General

Guideline Title

Coeliac disease: recognition, assessment and management.

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Coeliac disease: recognition, assessment and management. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Sep 2. 21 p. (NICE guideline; no. 20).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Institute for Health and Clinical Excellence (NICE). Coeliac disease. Recognition and assessment of coeliac disease. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 May. 86 p. (Clinical guideline; no. 86). [87 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): The guideline was developed by the Internal Clinical Guidelines Team on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Recognition of Coeliac Disease

Offer serological testing for coeliac disease to:

- People with any of the following:
  - Persistent unexplained abdominal or gastrointestinal symptoms
  - Faltering growth
  - Prolonged fatigue
  - Unexpected weight loss
  - Severe or persistent mouth ulcers

    - Unexplained iron, vitamin B12 or folate deficiency
    - Type 1 diabetes, at diagnosis
    - Autoimmune thyroid disease, at diagnosis
    - Irritable bowel syndrome (in adults)
- First-degree relatives of people with coeliac disease

Consider serological testing for coeliac disease in people with any of the following:

- Metabolic bone disorder (reduced bone mineral density or osteomalacia)
- Unexplained neurological symptoms (particularly peripheral neuropathy or ataxia)
- Unexplained subfertility or recurrent miscarriage
- Persistently raised liver enzymes with unknown cause
- Dental enamel defects
- Down's syndrome
- Turner syndrome

For people undergoing investigations for coeliac disease:

- Explain that any test is accurate only if a gluten-containing diet is eaten during the diagnostic process and
- Advise the person not to start a gluten-free diet until diagnosis is confirmed by a specialist, even if the results of a serological test are positive

Advise people who are following a normal diet (containing gluten) to eat some gluten in more than 1 meal every day for at least 6 weeks before testing.

If people who have restricted their gluten intake or excluded gluten from their diet are reluctant or unable to re-introduce gluten into their diet before testing:

- Refer the person to a gastrointestinal specialist and
- Explain that it may be difficult to confirm their diagnosis by intestinal biopsy

Advise people who have tested negative for coeliac disease, particularly first-degree relatives and people with type 1 diabetes, that:

- Coeliac disease may present with a wide range of symptoms and
- They should consult their healthcare professional if any of the symptoms listed in the recommendations above arise or persist

Do not offer serological testing for coeliac disease in infants before gluten has been introduced into the diet.

Serological Testing for Coeliac Disease

All serological tests should be undertaken in laboratories with clinical pathology accreditation (CPA) or ISO15189 accreditation.

When healthcare professionals request serological tests to investigate suspected coeliac disease in young people and adults, laboratories should:

- Test for total immunoglobulin A (IgA) and IgA tissue transglutaminase (tTG) as the first choice
- Use IgA endomysial antibodies (EMA) if IgA tTG is weakly positive
- Consider using IgG EMA, IgG deamidated gliadin peptide (DGP) or IgG tTG if IgA is deficient (IgA deficiency is defined as total IgA less than 0.07 mg per litre)

When healthcare professionals request serological tests to investigate suspected coeliac disease in children, laboratories should:

- Test for total IgA and IgA tTG as the first choice
- Consider using IgG EMA, IgG DGP or IgG tTG if IgA is deficient

When laboratories test for total IgA, a specific assay designed to measure total IgA levels should be used.

Do not use human leukocyte antigen (HLA) DQ2 (DQ2.2 and DQ2.5)/DQ8 testing in the initial diagnosis of coeliac disease in non-specialist settings.

Only consider using HLA DQ2 (DQ2.2 and DQ2.5)/DQ8 testing in the diagnosis of coeliac disease in specialist settings (for example, in children who are not having a biopsy, or in people who already have limited gluten ingestion and choose not to have a gluten challenge).

Laboratories should clearly communicate the interpretation of serological test results and recommended action to healthcare professionals.

