Short-term cost effectiveness and long-term cost analysis comparing laparoscopic Nissen fundoplication with proton-pump inhibitor maintenance for gastro-oesophageal reflux disease

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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 laparoscopic Nissen fundoplication (LNF) for the treatment of gastro-oesophageal reflux disease (GORD).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with a history of GORD and who had depended on a PPI for at least 3 months.

Setting
The setting was primary care and a hospital. The economic study was performed in the UK.

Dates to which data relate
The effectiveness evidence and most resource use data were gathered between June 1997 and August 2001. The price year was 2001.

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

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
Patients included in the study were referred by general practitioners (GP) participating in the trial. Of the 340 patients initially identified from June 1997 to August 2001, 217 had physiologically significant reflux and consented to participate. However, only the first 100 patients enrolled in the trial were included in the current economic evaluation. There were 50 patients in each group. It was not stated whether any power calculations had been performed. Other details of the patients' characteristics were not provided.

Study design
This was a prospective, randomised clinical trial. The 100 patients included in the current study came from the Norfolk and Norwich University Hospital Trust in Norwich. Details on the follow-up and outcome assessment were not reported. However, the outcomes were assessed at 3- and 12-month intervals. Some missing values were excluded from the analysis (they were assumed to be randomly distributed between the groups).

**Analysis of effectiveness**
The analysis of the clinical study appears to have been conducted on an intention to treat basis. Two primary health outcomes were used in the current analysis among all the outcomes assessed in the clinical trial:

- the DeMeester acid score at 3 months, and
- the combined Gastro-Intestinal and Psychological Well-being (GIPW) quality of life score at 12 months.

At baseline, the study groups were comparable in their age, gender, weight, endoscopic findings and clinical measures.

**Effectiveness results**
The estimated clinical outcomes were not reported.

**Clinical conclusions**
The clinical results were used as benefit measures in the cost-effectiveness analysis.

**Measure of benefits used in the economic analysis**
The summary benefit measures were the DeMeester acid score at 3 months (a score of 13.9 or less indicated physiological normality) and the GIPW quality of life score at 12 months. These were derived directly from the effectiveness analysis.

**Direct costs**
The analysis of the costs was undertaken from the perspective of the NHS. Thus, only direct medical costs were considered. The health services included in the economic evaluation were PPIs, GP visits, outpatient care (endoscopy, pH monitoring and manometry, and follow-up visits) and LNF (inpatient stay, staff and operating theatre, overheads and disposables). For most items, the unit costs were presented separately from the quantities of resources used. Resource use was derived mainly from the clinical trial using an intention to treat approach. Other resource use data came from experts' opinions and some published sources. The costs were estimated from the British Medical Formulary, Reference Costs, the Norfolk and Norwich University Hospital Trust, and the Personal Social Services Research Unit. In the long-term analysis of the costs, several assumptions were made in order to assess best and worst scenarios for LNF, where the costs of LNF were extrapolated into future years. Discounting was relevant only in the long-term analysis of costs, and an annual rate of 6% was applied. The price year was 2001.

**Statistical analysis of costs**
The costs were presented as average values with standard deviations and confidence intervals (CIs).

**Indirect Costs**
The indirect costs were not considered.

**Currency**
UK pounds sterling (£).
**Sensitivity analysis**
In the long-term analysis of costs, one-way and multi-way sensitivity analyses were used to analyse the uncertainty around several parameters. Such parameters included the reoperation rate, proportion of patients in the LNF group taking PPI medication, annual rate of relapse requiring endoscopy and pH monitoring in the PPI group, annual percentage change in the price of PPI medication, dose escalation rate after year 1, discount rate, and the hospital unit cost of uncomplicated LNF. The authors set the alternative ranges of values used. CIs surrounding cost-effectiveness estimates were calculated to address the issue of uncertainty. Two different approaches were used, namely, 1,000 bootstrap simulations and the net benefit approach (with the subsequent construction of cost-effectiveness acceptability curves representing the probability that LNF was cost-effective).

**Estimated benefits used in the economic analysis**
The estimated benefits measures were not reported.

**Cost results**
The average cost of LNF in year 1 was 2,687 (+/- 748) (range: 1,977 - 6,882), while the average cost of PPI therapy for one year was 440 (+/-113) (range: 219 - 768). Thus, the cost-difference was 2,247 (95% CI: 2,020 - 2,473).

