Serological testing for coeliac disease in patients with symptoms of irritable bowel syndrome: a cost-effectiveness analysis  
Mein S M, Ladabaum U

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  
Testing with tissue transglutaminase (TTG) antibodies alone, testing with a panel of antibodies (antigliadin IgG and antigliadin IgA), and up-front small bowel biopsy were compared with no testing for the detection of coeliac disease in patients with suspected irritable bowel syndrome (IBS).

Type of intervention  
Screening.

Economic study type  
Cost-effectiveness analysis and cost-utility analysis.

Study population  
The study population of the modelling study comprised a hypothetical cohort of 1,000 patients with suspected IBS. No further inclusion or exclusion criteria were reported.

Setting  
A setting was not explicitly stated, as the study was based on hypothetical patients. The economic study was carried out in the USA.

Dates to which data relate  
The effectiveness data were derived from studies published between 1994 and 2003. The cost data were derived from literature and other sources published between 1993 and 2003. All the costs were adjusted to reflect 2003 prices, using the annual medical services component of the Consumer Price Index.

Source of effectiveness data  
The effectiveness data were derived from a review and synthesis of completed studies, augmented by authors’ assumptions.

Modelling  
The authors constructed a decision analytic model, using Data-Pro (Tree-Age Software, Inc.), to estimate the clinical and economic consequences of the two serological testing strategies versus no testing. Also, to evaluate up-front endoscopic biopsy in all patients, or the addition of biopsy in patients already undergoing EGD. The results of the model depended on the critical assumption that uncovering coeliac in a patient with suspected IBS would lead, on average, to an improved quality of life. This assumption was based on the authors' clinical experience and on some evidence derived from the literature.
Outcomes assessed in the review

The input parameters in the decision analytic model were:

- age of the patients;
- the prevalence of coeliac disease in patients with suspected IBS;
- the prevalence of IgA deficiency in patients with coeliac disease;
- the sensitivity and specificity of TTG antibody testing for coeliac disease;
- the sensitivity and specificity of testing with an antibody panel for coeliac disease;
- the probability of major complications with EGD; and
- the probability of death given major complications with EGD.

All values for the variables, apart from age, were derived from the literature.

Study designs and other criteria for inclusion in the review

Not stated.

Sources searched to identify primary studies

MEDLINE was searched through September 2003 to identify primary studies.

Criteria used to ensure the validity of primary studies

Not reported.

Methods used to judge relevance and validity, and for extracting data

Not reported.

Number of primary studies included

The authors reported that 19 studies provided the effectiveness evidence.

Methods of combining primary studies

The authors do not seem to have used any particular method to combine the primary studies.

Investigation of differences between primary studies

No differences between the primary studies were reported.

Results of the review

The age of the patients was 35 years (range: 20 - 60).

The prevalence of coeliac disease in patients with suspected IBS was 3% (range: 1 - 5).

The prevalence of IgA deficiency in patients with coeliac disease was 2% (range: 1.7 - 10).

The IBS health state utility was 0.689 (range: 0.6 - 0.9).
The utility gain with a diagnosis of coeliac disease was 0.024 (range: 0.01 - 0.04).

The sensitivity of TTG antibody testing for coeliac disease was 94% (range: 87 - 97) and the specificity was 95% (range: 87 - 98).

The sensitivity of testing with an antibody panel for coeliac disease was 97% (range: 90 - 99) and the specificity was 87% (range: 80 - 91).

The probability of major complications with EGD was 0.2% (range: 0.05 - 0.5).

The probability of death given major complications with EGD was 5% (range: 2 - 10).

**Methods used to derive estimates of effectiveness**

Some estimates of effectiveness were supplemented by authors' assumptions.

**Estimates of effectiveness and key assumptions**

Patients without coeliac disease and those with undiagnosed coeliac disease were assumed to experience the natural history of IBS symptoms.

