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Cost Effectiveness of Medical versus Surgical Treatment in Patients with Severe or Refractory Gastroesophageal Reflux Disease in The Netherlands

G. VAN DEN BOOM, P. M. M. Y. H. GO, W. HAMEETEMAN, B. DALLEMAGNE
A. J. H. A. AMENT
Dept. of Health Economics, University of Limburg, and Academic Hospital Maastricht, Maastricht, The Netherlands, and Centre Hospitalier, St. Joseph-Esperance, Liège, Belgium


Background: For a significant number of patients with severe or refractory gastroesophageal reflux disease, maintenance treatment with omeprazole and reflux surgery (Nissen fundoplication) are alternative treatment options. In this study maintenance treatment with omeprazole is compared with open and laparoscopic Nissen fundoplication from a health-economic perspective. Methods: Meta-analysis of published articles to assess effectiveness and simple decision-analytic techniques to combine costs and effects are used. Findings and assumptions are submitted to sensitivity analysis. Results: It is estimated that it costs approximately 1880 Dutch guilders to initially heal a patient with severe or refractory esophagitis with 40 mg omeprazole daily. When medical maintenance therapy was compared with surgery, it appeared that medical maintenance therapy with omeprazole (20-40 mg daily) for a prolonged period of time (more than 4 years) is less cost effective than a Nissen procedure. It is estimated that a laparoscopic Nissen will shift this so-called break-even point towards 1.4 years, mainly due to a shorter hospital stay. Conclusions: Although caution is required in drawing conclusions, it appears that replacing treatment with (laparoscopic) Nissen fundoplications in these patients might lead to substantial savings.

Key words: Cost-effectiveness analysis; gastroesophageal reflux disease; laparoscopic surgery; Nissen fundoplication; omeprazole

Guido van den Boom, M.Sc., Dept. of Health Economics, University of Limburg, P.O. Box 616, 6200 MD Maastricht, The Netherlands (fax: +31 433670960)

Gastroesophageal reflux is a common problem in clinical practice, and it is estimated that ±5% of the adult Western population has it on a daily basis. Patients with gastroesophageal reflux disease (GERD) experience symptoms due to pathologic reflux, frequently resulting in complications. Despite the introduction of H₂-receptor antagonists a certain percentage of GERD patients do not respond well to medical treatment. Omeprazole offers a new and highly effective treatment option for these patients and has become standard medical treatment for patients with grade-III or -IV esophagitis (Savary–Miller classification (1)) in The Netherlands. Cessation of treatment, however, results in rapid relapse in almost all patients, necessitating prolonged or maintenance therapy. An alternative treatment option is surgery. The Nissen fundoplication is performed most frequently in The Netherlands. The introduction of a laparoscopic Nissen fundoplication might potentially lead to an increase in popularity, mainly due to a decrease in postoperative morbidity, resulting in a reduction of hospital stay. In this study medical treatment with omeprazole is compared with the open and the laparoscopic Nissen fundoplication, by means of cost-effectiveness analysis. The nature of the respective treatments and, accordingly, their outcome differ in many respects. Medical treatment is aimed at reducing gastric acidity, whereas surgery is aimed at restoring lower esophageal sphincter pressure. Medical therapy is accompanied by possible side effects (2), and surgery by possible complications (3), but both are ultimately aimed at the healing and prevention of esophagitis. The absence of esophagitis is the central comparator, and this study and the results presented are restricted to this comparator.

The objective of this study is threefold: first, to assess the cost effectiveness of treatment with omeprazole during the ‘healing phase’ in patients with severe GERD or patients unresponsive to treatment with H₂ blockers, and secondly, to compare medical maintenance treatment with its surgical alternative (that is, the Nissen fundoplication) in respective patients. Finally, an attempt is made to estimate the cost effectiveness of a laparoscopic Nissen fundoplication. A further attempt is made to put the results into perspective (both medically and economically).