Referral of People with Suspected Coeliac Disease

Refer young people and adults with positive serological test results to a gastrointestinal specialist for endoscopic intestinal biopsy to confirm or exclude coeliac disease. (In young people and adults, a positive serological test result is defined as unambiguously positive IgA tTG alone, or weakly positive IgA tTG and a positive IgA EMA test result. Note: In people who have IgA deficiency, a serologically positive result can be derived from any one of the IgG antibodies.)

Refer children with positive serological test results to a paediatric gastroenterologist or paediatrician with a specialist interest in gastroenterology for further investigation for coeliac disease. (Further investigation may include, but is not limited to, one or more of the following: an IgA EMA test to confirm serological positivity, HLA genetic testing, an endoscopic biopsy.)

Refer people with negative serological test results to a gastrointestinal specialist for further assessment if coeliac disease is still clinically suspected.

Healthcare professionals should have a low threshold for re-testing people identified in the recommendations above if they develop any symptoms consistent with coeliac disease.

Monitoring in People with Coeliac Disease

Consider referring people with coeliac disease for endoscopic intestinal biopsy if continued exposure to gluten has been excluded and:

- Serological titres are persistently high and show little or no change after 12 months or
- They have persistent symptoms, including diarrhoea, abdominal pain, weight loss, fatigue or unexplained anaemia

Do not use serological testing alone to determine whether gluten has been excluded from the person's diet.

Offer an annual review to people with coeliac disease. During the review:

- Measure weight and height
- Review symptoms
- Consider the need for assessment of diet and adherence to the gluten-free diet
- Consider the need for specialist dietetic and nutritional advice

Refer the person to a general practitioner (GP) or consultant if concerns are raised in the annual review. The GP or consultant should assess all of the following:

- The need for a dual-energy X-ray absorptiometry (DEXA) scan (in line with the NGC summary of the NICE guideline Osteoporosis: assessing the risk of fragility fracture) or active treatment of bone disease
- The need for specific blood tests
- The risk of long-term complications and comorbidities
- The need for specialist referral

Non-responsive and Refractory Coeliac Disease

Consider the following actions in people with coeliac disease who have persistent symptoms despite advice to exclude gluten from their diet:

- Review the certainty of the original diagnosis
- Refer the person to a specialist dietitian to investigate continued exposure to gluten
- Investigate potential complications or coexisting conditions that may be causing persistent symptoms, such as irritable bowel syndrome, lactose intolerance, bacterial overgrowth, microscopic colitis or inflammatory colitis

Diagnose refractory coeliac disease if the original diagnosis of coeliac disease has been confirmed, and exposure to gluten and any coexisting conditions have been excluded as the cause of continuing symptoms.

Refer people with refractory coeliac disease to a specialist centre for further investigation.

Consider prednisolone for the initial management of the symptoms of refractory coeliac disease in adults while waiting for specialist advice.

Information and Support

Explain to people who are thought to be at risk of coeliac disease that a delayed diagnosis, or undiagnosed coeliac disease, can result in continuing

ill health and serious long-term complications.

Give people with coeliac disease (and their family members or carers, where appropriate) sources of information on the disease, including national and local specialist coeliac groups and dietitians with a specialist knowledge in coeliac disease.

A healthcare professional with a specialist knowledge of coeliac disease should tell people with a confirmed diagnosis of coeliac disease (and their family members or carers, where appropriate) about the importance of a gluten-free diet and give them information to help them follow it. This should include:

- Information on which types of food contain gluten and suitable alternatives, including gluten-free substitutes
- Explanations of food labelling
- Information sources about gluten-free diets, recipe ideas and cookbooks
- How to manage social situations, eating out and travelling away from home, including travel abroad
- Avoiding cross contamination in the home and minimising the risk of accidental gluten intake when eating out
- The role of national and local coeliac support groups

Be aware that people with coeliac disease may experience anxiety and depression. Diagnose and manage these issues in line with the following NICE guidelines:

- Depression in adults with a chronic physical health problem
- Depression in children and young people: identification and management in primary, community and secondary care (see the NGC summary)
- Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. Management in primary, secondary and community care (see the NGC summary)
- Social anxiety disorder: recognition, assessment and treatment (see the NGC summary)

Advice on Dietary Management

Advise people with coeliac disease (and their family members or carers, where appropriate) to seek advice from a member of their healthcare team if they are thinking about taking over-the-counter vitamin or mineral supplements.