**Measure of benefits used in the economic analysis**

The benefits used were the cases of coeliac disease detected and the quality-adjusted life-years (QALYs) gained. The number of coeliac cases detected was derived from the model. The utilities used to calculate the QALYs of the IBS state and the treated coeliac disease state were derived using the Short Form-36 (SF-36) reported in published studies. The authors estimated QALYs based on a regression equation (see Other Publications of Related Interest), which predicts utilities from published SF-36 data. The utility of the treated coeliac disease state was derived from a published study (Hallert et al., 1998), and the authors used SF-36 data from this study to calculate a utility for patients with coeliac disease. The authors calculated remaining life expectancy as a function of age from the USA Life Tables, multiplying remaining life expectancy by the utility of the IBS state, or by the utility of the treated coeliac disease state, to calculate QALYs. The QALYs were discounted at an annual rate of 3%.

**Direct costs**

The costs to the health service were included in the analysis. These focused on the costs of IBS care per patient per year, the TTG antibody test, the antibody panel, EGD with biopsy, and major complications with EGD. As there were no available data comparing the costs of care for IBS and coeliac disease, the authors assumed that medical costs for treated coeliac disease were the same as for IBS care. The unit costs were reported. The authors discounted both the QALYs and costs at an annual rate of 3%, which was appropriate as the outcomes were calculated for the patients' lifetimes. All the costs were adjusted to 2003 levels, using the annual medical services component of the Consumer Price Index. The cost data were derived from published literature and appear to have been based on averages. The costs appear to have been estimated per patient (this was explicitly stated in some cases).

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**

No indirect costs were included.

**Currency**

US dollars ($).
Sensitivity analysis
A one-way sensitivity analysis was carried out on all input parameters to investigate variability in the data. The variable ranges tested were derived from published data (see Results of the Review). A two-way sensitivity analysis was also conducted. This examined the combinations of coeliac disease prevalence in suspected IBS and utility gain with a coeliac disease diagnosis under which TTG testing might be a cost-effective intervention. In addition, a probabilistic analysis (Monte Carlo simulation) was performed in which all model inputs were varied simultaneously for 5,000 iterations using the ranges reported already. The results of the Monte Carlo simulations were reported as medians with interquartile ranges.

Estimated benefits used in the economic analysis
Compared with no testing, the incremental coeliac disease cases detected were 28 with the TTG antibody test and 29 with the antibody panel.

Compared with no testing, the incremental QALYs per 1,000 patients with suspected IBS were 17.7 with the TTG antibody test and 18.1 with the antibody panel.

Cost results
The cost results were reported as the average cost per patient.

The discounted lifetime cost of caring for IBS in the absence of coeliac disease testing was $11,835 per patient. In the presence of testing, these costs were $11,965 per patient with the TTG antibody test and $12,089 per patient with the antibody panel.

Up-front EGD with biopsy in all patients, along with confirmatory antibody panel testing in those with abnormal histology, detected all cases of coeliac disease. It resulted in a total discounted cost per patient of $937 higher than no testing.

Synthesis of costs and benefits
Compared with no testing, TTG antibody testing resulted in a cost of $4,600 per case detected, while testing with the antibody panel resulted in a cost of $8,800 per case detected.

The incremental cost of coeliac disease testing using the antibody panel compared with the TTG antibody test was $135,000 per incremental case detected.

Compared with no testing, TTG antibody testing resulted in a cost of $7,400 per QALY gained, while testing with the antibody panel resulted in a cost of $14,000 per QALY gained.

The incremental cost per QALY gained of testing using the antibody panel compared with the TTG antibody test was $287,000 per incremental QALY gained. It is obvious that testing with the panel compared with TTG alone incurred a substantial incremental cost for only a small increase in quality-adjusted life expectancy.

When up-front EGD with biopsy in all patients, along with confirmatory antibody panel testing in those with abnormal histology, detected all cases of coeliac disease, the incremental cost per case detected was $450,000 compared with TTG testing, and $776,000 compared with antibody panel testing.

