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What is This?
Economic Evaluation of a Steroid-Eluting Sinus Implant following Endoscopic Sinus Surgery for Chronic Rhinosinusitis

Luke Rudmik, MD, MSc1, and Timothy L. Smith, MD, MPH2

Abstract

Objective. This study aimed to evaluate the cost-effectiveness of a mometasone steroid-eluting sinus implant compared to a nonsteroid-eluting sinus implant following endoscopic sinus surgery (ESS) for chronic rhinosinusitis.

Study Design. Economic evaluation using a decision tree model.

Setting. Academic and nonacademic otolaryngology practices.

Subjects. Patients with refractory chronic rhinosinusitis undergoing ESS.

Methods. The economic perspective was the health care third party payer. Effectiveness and probability data were obtained from a single meta-analysis of 2 randomized, double-blind, controlled trials. Costs were obtained from the Centers for Medicare & Medicaid Services database and wholesale pharmaceutical pricing. Multiple sensitivity analyses were performed including a probabilistic sensitivity analysis. Comparative treatment groups were (1) placement of the mometasone steroid-eluting sinus implant following ESS and (2) placement of a nonsteroid-eluting implant following ESS. The primary outcome was cost per postoperative intervention avoided within 60 days after ESS.

Results. The mean cost for the steroid-eluting and nonsteroid-eluting sinus implant strategies were $1,572.91 and $365.18, respectively. The steroid-eluting strategy incremental cost-effectiveness ratio was $5,489.68. The sensitivity analysis demonstrated a 74.3%, 87.2%, and 90.5% certainty that the steroid-eluting implant strategy is cost-effective at willingness-to-pay thresholds of $10,000, $25,000, and $50,000, respectively.

Conclusion. Results from this economic evaluation suggest that placement of a mometasone steroid-eluting sinus implant into the ethmoid cavity following ESS for refractory chronic rhinosinusitis is a cost-effective intervention for preventing a postoperative intervention within 60 days after surgery.

Keywords

chronic rhinosinusitis, sinusitis, implant, stent, spacer, Propel, cost-effectiveness, economic evaluation, topical corticosteroid, endoscopic sinus surgery

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Introduction

Following endoscopic sinus surgery (ESS) for chronic rhinosinusitis (CRS), steroid-eluting middle meatal spacers and implants are gaining popularity due to their ability to efficiently deliver topical steroid therapy to the sinus cavity during a time when traditional sprays and rinses have limited access.1-3 Furthermore, the use of steroid-eluting implants or spacers following ESS have the theoretic advantage of maintaining a patent middle meatus by medializing the middle turbinate as well as reducing the risk of patient noncompliance by potentially decreasing the need for self-applied topical steroid sprays and steroid rinses. However, it is important to note that patients with CRS will require continued long-term topical therapies for maintenance of their chronic inflammatory disease after the implants are dissolved or removed. Potential drawbacks of implants include the risk of inducing inflammation as a foreign material, the potential for unintended systemic absorption of the medication, and high costs for purchasing the device.4

The Propel Sinus Implant (Intersect ENT, Palo Alto, California, USA) is a new technology that has received US Food and Drug Administration (FDA) approval for use in patients with medically refractory CRS who undergo ESS. The Propel implant is a dissolvable mometasone furoate-eluting implant that is placed into a dissected ethmoid cavity and expands to contact the mucosa. The implant eludes 370 μg of mometasone over 30 days and dissolves over 30 to 45 days. Two randomized clinical trials, 1 prospective single cohort study, and a recent meta-analysis have demonstrated
effectiveness with reducing the need for sinus lysis of adhesions and reduced courses of rescue oral corticosteroids for polyp recurrence following ESS.\textsuperscript{5-8}

With more than 250,000 sinus surgery procedures performed in the United States every year,\textsuperscript{9} policy makers and third party payers must consider how the implementation of a novel CRS-related intervention will affect the overall efficiency of care delivered. Therefore, the high cost of the mometasone steroid-eluting sinus implant must be objectively evaluated in the context of its promising early postoperative effectiveness outcomes. The objective of this study is to evaluate the cost-effectiveness of the mometasone steroid-eluting sinus implant following ESS for patients with refractory CRS. We hypothesize that the steroid-eluting implant strategy will be a cost-effective intervention compared to using a nonsteroid-eluting implant.