Explain to people with coeliac disease (and their family members or carers, where appropriate) that they may need to take specific supplements such as calcium or vitamin D if their dietary intake is insufficient.

Explain to people with coeliac disease (and their family members or carers, where appropriate) that:

- They can choose to include gluten-free oats in their diet at any stage and
- They will be advised whether to continue eating gluten-free oats depending on their immunological, clinical or histological response

Definitions

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. The GDG uses similar forms of words (for example, 'Do not offer…') when confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

A National Institute for Health and Care Excellence (NICE) pathway titled "Coeliac Disease Overview" is available from the NICE Web site .

Scope

Disease/Condition(s)

Coeliac disease

Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Clinical Specialty

Allergy and Immunology

Family Practice

Gastroenterology

Internal Medicine

Medical Genetics

Nutrition

Pediatrics

Intended Users

Advanced Practice Nurses

Dietitians

Nurses

Patients

Physician Assistants

Physicians

Guideline Objective(s)

To offer best practice advice on the care of children, young people and adults with suspected or confirmed coeliac disease

Target Population

- Children (defined as below age 16 years), young people (defined as age 16 or 17 years), and adults (those 18 years or over) with symptoms or signs suggestive of coeliac disease
- Children, young people, and adults with confirmed coeliac disease
- Children, young people, and adults considered to be at high risk of coeliac disease, including people with autoimmune conditions such as type 1 diabetes and autoimmune thyroid disease, or those with a first-degree family history of coeliac disease
- Specific subgroups in whom the investigation and management of coeliac disease is known to be different

Note: The following groups are not covered within this guideline: children, young people, and adults with other gastrointestinal disorders (the guideline will only cover differential diagnosis of non-responsive coeliac disease); people with non-coeliac disease gluten sensitivity.

Interventions and Practices Considered

1. Identification of children and adults to whom serological testing should be offered
2. Dietary considerations prior to testing for coeliac disease
3. Serological testing
    - Immunoglobulin A (IgA) and IgA tissue transglutaminase (tTG) as first choice
    - IgA endomysial antibodies (EMA)
    - IgG EMA, IgG deamidated gliadin peptide (DGP) or IgG tTG (if IgA is deficient)
    - Human leukocyte antigen (HLA) DQ2 (DQ2.2 and DQ2.5)/DQ8 testing (in specialist settings only)
4. Referral to gastrointestinal specialist for endoscopic intestinal biopsy and/or further assessment
5. Monitoring in people with coeliac disease
6. Considerations for non-responsive coeliac disease
7. Providing information and support about coeliac disease
8. Diagnosis and management of anxiety and depression symptoms
9. Providing advice on dietary management (gluten-free diet, supplements such as calcium and vitamin D)

Major Outcomes Considered

- Health-related quality of life
- Mucosal recovery
- Contact with healthcare professionals
- Resolution of gastrointestinal and non-gastrointestinal symptoms
- Complications of coeliac disease, such as osteoporosis, ulcerative jejunitis, malignancy (intestinal lymphoma), functional hyposplenism, vitamin D deficiency and iron deficiency
- Serological response
- Dietary adherence
- Impact on carers
- Growth in children and young people
- Resource use and costs

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The guideline was developed by the Internal Clinical Guidelines Team on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing Review Questions and Protocols and Identifying Evidence

The technical team drafted review questions which were refined and validated by the Guideline Development Group (GDG), using a Population, Intervention, Comparator, Outcome (PICO) framework, and drafted review protocols based on the topics agreed with the stakeholders and included in the scope (see Appendix B in the full guideline appendices [see the "Availability of Companion Documents" field]) and prepared a protocol for each review question (see Appendix C in the full guideline appendices). These formed the starting point for systematic reviews of relevant evidence. Published evidence was identified by applying systematic search strategies (see Appendix C in the full guideline appendices) to the following databases: Medline (1950 onwards), EMBASE (1980 onwards), Cumulative Index to Nursing and Allied Health Literature (CINAHL; 1982 onwards), and three Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects). Searches to identify economic studies were undertaken using the above databases, the National Health Service Economic Evaluation Database (NHS EED) and the Health Technology Assessment (HTA) database.

