OBJECTIVE: To evaluate the cost-effectiveness of the Stretta procedure and that of competing strategies in the long-term management of gastroesophageal reflux disease.

METHODS: A Markov model was designed to estimate costs and health outcomes in Canadian patients with gastroesophageal reflux disease over five years, from a Ministry of Health perspective. Strategies included the use of daily proton pump inhibitors (PPIs), laparoscopic Nissen fundoplication (LNF) and the Stretta procedure. Probabilities and utilities were derived from the literature. Costs are expressed in 2006 Canadian dollars. Units of effectiveness were symptom-free months (SFMs) and quality-adjusted life years (QALYS), using a five-year time horizon.

RESULTS: In the analysis that used SFMs, the strategy using PPIs exhibited the lowest costs ($40 per SFM) and the greatest number of SFMs, thus dominating both the LNF and Stretta systems. But the cost-effectiveness analysis using QALYS as the measure of effectiveness showed that PPIs presented the lowest cost-effectiveness ratio, while both the LNF and Stretta strategies were associated with very high incremental costs (approximately $353,000 and $393,000, respectively) to achieve an additional QALY. However, the PPI strategy did not dominate the two other strategies, which were associated with better effectiveness.

CONCLUSIONS: If SFMs are used as the measure of effectiveness, PPIs dominate the Stretta and LNF strategies. However, if QALYS are used, the PPIs still present the lowest cost and LNF gives the best effectiveness. Regardless of the units of effectiveness or utility used in the present cost analysis, an approach of prescribing PPIs appears to be the preferred strategy.

Key Words: GERD; Proton pump inhibitors; Stretta procedure
Gastroesophageal reflux disease (GERD) is one of the most prevalent medical disorders in the United States, affecting 19 million people chronically (1), and generating an annual cost of $40 billion in health care expenditures (2).

In patients with uncomplicated reflux symptoms, the mainstays of treatment are proton pump inhibitors (PPIs) and antireflux surgery (3). Endoscopic therapies, such as the Stretta procedure, may potentially reduce or eliminate long-term drug use without the expense or complications of surgery (4).

The Stretta procedure (Curon Medical, USA) is a minimally invasive, endoscopic treatment of GERD in which radiofrequency energy is applied to the gastroesophageal junction (5). In principle, controlled injury causes scarring and stricturing of the lower esophageal sphincter, limiting free reflux of gastric contents (5). Damage to the gastroesophageal junction may also reduce nociception and the vagal impulses that drive transient lower esophageal sphincter relaxations (5).

A previous controlled study (6) of the Stretta procedure showed significant reductions in mean heartburn scores and quality-of-life measures after six months relative to a sham arm. Further, prospective studies of the Stretta procedure suggest that the response may persist for up to three years (7-10).

To date, no prospective trials comparing medical, surgical and endoscopic treatments of GERD have been published. Thus, third-party payers examining the relative costs and benefits of GERD therapies must draw their assessments from alternate sources. A decision model examining the costs and health outcomes of GERD treatment will therefore provide valuable insight into the cost-effectiveness of the different competing strategies.

METHODS

Model design
A Markov model was designed to simulate the management of patients with uncomplicated GERD. A Markov model is a mathematical construct containing multiple decision nodes and health states that estimate outcomes based on user-defined, repeated risks over time (11). The model was developed using 2005 TreeAge Pro Suite software (TreeAge Software Inc, USA).

Model cohort
The study population included adult patients with GERD, documented by an abnormal 24 h pH study, who were at least partially responsive to PPIs. The following criteria were met before enrolment: small (smaller than 2 cm) hiatal hernia, absence of significant esophagitis, stricture, Barrett’s esophagus or malignancy, and normal esophageal manometry. All patients were symptomatically stable and generally medically fit for endoscopic or surgical antireflux treatments.

Model structure
Three strategies were compared: medical therapy with once-daily PPI therapy, surgical therapy with laparoscopic Nissen fundoplication (LNF) and endoscopic therapy with the Stretta procedure (Figure 1). The model’s time horizon was five years, with a cycle length of six months to best reflect available evidence from fully published, controlled trials.

Medical arm (PPI): Patients in this arm received a once-daily PPI (omeprazole 20 mg tablets). Based on previous trial experiences, patients were presumed to be compliant with and tolerant of their medications. In the base cases, patients were assumed to be symptom-free on medications; however, symptom relapse requiring twice-daily PPI dosing was incorporated into the model as part of a sensitivity analysis (see below).

