NICE National Institute for Health and Care Excellence

2019 surveillance of coeliac disease: recognition, assessment and management (NICE guideline NG20)

Surveillance report

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Surveillance decision

We will not update the NICE guideline on coeliac disease.

Reasons for the decision

The reason for not updating the guideline at this time is that the totality of evidence identified from the surveillance review supports current recommendations or was not deemed sufficient to impact recommendations.

This included evidence in the following areas:

Recognition of coeliac disease: signs, symptoms and coexisting conditions

The guideline advises to consider serological testing for coeliac disease (CD) for people with various signs and symptoms, including unexplained subfertility, recurrent miscarriage and dental enamel defects. The new evidence supporting testing for CD in people with these conditions is consistent with this advice. New evidence showing a higher prevalence of CD in people with Down's syndrome (5.8%) than was found in the guideline evidence review (3.2% versus background population prevalence of 1%), and based on a larger pooled sample size, supports additional topic expert and stakeholder advice to strengthen the recommendation to 'offer' serological testing for CD to this group. However, the new evidence did not report the relative risk of CD for people with Down's syndrome compared with matched controls without Down's syndrome. In the absence of these data and evidence on the cost effectiveness of offering testing for CD to all people with Down's syndrome, there is unlikely to be any impact on the guideline advice.

Serological testing and referral for suspected coeliac disease

Approaches to testing

New evidence was identified on a range of different approaches to serological testing, including point-of-care testing, deamidated gliadin peptide testing, immunoglobulin A (IgA) anti-tissue transglutaminase antibody (IgA anti-tTG) testing, human leukocyte antigen

(HLA)-DQ2/8 testing and combined testing. This evidence was largely consistent with guideline recommendations or required further confirmatory research to signal an impact on the guideline.

Non-biopsy strategy in young people and adults

NICE guideline NG20 advises referral of young people and adults with positive serological test results to a gastrointestinal specialist for endoscopic intestinal biopsy to confirm or rule out CD. Despite stakeholder feedback indicating the value of non-biopsy diagnosis in adults, the collective new evidence does not indicate sufficient diagnostic accuracy of this approach in adults to justify a change to the recommendations. Although no ongoing trials were identified in the surveillance review, we recognise that this is a rapidly evolving area of research and further evidence will be considered when available. We will revisit this section of the guideline when the British Society of Gastroenterology publishes its updated guidance in this area.

Non-biopsy strategy in children

NICE guideline NG20 recommends referral of children with positive serological test results to a paediatric gastroenterologist or paediatrician with a specialist interest in gastroenterology for further investigation for CD. This allows for alternative confirmatory diagnosis to biopsy in certain circumstances. These alternatives could include a non-biopsy approach by using an IgA EMA (endomysial antibodies) test to confirm serological positivity or using genetic testing. The guideline committee recognised that an endoscopic intestinal biopsy is not always available as an option in paediatric populations because it can be highly distressing for both the children and their parents and also requires additional care and costs because of the need for general anaesthetic.

Topic experts and stakeholders highlighted that a non-biopsy approach, including serological and genetic testing, to diagnose CD in children, is being used increasingly in the NHS. Non-biopsy testing is a less invasive approach, which avoids the need for endoscopy and general anaesthesia, and is considered by some topic experts to be cost saving. The European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines for diagnosing coeliac disease 2020 state that if TGA-IgA is 10 or more times the upper limit of normal then non-biopsy diagnosis may be applied, provided IgA EMA will test positive in a second blood sample (this approach would be subject to carer or parent approval). The ESPGHAN guidelines also state that HLA DQ2-/DQ8 determination and symptoms are not obligatory additional criteria for the non-biopsy

approach. New evidence indicates that a non-biopsy approach in children has high diagnostic accuracy under the ESPGHAN criteria. This approach could avoid risks and costs of endoscopy for a significant proportion of children with suspected CD, and therefore we will revisit this section of the guideline once the British Society of Gastroenterology publishes its updated guidance in this area.

Monitoring in people with coeliac disease

Annual monitoring

Topic experts advised on standard follow-up serology as part of annual review, in addition to nutrition screening and the need for guidance on dual energy X-ray absorptiometry (DEXA) scanning for osteoporosis. However, recommendation 1.4.3 in NICE guideline NG20 already advises offering annual review to include consideration of the need for assessment of diet and dietary adherence, plus the need for specialist dietetic and nutritional advice. Recommendation 1.4.4 also advises referral to a GP or consultant to assess the need for a DEXA scan for osteoporosis, and the need for specific blood tests. No new evidence was identified to signal any need for change to the existing advice.

