Polymorphisms and the pocketbook: the cost-effectiveness of cytochrome P4502C19 genotyping in the eradication of Helicobacter pylori infection associated with duodenal ulcer

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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 cytochrome P4502C19 genotyping in the eradication of Helicobacter pylori (H. pylori) infection associated with duodenal ulcer (DU). This health technology was compared with no genotyping prior to the initiation of anti-H. pylori treatment.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised two hypothetical patient cohorts with newly diagnosed duodenal ulcer and H. pylori infection at entry to hospital.

Setting
The study setting was secondary care. The economic study was carried out at SUNY upstate Medical University, Syracuse, USA.

Dates to which data relate
The effectiveness data were derived from sources published between 1984 and 2001. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of published sources.

Modelling
A decision analytic model was used to derive the cost-effectiveness of genotyping. In the model, one cohort of patients underwent CYP219 genotyping prior to the initiation of anti-H. pylori treatment, while the other did not undergo genotyping. Homozygous extensive metabolisers in the genotyped cohort received a non proton-pump inhibitor (PPI)-based regimen, which comprised bismuth, metronidazole, and tetracycline with ranitidine (BMTR). All other patients in both cohorts received a PPI-based regimen of omeprazole, amoxicillin and clarithromycin (OAC). All initial H. pylori eradication regimens were given for a week. DU recurrences associated with failure of the initial H. pylori treatment regimen in homozygous and heterozygous extensive metabolisers in the genotyped cohort were treated with high-dose lansoprazole plus amoxicillin for 2 weeks, whereas poor metabolisers in the genotyped cohort and non-genotyped patients received BMTR.
Outcomes assessed in the review
The outcomes assessed were:

- the H. pylori eradication rates according to the three treatment regimens for the three genotypes;
- the ethnic distribution of the CYP2C19 genotype;
- the regional US ethnic distribution;
- the DU recurrence rate when H. pylori was successfully eradicated and when eradication failed; and
- the DU complication rate requiring hospitalisation when H. pylori eradication failed.

Study designs and other criteria for inclusion in the review
The designs of the studies included in the review were not reported. However, the authors did report that the regional US ethnic distribution was derived from the 2000 Census.

Sources searched to identify primary studies
Not reported.

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
Approximately 21 published studies were included in the review. Data from the 2000 US Census were also included.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The H. pylori eradication rate with OAC was 0.98 for a poor metaboliser of the CYP2C19 genotype, 0.92 for a heterozygous extensive metaboliser of the CYP2C19 genotype, and 0.73 for a homozygous extensive metaboliser of the CYP2C19 genotype.

The H. pylori eradication rate with BMTR was 0.86 for all three genotypes.

The H. pylori eradication rate with lansoprazole plus amoxicillin was 1.0 for those with heterozygous and homozygous extensive metaboliser genotypes.

The distribution of the CYP2C19 genotype in Asian or Pacific Islanders was 0.17 for poor metabolisers, 0.48 for heterozygous extensive metabolisers, and 0.35 for homozygous extensive metabolisers.
The distribution of the CYP2C19 genotype in other ethnic groups was 0.03 for poor metabolisers, 0.30 for heterozygous extensive metabolisers, and 0.67 for homozygous extensive metabolisers.

The regional distribution of Asian or Pacific Islanders ranged from 0.019 in the Midwest to 0.51 in Hawaii. The distribution of other ethnic groups ranged from 0.981 in the Midwest to 0.49 in Hawaii.

The DU recurrence rate was 0.2 with successful eradication of H. pylori and 0.85 with failed H. pylori eradication. The DU complication rate requiring hospitalisation was 0.027 with failed H. pylori eradication.

**Measure of benefits used in the economic analysis**
The measure of health benefit used was the ulcer episodes prevented.

**Direct costs**
The resource quantities and the costs were reported separately. The direct costs included in the analysis were those of the health service. These comprised the costs of endoscopy (facilities and physician), primary physician office visits, gastroenterologist office visits, hospitalisation, inpatient initial and follow-up visits, and drug regimens. The authors assumed that the direct medical costs were equal to the 2001 Medicare reimbursement rates for drug use, procedures, physician visits, and hospitalisations. Emergency department visits with home discharges were not included. Discounting was not relevant, as all the costs were incurred during one year, and was not performed. The price year was 2001. The average costs were reported.

