Coeliac disease
How can case-finding improve outcomes and reduce avoidable costs?
What is the importance of an early diagnosis in coeliac disease?

- The average time from symptom onset to correct diagnosis of coeliac disease is 13 years\(^1\).
- Untreated patients are more likely to develop long-lasting complications\(^2\).

Who is at risk?

- Screening for **first-degree relatives**, as recommended by guidelines\(^3\), and case-finding in **second-degree relatives**\(^4\) can help identify patients earlier, thus reducing the risk of complications\(^3\).
- Screening for coeliac disease in **patients with IBS**, as recommended by national and international guidelines\(^3, 5-7\), can help resolve symptoms\(^8\), improve the quality of life of these patients\(^9\) and is cost-effective\(^3, 9, 10\).
- As recommended by national and international guidelines\(^3, 6, 11-15\), **type 1 diabetes patients** should be screened for coeliac disease at the time of diagnosis and, if negative, annually for the first two years after diagnosis\(^15\). Identifying patients thorough screening can help: improve quality of life, improve diabetic control and decrease the risk of complications associated with type 1 diabetes and coeliac disease\(^16\).
- **NICE** recommends that coeliac disease testing is considered for **all couples with unexplained infertility or recurrent miscarriage**. A gluten-free diet, started prior to conception, could improve fertility\(^3, 4\).

Which serological tests should be used to help diagnose these at-risk patients?

- Several serological tests are available to help diagnose coeliac disease. Testing is specific, easy and cheap. **NICE** recommends that when requesting serological tests to investigate suspected coeliac disease, laboratories should test for total IgA and IgA tTG as first choice\(^3\).

Why will identifying high-risk patients benefit clinical outcomes?

- The early identification and appropriate management of patients with coeliac disease improves clinical outcomes including reducing the risk of cancer, reversing symptoms, and improving QoL\(^3, 15, 17-21\).

Why is this approach cost effective?

- Diagnosis and treatment of coeliac disease significantly reduces costs of other irrelevant tests by 29% and referral by 37%\(^21\).

*Management plans must be adhered to by the patient.*
What is the importance of an early diagnosis in coeliac disease?

- Coeliac disease is a chronic autoimmune condition, in genetically susceptible persons, perpetuated by the ingested gluten from cereals (wheat, rye, and barley)\(^3\)

In the UK, coeliac disease affects approximately **1% of the population**, although most people with this condition remain undiagnosed\(^3\)

The average time from symptoms onset to correct diagnosis of coeliac disease is **13 years**\(^1\)

- Coeliac disease can present at any age and despite the fact that it primarily affects the small intestine, symptoms of coeliac disease can manifest in organs outside of the gut – the nature of coeliac disease is much more than simply intestinal malabsorption\(^3\)

- Coeliac disease is manageable, and symptoms can be resolvable, by strictly adhering to a lifelong gluten-free diet\(^3\)

- The symptoms of untreated coeliac disease can include, but aren’t limited to:\(^3\)

<table>
<thead>
<tr>
<th>GASTROINTESTINAL</th>
<th>NON-GASTROINTESTINAL</th>
<th>ADDITIONAL SYMPTOMS IN CHILDREN</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Indigestion</td>
<td>• Fatigue</td>
<td>• Delayed puberty</td>
</tr>
<tr>
<td>• Diarrhoea</td>
<td>• Unexplained iron, vitamin B12 or folate deficiency</td>
<td>• Faltering growth</td>
</tr>
<tr>
<td>• Abdominal pain</td>
<td>• Severe or persistent mouth ulcers</td>
<td>• Static weight</td>
</tr>
<tr>
<td>• Bloating</td>
<td>• Osteoporosis</td>
<td>• Progressive weight loss</td>
</tr>
<tr>
<td>• Distension</td>
<td>• Reproductive problems</td>
<td></td>
</tr>
<tr>
<td>• Constipation</td>
<td>• Neuropathy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Ataxia</td>
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</tbody>
</table>

**Untreated patients are more likely to develop long-lasting complications:**\(^2\)

- Central and peripheral system disorders
- Iron deficiency anaemia
- Intestinal non-Hodgkin’s lymphomas
- Gall bladder malfunction
- Vitamin K deficiency associated with risk for haemorrhaging
- Early onset osteoporosis or osteopenia – up to **40%**
- Pancreatic insufficiency
- Sub-fertility
Who is at risk? The benefits of case-finding for coeliac disease in high-risk populations

Who: Coeliac Disease, first- & second-degree relatives

- 7.5% of first-degree relatives and 2.3% of second-degree relatives of patients with coeliac disease will have coeliac disease.
- First- and second-degree relatives, who often suffer from silent or sub-clinical coeliac disease, should be investigated for coeliac disease.
- Screening for first-degree relatives, as recommended by guidelines, and case-finding in second-degree relatives can help identify patients earlier, thus reducing the risk of complications.