Stakeholders also highlighted the need for more detailed advice on how adherence to a gluten-free diet should or should not be assessed at annual review. In developing the guideline, the committee 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 guideline advises that serological testing should not be used alone to measure adherence.

The guideline committee highlighted, based on their own expertise and clinical experience, that people with CD benefit from regular dietetic assessment to monitor adherence to the gluten-free diet, review symptoms, and provide nutritional advice, and that this would represent a gold standard for annual review. However, there was a lack of good quality evidence to support this, and in view of the significant implementation ramifications of offering all people with CD access to a specialist dietitian, the guideline committee agreed that the recommendation should reflect that dietetic input should be considered as part of an annual review. A research recommendation was also made to stimulate investigation into the use of dietetic support as an integral component of an annual review for people with CD. The surveillance review did not identify any new evidence to inform more detailed advice to assess adherence to a gluten-free diet, or to address the research recommendation.

Stakeholders commented on the lack of guidance on serology as a marker for persistent villous atrophy. New evidence indicated that tests for serum IgA tTG and IgA EMA levels had low accuracy in monitoring CD patients for persistent villous atrophy. The evidence suggested that in the absence of these markers, signs and symptoms for this complication should be assessed at annual review and onward referral should be considered if concerns arise. This is consistent with recommendation 1.4.4 for assessing the risk of long-term complications or comorbidities.

Pneumococcal immunisation

New evidence and feedback from topic experts and stakeholders indicated a higher risk of hospital-acquired and community-acquired pneumococcal infection for people with CD, suggesting that preventive pneumococcal vaccination should be considered for these people, in addition to those with functional hyposplenism. However, vaccination guidance is set at a national level by the UK government through the Joint Committee on Vaccination and Immunisation and is not within the scope of NICE guideline NG20. New evidence identified in the current surveillance review is therefore unlikely to impact on the guideline.

Advice on dietary management

Folic acid supplementation

Topic experts and stakeholders highlighted an inconsistency between the guideline, which does not advise on folic acid supplementation, and the NICE clinical knowledge summary (CKS) on coeliac disease management, which advises high-dose folic acid supplementation (5 mg once daily) for women with CD who are pregnant, or who are planning a pregnancy. The basis for this advice is that women with CD are considered at high risk of having a child with a neural tube defect. However, the CKS topic states that this is based on expert advice, rather than evidence, and what CKS considers to be good medical practice based on the potential risk of poor absorption of folic acid in women with CD. No evidence was identified to substantiate the CKS advice, which does not constitute formal NICE guidance, and until evidence indicates otherwise, no impact on the guideline is anticipated. The CKS advice will be amended to align with NICE guideline NG20. NICE's guideline on maternal and child nutrition provides further advice in this area.

Role of the dietitian

Topic experts and stakeholders asserted that the value of the dietitian should be made more prominent in both NICE guideline NG20 and NICE's quality standard on coeliac disease. The specialist knowledge and training of dietitians includes behavioural modification and counselling skills to support patients around early dietary management of CD. It was noted that there is an important role for dietitians to play in the community and that this should be reflected in the guideline. However, the role of the dietitian is already outlined in NICE guideline NG20, recommendations 1.5.1 and 1.6.2, which include referral to and information on specialist dietitians. There is also a research recommendation in this area, which remains ongoing.

Other areas

Prescription of gluten-free foods

Topic experts and stakeholders highlighted a need for the guideline to recommend the prescription of gluten-free foods following changes in the legislation, the NHS (General Medical Services Contracts) (Prescription of Drugs etc.) (Amendment) Regulations 2018.

However, the guideline does not make recommendations on prescribing of gluten-free foods because policy and legislation in this area is set at a national level by the Department for Health and Social Care, with implementation passed to clinical commissioning groups at a local and regional level. Therefore, no impact is anticipated on the guideline.

Implementation issues

Stakeholders raised 2 guideline implementation issues concerning serological testing; NICE guideline NG20 recommends testing for total IgA and IgA tTG as the first-choice serological test. A stakeholder noted anecdotal evidence that the request to test for total IgA is not always automatically carried out. The guideline also advises using IgA EMA if IgA tTG is weakly positive. A stakeholder noted further anecdotal evidence that some healthcare professionals, including some secondary care settings, do not have access to EMA. These issues have been passed to the NICE system support for implementation team for further investigation.

Irritable bowel syndrome

Stakeholders highlighted that more work is needed to reduce the number of misdiagnoses of irritable bowel syndrome (IBS) in people with CD. The national charity Coeliac UK is in the process of commissioning epidemiology research, which will provide the incidence and prevalence of these conditions in the UK as of 2019. Information on prior diagnosis of IBS will also be available and preliminary prevalence figures are anticipated by May 2020. This research will help to identify key areas of underdiagnosis. This will be monitored for potential impact on NICE guideline NG20 and NICE's guideline on IBS in adults. No other evidence was identified to signal an impact in this area.