**Statistical analysis of costs**
Resource use and the costs were treated as point estimates (i.e. the data were deterministic).

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

**Currency**
US dollars ($).

**Sensitivity analysis**
The authors performed a break-even analysis to provide the dollar amount per genotype test required to eliminate the savings realised from ulcer prevention by the use of genotyping. The authors also determined the relative impact that ethnicity would be expected to have on cost-effectiveness, by using data from the sensitivity analysis most unfavourable for CYP2C19 genotyping in the sub-group of homozygous extensive metabolisers.

**Estimated benefits used in the economic analysis**
The estimated number of ulcer episodes prevented by the use of genotyping was not reported. However, from the authors' results, it can be derived that genotyping was at least as effective as non-genotyping.

**Cost results**
The costs of the two strategies were not reported. However, from the authors' results, it can be derived that genotyping was less costly than non-genotyping.

**Synthesis of costs and benefits**
As in the reference case analysis, the use of CYP2C19 genotyping prior to initiating anti-H. pylori therapy was
dominant (i.e. costs were saved with each ulcer recurrence episode prevented) in all geographical regions of the USA. Therefore, the costs and benefits were not combined. The subsequent break-even analysis showed that the dollar amount per genotype test required to eliminate the savings realised from ulcer prevention by using genotyping ranged from $89.20 (Hawaii) to $118.96 (Midwest) per genotype test. Using probabilities most unfavourable to genotyping, the variation of people with Pacific Rim origins from 0% to 100% altered the cost-effectiveness from $495 to $2,125 per ulcer prevented.

Authors' conclusions
The results suggested that treatment decisions for Helicobacter pylori (H. pylori) infection associated with duodenal ulcer (DU), which were based on a patient's CYP2C19 genotype, could decrease expenses for health plans that implement testing.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used. It represented current practice in the authors' setting. 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 had been undertaken to identify relevant research and minimise biases. The methods used in the review were not reported, nor did the authors report how estimates of effectiveness from the primary studies were combined, or if differences between the primary studies were investigated. The authors also reported sensitivity analysis ranges for several of the model probabilities, which were then used in the break-even and sensitivity analysis.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. However, the authors did not report the number of ulcers prevented using both strategies. This limits the validity and the generalisability of their results.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. However, some relevant costs such as emergency department visits with home discharges were not included. It is unlikely that these omissions would have affected the authors' conclusions. The costs and the quantities were reported separately, which will enhance the generalisability of the results. Resource use was derived from a published study. It would appear that no sensitivity analysis of the quantities was conducted, thereby limiting the interpretation of the study findings. The prices were derived from Medicare reimbursement rates, hence charges were used to proxy prices. No sensitivity analysis of the prices was conducted. The price year was reported, which will aid any potential inflation exercises.

Other issues
The authors did not compare their findings with those from other studies. The issue of generalisability to other settings was partly addressed in the sensitivity analysis, although this was not as comprehensive as it could have been, as it did not include prices or resources. The authors do not appear to have presented their results selectively, although the costs and benefits were not reported separately for each of the two strategies. The methodology used to conduct the review of the literature could have been reported in more detail. The authors' conclusions reflected the scope of the analysis. The authors reported a number of further limitations to their study. First, they did not include societal perspectives. Second, the only existing probability data were derived from small studies of CYP2C19 genotyping. Finally, the analysis did not consider the impact of antimicrobial resistance on H. pylori eradication rates.

Implications of the study
The authors reported that their results provided an economic margin to complement recent calls for the routine use of
CYP genotyping to decrease the risk of toxicity from narrow therapeutic index drugs, which are extensively cleared by enzymes subject to genetically determined polymorphisms, particularly CYP2D6.

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None stated.

**Bibliographic details**

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**Other publications of related interest**

Evans DA, Krahn P, Narayanan N. The mephenytoin (cytochrome P450 2C19) and dextomethorphan (cytochrome P450 2D6) polymorphisms in Saudi Arabians and Filipinos. Pharmacogenetics 1995;5:64-71.


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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