Where a question was updated directly from the previous guideline (CG68) the search strategies used in the CG68 were updated. However for the review question on signs and symptoms, coexisting conditions and first-degree relatives and long-term consequences, the GDG requested some new search for additional terms and these additional searches had no date restriction. No date restrictions were placed on the searches for all new questions.

Searches in EMBASE and Medline were limited to English language and studies in humans. None of the other searches were limited by language of publication (although publications in languages other than English were not reviewed). Validated search filters were used to identify particular study designs, such as randomised controlled trials (RCTs). There was no systematic attempt to search grey literature (conference abstracts, theses or unpublished trials), nor was hand searching undertaken of journals not indexed on the databases.

Towards the end of the guideline development process, the searches were updated and re-executed to include evidence published and indexed in the databases by 5th December 2014.

Study Identification

Identified titles and abstracts were sifted for relevance and data were extracted by 1 reviewer. A second reviewer checked a random 10% of sifted out titles and abstracts, and all excluded studies with the reason for exclusion, and all data extracted for the included studies.

Health Economics

Literature reviews seeking to identify published cost–utility analyses of relevance to the issues under consideration were conducted for all questions, with the exception of those detailed in Sections 4.1, 4.2 and 4.3 (which provided data for the health economic question considered in Section 4.4) and 7.1 and 7.2 in the full version of the guideline (which were information questions without a substantive health economic component). In each case, the search undertaken for the clinical review was modified, retaining population and intervention descriptors, but removing any study-design filter and adding a filter designed to identify relevant health economic analyses. Search strategies are provided in full in Appendix C in the full guideline appendices. In assessing studies for inclusion, population, intervention and comparator criteria were always identical to those used in the parallel clinical search; only cost–utility analyses were included.

See Sections 4 to 7 in the full guideline for specific inclusion/exclusion criteria for each question.

Number of Source Documents

See Sections 4-7 in the full guideline as well as Appendix D in the full guideline appendices (see the "Availability of Companion Documents" field) for detailed information on results of literature searches, number of included and excluded studies, and evidence tables for each review question. Also see Appendix F for a list of excluded studies.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The guideline was developed by the Internal Clinical Guidelines Team on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Outcomes

The outcomes prioritised in the review questions and protocols reflect the treatment objectives outlined in each question. The minimum important difference (MID) for both dichotomous and continuous outcomes would be decided by looking at appropriate published evidence or under agreement with the Guideline Development Group (GDG) following discussion within committee meetings. On the occasion that no published literature on the minimal important difference was identified and the GDG were unable to specify on a default option was used, for example, in the case of dichotomous outcomes was defined as a relative risk reduction or an increase of 25% or more to be considered clinically important.

For this guideline, the effectiveness of interventions/diagnostic strategies to manage coeliac disease has been assessed against a variety of outcomes. The justification for using these outcomes is based on their relevance to people with the condition and the expert consensus opinion of members of the multidisciplinary GDG. When assessing the effectiveness of a particular treatment, information about the effect of that treatment on one or more primary outcomes was sought.

Process

Data Extraction

Basic characteristics of each included study were summarised into standardised evidence tables for each review question (see Appendix D in the full guideline appendices [see the "Availability of Companion Documents" field) along with the quality assessment of the evidence. Where outcome data were presented, results were entered as reported in the full-text report of the study.

Some studies were excluded from the guideline reviews after obtaining copies of the publications because they did not meet inclusion criteria specified by the GDG (see Appendix C in the full guideline appendices). These studies are listed in alphabetical order for each question and the reason for exclusion provided for each one.

Missing Continuous Data

Where the standard deviation of the mean change from baseline was not reported, the GDG imputed this using either the baseline standard deviation (SD) from the control group or the SD from a similar group.