PATIENTS AND METHODS

Patients
In the assessment of the cost effectiveness of omeprazole during the ‘healing phase’ studies were included in which
patients had esophagitis grade I or worse (Savary–Miller). A differentiation was made between refractory esophagitis and esophagitis that was not further specified. Refractory patients were defined as patients who underwent treatment with normal or higher dosages of H2-receptor antagonists for at least 3 months but failed to respond to therapy. The medical results obtained in refractory patients are used in the calculation of cost effectiveness.

Surgery was also performed in patients with complaints for prolonged periods of time who were unresponsive to medical treatment. The severity of esophagitis as expressed in Savary–Miller gradings was not always known. Since long-term results of the Nissen procedure were analyzed, the results were mostly obtained in the pre-omeprazole era.

Estimation of cost effectiveness

Assessment of effectiveness of both medical and surgical treatment was established by means of meta-analysis. This was performed in accordance with ter Riet & Bouter (4). Articles were selected using CD-ROM-derived references (MEDLINE: 1966–March 1993). A correction was made for quality and significance of the published studies by means of a weighing procedure. Since information on all the weighing factors proposed by ter Riet & Bouter were not available, the following simplified weighing scheme is applied:

- Design, in accordance with RCT principle: 3 points
- Analysis performed on basis of ‘intention to treat’ principle: 2 points
- Experimental group size >50: 1 point
- Number of drop-outs <10%: 1 point
- Comparison versus placebo: 1 point
- Minimum weight: 1 point

If weighted results do not differ statistically from the unweighted, unweighted results will be presented.

Effectiveness of medical treatment during the 'healing phase' was defined as: ‘the percentage of patients whose esophagitis was cured (gastroscopically proven grade 0)’. In the comparison of medical maintenance treatment with omeprazole versus the (laparoscopic) Nissen fundoplication, effectiveness was defined as: ‘the ability (of respective treatments) to retain patients in full remission of esophagitis during a certain period of time’, expressed in patient-years.

Costs were estimated using modeling techniques. Only direct medical costs due to treatment were regarded. Costs due to side effects or complications were ignored. Costs for medication were valued using market prices; other cost factors were estimated using (weighted) reimbursement data as proxies of actual costs. Information concerning the laparoscopic procedure was gathered by means of interviews with experts in the field. Both costs and effects are discounted at a 5% rate, in accordance with the Dutch guidelines (5). For cross-study comparison a second approach to discounting is chosen in which costs are discounted at a 5% rate and effects are not discounted (that is, 0%).

The level of the discount rate is varied from 2% to 8% in the final sensitivity analysis.

RESULTS

Cost effectiveness of omeprazole in the healing phase

The analysis included 25 studies (6–31) with a total of 69 results (healing rates). Results of the analysis are presented in Fig. 1 (unweighted results).

Weighing did not result in significant changes. The calculation of cost effectiveness is based on medical therapy with 40 mg omeprazole once daily (20 mg is suboptimal). It is assumed that assessment of healing (gastroscopy) takes place 8 weeks after therapy initiation, which meets clinical practice in The Netherlands. On the basis of the meta-analysis 84% of all patients are cured during the first 8 weeks. Patients who do not respond well to therapy will receive an additional 4 weeks of treatment. After this period an additional gastroscopy will take place. Forty-eight per cent of these patients respond well to this prolonged therapy, resulting in a total healing rate of 91% after 12 weeks. The remaining 9% are considered unresponsive to treatment with omeprazole, although it is reported that additional healing is achievable with higher doses.

The calculation of cost effectiveness of omeprazole treatment (40 mg) in severe or refractory esophagitis is based on:

- Medication costs (on average per patient): Dfl.782.60*
- Costs due to gastroscopic assessment (on average per patient): Dfl.935.75†
- Effectiveness (ability to cure): 91%

It will cost approximately 1880 Dutch guilders (1 US$ = ±Dfl. 1.60) on average to initially heal esophagitis with omeprazole.

