Cost-effectiveness of proton pump inhibitor cotherapy in patients taking long-term, low-dose aspirin for secondary cardiovascular prevention

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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.

CRD summary
The study examined the cost-effectiveness of long-term therapy with low-dose aspirin (ASA) plus proton-pump inhibitor (PPI) co-therapy, compared with ASA alone, for the prevention of upper gastrointestinal bleeding in patients with coronary heart disease. The authors concluded that PPI co-therapy was a cost-effective strategy when over-the-counter costs of drugs were considered. At the higher prescription cost of PPI, co-therapy was cost-effective only in high-risk patients. Overall, the quality of the study methodology was good, with clear reporting of the methods and results.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective of the study was to examine the cost-effectiveness of long-term therapy with low-dose aspirin (ASA) plus proton-pump inhibitor (PPI) co-therapy, compared with ASA alone, for the prevention of upper gastrointestinal bleeding (UGIB) in hypothetical patients with coronary heart disease who were at least 50 years of age. The analysis considered the cost-effectiveness of low-cost over-the-counter PPIs such as omeprazole magnesium, as well as that of higher cost prescription PPIs such as esomeprazole magnesium, rabeprazole sodium and pantoprazole sodium, in different groups of patients.

Interventions
The study examined co-therapy with PPI as a preventive measure against the development of UGIB in patients with coronary heart disease. ASA (75 to 325 mg daily) with PPI co-therapy was compared with ASA alone. Those receiving ASA alone were switched to gastroprotection (ASA plus PPI) only if a UGIB event occurred; those receiving ASA plus PPI were switched to clopidogrel bisulphate plus PPI in the event of UGIB.

Location/setting
USA/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a Markov model, which was developed to simulate the management of patients eligible for treatment and the risk of UGIB, cardiovascular events and death associated with the two alternative strategies. A patient's lifetime horizon was considered. The authors stated that the analysis was undertaken from the perspective of a long-term payer such as Medicare.

Effectiveness data:
The clinical estimates were derived from the literature. The risk of UGIB was estimated from a review of the literature that involved a search of MEDLINE; this identified three recent systematic reviews. An age-dependent, dynamic UGIB risk was modelled on the basis of these sources. A further review of the literature was undertaken to estimate treatment effectiveness (effect of PPI co-therapy in reducing UGIB risk), which was derived from two randomised clinical trials (RCTs).

Monetary benefit and utility valuations:
Measure of benefit:
The summary benefit measure was the expected number of life-years (LYs). These were estimated using the decision model. UGIB events and UGIB-related deaths were also reported as model outputs.

Cost data:
The analysis of the costs included the health services related to hospitalisation for UGIB and various medications. The hospital cost was derived from the Health-care Cost and Utilization Project Nationwide Inpatient Sample. Over-the-counter costs for drugs were derived from average wholesale prices available to large health insurance companies or governmental payers. Other medication costs were obtained from the 2007 Thomson Red Book and the Consumer Union. The long-term costs were discounted at an annual rate of 3%. The price year was 2007. The costs were in US dollars ($).

Analysis of uncertainty:
Univariate sensitivity analysis was performed in order to address the issue of uncertainty. The effectiveness of treatment was varied from 25 to 75%, as suggested in the literature. Hospital costs were arbitrarily varied by +/-33% of their baseline values. Other ranges were derived from published sources, whenever possible. A probabilistic sensitivity analysis was also carried out by randomly varying the eight key inputs of the decision model. Statistical distributions associated with each parameter were provided.

Results
In a hypothetical 65-year-old patient at average risk of UGIB, the expected lifetime costs were $1,269 with ASA alone and $2,847 with ASA plus PPI, using over-the-counter prices. The expected LYs were 9.60 with ASA alone and 9.64 with ASA plus PPI. The incremental cost-effectiveness ratio (ICER; i.e. the incremental cost per LY gained) was $40,090. The probabilistic sensitivity analysis showed that nearly 75% of trials remained below a willingness-to-pay threshold of $50,000 per LY saved in this population.

The sensitivity analysis showed that the study findings were sensitive to assumptions on treatment effectiveness (range from $35,315 to $94,718 per LY gained) and drug prices, as already reported.

Authors’ conclusions
The authors concluded that PPI co-therapy in patients on ASA for the secondary prevention of coronary heart disease was a cost-effective strategy when over-the-counter costs of drugs were considered. At the prescription cost of PPI, co-therapy was cost-effective only in high-risk patients.

CRD commentary
Interventions:
The rationale for the choice of the interventions was clear since the addition of PPI to ASA represents a valid alternative to ASA alone. They are likely to represent relevant comparators in many settings.

Effectiveness/benefits:
The clinical estimates were derived from systematic reviews of the literature, the methods and conduct of which were described in part. The final sources used to estimate treatment effectiveness and other parameters of underlying disease were robust given the characteristics of their design. RCTs and literature reviews are usually considered good sources of clinical data. Uncertainty in some estimates was extensively addressed in the sensitivity analysis. The derivation of the benefit measure was clear, but it was unclear whether a discount rate was applied to the LYs.

Costs:
The analysis of the costs appears to have been consistent with the perspective adopted. The cost of hospitalisation was presented as a macro-category, reflecting the accounting system used in the authors' setting. Alternative sources of drug costs were used; the authors also considered the perspective of large payers that may be able to achieve considerable discounts. The impact of variation in the costs was the focus of the analysis and was considered globally in the sensitivity analysis. The sources of the costs were reported, together with other characteristics of the analysis such as the price year and use of discounting.

Analysis and results:
The synthesis of the costs and benefits was appropriate. The authors provided an extensive presentation of the results of the analysis considering different combinations of patient age and risk of disease. The issue of uncertainty was addressed extensively in the sensitivity analysis, the alternative assumptions being mainly based on published evidence. Furthermore, the authors compared their findings with other published economic evaluations, showing similar results. Finally, limitations and strengths of the analysis were appropriately highlighted.

Concluding remarks:
The quality of the study methodology appears to have been satisfactory, with good reporting of the methods and sources, and clear presentation of the study results. The authors’ conclusions appear valid and robust.

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