Surgical arm (LNF): Patients in this arm underwent LNF. Patients who were symptomatic immediately after surgery (‘LNF failures’) or who developed symptom recurrence during follow-up were managed with once-daily PPI use. The model captured in-hospital and early postoperative complications that required intervention (namely esophageal stricture). Non-GERD complications, such as the gas-bloat syndrome, were not included. Complication rates did not have an impact on treatment response. Neither surgical revisions nor mortality were included.

Endoscopic arm (Stretta): Patients in this arm underwent the Stretta procedure as per published protocols (6). Health states were derived from the prospective cohort and controlled trial experience. Postprocedural complications that required intervention (namely bleeding esophageal ulcer) were included in the model. Patients not responding to the Stretta procedure (‘Stretta failures’) or subsequently developing symptoms during follow-up were treated with once-daily PPIs. As with the LNF arm, treatment response rates were not influenced by previous complications, and mortality was not included in the model.

Transition probabilities
All model parameters were derived from the medical literature, and fixed-time probabilities (such as annual rates) were converted to six-month transition estimates using established methods (12) (Table 1). A MEDLINE search of studies published before November 2004 was conducted using the terms “gastroesophageal reflux”, “fundoplication” and the keyword “Stretta”. Also, published reviews and key conference abstracts were hand-reviewed for relevant material.

Health utility estimates
Symptom-free months (SFM) was one of two units of effectiveness adopted. The values are directly based on the probabilities of success and relapse shown in Table 1. In addition, quality-adjusted life years (QALYs) experienced in a health state were also used as the unit of effectiveness (utility) for a separate analysis. QALYs were estimated by multiplying the time spent in a specific health state by its associated utility.
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**TABLE 1**

Base case estimates and ranges for transition probabilities and utility weights used in the model

| Parameter                        | Transition probability, % | Base case | Range          | References |
|----------------------------------|---------------------------|----------|----------------|------------|
| Stricture rate post-LNF          |                           | 4.1      | 0.3 to 0.6     | 31,32      |
| Initial LNF success rate         |                           | 95.0     | 93 to 97       | 28,33-36   |
| (symptom-free within first six months) |                       |          |                |            |
| GERD relapse after successful LNF (six-month rate) |                       | 6.5      | 0 to 13        | 37-39      |
| GERD relapse rate on daily PPI   |                           | 0.0      | 0 to 0.1       | 40         |
| Bleeding esophageal ulcer post-Stretta procedure |                       | 3.0      | 1 to 5         | 6          |
| Initial Stretta success rate     |                           | 61.0     | 50 to 100      | 6,9,10,36  |
| (symptom-free within first six months) |                       |          |                |            |
| GERD relapse after successful Stretta procedure (six-month rate) |                       | 6.5      | 0 to 13        | *          |

| Utility weight                   | Parameter                  | Base case | Range          | References |
|----------------------------------|---------------------------|----------|----------------|------------|
| Symptomatic GERD                 |                           | 0.94     | 0.89 to 0.98   | 13,41,42   |
| GERD-free                        |                           | 1.00     | 0.95 to 1.00   | †          |
| Daily medication consumption     |                           | 0.99     | 0.98 to 1.00   | 43         |
| Stretta procedure – two weeks    |                           | 0.75     | 0.50 to 1.00   | †          |
| LNF procedure – two weeks        |                           | 0.50     | 0.25 to 0.75   | 44         |
| Dysphagia – two weeks            |                           | 0.62     | 0.59 to 0.67   | 45         |
| Bleeding esophageal ulcer        |                           | 0.62     | 0.59 to 0.67   | †          |

*The authors assumed that the probability was the same as laparoscopic Nissen fundoplication (LNF). †Assumption by the authors; ‡The authors assumed that the probability was the same as dysphagia. GERD Gastroesophageal reflux disease; PPI Proton pump inhibitor

Final health outcomes included SFMs and QALYs, with the model rolled back successively for each measure of effectiveness. Strategies were ranked in descending order by total costs, and comparisons were made with the next most costly, nondominated treatment alternatives (dominated strategies are less effective and more costly). Incremental cost-effectiveness ratios were calculated for all nondominated strategies.