Who: Coeliac Disease & Irritable Bowel Syndrome (IBS)

- Up to 4.7% of IBS patients have coeliac disease.
- Likely as a result of similar symptoms, 35% of coeliac disease patients first receive treatment for irritable bowel syndrome.
- Screening for coeliac disease in patients with IBS, as recommended by national and international guidelines, can help resolve symptoms and improve the quality of life for patients and is cost-effective.
As recommended by national and international guidelines, type 1 diabetes patients should be screened for coeliac disease at the time of diagnosis and, if negative, annually for the first two years after diagnosis. Screening can: improve quality of life, improve diabetic control and decrease the risk of complications associated with type 1 diabetes and coeliac disease.

Who: Coeliac Disease & Type 1 Diabetes

- Up to 16% of patients with type 1 diabetes will also have coeliac disease.
- Up to 70% of patients with type 1 diabetes and coeliac disease are asymptomatic for coeliac disease.
- The presence of undiagnosed coeliac disease increases the risk of complications, e.g. neuropathy, cardiovascular disease, and mortality in type 1 diabetes patients.

Who: Coeliac Disease, sub-fertility & pregnancy outcomes

- Up to 8% of couples with unexplained infertility may have an underlying undiagnosed coeliac disease.
- Untreated coeliac disease is a risk factor during pregnancy and has been shown to be associated with recurrent miscarriage, intrauterine growth retardation, low birth weight and preterm birth.
- NICE recommends that coeliac disease testing is considered in all couples with unexplained infertility or recurrent miscarriage; a gluten-free diet, started prior to conception, could improve fertility.
Who is at risk? The benefits of case-finding for coeliac disease in high-risk populations

Who: Other risk groups

In addition to the previous groups, NICE recommends that serological testing for coeliac disease is considered in people with:

- 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
- Autoimmune thyroid disease, at diagnosis
- Metabolic bone disorder (reduced bone mineral density or osteomalacia)
- Unexplained neurological symptoms (particularly peripheral neuropathy or ataxia)
- Persistently raised liver enzymes with unknown cause
- Dental enamel defects
- Down’s syndrome
- Turner syndrome

is offered to people with:

is considered in people with:
How should **serology** be used to help diagnose these at-risk patients?

When requesting serological tests to investigate suspected coeliac disease in children NICE recommends that laboratories should:

- Test for total IgA and IgA tTG as **first choice**
- Consider using IgG deamidated gliadin peptide (DGP), IgG tTG or IgG EMA if total IgA is deficient
- Communicate the serological test results, their interpretation and recommended actions to the healthcare professional
- Recommend that patients with **positive serological test results** should be referred to a paediatric gastroenterologist for additional investigations to coeliac disease

When requesting serological tests to investigate suspected coeliac disease in young people and adults, NICE recommends that laboratories should:

- Test for total IgA and IgA tTG as **first choice**
- Use IgA EMA if IgA tTG is weakly positive. Consider using IgG EMA, IgG DGP or IgG tTG if total IgA is deficient
- Communicate the serological test results, their interpretation and recommended actions to the healthcare professional
- Recommend that patients with **positive serological test results** should be referred to a gastrointestinal specialist for a biopsy to confirm coeliac disease

Recommend, if coeliac disease is still suspected, people with **negative serological test results** are referred to a gastrointestinal specialist for further assessment

Patients with coeliac disease should be considered for referral for 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
How can **serology** be used to help diagnose these at-risk patients?

**tTG IgA** levels positively correlate with histological lesions in coeliac disease – this can be used to determine the severity of disease pre- and post-diagnosis. Current research suggests that the serological workup for the diagnosis of coeliac disease could be significantly improved by the routine introduction of deamidated gliadin IgG together with tTG IgA:

- A combination of tTG IgA and deamidated gliadin, as first choice, ensures more patients (including IgA deficient patients and children) are identified correctly – reducing the number of avoidable intestinal biopsies.

