Cost-effectiveness analysis of high-dose omeprazole infusion as adjuvant therapy to endoscopic treatment of bleeding peptic ulcer


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 intravenous (i.v.) administration of a high-dose proton-pump inhibitor (PPI), namely omeprazole, after the endoscopic treatment of bleeding peptic ulcers. The dosage considered was bolus i.v. injection of 80 mg followed by an infusion of 8 mg/hour for 72 hours.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing endoscopic treatment of a bleeding peptic ulcer.

Setting
The setting was a hospital. The economic study was carried out in Hong Kong.

Dates to which data relate
The dates when the effectiveness and resource use data were collected were not provided. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a published study (Lau et al., see Other Publications of Related Interest).

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

Study sample
Limited information on the original study was provided. An overall sample of 240 patients was enrolled, of which 120 were allocated to the omeprazole group and 120 to the placebo group. The method used to select the sample was not described.

Study design
This was a prospective, randomised, placebo-controlled clinical trial. The length of follow-up was one month after the
endoscopic intervention. Final assessment data were available for 115 patients in the omeprazole group and 117 patients in the placebo group. Other details of the primary study were not reported.

Analysis of effectiveness
The analysis of the clinical study was carried out on the patients available at the last follow-up assessment (only to match effectiveness and cost data, with the latter being unavailable for a few patients in both groups). The primary outcome measure was the percentage of patients without recurrent bleeding. The number of patients with early or late recurrent bleeding and the relative risk of recurrent bleeding were also reported. The study groups were comparable at baseline in terms of the demographic variables, co-morbid illnesses, severity of bleeding at presentation, ulcer etiology, ulcer location, ulcer size, and stigmata of bleeding.

Effectiveness results
The proportion of patients without recurrent bleeding was 77.8% in the placebo group and 93.9% in the omeprazole group.

There were 23 patients with early recurrent bleeding in the placebo group and 4 in the omeprazole group.

There were 3 patients with late recurrent bleeding in each group.

The relative risk of recurrent bleeding was 0.274.

Clinical conclusions
The effectiveness analysis showed that omeprazole led to fewer patients with recurrent bleeding after the endoscopic intervention than placebo.

Measure of benefits used in the economic analysis
The summary benefit measure was the percentage of patients without recurrent bleeding. This was estimated directly from the effectiveness study.

Direct costs
Discounting was not relevant as the costs were incurred during a short timeframe. The unit costs were not reported separately from the quantities of resources used. The costs were presented as macro-categories. The health services included in the economic evaluation were hospitalisation, endoscopic treatment (with or without haemostatic therapy), omeprazole and surgery. The cost of blood transfusion was restricted to administration sets and related consumables. The cost/resource boundary of a public health organisation was used. Resource use was estimated using patient-level data, which were derived from the sample of patients included in the effectiveness study. However, 8 patients (5 in the omeprazole group and 3 in the placebo group) were not included in the pharmacoeconomic analysis. The costs were estimated from the hospital pharmacy department and the Hong Kong Government Gazette. The price year was not reported.

Statistical analysis of costs
The two-sample Kolmogorov-Smirnov test was carried out to assess the difference between the medical costs of the two groups. Owing to the skewed distribution, the costs were presented as the median (25th and 75th percentile) value.

Indirect Costs
The indirect costs were not considered.
Currency
The costs were estimated in Hong Kong dollars (HK$) and were also presented in US dollars ($). The exchange rate was $1 = HK$7.8.

Sensitivity analysis
One-way sensitivity analyses were carried out. These assessed the impact of variations in the rates of recurrent bleeding (+/- 20%) and total direct medical costs (25th and 75th percentiles) on the estimated cost-effectiveness ratios. The impact of varying some cost estimates was also investigated.

Estimated benefits used in the economic analysis
The percentage of patients without recurrent bleeding was 77.8% in the placebo group and 93.9% in the omeprazole group.