When the standard deviation of the point estimate at study end was not reported, the GDG imputed this using either the baseline SD from the control group or the SD from a similar group.

Missing Dichotomous Data

Where the raw numbers for an outcome were not reported and a percentage was reported, the raw numbers were calculated manually from the reported percentage. When a decimal was calculated the number was rounded up if the decimal was over 0.5 and down if below 0.5.

When the outcome is negative (for example, adverse effects or failure rate) the denominator used equalled the total number of the study arm. When the outcome is positive (for example, effectiveness) the denominator used was the number completing in the study arm.

Quality Assessment Checklists

For randomised controlled trials (RCTs), the NICE methodological checklist for RCTs was used for quality assessment of the evidence. For cohort studies, the NICE methodological checklist for cohort study was used for quality assessment. For diagnostic studies, the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) checklist was used for quality assessment. For qualitative studies, the Critical Appraisal Skills Programme (CASP) checklist for qualitative research design was used for quality assessment. For prognostic studies, a prognostic study checklist designed by Hayden and colleagues was used.

Meta-analyses

Where possible, meta-analyses were conducted to combine the results of studies for each outcome. For continuous outcomes, where change from baseline data were reported in the trials and were accompanied by a measure of spread (for example standard deviation), these were extracted and used in the meta-analysis.

Dichotomous outcomes were presented as relative risks (RRs) with 95% confidence intervals (CIs), and continuous outcomes were presented as mean differences with 95% CIs or SDs.

Software

Data for intervention reviews were analysed using Review Manager 5.1 while data for diagnostic reviews was analysed using Meta Disk. An online calculator (http://vassarstats.net) was used to calculate confidence intervals around proportions for single studies.

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Process

The body of evidence identified for each therapy or treatment review question (or part of a review question) was presented in the form of a GRADE evidence profile summarising the quality of the evidence and the findings (pooled relative and absolute effect sizes and associated CIs). Where possible, the body of evidence corresponding to each outcome specified in the review protocol was subjected to quantitative meta-analysis. In such cases, pooled effect sizes were presented as pooled RRs, pooled odds ratios (ORs), or mean differences. A random-effects model was used as default.

Where quantitative meta-analysis could not be undertaken, the range of effect sizes reported in the included studies was presented in a GRADE profile.

GRADE was used to assess the quality of evidence for the selected outcomes as specified in 'The guidelines manual (2012)' (see the "Availability of Companion Documents" field). The type of review question determines the highest level of evidence that may be sought. For issues of therapy or treatment, the highest possible evidence level is a well conducted systematic review or meta-analysis of RCTs, or an individual RCT. In the GRADE approach, a body of evidence based on RCTs has an initial quality rating of high, but this may be downgraded to moderate, low or very low if the factors listed above are not addressed adequately. For diagnostic review questions on prognosis, the highest possible level of evidence is a controlled observational study (a cohort study or case–control study), and a body of evidence based on such studies would have an initial quality rating of low, which might be downgraded to very low or upgraded to moderate or high, depending on the factors listed above.

For each review question the highest available level of evidence was sought. Where appropriate, for example, if a systematic review, meta-analysis or RCT was identified to answer a question directly, studies of a weaker design were not considered. Where systematic reviews, meta-analyses and RCTs were not identified, other appropriate experimental or observational studies were sought.

GRADE Profiles for Interventional Evidence

The quality ratings for each study are reported the study's evidence table and are summarised in the footnotes of each GRADE profile. For this guideline, the GDG inserted footnotes to explain the choice made while assessing the quality of evidence for each outcomes. These footnotes indicated if the GDG upgraded the evidence level, downgraded the evidence level or left the evidence level unchanged, and gave the rationale for doing this.

The quality of the evidence for each outcome was downgraded where appropriate for the reasons outlined in Table 1 in the full version of the guideline.

Modified GRADE for Diagnostic Evidence

GRADE has not been developed for use with diagnostic studies; therefore a modified approach was applied using the GRADE framework.