- A combination of the EliA™ tTG IgA and the EliA™ deamidated gliadin IgG increases the clinical sensitivity from 77.9% to **84.2%**, maintaining the specificity (100%) – resulting in more patients, including young children, being identified correctly.

The specificity of the test, in children, takes greater prominence in its impact upon estimates of cost effectiveness. This is driven by the fact that a biopsy is more than double the cost in children as it is in adults – combination approaches that include one or more DGP assay appear attractive strategies.

In adults, the most sensitive diagnostic strategies are likely to be the most cost-effective – people can be considered serologically positive if they are positive on either IgA tTG or IgA EMA.

**IT IS CLINICALLY EFFECTIVE AND COST EFFECTIVE TO USE tTG IgA AND DEAMIDATED GLIADIN TO DETERMINE THE NEED FOR ENDOSCOPY IN PATIENTS WITH SUSPECTED COELIAC DISEASE**
**Why** will identifying high-risk patients benefit outcomes?

The identification and appropriate management of patients with coeliac disease early improves clinical outcomes.

**Why** is this approach cost effective?

It is cost effective to identify and manage patients with coeliac disease early:

- Coeliac disease patients benefit from being correctly diagnosed and treated with a gluten-free diet, since this reduces both symptoms and healthcare consumption; the average cost of a coeliac disease patient who is untreated and undiagnosed is 37% higher than for a patient who receives a correct diagnosis and appropriate treatment.

Diagnosis and treatment of coeliac disease significantly reduces costs of tests by 29% and referral to secondary care by 37%.

Screening and then treating for coeliac disease is cost-effective in:

<table>
<thead>
<tr>
<th>Category</th>
<th>£ (1000's) per QALY gained (ICER)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-Degree Relatives</td>
<td>£14,000 - £18,000</td>
</tr>
<tr>
<td>IBS Patients</td>
<td>£20,800</td>
</tr>
<tr>
<td>Type 1 Diabetes Patients</td>
<td>£17,100 - £20,600</td>
</tr>
</tbody>
</table>

DECREASE THE RISK OF:

- Delayed puberty
- Some cancers
- Complications in type 1 diabetes
- Low birth weight babies

IMPROVE:

- Symptoms
- The condition of the intestinal mucosa
- Anaemia
- Diabetic control
- Low bone mineral density, if made at young age
- Persistent dermatitis herpetiformis skin lesions

RESOLVE:

- Infertility
- Menstrual problems
- Spontaneous abortions

*Early diagnosis and treatment of coeliac disease can: 3, 15, 17-21

*Management plans must be adhered to by the patient

†QALY: Quality-Adjusted Life-Year

**ICER: Incremental Cost-Effectiveness Ratio
What does the Royal College of General Practitioners e-learning course for coeliac disease suggest for increasing the pickup rate of these at-risk patients?

To see if they have had coeliac serology performed, the RCGP e-learning course on coeliac disease suggests running individual searches on patients with:

- IBS
- Type 1 diabetes
- Autoimmune thyroid diseases

The RCGP also suggests, offering tTG IgA to these patients next time they present:

- Patients with mildly abnormal iron studies
- Patients with vitamin deficiencies
- Patients with abnormal full blood counts who have been complaining about diffuse abdominal symptoms

How are other Clinical Commissioning Groups doing it?

Patient <45 years who presents with recurring GI symptoms and no red flag symptoms*

<table>
<thead>
<tr>
<th>Coeliac serology</th>
<th>Faecal calprotectin</th>
<th>Full blood count</th>
<th>Thyroid stimulating hormone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive (&gt;50 mg/kg)</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Investigative scope</td>
<td>Investigative scope</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnose coeliac disease and manage accordingly</td>
<td>Consider genetic testing or alternative diagnosis</td>
<td>Diagnose IBD</td>
<td>Non-inflammatory functional bowel disease likely</td>
</tr>
<tr>
<td>If patient has anaemia follow local pathway</td>
<td>If patient has hypothyroidism follow local pathway</td>
<td></td>
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</tbody>
</table>

*Adapted from the Coventry and Warwickshire NHS Trust Primary Care clinical pathway for patients <45 years with symptoms of IBS for more than one month and no red flag symptoms.
Implement a diagnostic pathway to actively screen at risk patients for coeliac disease as and when they arrive.

Audit GP databases to identify patients who have not been tested and test them.

Continue to test for coeliac disease in patients who present with recurrent GI symptoms and increase awareness of non-GI symptoms.

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