Cost effectiveness of omeprazole in the maintenance phase

Once healing with omeprazole has been accomplished, cessation of treatment in patients with severe or refractory esophagitis will result in relapse of esophagitis in more than 80% of all cases within 6 months (6, 8). Maintenance treatment with H2-receptor antagonists is not likely to prevent relapse (31). Temporary cessation of maintenance therapy with omeprazole in patients with refractory esophagitis was accompanied by relapse of esophagitis in all patients (32). This implies that patients with refractory reflux esophagitis require maintenance treatment for prolonged periods of time, perhaps even for the rest of their lives. Studies on the efficacy of long-term treatment with omeprazole reveal its potential to

* Wholesale price per daily dose (40 mg) is Dfl. 11.98 (Oct. 1992) + 6% VAT + Dfl. 11.50 per recipe (pharmacist’s expenses).
† Costs of gastroscopy are calculated as the weighted mean of reimbursements by National Health Insurance (NHI) and private insurers. The weighing corresponds with the number of people insured by the respective insurances.
Cost Effectiveness of Treatment in GERD

Fig. 1. Effectiveness of omeprazole in the ‘healing phase’: dose- and duration-specific. n = experimental group size. *Refractory esophagitis with Barrett's epithelium.

retain patients in full remission of esophagitis. Four studies were found with follow-up periods ranging from 12 to 36 months (23, 33–35). Three of them show little variation: 68% to 73% of patients remained in remission of esophagitis for the entire study period with 20 mg omeprazole once daily. In one study (23) all patients remained in remission, but this result is invalidated by its small sample size (n = 10) and is therefore omitted. Relapses predominantly occurred during the first 6 to 9 months of maintenance treatment. Most relapses, however, responded well to an increase in dose to 40 mg (33, 35).

For use of these results in the calculation of the cost-effectiveness ratio a conservative estimate is chosen, mainly because results are slightly invalidated by small sample sizes, moderately high drop-out rates, and limited follow-up periods. It is assumed that two-thirds of patients remain in remission throughout maintenance treatment of whatever duration with 20 mg. The relapses in the remaining one-third are assumed to occur evenly divided in time (linearity assumption). Eighty per cent of these cases respond well to an increase in dose to 40 mg. These patients receive this dose for the entire maintenance period. Assessment of success (by means of gastroscopy) takes place 6 months after therapy initiation and at 12 months in patients who relapsed during the first 6 months. Patients unresponsive to 40 mg are considered resistant to maintenance treatment with omeprazole. Calculations are based on a cohort of 100 patients entering the maintenance phase after complete healing of esophagitis. The total number of months in remission during the first 12 months adds up to 1060 months (effectiveness = 88.3%). In the years to follow, patients who respond well to maintenance treatment continue to receive their efficacious dose and are monitored once a year by means of gastroscopy. Since the effects and costs are considered to be constant from then on, the cost effectiveness is constant for every future year.

First 6 months
- Medication costs: Dfl. 117,859
- Costs due to gastroscopic assessment: Dfl. 43,254

Second 6 months
- Medication costs: Dfl. 154,925
- Costs due to gastroscopic assessment: Dfl. 14,418
- Effectiveness: ability to retain patients in remission (patient-years): 88.3%

Cost effectiveness first year: Dfl. 3,741
Consecutive years (93.33 patients)
- Medication costs: Dfl. 278,103
- Costs due to gastroscopic assessment: Dfl. 40,370
- Effectiveness (patient-years): 93.33
- Cost effectiveness consecutive years: Dfl. 3,412

The cost-effectiveness ratio of consecutive years is lower than the first because during the first year all 100 patients receive treatment and more gastroscopies are performed (higher costs) and because not all patients receive an efficacious dose during the first year (lower effectiveness). Given these assumptions and results, one is now able to project the cost effectiveness of maintenance treatment over time (Table I).
The data show that it is costly to keep a patient in remission; for example, it will cost approximately 27,800 Dutch guilders to keep a patient in remission for a period of 10 years, given a statistical chance of 93.33% that medical therapy will be successful in this patient.

Cost effectiveness of anti-reflux surgery

To assess the effectiveness of the Nissen procedure, 23 studies are reviewed (36–58). Unfortunately, not all studies present gastroscopic findings. The results of this review are summarized in Table II.