Cohort studies within the GRADE approach start at the low quality level due to accepted inherent study design limitations. Within a modified approach, where evidence from cohort studies has been deemed to be the most appropriate source of information to answer a given review question, studies start from a presumption of 'high quality' The same criteria (risk of bias, inconsistency, imprecision and indirectness) were used to downgrade the quality of evidence as detailed in Table 2 in the full version of the guideline.

Modified GRADE for Qualitative Studies

GRADE has not been developed for use with qualitative studies; therefore a modified approach was applied using the GRADE framework.

Qualitative studies within the non-modified GRADE approach start at the very low quality level due to accepted inherent study design limitations. Within a modified approach where qualitative evidence has been deemed to be the most appropriate source of information to answer a given review question, it is acceptable to initially indicate a high quality level to this study type and to assess the quality of evidence from this point. The same criteria (risk of bias, inconsistency, imprecision and indirectness) were used to downgrade the quality of evidence as detailed in Table 3 in the full version of the guideline.

Health Economics

Economic evidence profiles, including critical appraisal according to the Guidelines manual, were completed for included studies; these are shown in Appendix G in the full guideline appendices.

Economic studies identified through a systematic search of the literature are appraised using a methodology checklist designed for economic evaluations. This checklist is not intended to judge the quality of a study per se, but to determine whether an existing economic evaluation is useful to inform the decision-making of the GDG for a specific topic within the guideline. There are two parts of the appraisal process; the first step is to assess applicability (i.e., the relevance of the study to the specific guideline topic and the NICE reference case) (see Table 4 in the full version of the guideline).

In the second step, only those studies deemed directly or partially applicable are further assessed for limitations (i.e., the methodological quality, see Table 5 in the full version of the guideline).

Where relevant, a summary of the main findings from the systematic search, review and appraisal of economic evidence is presented in an economic evidence profile alongside the clinical evidence.

Original health economic modelling was conducted for 3 questions that were prioritised by the GDG for detailed analysis: order and sequencing of serological tests (see Section 5.2 in the full version of the guideline), active case-finding (see Section 4.4 in the full version of the guideline) and dietetic involvement in follow-up (considered as part of the review on frequency of follow-up; see Section 5.4 in the full version of the guideline). Each analysis relied on broadly the same model, which was originally developed for the serological testing question and subsequently modified to address other questions. Full details of the methods of the models are provided in Appendix G in the full guideline appendices.

In questions for which no published evidence was identified and original analysis was not prioritised, the GDG made a qualitative judgement about cost-effectiveness by considering potential differences in resource use and cost between the options alongside the results of the review of evidence of clinical effectiveness.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): The guideline was developed by the Internal Clinical Guidelines Team on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Agreeing the Recommendations

For each review question, recommendations for clinical care were derived using, and linked explicitly to, the evidence that supported them. In the first instance, informal consensus methods were used by the Guideline Development Group (GDG) to agree short clinical and, where appropriate, cost effectiveness evidence statements, which were presented alongside the evidence profiles. Statements summarising the GDG's interpretation of the evidence and any extrapolation from the evidence used to form recommendations were also prepared to ensure transparency in the decision-making process. The 'Linking evidence to recommendations' (LETR) criteria used in moving from evidence to recommendations were:

- Relative value placed on the outcomes considered
- Consideration of the clinical benefits and harms
- Consideration of net health benefits and resource use
- Quality of the evidence
- Other considerations (including equalities issues)

In areas where no substantial clinical research evidence was identified, the GDG considered other evidence-based guidelines and consensus statements or used their collective experience to identify good practice. The health economics justification in areas of the guideline where the use of National Health Service (NHS) resources (interventions) was considered was based on GDG consensus in relation to the likely cost-effectiveness implications of the recommendations. The GDG also identified areas where evidence to answer their review questions was lacking and used this information to formulate recommendations for future research.

The wording used in the recommendations in this guideline denotes the certainty with which the recommendations were made. Some recommendations were made with more certainty than others. Recommendations are based on the trade-off between the benefits and harms of an intervention, whilst taking into account the quality of the underpinning evidence.