**Methods**

The perspective of this economic evaluation was from a US health care third party payer. All costs are expressed in US dollars (USD) as of February 2014. The primary outcome is the cost per postoperative intervention avoided. The time horizon for this economic evaluation is 60 days after ESS. All costs and effects are presented in disaggregated and aggregated form and incremental cost-effectiveness ratios (ICERs) are presented for the primary outcome. The ICER is a commonly used equation in health economics to provide important information to resource allocation decision makers. It is the ratio of change in costs between 2 strategies to the change in effectiveness between the 2 strategies: (cost strategy A – cost strategy B) / (effectiveness strategy A – effectiveness strategy B). Therefore, the ICER provides the additional cost associated with the additional benefit of the new intervention being evaluated. The advantages of using the ICER are that it can be used to compare the multiple different treatment modalities and provides helpful information to decision makers regarding the additional costs associated with a new intervention in the context of the newly added benefit.\textsuperscript{10} Costs were not discounted since the time horizon was within 1 year. Institutional ethics review board approval was not obtained since all data were obtained from published studies and no individual patient data were used in the analysis.

**Economic Model**

A decision tree model was constructed to simulate the clinical management of a patient with refractory CRS undergoing ESS. Refractory CRS was defined as persistent disease despite a minimum of 3 months of topical sinonasal corticosteroids along with a minimum of a 7-day course of systemic corticosteroids \textsuperscript{6} a 2-week course of broad-spectrum antibiotics.\textsuperscript{11} A decision tree was elected because of the short time horizon (60 days) of the mometasone steroid-eluting implant effectiveness on patient outcomes.

In the model, the 2 comparative treatment groups were (1) placement of the mometasone steroid-eluting sinus implant within the middle meatus following ESS and (2) placement of a nonsteroid-eluting implant within the middle meatus following ESS. In each treatment strategy, there were 2 potential postoperative complications that would require a clinical intervention: (1) severe ethmoid adhesions that require a lysis procedure (this procedure was poorly defined in the primary studies and may represent a division of a minor synechiae) and (2) recurrent polyposis requiring a course of rescue oral corticosteroids (Figure 1). For the reference case, it was assumed that the “lysis of adhesion” procedure occurred at a medical encounter outside of the standard-of-care postoperative follow-up visits. The sensitivity analysis modeled a scenario where all lysis of adhesion procedures occurred within 1 of the standard postoperative care visits with a normally scheduled sinus debridement. Therefore, in this scenario, there was no additional cost for the lysis of adhesion intervention since it occurred in a regularly scheduled visit that was common to both groups. The model was programmed using the software TreeAge Pro 2012 (TreeAge Pro, Inc, Williamstown, Massachusetts, USA).

![Figure 1. Decision tree model for steroid-eluting sinus implant versus nonsteroid-eluting implant. Outlines the potential early postoperative clinical pathways (bold) along with each probability variable (not bold). The costs and effects for each pathway are presented at the end of each potential clinical pathway.](image-url)
Effectiveness Outcomes

The clinical effectiveness outcomes were obtained from a meta-analysis\(^6\) of 2 randomized trials evaluating the Propel sinus implant in patients with CRS (Murr et al\(^8\) and ADVANCE II\(^5\)). The designs of the Murr et al and ADVANCE II trials are presented in Table 1. For this model, effectiveness was defined as an avoided postoperative intervention within 60 days following ESS. The model pathways in which there were no postoperative interventions received an effect value of 1 (\(e_{\text{NoInterventionrequired}}\)), whereas all other pathways received an effect value of 0 (\(e_{\text{Interventionrequired}}\)) (Table 2).

Probabilities

The pooled results from the meta-analysis provided the following probabilities for the model: (1) probability of patients needing a postoperative lysis of adhesions (\(p_{\text{Propel\_Lysisadhesions}}\) and \(p_{\text{NoPropel\_Lysisadhesions}}\)) and (2) probability of patients...
needing a postoperative course of rescue oral corticosteroids (\(p_{\text{Propel\_Oralsteroidrescue}}\) and \(p_{\text{NoPropel\_Oralsteroidrescue}}\)) (Table 2).

Cost Estimation
The cost perspective was the US health care third party payer. It was assumed that interventions related to both ethmoid adhesions and recurrent nasal polyposis would be managed in an outpatient setting. Postoperative intervention costs were obtained from the Centers for Medicare & Medicaid Services (CMS) Physician Fee Schedule\(^\text{12}\) using the corresponding CPT code and wholesale pricing for pharmaceuticals.\(^\text{13}\) For the reference case, CMS costs were averaged from all regional fees. The sensitivity analysis applied the upper and lower limit CMS cost for carrier locality. For this model, a postoperative lysis of adhesion (\(c_{\text{Lysisadhesion}}\)) would require a physician visit (CPT# 99214), endoscopy (CPT# 31231), and in-office lysis procedure (CPT# 30560).\(^\text{12}\) Postoperative severe polyyp recurrence (\(c_{\text{Oralsteroidrescue}}\)) would require a physician visit (CPT# 99214), endoscopy (CPT# 31231), and course of prednisone 30 mg for 14 days.\(^\text{12,13}\)

