

The impact of asthma on the cost effectiveness of surgery for chronic rhinosinusitis with nasal polyps

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Background: The objective of this work was to evaluate the impact of asthma on the cost-effectiveness profile of endoscopic sinus surgery (ESS) compared to medical therapy for patients with chronic rhinosinusitis with nasal polyps (CRSwNP).

Methods: The study design consisted of a cohort-style Markov decision-tree cost utility analysis with a 35-year time horizon. Matched cohorts of CRSwNP patients with (n = 95) and without (n = 95) asthma who underwent ESS were compared with cohorts of patients from the national Medical Expenditures Survey Panel (MEPS) database who underwent medical management for chronic rhinosinusitis (CRS). Baseline, 1-year, and 2-year health utility values were calculated from responses to the EuroQol-5 Dimension (EQ-5D) instrument in both cohorts. The primary outcome measure was the incremental cost effectiveness ratio (ICER) for each cohort.

Results: The reference cases for CRSwNP patients with and without asthma yielded ICERs for ESS vs medical therapy alone of \$12,066 per quality-adjusted life year (QALY) and \$7,369 per QALY, respectively. At a willingness-to-pay

threshold of \$50,000/QALY, the ICER scatter plots demonstrated 86% and 99% certainty that the ESS strategy was the most cost-effective option for CRSwNP patients with and without asthma, respectively. ESS was not significantly more cost effective for CRSwNP patients without asthma ($p = 0.494$).

Conclusion: ESS remains cost effective compared to medical therapy for patients both with and without asthma. While the comorbidity of asthma results in an inferior ICER result, it does not result in a statistically significant negative impact on the overall cost effectiveness of ESS. © 2017 ARS-AAOA, LLC.

Key Words:

sinusitis; quality of life; patient reported outcome measures; cost-benefit analysis; paranasal sinuses

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The presence of asthma in patients who suffer from chronic rhinosinusitis (CRS)^{1,2} often results in reduced quality-of-life (QOL)^{3,4} and inferior disease-specific

outcomes after endoscopic sinus surgery (ESS).^{5,6} In light of these inferior outcomes, the clinical question remains whether surgical treatment is cost effective for CRS patients with asthma. This question takes on even greater relevance for CRS with nasal polyps (CRSwNP), where up to 50% of patients have been shown to carry a comorbid diagnosis of asthma.⁷

Several studies have examined asthma-specific and CRS-specific outcomes following ESS in patients with CRSwNP. A 2013 meta-analysis by Vashishta et al.⁸ reported that ESS improved clinical asthma outcome measures, but had no significant effect on pulmonary function tests (PFTs). Similarly, a 2015 meta-analysis by Rix et al.³ concluded that while CRS-specific symptoms significantly improve post-ESS, existing data does not demonstrate any significant improvement in PFTs or asthma medication usage. A 2017 prospective study by Schlosser et al.⁹ reported that validated asthma-specific outcomes improve post-ESS, but

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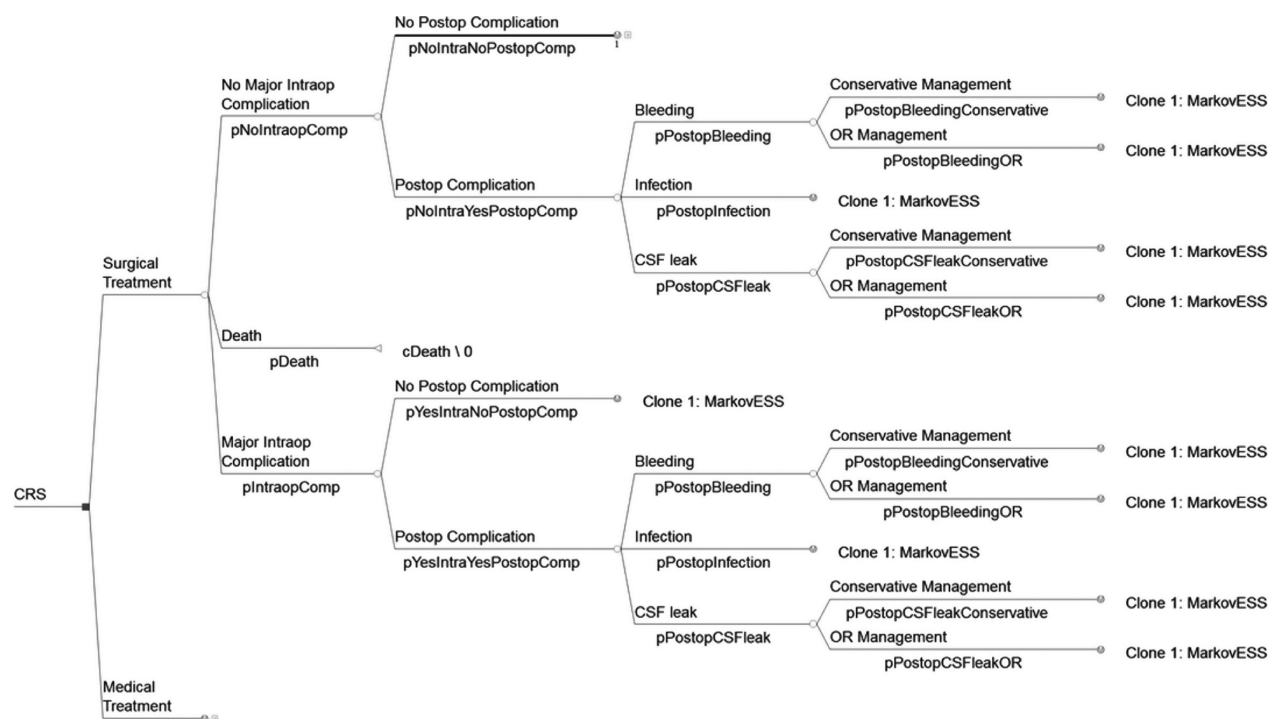