The studies indicate that the Nissen fundoplication is highly effective in controlling gastroesophageal reflux and its symptoms. Good to excellent results range from 67% up to 92%. A more standardized outcome measure, the Visick grading (grade I or II), ranges from 83.3% up to 100%. The percentage of patients who underwent a Nissen procedure and who remained in remission during the entire period of the respective study ranges from 75% to 100%. There are minor indications that the efficacy of the procedure decreases with time; however, results of studies with a long follow-up period (range, 1–20 years) are comparable to those with a shorter time span. On the basis of these results, we assume that the effectiveness of the Nissen fundoplication is constant in time. The percentage of patients in remission of esophagitis is calculated on the basis of individual cases. This resulted in an effectiveness of 90.5%. The last column in Table II gives an impression of the ‘healing capacity’ of the operation: if esophagitis was present preoperatively, the Nissen fundoplication resulted in healing of the esophagitis and keeping the patient in remission during the entire follow-up period in about 85% of all cases. This figure might be regarded as a lower estimate and will be used in the sensitivity analysis.

The following costs are calculated on the basis of reimbursements to university hospitals:

<table>
<thead>
<tr>
<th>Diagnostic actions</th>
<th>Personnel cost</th>
<th>Hospital’s residence</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dfl. 865.00</td>
<td>Dfl. 955.25</td>
<td>Dfl. 9307.65</td>
<td>90.05%</td>
</tr>
<tr>
<td>2 × gastroscopy (pre- and post-operatively)†</td>
<td>Surgeon</td>
<td>10 days’ hospitalization§</td>
<td></td>
</tr>
<tr>
<td>(24-h pH-metry study) (manometry) †</td>
<td>Assistant</td>
<td>2 outpatient control visits¶</td>
<td></td>
</tr>
<tr>
<td>Hospital’s residence</td>
<td>Anesthesiologist ‡</td>
<td>Total costs per operation</td>
<td></td>
</tr>
</tbody>
</table>

Cost effectiveness of a laparoscopic Nissen fundoplication

The first results of a large series of laparoscopic fundoplications (59) are promising. A total of 197 patients were operated on. At 3 months 67 patients underwent

* For calculation, see cost-effectiveness omeprazole.
† 24-h pH-metry and manometry were not reimbursed by insurers in The Netherlands at the time of this study.
‡ Calculated as the weighed mean of reimbursements by NHI (0.62 * (Dfl. 420 (surgeon) + Dfl. 175 (assistant) + Dfl. 175 (anesthesiologist))) and private health insurers (0.38 * (Dfl. 932 (surgeon) + Dfl. 319 (anesthesiologist))).
§ Calculated as the weighed reimbursement for a treatment day, the use of an operating room included; 10 days is the average length of admission in The Netherlands.
¶ Based on the weighed reimbursement of a reference card (NHI: Dfl. 40.50) and two consultations for the privately insured (first visit, Dfl. 51.00; second visit, Dfl. 32.50).

Table I. Costs and effects of maintenance treatment with omeprazole (on the basis of a cohort of 100 patients) and the impact of discounting