For all recommendations, it is expected that a discussion will take place with the patients about the risks and benefits of the interventions, and their values and preferences. This discussion should help the patient reach a fully informed decision. Terms used within this guideline are:

- 'Offer' – for the vast majority of patients, an intervention will do more good than harm
- 'Do not offer' – the intervention will not be of benefit for most patients
- 'Consider' – the benefit is less certain, and an intervention will do more good than harm for most patients. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for an 'offer' recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient

Towards the end of the guideline development process, formal consensus methods were used to consider all the clinical care recommendations and research recommendations that had been drafted previously.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. The GDG uses similar forms of words (for example, 'Do not offer…') when confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other

options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

The original health economic modelling the Guideline Development Group (GDG) undertook for this guideline addressed 3 topics: active case-finding in populations at increased risk of coeliac disease (see Section 4.4 in the full version of the guideline [see the "Availability of Companion Documents" field), serological diagnosis of coeliac disease (see Sections 5.1 and 5.2 in the full version of the guideline) and dietitian-led follow-up of people with coeliac disease (see Section 5.4 in the full version of the guideline). Because modelling for active case-finding and dietitian-led follow-up was based on modified versions of the model developed for serological diagnosis, questions are presented out of guideline order. Refer to Appendix G in the full guideline appendices (see the "Availability of Companion Documents" field) for the 'Full health economics report'.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was validated through two consultations.

1. The first draft of the guideline (the full guideline and the National Institute for Health and Care Excellence [NICE] guideline) were consulted with stakeholders and comments were considered by the Guideline Development Group (GDG).
2. The final consultation draft of the full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- The benefit of implementing immunoglobulin A tissue transglutaminase (IgA tTG) as the first-choice test will result in optimal sensitivity and specificity in serological testing. However, there is no clear guidance on how to interpret weakly positive IgA tTG results. Conducting an endomysial antibody test to follow up people with weakly positive IgA tTG test results will provide the opportunity for a secondary serological screen to inform the decision to biopsy in people with suspected coeliac disease.
- The advice and support of a healthcare professional with specialist knowledge of the dietary requirements of coeliac disease is one approach to help ensure lifelong adherence to a gluten-free diet.
- One of the major benefits of routine monitoring is the increased level of contact between the person with coeliac disease and healthcare professionals.

Refer to the "Trade-off between benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents"

field) for details about benefits of specific interventions.

Potential Harms

- False-negative or false-positive results of diagnostic tests
- Harms of investigative procedures were discussed in terms of their invasive nature, which could cause these patients, who are likely very unwell, further discomfort.

Refer to the "Trade-off between benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for details about harms of specific interventions.

Contraindications

Contraindications

The limitations of capsule endoscopy were discussed in terms of the presence of lesions such as ulcerative jejunitis and malignancy being contraindications for the capsule to successfully pass through the intestines. If the capsule becomes lodged in the intestine, an operation is required to remove it and this can be distressing for people with non-responsive coeliac disease (RCD).

Qualifying Statements

Qualifying Statements

- Healthcare professionals are expected to take the National Institute for Health and Care Excellence (NICE) clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
- The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients.
- For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also "Patient-centred care" in the full version of the guideline [see the "Availability of Companion Documents" field]).

Implementation of the Guideline

Description of Implementation Strategy

See "Implementation: getting started" in the original guideline document for information about putting the recommendations about laboratory testing and making sure patients have access to trained professionals into practice.

