Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study examined screening strategies for coeliac disease (CD). The screening tests evaluated were non-invasive serologic tests, the immunoglobulin (Ig)A antiendomysial antibodies (EMA) and IgA human anti-tissue transglutaminase antibodies (TTG). All strategies were examined with and without simultaneous screening for IgA deficiency as this can lead to a false-negative serology. If IgA deficiency were identified, then antigliadin IgG was performed. In all screening strategies, a small intestinal biopsy was performed to confirm the diagnosis of CD.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adults aged 18 years. Other ages (range: 6 to 30 years) were examined in the sensitivity analyses.

Setting
The setting was the community. The economic study was carried out in the USA.

Dates to which data relate

Source of effectiveness data
The effectiveness data were derived from a review of published studies.

Modelling
A Markov state transition model was built to estimate the lifetime costs and health outcomes associated with each screening strategy and no treatment. The model consisted of six health states:

no CD;

CD but undiagnosed and considered healthy by patient and health system;

CD diagnosed but treatment failure;

CD diagnosed and adhering to a strict gluten-free diet (GFD); and
death.

The cycle length was one year. The model assumed that, in the no-screening strategy, all CD patients will eventually be diagnosed as having CD uniformly overtime.

Outcomes assessed in the review
The outcomes assessed included CD prevalence, CD mortality rate, the sensitivity and specificity of the screening tests, and levels of compliance with a GFD.

Study designs and other criteria for inclusion in the review
The authors did not specify study designs for inclusion in the review. The inclusion criteria specified studies published in the English language from January 1986 to December 2004. In addition, the authors stated that variable estimates were based only on published data on cohorts of patients, but it was unclear what was meant by that statement.

Sources searched to identify primary studies
The authors searched MEDLINE (via Ovid), the Cochrane Library and the Web of Science databases.

Criteria used to ensure the validity of primary studies
The authors stated that they did not use systematic methods to identify relevant articles.

Methods used to judge relevance and validity, and for extracting data
It appears that the validity of the primary studies was not assessed.

Number of primary studies included
The review included at least 13 primary studies.

Methods of combining primary studies
The primary studies were used to inform author assumptions about the input parameter values and their potential ranges. The results from the primary studies were reported in a narrative.

Investigation of differences between primary studies
The authors did not report investigating differences between the primary studies. They made selective use of the data and in some cases discarded outlying values.

Results of the review
The prevalence of CD was 1/200 (range: 1/1,000 to 1/100).

The prevalence of IgA deficiency was 1/500 (range: 1/1,000 to 1/200).

The standardised mortality ratio (SMR) for patients with CD was 1.6 (range: 1.3 to 2.6).

The sensitivity of TTG was 85% (range: 60 to 98) and the specificity was 90% (range: 85 to 99).

The sensitivity of EMA was 85% (range: 20 to 98) and the specificity was 98% (range: 95 to 99).

The sensitivity of antigliadin IgG was 76% (range: 52 to 99) and the specificity was 78% (range: 76 to 80).
Methods used to derive estimates of effectiveness
The authors made assumptions to estimate the SMR for patients with CD who complied with a GFD. The sensitivity and specificity of the screening strategy combining TTG and EMA were calculated.

Estimates of effectiveness and key assumptions
The sensitivity of TTG followed by EMA if TTG positive was 73% and the specificity was 99%.

Adherence to a GFD was estimated to reduce the SMR for patients with CD to 1.1 (range: 1.0 to 1.3).

Measure of benefits used in the economic analysis
The measure of benefits used was the life-years gained. The authors stated that they did not use quality-adjusted life-years because of the lack of validated utilities for CD. Life-years were discounted at a rate of 3%.

Direct costs
The resource use data were not reported separately from the costs. The study included direct health care costs to a third-party payer. These covered the costs of IgA, antigliadin IgG, TTG, EMA, endoscopy plus biopsy (including average cost of endoscopy and its complications), evaluation of symptoms (including office visits, routine blood tests, serological test and endoscopy), and the annual follow-up cost of CD (including a general medicine office visit and a TTG test). The cost data were derived from the Medicare Fee Schedule, then used in a Markov state-transition model to estimate the lifetime cost of each strategy examined. The costs were derived from actual data but, as this was the reimbursement schedule for a third-party payer, they might not represent the market value of the resources used. This may limit the generalisability of the results. Discounting was relevant and a rate of 3% per annum was used. The study reported the average costs.

Statistical analysis of costs
Primary sampled data for costs were not available, so a statistical analysis was not possible.

Indirect Costs
The indirect costs were not included in the analysis. The authors stated that this was because of the lack of valid estimates of indirect costs. The exclusion of the indirect costs was appropriate given the third-party payer perspective.