<table>
<thead>
<tr>
<th>Years</th>
<th>Present value of cost*</th>
<th>Cumulative effects†</th>
<th>Cumulative effects‡</th>
<th>C/E ratio§</th>
<th>C/E ratio¶</th>
<th>Costs per patient*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>330,456</td>
<td>88.33</td>
<td>88.33</td>
<td>3741</td>
<td>3741</td>
<td>3741</td>
</tr>
<tr>
<td>2</td>
<td>648,931</td>
<td>177.22</td>
<td>181.66</td>
<td>3576</td>
<td>3489</td>
<td>6791</td>
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<tr>
<td>3</td>
<td>967,405</td>
<td>261.87</td>
<td>274.99</td>
<td>3523</td>
<td>3355</td>
<td>9886</td>
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<tr>
<td>4</td>
<td>1,285,879</td>
<td>342.49</td>
<td>368.32</td>
<td>3497</td>
<td>3252</td>
<td>12,833</td>
</tr>
<tr>
<td>5</td>
<td>1,604,353</td>
<td>419.27</td>
<td>461.65</td>
<td>3482</td>
<td>3162</td>
<td>15,641</td>
</tr>
<tr>
<td>10</td>
<td>3,196,724</td>
<td>751.70</td>
<td>928.30</td>
<td>3451</td>
<td>2794</td>
<td>27,795</td>
</tr>
<tr>
<td>15</td>
<td>4,789,094</td>
<td>1012.17</td>
<td>1394.95</td>
<td>3441</td>
<td>2497</td>
<td>37,318</td>
</tr>
<tr>
<td>20</td>
<td>6,381,465</td>
<td>1216.25</td>
<td>1861.60</td>
<td>3436</td>
<td>2245</td>
<td>44,780</td>
</tr>
<tr>
<td>25</td>
<td>7,973,835</td>
<td>1376.16</td>
<td>2328.25</td>
<td>3433</td>
<td>2029</td>
<td>50,026</td>
</tr>
<tr>
<td>30</td>
<td>9,566,206</td>
<td>1501.45</td>
<td>2794.90</td>
<td>3432</td>
<td>1844</td>
<td>55,207</td>
</tr>
</tbody>
</table>

* Cumulative total costs (in Dutch guilders) in respective year, discounted at a 5% rate.
† Cumulative effects, expressed as (patient) years in remission of esophagitis, discounted at a 5% rate.
‡ Cumulative effects, expressed as (patient) years in remission of esophagitis, not discounted.
§ Cost effectiveness: cumulative costs (5%) divided by cumulative effects (5%).
¶ Cost effectiveness: cumulative costs (5%) divided by cumulative effects (0%).
* Total costs (5%) to keep one patient in remission of esophagitis during a particular number of years: a patient has a statistical chance of 93% that therapy will be successful.
Table II. The effectiveness of the Nissen fundoplication: results of a meta-analysis

<table>
<thead>
<tr>
<th>Control of GER*</th>
<th>Visick grading†</th>
<th>Remaining in remission‡</th>
<th>‘Healing capacity’§</th>
</tr>
</thead>
<tbody>
<tr>
<td>67%–92%</td>
<td>83%–100%</td>
<td>75%–100%</td>
<td>73%–100%</td>
</tr>
<tr>
<td>n = 1019</td>
<td>n = 159</td>
<td>n = 660</td>
<td>n = 221</td>
</tr>
<tr>
<td>Refs. 35,37,39–43, 46,47,52–54</td>
<td>Refs. 36,43,49</td>
<td>Refs. 23,33,35–39, 41,44–46,48–51</td>
<td>Refs. 23,34,36,48, 50,51</td>
</tr>
</tbody>
</table>

* Control of gastroesophageal reflux is assessed in various ways and measured with various instruments: good to excellent results range from 67% to 92%.
† Grades I and II.
‡ Central effect factor: percentage of patients remaining in full remission of esophagitis during the entire follow-up period of the respective studies.
§ Percentage of patients who had esophagitis (grade I or worse) pre-operatively and who remained in full remission post-operatively.
|| Total number of subjects participating in the respective studies.

Analysis of data showed that utilization of resources and duration of the operation and admission developed along a 'learning curve'. The most recent data indicate that the costs of the operation are very much similar to those of the 'open' variant. Hospital stay, however, is significantly reduced to 2–3 days, including pre-operative stay. On the basis of effectiveness reported and the reduction of costs due to hospital admission (from 10 to 3 days), the cost effectiveness of the laparoscopic Nissen fundoplication is Dfl. 4748 (4676/0.985).

Comparison of medical maintenance therapy versus surgery

Since costs and effects are expressed in the same units, the cost effectiveness of the respective therapies can now be compared. In Fig. 2 the cost effectiveness in time of the three therapeutic options is illustrated.