The cost of the mometasone steroid-eluting sinus implant (\(c_{\text{Propelstent}}\)) was obtained from Intersect ENT Inc\(^\text{14}\) and was $700 per implant when purchased as a 5 pack. Using 2 implants per ESS case produced an overall cost of $1,400. Since there is a large variety of nonsteroid-eluting spacers/
stents available, we provided an estimated cost of $40 based on the use of 2 Salman middle meatal nonsteroid stents (c_Nondrugstent). All costs are summarized in Table 2.

Sensitivity Analysis

To test the effect of single variables on the overall economic conclusion from this model, we performed multiple 1-way sensitivity analyses. The tornado diagram is used to visually demonstrate the resulting ICERs when 1 variable is changed to become either the maximum or minimum value of the range provided. It is used to identify the relative importance of a variable since it can demonstrate if the economic conclusion changes based on changing the variable.

Based on the original randomized controlled trials (RCTs) and meta-analysis, the timing of the lysis of adhesion procedure within the first 60 days after ESS is unknown. Therefore, there is a chance that this intervention occurred within 1 of the regularly scheduled standard-of-care postoperative follow-up visits with a standard debridement. If this is true, then there would be no additional cost of the lysis of adhesion intervention since it occurred within a standard postoperative medical encounter that would have been common to both study groups. To model this potential scenario, we changed the probability of requiring a lysis of adhesion intervention to equal zero and thus the only additional postoperative intervention would be the need for a course of rescue oral corticosteroid.

A probabilistic sensitivity analysis (PSA) using a Monte Carlo simulation with 15,000 scenarios was performed. For each parameter category, the following data distributions were applied: cost = gamma distribution and probabilities = beta distribution. All variables in the model received ranges based on the 95% confidence intervals published in the meta-analysis. Variables with underlying assumptions possess higher levels of uncertainty and therefore received higher standard deviations to test several plausible values in the Monte Carlo simulation. Results are presented in both a cost-effectiveness acceptability curve (CEAC) and ICER scatter plot.

The CEAC is a technique used to graphically represent the uncertainty in an economic evaluation. It is a very important outcome for policy makers since it provides the degree of certainty in an economic conclusion at several different willingness-to-pay (WTP) thresholds. The ICER scatterplot is a technique used to visually demonstrate the cost-effectiveness of all the different ICERs generated from the 15,000 iterations of the PSA. The ICERs are plotted onto the cost-effectiveness plane (CEP), which is divided into 4 quadrants. Quadrant II ICERs are both cheaper and more effective and therefore are defined as the dominant intervention. On the other hand, quadrant IV ICERs are more expensive and are less effective and therefore are considered dominated and typically rejected. Decisions to accept the alternative intervention in quadrants I and III depend on the maximum ICER that policy makers are willing to accept (ie, WTP threshold).

Results

Reference Case

A patient receiving the mometasone steroid-eluting sinus implant strategy had a 67% chance of avoiding a postoperative intervention (ie, rescue course of oral corticosteroids or lysis of adhesions) compared to a 45% chance in the nonsteroid eluting stent strategy arm. Despite the mometasone steroid-eluting sinus implant strategy costing more ($1,572.91 vs $365.18), it resulted in an ICER of $5,489.68 per postoperative intervention avoided within 60 days after ESS (Table 3).

Sensitivity Analysis

Multiple 1-way sensitivity analyses were performed and presented in an ICER tornado diagram (Figure 2). The results demonstrated that the conclusion of this model was most sensitive to the probabilities of patients in the mometasone steroid-eluting and nonsteroid-eluting implant strategies who required either a rescue course of oral corticosteroids or lysis of adhesions following ESS. None of the variables exceeded an ICER of $8,500 per intervention avoided. Overall, the 1-way sensitivity analysis demonstrated that changes to no 1 variable resulted in a change in the economic conclusion that the mometasone steroid-eluting sinus implant strategy is the cost-effective clinical intervention.

To test the possibility that all postoperative lysis of adhesion procedures occurred during 1 of the standard postoperative care follow-up visits, we turned the probability of requiring an extra medical encounter for lysis of adhesions to zero. When the only postoperative intervention avoided was recurrence of severe polyposis requiring a course of...
rescue oral corticosteroids, the steroid implant strategy ICER was $8,903.80 (Table 3).