Cost results
The median cost per patient was HK$28,780 (3,690; 25th and 75th percentile: 25,650 and 41,300) in the placebo group and HK$27,010 (3,463; 25th and 75th percentile: 23,880 and 33,270) in the omeprazole group. The difference between the groups was statistically significant, (p=0.0174).

The cost-saving per patient was HK$1,770 (7%).

The use of an alternative source of cost from a US diagnosis-related group (DRG) confirmed the cost-savings associated with omeprazole.

Synthesis of costs and benefits
The costs and benefits of the alternative strategies were combined by calculating the average cost-effectiveness ratios.

The median cost per recurrent bleeding averted was HK$36,992 (25th and 75th percentile: 32,969 and 53,080) or US$4,743 (25th and 75th percentile: 4,227 and 6,806) in the placebo group and HK$28,764 (25th and 75th percentile: 25,431 and 35,430) or US$3,688 (25th and 75th percentile: 3,260 and 4,542) in the omeprazole group.

The use of an alternative PPI, for example, pantoprazole which was widely prescribed in the USA, led to a cost of HK$30,705 (US$3,936) for the treatment group.

The sensitivity analysis showed that omeprazole was more cost-effective than placebo providing the total direct costs for patients without recurrent bleeding in the omeprazole group did not exceed HK$29,000 (US$3,718).

Authors' conclusions
High-dose intravenous (i.v.) omeprazole therapy was a cost-effective strategy in reducing the recurrence of bleeding and the need for surgery in patients with active bleeding ulcer after endoscopic treatment. Compared with endoscopic treatment alone, the costs were reduced and better clinical outcomes were observed with omeprazole.

CRD COMMENTARY - Selection of comparators
The comparator (placebo) was selected so that the actual value of omeprazole could be assessed. It also reflected the traditional approach based on endoscopic treatment alone. The authors replicated the analysis of costs using an alternative PPI, such as pantoprazole. Nevertheless, the clinical impact of alternative treatments was not investigated. You should decide whether endoscopic treatment alone represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a clinical trial, which was appropriate for the study question. The length of follow-up was appropriate and the study groups were comparable at baseline. Few details were provided on the methods and design of the trial, which had been published elsewhere. In general, the design of the study ensured the validity of the primary estimates, although it would have been interesting to have known whether any justification for the sample size was provided. Similarly, it was not easy to assess whether the study sample was representative of the study population.

**Validity of estimate of measure of benefit**
The summary benefit measure was derived directly from the effectiveness study and was specific to the disease considered in the analysis. Therefore, it would be difficult to compare with the benefits of other health care interventions. However, the rate of patients without bleeding represents a commonly used measure to assess the impact of the interventions on the patients' health.

**Validity of estimate of costs**
The authors explicitly stated the perspective adopted in the study. As such, it appears that all the relevant categories of costs have been included in the analysis. A detailed breakdown of the costs was not provided and the costs were presented as macro-categories. The charges were derived from the hospital, and the authors stated that these charges were likely to be reasonably close to the true costs of the services. Alternative sources of the costs were also used. All economic estimates were varied in the sensitivity analysis. Discounting was not relevant due to the short time horizon of the analysis. Statistical tests were conducted, not only to deal with the skewed distribution of the costs, but also to test the statistical significance of differences in the estimated costs.

**Other issues**
The authors reported some results from other economic evaluations and noted the limitations of other studies, such as the use of inappropriate economic data or the lack of a cost-effectiveness ratio. They also stated that their cost-effectiveness ratios were specific to the study setting and could not be easily transferred to settings with different economic and clinical characteristics. The issue of the generalisability of the study results to other settings was addressed partially through the sensitivity analysis, in which plausible ranges of variations for the base-case data were investigated.

**Implications of the study**
The authors stated that i.v. high-dose omeprazole treatment as adjuvant therapy to the endoscopic treatment of bleeding peptic ulcers should be recommended in countries with similar publicly funded hospitals.

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Other publications of related interest


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