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Recognition of Coeliac Disease

Offer serological testing for coeliac disease to:

- People with any of the following:
  - Persistent unexplained abdominal or gastrointestinal symptoms
  - Faltering growth

    - Prolonged fatigue
    - Unexpected weight loss
    - Severe or persistent mouth ulcers
    - Unexplained iron, vitamin B12 or folate deficiency
    - Type 1 diabetes, at diagnosis
    - Autoimmune thyroid disease, at diagnosis
    - Irritable bowel syndrome (in adults)
- First-degree relatives of people with coeliac disease

For people undergoing investigations for coeliac disease:

- Explain that any test is accurate only if a gluten-containing diet is eaten during the diagnostic process and
- Advise the person not to start a gluten-free diet until diagnosis is confirmed by a specialist, even if the results of a serological test are positive

Serological Testing for Coeliac Disease

When healthcare professionals request serological tests to investigate suspected coeliac disease in young people and adults, laboratories should:

- Test for total immunoglobulin A (IgA) and IgA tissue transglutaminase (tTG) as the first choice
- Use IgA endomysial antibodies (EMA) if IgA tTG is weakly positive
- Consider using IgG EMA, IgG deamidated gliadin peptide (DGP) or IgG tTG if IgA is deficient (IgA deficiency is defined as total IgA less than 0.07 mg per litre)

When healthcare professionals request serological tests to investigate suspected coeliac disease in children, laboratories should:

- Test for total IgA and IgA tTG, as the first choice
- Consider using IgG EMA, IgG DGP or IgG tTG if IgA is deficient

Monitoring in People with Coeliac Disease

Offer an annual review to people with coeliac disease. During the review:

- Measure weight and height
- Review symptoms
- Consider the need for assessment of diet and adherence to the gluten-free diet
- Consider the need for specialist dietetic and nutritional advice

Non-responsive and Refractory Coeliac Disease

Consider the following actions in people with coeliac disease who have persistent symptoms despite advice to exclude gluten from their diet:

- Review the certainty of the original diagnosis
- Refer the person to a specialist dietitian to investigate continued exposure to gluten
- Investigate potential complications or coexisting conditions that may be causing persistent symptoms, such as irritable bowel syndrome, lactose intolerance, bacterial overgrowth, microscopic colitis or inflammatory colitis

Information and Support

A healthcare professional with a specialist knowledge of coeliac disease should tell people with a confirmed diagnosis of coeliac disease (and their family members or carers, where appropriate) about the importance of a gluten-free diet and give them information to help them follow it. This should include:

- Information on which types of food contain gluten and suitable alternatives, including gluten-free substitutes
- Explanations of food labelling
- Information sources about gluten-free diets, recipe ideas and cookbooks
- How to manage social situations, eating out and travelling away from home, including travel abroad
- Avoiding cross-contamination in the home and minimising the risk of accidental gluten intake when eating out
- The role of national and local coeliac support groups

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Coeliac disease: recognition, assessment and management. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Sep 2. 21 p. (NICE guideline; no. 20).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2009 May (revised 2015 Sep 2)

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

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National Institute for Health and Care Excellence (NICE)

Guideline Committee

Guideline Development Group (GDG)

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Financial Disclosures/Conflicts of Interest

Guideline Development Group (GDG) declarations of interest are provided in Appendix A in the full guideline appendices (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Institute for Health and Clinical Excellence (NICE). Coeliac disease. Recognition and assessment of coeliac disease. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 May. 86 p. (Clinical guideline; no. 86). [87 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available in ePub or eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Coeliac disease: recognition, assessment and management. Full guideline. London (UK): National Institute for Health and Care Excellence; 2015 Sep. 145 p. (NICE guideline; no. 20). Available from the NICE Web site .
- Coeliac disease: recognition, assessment and management. Appendices. London (UK): National Institute for Health and Care Excellence; 2015 Sep. (NICE guideline; no. 20). Available from the NICE Web site .
- Coeliac disease: recognition, assessment and management. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence; 2015 Sep. (NICE guideline; no. 20). Available from the NICE Web site .
- Coeliac disease: recognition, assessment and management. Costing statement. London (UK): National Institute for Health and Care Excellence; 2015 Sep. 4 p. (NICE guideline; no. 20). Available from the NICE Web site .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Available from the NICE Web site .

Patient Resources

The following is available:

- Coeliac disease: recognition, assessment and management. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Sep. 9 p. (NICE guideline; no. 20). Available from the National Institute for Health and Care Excellence (NICE) Web site. Also available for download in ePub or eBook formats from the NICE Web site. Also available in Welsh rom the NICE Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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