**TABLE 2**

Base case estimates and ranges for costs and length of stay used in the model

| Parameter                        | Cost, $ | Base case | Range          | Reference |
|----------------------------------|---------|----------|----------------|-----------|
| Omeprazole 20 mg tablet          |         | 1.25     | 1 to 6         | 17        |
| Hospitalization for LNF          |         | 5,761.00 | 4,859 to 10,624 | 40        |
| Surgical fee for LNF             |         | 550.60   | 275 to 1,102   | 18        |
| Anesthesia fee                   |         | 225.47   | 112 to 451     | 18        |
| Surgical consult fee             |         | 81.60    | 40 to 164      | 18        |
| Outpatient surgical follow-up fee|         | 29.20    | 14 to 59       | 18        |
| Inpatient surgical follow-up fee |         | 29.20    | 14 to 59       | 18        |
| Esophageal dilation fee           |         | 30.65    | 15 to 62       | 18        |
| Hospital cost for endoscopy      |         | 185.00   | 92 to 370      | 18        |
| Endoscopy fee                    |         | 102.75   | 51 to 206      | 18        |
| Stretta catheter cost            |         | 1,398.00 | 699 to 2,796   | 21        |
| Stretta guidewire cost           |         | 67.00    | 33 to 134      | 21        |
| Annual equivalent expenditure    |         | 7,232.00 | 3,616 to 10,848| 21        |
| Stretta procedure*               |         | 146.60   | 73 to 294      | 18        |
| Outpatient medical follow-up fee |         | 29.20    | 14 to 59       | 18        |
| Physician fee for UGIB           |         | 171.40   | 85 to 343      | 18        |
| Hospitalization for UGIB         |         | 4,124.00 | 2,150 to 6,661 | 19        |
| Inpatient medical follow-up fee  |         | 29.20    | 14 to 59       | 18        |
| Weekly frequency of the use of the model, n | | 5 | 2 to 10 | † |
| Yearly frequency of the use of the model, n | | 50 | 45 to 52 | † |
| Length of stay for UGIB, days    |         | 4.6      | 1 to 10        | 46        |
| Length of stay for LNF, days     |         | 4.8      | 3 to 10        | 19        |

All costs are expressed in 2006 Canadian dollars. *Based on an acquisition cost of $36,002 (ie, a value of $28.20 per use); †Assumption based on the information given by the manufacturer and based on the use at the Montreal General Hospital (Montreal, Quebec). LNF Laparoscopic Nissen fundoplication; UGIB Upper gastrointestinal bleeding

Cost data

**General considerations:** In Canada, health care (including physician remuneration) is publicly funded and is administered locally by provincial ministries. Subsidization of prescription drugs varies by province, and is subject to inclusion in local formularies. The perspective of a provincial Ministry of Health (third-party payer) was adopted for direct medical costs (drug, physician and hospital costs) (Table 2). All costs are expressed in 2006 Canadian dollars and are discounted by 3% over the five-year study period, as per established guidelines (15,16).

**Drug costs:** The generic price of omeprazole 20 mg tablets, derived from a national database (17), was used. The price does not include the pharmacist’s professional fees. Boundaries for price ranges used in the sensitivity analysis are presented in Table 2.

**Physician remuneration:** In Canada, physicians bill the provincial Ministry of Health on behalf of patients for services provided. Consultation and procedural fees used in the model were derived from the Ontario Ministry of Health and Long-Term Care Schedule of Benefits (18). Current fee weight. Symptom-free health had a utility weight of 1.0, with all other states assigned a disutility of varying degrees. Utility weights in the present model were derived from a variety of published sources, including those derived from expert consensus and from validated statistical methods (Table 1). The principal utility value for GERD was adapted from a Canadian study (13). The transient disutility for undergoing the Stretta procedure was assumed to be similar to esophageal dilation by consensus (Dan Comay, Alan N Barkun, Serge Mayrand). QALYs were discounted by 3% over the five-year study period, as per established guidelines (14).

**Cost-effectiveness determination**

For each intervention, the clinical end points examined were time without GERD symptoms and reduction in PPI usage. For each intervention, the clinical end points examined were time without GERD symptoms and reduction in PPI usage. Final health outcomes included SFMs and QALYs, with the model rolled back successively for each measure of effectiveness. Strategies were ranked in descending order by total costs, and comparisons were made with the next most costly, nondominated treatment alternatives (dominated strategies are less effective and more costly). Incremental cost-effectiveness ratios were calculated for all nondominated strategies.