Currency
US dollars ($).

Sensitivity analysis
The authors undertook a full probabilistic sensitivity analysis to examine the impact of variability in the data. One-way sensitivity analyses were then used for those variables found to be most influential in the probabilistic sensitivity analysis. In addition, first- and second-order Monte Carlo simulations (based on 100,000 simulations) were conducted under the assumptions of accordant beta distribution in chance nodes and accordant normal distribution for cost outcomes.

Estimated benefits used in the economic analysis
No screening was estimated to result in a life expectancy of 44.21556 years for adults aged 18 years.

The estimated life expectancies resulting from the 6 screening strategies were as follows:
screening with EMA, 44.21792;
screening with TTG followed by EMA, 44.21757;

screening with TTG, 44.21806;

screening for IgA deficiency followed by TTG then EMA, 44.21757;

screening for IgA deficiency followed by EMA, 44.21792; and

screening for IgA deficiency followed by TTG, 44.21792.

A discount rate of 3% per annum was used in calculating the health outcomes.

**Cost results**
The lifetime cost per person screened was:

- $1.36 for no screening;
- $107.25 for screening with EMA;
- $156.65 for screening with TTA followed by EMA;
- $186.62 for screening with TTA;
- $196.53 for screening for IgA deficiency then TTG followed by EMA;
- $217.10 for screening for IgA deficiency followed by EMA; and
- $226.24 for screening for IgA deficiency followed by TTG.

A discount rate of 3% per annum was used in calculating the costs.

**Synthesis of costs and benefits**
The costs and benefits were synthesised to calculate the incremental cost per life-year gained. Four screening strategies were found to be dominated in the incremental analysis, all of which contained multiple screening tests.

The strategy of screening with EMA was estimated to cost $44,941 per life-year gained compared with no screening.

The strategy of screening with TTG was estimated to cost $572,616 per life-year gained compared with screening with EMA alone.

The authors estimated a 95% confidence interval (CI) for the incremental cost-effectiveness ratio (ICER) of screening with EMA (95% CI: $2,651 to dominant) using a non-parametric bootstrapping method.

The ICER for screening with EMA compared with no treatment was less than $50,000 in 81.2% of bootstrapped samples.

The most sensitive parameters were the discount rate on outcomes, the prevalence of CD, the SMR for patients with CD and the effect of a GFD on this SMR, the cost of EMA and the sensitivity of EMA.

**Authors’ conclusions**
Mass screening would be cost-effective in populations with a high prevalence of coeliac disease (CD). Immunoglobulin (Ig)A antiendomysial antibodies (EMA) would be the preferred serological marker.
CRD COMMENTARY - Selection of comparators
The comparator of no screening represented current practice in the study setting. The study examined combinations of two non-invasive serologic tests for alternative screening strategies. The serologic tests examined were selected for their high sensitivity and specificity and do not represent the full range of available tests. You must decide whether the comparisons included are relevant in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from a review of published studies. The authors stated that the review was not systematic and that they tried to bias the parameter estimates in favour of no screening. As such, the authors used data from the available studies selectively. The authors did not consider the impact of differences between the primary studies when estimating effectiveness.

Validity of estimate of measure of benefit
The estimation of lifetime benefits was modelled using a Markov state transition model. The results were very sensitive to the assumed SMR of CD and the effectiveness of treatment with a GFD. The authors stated that validated utility estimates were not available for CD, and so the main outcome was life-years. Although the life-years gained were adopted as the measure of health benefits, the authors proposed cost-effectiveness thresholds based on quality-adjusted life-years.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. The costs were not reported separately from the quantities, which may limit the generalisability of the results. The cost data were derived from Medicare reimbursement rates, which may have limited generalisability to other third-party payers, both in the USA and other countries. A sensitivity analysis of the costs was conducted. The costs were discounted as they were all incurred over a lifetime horizon. The price year was reported, which will aid any possible inflation exercises.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, which were found to be in broad agreement with each other. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported several further limitations of their study, in which the effect of CD on many related health states was not reflected because of a lack of data, and the value of reduced working capacity due to CD was not evaluated.

Implications of the study
The authors recommended further studies to establish the prevalence of CD, as this would have an impact on the potential cost-effectiveness of mass screening strategies. In addition, the authors suggested that targeted screening is still justified in high-risk groups such as first-degree relatives, as well as those with insulin-dependent diabetes mellitus, thyroid auto-immune disease or Down syndrome. Finally, the authors suggested that the true sensitivity of EMA in mass screening should be established before settling on it as a mass-screening tool.

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Bibliographic details

PubMedID