The long-term analysis of costs showed that LNF broke even towards the end of year 8, with a cost differential between LNF and PPI therapy of 1,476 per patient at year 3 and 801 at year 5.

The long-term costs were affected by the costs of LNF and PPI therapy.

The break-even point was also affected by hospital unit costs. However, it was less sensitive to the PPI ingestion rate after LNF, LNF reoperation rate, PPI relapse rate, future PPI price, PPI dose escalation and the discount rate.

LNF broke even in 6 years in a combined best LNF scenario, and in 13 years in a combined worst LNF scenario.

**Synthesis of costs and benefits**
Incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the two treatments.

The incremental cost per patient returned to physiologically normal acid score at 3 months with LNF over PPI therapy was 5,515 (non-parametric CI: 3,650 - 16,400; parametric CI: 3,655 - 13,400).

The incremental cost per point improvement in GIPW quality of life at 12 months with LNF over PPI therapy was 293 (non-parametric CI: 140 - 7,000; parametric CI: 149 - 5,250).

**Authors' conclusions**
From the perspective of the National Health Service (NHS), the use of laparoscopic Nissen fundoplication (LNF) to treat gastro-oesophageal reflux disease (GORD) may be cost-saving after 8 years in comparison with proton-pump inhibitor (PPI) maintenance therapy.

**CRD COMMENTARY - Selection of comparators**
The rationale for the selection of the comparators was clear and appropriate. LNF and PPI were two available treatment approaches for the treatment of GORD. It was not stated which type of PPI medication was used as the comparator since several medications are contained within the PPI group. In addition, dosages were not reported. You should decide whether they are valid comparators 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. However, limited
information on the design and other characteristics of the primary study were reported since it had been published already. The method of sample selection was reported and it was stated that the study groups were comparable at baseline, which enhances the validity of the comparison. However, details on patient demographics, follow-up and the outcome assessment were not provided, nor was a justification for the sample size. The current analysis used a subgroup of patients enrolled in the primary trial. The results of the effectiveness analysis were not reported.

Validity of estimate of measure of benefit
The summary benefit measures were specific to the disease considered in the study. They would not be comparable with the benefits of other health care interventions. The impact of the two treatment options on quality of life was addressed, but the authors stated that no validated approach was available to translate the GIPW score into the quality-adjusted life-years required to perform a cost-utility analysis.

Validity of estimate of costs
The cost analysis was the main focus of the current study. Extensive information on the sources used to derive the costs, quantities of resources used and unit costs was provided, which enhances the possibility of replicating the analysis in other settings. The costs included were consistent with the perspective adopted in the study. The impact of the indirect costs was not considered, although it would have been helpful as patients in the LNF group took a mean of 17 days off work. The authors noted that the inclusion of the indirect costs would have favoured the PPI strategy in the short-term, whereas the impact in the long-term analysis was unclear. The estimation of the long-term costs relied on several assumptions about the efficacy of the interventions and resource consumption. All of these assumptions were tested in the sensitivity analysis. Similarly, the costs were specific to the study setting but extensive sensitivity analyses were performed to assess the robustness of the cost estimates to variations in several parameters. The price year was reported, which makes reflation exercises in other settings possible.

Other issues
The authors did not compare their findings with those from other studies. They also did not explicitly address the issue of the generalisability of the study results to other settings. However, the extensive sensitivity analyses enhance the external validity of the study to some extent. The authors noted that the analysis did not consider the clinical and economic issues of the training of surgeons in laparoscopic techniques and associated learning-curve effects. It was also pointed out that the majority of the uncertainty related to the effectiveness side of the analysis, given that the clinical trial found a small improvement in quality of life for LNF patients in comparison with PPI patients. However, such an improvement was at the limit of statistical significance, which might suggest that the central economic issue relates to the long-term cost of LNF rather than to its short-term cost-effectiveness. Further, the issue of crossover from PPI therapy to LNF was not addressed.

Implications of the study
The study results suggested that the use of LNF for the long-term treatment of GORD would break even in approximately 7 years.

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