In 2006 Canadian dollars and are discounted by 3% over the five-year study period, as per established guidelines (15,16).
schedules do not reimburse directly for the Stretta procedure. However, in anticipation of future inclusion, a fee equal to esophagoscopy/gastroscopy for active bleeding with removal of a foreign body was used. All ranges of sensitivity analyses for physician fees were calculated by subtracting or adding one-half of the point estimate value (Table 2).

**Hospital-related costs**: Health care resource profiles were constructed for each health state, and costs per resource unit were adapted from various sources (see below). Hospital costs (excluding endoscopy) were extracted from the Canadian Institute for Health Information (CIHI) database (19). The CIHI is a national, not-for-profit organization that maintains a comprehensive health information system, which includes patient and hospital data from a discharge abstract database. CIHI data do not include physician fees. Discharges from acute care hospitals are assigned both a case-mix group identifier (similar to American diagnosis-related groups) and a complexity level based on the health status of the patient. The low and high bounds for the range of sensitivity analysis were based on lower and higher complexity levels for the diagnosis in the CIHI database (19). Costs for gastrointestinal endoscopy were previously reported from an activity-based costing study conducted in a major academic centre in Quebec (20). Boundaries for sensitivity analysis are presented in Table 2.

**Stretta costs**: Total costs for the Stretta procedure were divided among three costing units: endoscopy costs, disposable equipment costs and the per-use costs of the light-emitting Stretta module (21). The purchase price for all disposable instruments (Stretta catheter and guidewire) were drawn from the literature (21). All United States costs were converted into Canadian dollars. The acquisition cost of the Stretta module was updated using the consumer price index (similar to American diagnosis-related groups) and a complexity level based on the health status of the patient. The low and high bounds for the range of sensitivity analysis were based on lower and higher complexity levels for the diagnosis in the CIHI database (19). Costs for gastrointestinal endoscopy were previously reported from an activity-based costing study conducted in a major academic centre in Quebec (20). Boundaries for sensitivity analysis are presented in Table 2.

**Sensitivity analysis**

**Deterministic analysis**: To test the effects of variability in the choice of model parameters, one-way sensitivity analyses were performed using a range of values obtained from the literature, or were determined a priori by consensus (Dan Comay, Alan N Barkun, Serge Mayrand) when base case probabilities were less established (Tables 1 and 2). Sensitivity analysis specifically targeted the probability and cost assumptions that altered cost-effectiveness results by at least 20% (22).

**Probabilistic analysis**: Probabilistic analyses were also conducted to further assess the impact of uncertainty in model estimates by adapting reference ranges to beta and normal distributions for cost inputs and transition probabilities (23). Using Monte Carlo stochastic methods, values were sampled at random per distribution over 10,000 unique model simulations (24).

**Cost-effectiveness acceptability curves**: Cost-effectiveness acceptability curves were constructed to better interpret cost effectiveness (25). Derived from Monte Carlo simulations, cost-effectiveness acceptability curves represent the proportion of incremental cost and incremental effect points where the intervention is cost-effective over varying willingness-to-pay (WTP) values. WTP thresholds are the maximum ceiling costs per unit of benefit below which a payer deems an intervention to be cost-effective (26).

### RESULTS

#### Base case analysis

Administering PPI therapy was the cheapest strategy among the three tested in the present model, and was the dominant strategy according to the analysis, which used SFM as an effectiveness measure. Table 3 shows that PPI treatment was the most effective strategy, with a mean cost-effectiveness ratio of approximately $40 per SFM. The other two strategies were dominated by the PPI treatment, because they were less effective and more expensive.

For the analysis in which effectiveness was measured in QALYs (Table 4), the PPI strategy presented the lowest value of QALYs (0.013 less than the highest value obtained by the LNF strategy). However, the PPI arm still had the lowest cost-effectiveness ratio ($316.45 per QALY). The incremental cost-effectiveness ratios of the other two strategies were both above $350,000 per additional QALY.

**Sensitivity analysis**

The results of the present study were only sensitive to the price of omeprazole (20 mg tablet) when it increased to $2.20. Indeed, the sensitivity analysis showed that, with regard to the SFM analysis, when the price of omeprazole rose over $2.40, the Stretta strategy was associated with the lowest cost-effectiveness ratio (Figure 2), and the LNF strategy was still dominated.

