Noninvasive tests as a substitute for histology in the diagnosis of Helicobacter pylori infection


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 use of invasive and noninvasive tests for the diagnosis of Helicobacter pylori (H. pylori) infection in patients with a negative rapid urease test (RUT). The diagnostic tests considered were histology (based on 1 fundic and 2 antral biopsies), 13-C Urea Breath Test (UBT), FlexSure HP whole blood test, FlexSure HP serum test, QuickVue, AccuStat, Stat-Simple Pylori and HM-CAP enzyme-linked immunoassay (EIA). RUT and histology are invasive tests, while UBT is a noninvasive test. FlexSure HP whole blood test, QuickVue, AccuStat and Stat-Simple Pylori are noninvasive capillary whole blood-based rapid serologies. EIA and FlexSure HP serum test are noninvasive rapid serum-based serologies.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing endoscopy for dyspepsia, testing negative for H. pylori on RUT. The exclusion criteria were prior treatment for H. pylori, the use of proton-pump inhibitors, antibiotics or bismuth within 4 weeks, the presence of underlying malignancy, prior gastric surgery, pregnancy, breast-feeding, and the inability to give informed consent.

Setting
The setting of the clinical study was secondary care. The economic study was carried out in Portland (OR), USA.

Dates to which data relate
The effectiveness evidence and resource use data were gathered between March and November 1997. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was performed prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations to determine the sample size were not performed. Of 100 consecutive patients undergoing endoscopy for dyspepsia, 67 tested negative for H. pylori on RUT and were included in the study. The mean age was 58 (+/- 14) years, 61 patients were men (91%), 66 were white (98.5%), and 23 (34%) had a history of peptic ulcer disease. The authors stated that this sample was representative of the patient population examined for H. pylori in their hospitals. No patient included in the final sample refused to participate or was excluded from the effectiveness analysis.

**Study design**
This was a diagnostic cohort study that was performed in two medical centres. All of the patients received all the invasive and noninvasive tests included in the analysis. The six noninvasive rapid antibody tests were all performed on each patient on the same day. With the exception of EIA, the noninvasive rapid tests were performed in randomised order to avoid bias from one or several test results. One expert gastrointestinal pathologist reviewed the results of the histological examinations and was blinded to the results of the other tests for H. pylori. The patients were not followed up to assess the future costs and future effectiveness results.

**Analysis of effectiveness**
All of the patients included in the study sample were considered for the effectiveness analysis. The primary health outcomes used in the analysis were the positive and negative predictive values (PPV and NPV, respectively) of the tests. In other words, the ratio between true-positive patients and all positive patients for H. pylori (PPV), and the ratio between false-negative patients and all negative patients for H. pylori (NPV). All patients testing positive with one individual test were called "all positives" for this test. The patients were considered true positive when chronic gastritis was present on histology and at least two of the three reference standard tests (histology, UBT and EIA) were positive. Similarly, the patients were considered "all negatives" when an individual test was negative, and true negative when at least two of the three reference standard tests were negative.

**Effectiveness results**
Histology based on the presence of chronic gastritis plus H. pylori had no false positives (PPV=100%) and a NPV of 95% (63 true negatives out of 66 all negatives). However, it failed to diagnose 3 out of 4 infected patients (sensitivity 25%).

Histology based only on the presence of chronic gastritis showed a NPV of 97% (59 true negatives out of 61 all negatives), but a PPV of 33% (only 2 true positives out of 6 all positives).

The UBT had a NPV of 100% but a PPV of only 31% (4 out of 13).

All six rapid antibody noninvasive tests had a NPV of 100%. All of the tests detected the four infected patients (sensitivity 100%).

The PPV was 36% for the FlexSure HP whole blood test (4 out of 11), 50% for the FlexSure HP serum test and for the EIA (4 out of 8), 57% for the QuickVue and the AccuStat (4 out of 7) and 80% for the Stat-Simple Pylori (4 out of 5).