The break-even point in time is the number of years at which the cost effectiveness of the alternatives are equal. If medical maintenance treatment with omeprazole is to last longer than approximately 4 years, it is more cost-effective to operate (open Nissen). If medical treatment is compared with the laparoscopic Nissen fundoplication, this break-even point is approximately 1.4 years; this shift is mainly due to a reduction in hospital stay. From an economic point of view, if one knows in advance that a patient requires medical therapy for, say, 10 years, a Nissen fundoplication is the more cost-effective treatment for this patient. Substantial savings will

![Fig. 2. Comparison of medical treatment with omeprazole versus the (laparoscopic) Nissen fundoplication, on the basis of cost effectiveness.](image-url)
Table III. Cost effectiveness of the Nissen fundoplication and the impact of discounting

<table>
<thead>
<tr>
<th>Years</th>
<th>Cumulative effects*</th>
<th>Cumulative effects†</th>
<th>C/E ratio‡</th>
<th>C/E ratio§</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>90.5</td>
<td>90.5</td>
<td>12,356</td>
<td>12,356</td>
</tr>
<tr>
<td>2</td>
<td>176.7</td>
<td>181.7</td>
<td>6329</td>
<td>6156</td>
</tr>
<tr>
<td>3</td>
<td>258.8</td>
<td>275.0</td>
<td>4321</td>
<td>4066</td>
</tr>
<tr>
<td>4</td>
<td>337.0</td>
<td>368.3</td>
<td>3319</td>
<td>3036</td>
</tr>
<tr>
<td>5</td>
<td>411.4</td>
<td>461.7</td>
<td>2718</td>
<td>2422</td>
</tr>
<tr>
<td>10</td>
<td>733.8</td>
<td>928.3</td>
<td>1524</td>
<td>1205</td>
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<tr>
<td>15</td>
<td>986.3</td>
<td>1395.0</td>
<td>1134</td>
<td>802</td>
</tr>
<tr>
<td>20</td>
<td>1184.2</td>
<td>1861.6</td>
<td>944</td>
<td>601</td>
</tr>
<tr>
<td>25</td>
<td>1339.3</td>
<td>2328.3</td>
<td>835</td>
<td>480</td>
</tr>
<tr>
<td>30</td>
<td>1460.8</td>
<td>2794.9</td>
<td>766</td>
<td>400</td>
</tr>
</tbody>
</table>

* Cumulative effects, discounted at a 5% rate.
† Cumulative effects, undiscounted.
‡ Cost effectiveness, based on discounted effects (5%).
§ Cost effectiveness, based on undiscounted effects.

SSS

Sensitivity analysis

Since calculations are based on assumptions and modeling, uncertainty should be resolved by means of sensitivity analysis (Fig. 3). The influence of changing a single assumption or estimation on the final result (that is, the break-even point) is displayed here.

It is notable that fairly sensitive assumptions such as duration of admission of the open Nissen procedure and the price of a daily dose of omeprazole are well documented and thus certain. On the other hand, the estimations that were less certain are fairly insensitive. For example, a 25% change in costs of gastroscopy has no significant effect on the break-even point. It has recently been claimed that endoscopy should only be performed once every 5 years; this would not radically change our results and conclusions. The insensitivity of the discount factor can be explained by the fact that the break-even points are reached in fairly short time periods: the impact of discounting becomes increasingly evident when longer time spans are involved.

DISCUSSION

Many articles have been published on the efficacy of anti-reflux treatment, but only a few are focused on cost effectiveness. Bate (60) compared two medical alternatives: treatment of reflux esophagitis with either omeprazole or H2-antagonists (ranitidine). He concluded that omeprazole is the more cost-effective option: the higher costs of omeprazole are more than compensated for by its higher effectiveness with regard of healing esophagitis and relieving symptoms. More recently, Barradell & McTavish assessed the cost effectiveness of omeprazole in the treatment of reflux esophagitis and duodenal ulcer (61) and concluded that omeprazole is a cost-effective treatment option both in healing esophagitis and in preventing relapses. The results of these studies cannot be compared with our findings since

![Fig. 3. Results of sensitivity analysis: the influence of changing single variables on the break-even point.](image-url)
Costs and drug regimens are not comparable; however, with regard to assessing drug effectiveness, findings and assumptions do agree well with this study. Most recently, health-economic aspects in the management of acid-related diseases were the topic of discussion during a symposium held in Paris (62). The importance of economic evaluation and its role in decision-making and the need for standardization were emphasized. The presented studies (duodenal ulcer and persistent GERD) confirm the above findings, but these studies were not set up to compare medical treatment with anti-reflux surgery. Studies concerning the cost effectiveness of anti-reflux surgery were not found.