The multi-way PSA produced the CEAC seen in Figure 3. The results demonstrated that the steroid-eluting sinus implant strategy was the most cost-effective decision for any WTP threshold greater than $10,000 (Table 4). When the ICERs from the PSA are plotted onto the cost-effectiveness plane, it demonstrates that 90.5%, 87.2%, and 74.3% of outcomes are located to the right (ie, cost-effective) of the $50,000, $25,000, and $10,000 WTP lines in quadrant I, respectively (Figure 4).

**Discussion**

This study evaluated the cost-effectiveness of a mometasone steroid-eluting sinus implant compared to a nonsteroid-eluting implant following ESS for refractory CRS. The result from this modeling economic evaluation suggests that the steroid-eluting sinus implant strategy is the cost-effective decision for preventing the need for a clinical intervention (ie, course of rescue oral corticosteroids and/or lysis of adhesions) within the first 60 days after ESS. The sensitivity analyses performed demonstrated that there is greater than 74% certainty for this economic conclusion with any WTP threshold greater than $10,000.

Endoscopic sinus surgery is an effective intervention for patients with refractory CRS, and the rates for this procedure appear to be increasing in the United States.18 Therefore, it is important to identify novel interventions related to the delivery of care for ESS in order to improve the quality of care provided. Avoidance of postoperative complications is not only an important quality-of-care outcome to patients but it also reduces potentially wasted resources used by the interventions required to fix the complication.19,20 Policy makers and third party payers recognize the importance of complication avoidance and therefore place value on the interventions that achieve this endpoint.

This study evaluated the Propel mometasone sinus implant, which is a new steroid-eluting technology to improve the delivery of topical steroid therapy to the sinonasal mucosa. The results from this study suggest that it may be a cost-effective intervention for preventing a postoperative intervention within 60 days compared to a nonsteroid-eluting implant following ESS. Despite the convincing outcomes from this economic evaluation, there are several factors that should be considered when interpreting the results.

First, the conclusion that the mometasone steroid-eluting sinus implant is cost-effective must be taken into context of the primary endpoint, which was the avoidance of a...
such as Nasopore soaked in triamcinolone\textsuperscript{21,22} or no spacer. The surgeon would use either an off-label steroid-eluting spacer therefore, the results cannot be applied to cases when the mometason steroid-eluting implant to a nonsteroid-eluting spacer; Second, this economic evaluation compared the mometa-

doctrine making a decision for resource allocation and funding. Third, the time horizon for this economic evaluation is relatively short (60 days) when considering the chronicity of care needed to manage postoperative patients with CRS. Although the time horizon was appropriate for the primary objective of the 2 initial RCTs evaluating the mometasone steroid-eluting implant, future RCTs will need to expand their follow-up to allow for more accurate long-term economic evaluation of this intervention, which will likely be of more value to decision makers. Fourth, the majority of patients included in the meta-analysis by Han et al\textsuperscript{6} consisted of CRS patients with nasal polyposis. Therefore, the results from this economic evaluation are most relevant for this patient cohort and it is difficult to apply the results to a cohort of CRS patients without polyps. Fifth, this study did not take into account the possibility of a potential nonroutine postoperative visit to remove the steroid-eluting implant. Although this outcome was not reported, if this scenario is required (based on surgeon or patient preference), then the steroid implant strategy would have an added cost of a few hundred dollars.

Last, the US WTP threshold of $50,000, commonly quoted as being “cost-effective,” is arbitrary and the ultimate decision to adopt a novel intervention is complex and multifactorial. To improve the policy maker’s ability to make an informed decision pertaining to the use of the mometasone steroid-eluting sinus implant following ESS, this study provided multiple clinical scenarios and the CEAC in order to explicitly report the degree of uncertainty associated with the conclusions at WTP thresholds of $50,000, $25,000, and $10,000.

**Conclusion**

Endoscopic sinus surgery is an important surgical procedure for patients with refractory CRS. The mometasone steroid-eluting sinus implant is a novel adjunctive intervention to ESS and has been shown to be effective in reducing early postoperative complications requiring an intervention. However, implementing this steroid-eluting implant into routine practice comes with a higher cost compared to the use of other standard nonsteroid-eluting spacers and thus warranted a cost-effectiveness analysis. Results from this modeling economic evaluation suggest that the mometasone steroid-eluting sinus implant appears to be a cost-effective strategy for avoiding early postoperative interventions within the first 60 days following ESS compared to the use of a nonsteroid-eluting implant.

**Author Contributions**

Luke Rudmik, idea, data analysis, manuscript preparation; Timothy L. Smith, idea, manuscript preparation.

**Disclosures**

**Competing interests:** Timothy L. Smith is a consultant for Intersect Inc.

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