None of these differences reached statistical significance. Only the comparison between UBT versus Stat Simple Pylori approached statistical significance for a difference in PPV, (p=0.06).

These results could be due to the small sample size used in the study.

**Clinical conclusions**
Compared with histological examinations, the rapid antibody noninvasive tests resulted in a higher NPV and a higher ability to detect patients infected by H. pylori. However, none of these differences were statistically significant.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used. A cost-consequences analysis was therefore carried out.
Direct costs
Discounting was not carried out as it was not relevant to the analysis. The cost categories included in the study were all the tests performed and triple therapy for H. pylori for 10 days. Other potential costs, such as inducing metronidazole resistance, not treating some infected patients or treating false positive patients, were not included since they were likely to be similar among the alternatives studied. The unit costs and the quantities of resources used were reported separately. The quantity/cost boundary appears to have been that of the hospital. Resource use was derived from the same sample of patients as that used in the effectiveness analysis, whereas the source of the unit cost data was unclear. The resource use data were gathered between March and November 1997, but the price year was not indicated.

Statistical analysis of costs
T-tests were carried out to estimate the statistical significance of the difference in costs of the alternative tests.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not carried out

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The cost per patient (cost per test plus cost of H. pylori therapy for all patients testing positive with respective tests) of the tests included in the analysis was:

$217 for histology based on chronic active gastritis,
$202 for histology based on chronic active gastritis plus H. pylori,
$164 for UBT,
$105 for EIA,
$43 for FlexSure HP whole blood,
$34 for FlexSure HP serum and QuickVue,
$31 for AccuStat, and
$27 for Stat-Simple Pylori.

Histological examinations were significantly more expensive than all the rapid antibody noninvasive tests, (p<0.001). UBT and EIA were also significantly more expensive than the other five noninvasive tests.

Synthesis of costs and benefits
Not relevant because a cost-consequences analysis was performed.

**Authors' conclusions**
The noninvasive rapid antibody tests were at least as accurate (if not more accurate) as 13-C urea breath test (UBT) and histology in detecting Helicobacter pylori (H. pylori) in patients with a negative rapid urease test (RUT), and were significantly less expensive. In addition, the rapid antibody noninvasive tests provided an immediate result. Histology was the least cost-effective strategy as it missed a substantial percentage of infected patients in this population.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear. The newer noninvasive rapid antibody tests were compared with standard invasive and noninvasive tests such as histology or UBT. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness analysis used a diagnostic cohort study, which can be considered appropriate for the study question. However, the small sample size reduced the ability of the analysis to detect significant differences in the degree of accuracy of the alternative tests. The exclusion and inclusion criteria were reported in detail, as were disease classifications. The sample characteristics reflected the patient population of the medical centres where the study was carried out.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the economic analysis. The analysis was therefore categorised as a cost-consequences study. However, it is important to note that the differences between the alternative tests in terms of the key effectiveness parameters were not statistically significant. Thus, the analysis could also be classified as a cost-minimisation analysis.

**Validity of estimate of costs**
The cost categories included in the analysis were relevant to the study perspective. The authors stated clearly the rationale for excluding some categories of costs, and reported the unit costs and resource use separately. Appropriate statistical analyses were performed to estimate the significance of cost differences among the tests. However, no sensitivity analyses were carried out, thus reducing the generalisability of the economic results. Also, the source of the unit costs was not given.

**Other issues**
The issue of generalisability was partly addressed by comparing the results of the effectiveness analysis with the sensitivity and specificity of the tests found in other published studies. However, the authors did not perform sensitivity analyses and the cost results might not be transferable to other contexts. Also, the patient population was specific to the study medical centre, although the authors stated that this is unlikely to have influenced the results significantly.

**Implications of the study**
For patients undergoing endoscopy for dyspepsia with a negative RUT test for H. pylori, a rapid antibody test can be an accurate and cheap substitute for histology.

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