Dermatitis herpetiformis

Feedback from experts and stakeholders highlighted the absence of any reference to testing in people who have dermatitis herpetiformis in NICE guideline NG20. However, the guideline committee did not find any evidence meeting the search protocols to indicate that testing for the existence of dermatitis herpetiformis would be a reliable indicator of CD. The developers were therefore unable to include it in the list of criteria on when to offer serological testing in recommendation 1.1.1. No additional eligible evidence was identified in the 2019 surveillance review.

For further details and a summary of all evidence identified in surveillance, see appendix A.

Overview of 2019 surveillance methods

NICE's surveillance team checked whether recommendations in coeliac disease (NICE guideline NG20) remain up to date.

The surveillance process consisted of:

- Feedback from topic experts via a questionnaire.
- A search for new or updated Cochrane reviews.
- Examining related NICE guidance and quality standards and NIHR signals.
- A search for ongoing research.
- Examining the NICE event tracker for relevant ongoing and published events.
- Literature searches to identify relevant evidence.
- Assessing the new evidence against current recommendations to determine whether or not to update sections of the guideline, or the whole guideline.
- Consulting on the proposal with stakeholders.
- Considering comments received during consultation and making any necessary changes to the proposal.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Evidence considered in surveillance

Search and selection strategy

We searched for new evidence related to the whole guideline.

We found 54 studies in a search for systematic reviews, randomised controlled trials and observational studies published between 1 December 2014 and 31 August 2019.

We also included 2 studies identified in comments received during consultation on the 2019 surveillance review.

From all sources, we considered 56 studies to be relevant to the guideline.

See appendix A for details of all evidence considered, and references.

Ongoing research

We checked for relevant ongoing research; of the ongoing studies identified, 2 were assessed as having the potential to change recommendations. Therefore, we plan to check the publication status regularly and evaluate the impact of the results on current recommendations as quickly as possible. These studies are:

- Non-invasive markers of gluten ingestion in celiac disease patients
- Assessment of adherence to gluten free diet in children and adolescents by detection of gluten in faecal samples

Intelligence gathered during surveillance

Views of topic experts

We considered the views of topic experts who were recruited to the NICE Centre for Guidelines Expert Advisers Panel to represent their specialty. For this surveillance review, topic experts completed a questionnaire about developments in evidence, policy and services related to the guideline.

We sent questionnaires to 18 topic experts and received 6 responses.

Overall, 3 topic experts thought that the guideline should be updated and 3 thought that an update was not necessary. The issues that topic experts thought could be addressed in an update covered recognition of coeliac disease in people with coexisting conditions, non-biopsy diagnosis, annual monitoring and the role of the dietitian. See the section on reasons for the decision for further details of these issues.

Other sources of information

We considered all other correspondence received since the guideline was published. Issues raised included:

- **Neurological damage**. Feedback was received from a member of the public in February 2016 stating the need to extend the scope of the guideline to include neurological damage, and in response, NICE stated that the area is out of scope and therefore no recommendations were made, but that new evidence will be considered in this area in the next scheduled surveillance review, that is, the current 2019 review. It was also noted that in the public consultation on the draft recommendations of NICE guideline NG20, this was not highlighted by any of the stakeholders. The NICE guideline on suspected neurological conditions cross refers to NICE guideline NG20 to consider serological testing for gluten sensitivity in adults with gradually progressive unsteady gait, in addition to referral for neurological assessment.

Views of stakeholders

Stakeholders are consulted on all surveillance reviews except if the whole guideline will be updated and replaced. Because this surveillance proposal was to not update the guideline, we consulted with stakeholders.

Overall, 11 stakeholders commented, of whom 3 agreed and 8 disagreed with the decision not to update the guideline. Responses were received from national charities, professional bodies, a general practice and an NHS trust.

After reviewing the comments, very few of the references provided by stakeholders were included for further consideration, mostly because the study designs did not match the inclusion criteria for the guideline. Two studies were added as a result of stakeholder consultation, but the findings were consistent with current recommendations.

Stakeholders highlighted several areas where they felt an update was necessary. These included testing for people with irritable bowel syndrome, Down's syndrome and dermatitis herpetiformis; non-biopsy approach to diagnosis in children and adults; annual monitoring for measuring adherence to a gluten-free diet and for scanning for bone fragility; dietary advice and the importance of the dietitian's role in treatment and monitoring. For further details, see the section on reasons for the decision and appendix B for full details of stakeholders' comments and our responses.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all evidence and other intelligence and the impact on current recommendations, we decided that no update is necessary.

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