Cost-effectiveness studies are often based on modeling and estimating instead of measuring actual costs, alongside clinical trials. There are two major shortcomings in assessing cost effectiveness retrospectively by means of modeling. First, data on many cost factors are lacking. Data on some core factors, such as in this case the amount of medication prescribed or the average duration of admission, are available or can be estimated with reasonable accuracy. But data on other relevant factors such as the costs due to treatment failures, side effects, or absenteeism from work are often unavailable. Secondly, factors indicating effectiveness are not uniform. Individual studies are seldom set up to be used for comparison across studies. In this particular case the outcome of medical treatment is, as mentioned, different from the outcome of surgery. A single measure of effectiveness is defined (retaining patients in remission), but that does not make results truly comparable; again it is stated that the results are restricted to this single measure.

Despite the above-mentioned disadvantages these comparisons do have informational value. For example, the fact that patients may have postoperative morbidity or even mortality due to surgery is not accounted for in this study. Suppose, for the purpose of simplicity, that the only negative outcome of surgery would be that 2 of 1000 patients die as a result of the Nissen operation. The outcome of studies like this makes it possible to weigh these negative effects against the possible savings: substituting surgery for omeprazole in 1000 patients will generate savings in excess of 20 million guilders in 10 years. The question remains: is this worth giving up two lives for? This may sound very harsh and unethical, but (allocation) decisions at local and national levels implicitly value such negative effects. Economic evaluations only elicit these valuations and make them explicit, without being judgemental.

There are some significant advantages of assessing cost effectiveness in a manner such as presented in this study. For one, it may serve as a means to estimate the cost-effective potential of a new therapy, even in a very early stage in the product life cycle of a therapy/intervention. In this instance a laparoscopically performed Nissen operation is tested in an early stage of development. Although a broad range of uncertainty is introduced in the sensitivity analysis, our findings indicate that surgery and especially laparoscopic surgery is a cost-effective alternative for medical treatment and that substantial savings might occur if the present medical therapy is replaced. These findings are a strong advocate for cost-effectiveness studies of medical treatment versus laparoscopic surgery in clinical trials.

Modeling with the aid of a spreadsheet may be of use in determining threshold levels for either costs or effects in the comparison of therapies. New cost-effectiveness ratios due to fluctuation in prices or due to new data on effectiveness or protocols can easily be computed.

CONCLUSIONS AND RECOMMENDATIONS

Although caution is required in drawing substantial conclusions, it appears that surgery (Nissen fundoplication) is a cost-effective treatment option in patients with severe or refractory GERD as compared with medical treatment (omeprazole) if this medical treatment is to last longer than approximately 4 years. If effectiveness is solely expressed in terms of keeping patients in full remission of their esophagitis, changing to surgery will lead to substantial savings from this point in time onwards. A laparoscopic Nissen procedure might be even more cost effective: due to a substantial reduction in hospital stay, a laparoscopic Nissen fundoplication is more cost effective than medical treatment if this treatment is to last longer than approximately 17 months. Besides potential clinical superiority owing to a decrease in postoperative morbidity, laparoscopic surgery is likely to be superior from a health-economic perspective. A well-designed clinical trial in which medical maintenance treatment is compared with the laparoscopic Nissen fundoplication should be set up. It should incorporate an economic evaluation. All relevant cost factors, including costs due to side effects and morbidity and so-called indirect costs due to production losses, should be measured prospectively and valued properly (cost prices). Quality of life and patient preferences should be assessed by means of generic (utilities) and disease-specific instruments.

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