Authors' conclusions
The authors concluded "serological testing can detect most cases of coeliac disease present in a population of patients with symptoms consistent with a diagnosis of IBS (irritable bowel syndrome) at acceptable cost per case detected and per QALY (quality-adjusted life-year) gained". Up-front oesophago-gastroduodenoscopy (EGD) plus biopsy in all patients with symptoms of IBS was always dominated by serological testing.
CRD COMMENTARY - Selection of comparators
The authors did not justify their choice of the comparators. However, no testing for coeliac disease in patients with suspected IBS would seem to represent the standard practice in the authors' setting. Small bowel biopsy was assumed to be a perfect diagnostic 'gold' standard in the clinical setting of suspected coeliac disease and the presence of coeliac disease antibodies. You should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature was undertaken. It is therefore possible that the data from the available studies were used selectively. The authors did not note any differences between the efficacy estimates from the primary studies. There was no commentary on the quality of the retrieved studies, making it difficult to comment on the quality of the efficacy estimates. However, the authors conducted several sensitivity analyses relating to the efficacy estimates. These analyses improved both the internal validity and the generalisability of the study, by demonstrating the robustness of the results to changes in the base-case estimates. The authors acknowledged that they restricted the benefits of coeliac disease diagnosis to improvement in symptoms, and thus improvements in quality of life, due to the absence of more detailed data. They reported that if treatment of coeliac disease prevented long-term complications, increased life expectancy, or decreased long-term costs, the benefits of coeliac disease testing in suspected IBS would be greater than predicted in their analysis.

Validity of estimate of measure of benefit
The estimation of coeliac disease cases detected was obtained directly from the effectiveness analysis, and was mainly based on the sensitivity of the tests. The authors estimated QALYs using a regression equation that predicts utilities from published SF-36 data. The authors acknowledged that direct utility measurements would have been superior but, at the time of the study, such data were unavailable. The efficacy and the benefit measures were reported separately. This allows the reader to recreate the results and better understand the key factors impacting on the cost-effectiveness ratios.

Validity of estimate of costs
The authors did not explicitly state the perspective adopted in the study, but since the indirect costs were not included, it could not have been a societal perspective. It is unclear whether all the relevant costs were included. The quantities were derived from the model, while the unit prices were taken from the literature. Sensitivity analyses were conducted on ranges of all unit cost inputs. The unit costs, price year, inflation adjustment and discounting were all reported, all of which improve the generalisability of the results.

Other issues
The authors did not make appropriate comparisons of their finding with those from other studies. However, this might have been because of the lack of published literature in this specific area. The issue of generalisability of the results to other settings was discussed in terms of the prevalence of coeliac disease in suspected IBS patients. This was a critical variable in the authors' analysis and could be different in other settings, depending on the clinical population seen by individual physicians. The authors reported that their results suggest that, even at relatively low coeliac disease prevalence in suspected IBS, serological testing for coeliac disease is likely to be considered cost-effective. The cost and efficacy estimates for different settings may be compared with the sensitivity analysis ranges in order to obtain a preliminary understanding of cost-effectiveness in alternative settings. The authors do not appear to have presented the results selectively and their conclusions reflect the scope of the analysis.

The authors reported a number of further limitations to their study. For example, the lower specificity of the antibody panel test in comparison to the TTG testing was not taken into consideration. This may result in more patients having false positive results and thus undergoing "unnecessary" EGD with biopsy and becoming at risk of the associated complications. The authors also commented on the uncertainties surrounding some input parameters in the model, such as the true prevalence of coeliac disease in suspected IBS and the change in quality of life after diagnosing coeliac disease.
Implications of the study
The authors did not provide any explicit recommendations for policy change. They did, however, identify specific areas for further research. Future research should address patient preferences in relation to IBS symptoms and coeliac disease testing, and determine whether diagnosing coeliac in patients with IBS symptoms yields meaningful improvements in quality of life. Further research should also be performed in patients with suspected IBS found to have coeliac disease, in order to compare quality of life before and after instituting a gluten-free diet.

Source of funding
None stated.

Bibliographic details

PubMedID
15153173

DOI
10.1111/j.1365-2036.2004.01958.x

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Celiac Disease /diagnosis /economics; Colonic Diseases, Functional /complications /economics; Cost-Benefit Analysis; Decision Support Techniques; Endoscopy, Gastrointestinal /economics; Humans; Monte Carlo Method; Prognosis; Sensitivity and Specificity; Serologic Tests /economics

AccessionNumber
22004000772

Date bibliographic record published
28/02/2005

Date abstract record published
28/02/2005