With regard to the QALYs analysis, the Stretta strategy also became the preferred option according to the cost-effectiveness ratios when the price of omeprazole increased to more than $2.20 (Figure 3).
Probabilistic analyses

The Monte Carlo analysis was performed, generating 10,000 simulations. The values were almost unchanged across the set of simulations based on the distribution of the probabilistic variables. Mean and median values for the cost and effectiveness measures obtained by the 10,000 simulations were the same as the mean values presented in the results of the present study (Tables 3 and 4), confirming their stability robustness.

The results of the probabilistic analysis for the SFM and QALY units of effectiveness are displayed graphically as acceptability curves in Figures 2 and 3, respectively.

Whatever the amount of WTP, the PPI strategy was most likely to be cost-effective when SFM was used as a unit of effectiveness. The acceptability curves for the QALY analysis (Figure 4) show that under a WTP of $350,000, the PPI strategy is also most likely to be cost effective. For a WTP between approximately $350,000 and $400,000, the Stretta option would most likely be preferred. Above $400,000, it is the LNF strategy that displays the highest probability of being cost effective.

**DISCUSSION**

As with all cost-effectiveness analyses, limitations based on model assumptions reflect unknowns or inconsistencies in the literature, and deserve further discussion. First, for patients on daily PPI therapy, a step down to less costly or in-demand treatment strategies were not studied. Although selected patients with GERD may tolerate these strategies, we chose to examine a population having sufficient burden of disease to require daily PPI medication. Indeed, it is unlikely that endoscopic or surgical options would be considered for patients with symptoms controlled by more infrequent or less potent pharmacotherapy. Second, postfundoplication symptoms, such as diarrhea and gas-bloat syndrome, were not modelled, because these complications typically resolve within six months with lifestyle and dietary changes (27). We acknowledge that, for some patients, these complications may be more bothersome than the inciting GERD. If anything, this approach favours the calculated effectiveness and utilities of the LNF and Stretta options in the model. Third, postoperative mortality was not considered in the model, based on a recent meta-analysis of randomized, controlled trials (28). These studies, however, amalgamated results from large-volume, academic centres and may not reflect rates in smaller community settings. Therefore, caution should be used before generalizing these assumptions to local centres. Cumulative experience to date has shown that the Stretta procedure is reasonably safe, with
Cost-effectiveness analysis of the Stretta procedure

The potential for a decrease in PPI costs was identified during study conception and was addressed by sensitivity analysis. Our base case drug price for generic omeprazole ($1.25 per 20 mg tablet) was derived from a national registry.

We chose a reasonable time horizon of five years to study the cost-effectiveness of the Stretta procedure, despite the lack of long-term data on the durability of the Stretta procedure. Published experience to date is limited to three years, but these data do suggest a sustained clinical effect (7). Additional clinical trial-derived and generalizable data are now needed to better determine these important clinical parameters, thus allowing for more confident decision-making.

As generic and cheaper PPI medications become increasingly available in Canada, the cost advantage of the Stretta procedure diminishes. In conclusion, regardless of the units of effectiveness or utility used in the present cost analysis, an approach of prescribing PPIs appears to be more cost-effective than using LNF or the Stretta procedure.

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lessening frequency and severity of complications, particularly in experienced hands (29).

The conclusions favour the PPI strategy, because in the case of SFM, it is dominant and in the case of QALYs, the other two options display incremental cost-effectiveness ratios much greater than what would usually be deemed a cost-effective choice for decision-makers. Nonetheless, there are differences in the results when using SFM versus QALYs as measures of effectiveness or utilities, which may reflect disparate sources in the literature for the different estimates, and perhaps, patient populations that may have varied in certain characteristics that are difficult to characterize. The ‘fron-loaded’ nature of the benefits attributable to the endoscopic and surgical treatments may also be an explanation when compared with the more prolonged disutility associated with the ongoing consumption of PPIs.

By necessity, several United States cost inputs were converted and used in our Canadian model when comparable Canadian data were not available. Although simple currency conversion may not accurately reflect differences in transnational health care resource costing and the proportioning of certain costs (30), we accounted for these variances in the sensitivity analyses.

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