FIGURE 1. Intraoperative and postoperative decision tree for ESS and medical treatment. All terminal nodes are represented as Markov Nodes. ESS = endoscopic sinus surgery.

they were unable to identify novel CRS-specific factors that were associated with this improvement.

In a resource constrained healthcare system, recent efforts have focused on the comparative benefits and costs of various treatments for CRS.^{10,11} To date, a rigorous economic analysis of the cost effectiveness of surgical intervention for CRSwNP with and without asthma has not been performed. The aim of the current study was to perform a Cost Utility Analysis (CUA) to estimate the long-term cost-effectiveness of sinus surgery compared to continued medical therapy in CRSwNP patients with and without asthma.

Materials and methods

Economic model and study cohorts

A decision tree with 10 health state Markov microsimulation models was created and used to track patients in 2 arms: ESS with postoperative medical treatment vs medical therapy alone. The surgical health utility data were obtained from cohorts of CRSwNP patients with ($n = 95$) and without ($n = 95$) asthma who failed medical therapy and underwent ESS at Massachusetts Eye and Ear between 2011 and 2015. Subjects were enrolled from 11 different otolaryngology practices (4 academic and 7 private). The methods of data collection as well as the inclusion/exclusion criteria have been described by the authors.^{12–14} Patients were followed prospectively and completed the EuroQol-5 Dimension (EQ-5D) and 22-item Sino-Nasal Outcome Test (SNOT-22) surveys at the time of surgery, as well

as 3, 12, and 24 months postsurgery. Institutional review board (IRB) study approval was given by the Human Studies Committee of Massachusetts Eye and Ear.

The surgical cohorts first moved through the branches of a perioperative decision tree (Fig. 1). Major intraoperative complications were defined as death, cerebrospinal fluid (CSF) leak, intraoperative orbital injury, or major hemorrhage. Possible postoperative complications included in the model were moderate or severe epistaxis, infection, or CSF leak.¹⁵ Patients then entered the Markov microsimulation model at the terminal node of each branch.

Matched medical treatment cohorts consisting of 85 CRS patients without asthma and 10 CRS patients with asthma were chosen from the Medical Expenditures Panel Survey (MEPS) national database.¹⁶ The MEPS is an annual review providing information on health insurance status, health-care cost and expenditures, and patient-reported health of the U.S. general population. Patients were included based on matching the International Classification of Diseases, 9th edition (ICD-9) code for CRS, having 2 recorded responses to the EQ-5D instrument 1 year apart, and by their asthma distinction.¹⁷ Those patients with relevant surgical codes such as “nasal sinus operations” or “operations on nose” were excluded. Medical and surgical cohorts were matched using general demographic factors (age, sex, race, ethnicity, and smoking status), according to methodology previously utilized in robust utility studies of heart disease and diabetes.^{18,19}

The economic perspective of this CUA was from the U.S. government payer. As CRS remains a chronic disease, the

time horizon (35 years) was chosen as the difference between the conditional U.S. life expectancy and the average age of the cohort patients. Per standard CUA guidelines, a discount rate of 3% was applied to both utilities and costs. Half-cycle corrections were applied to upfront and final reward values.²⁰ The primary outcome was the overall cost effectiveness of ESS for CRSwNP with and without asthma compared to medical treatment alone, which is represented as an Incremental Cost Effectiveness Ratio (ICER).²¹ Thorough probabilistic sensitivity analyses were conducted. To determine whether ESS in asthma patients was more or less cost-effective than ESS in non-asthma patients, a Kruskal-Wallis test was conducted to determine whether the 10,000 ICER results from each CUA were statistically significantly different from each other.

Effectiveness

Multiyear Health Utility Values (HUVs) for each cohort were calculated from responses to the EQ-5D, a general QOL instrument that measures responses across 5 health domains.¹² HUVs represent a patient's preference at a given time point for living in a certain health state. HUVs range from 0 to 1, where 0 and 1 denote health states equivalent to death and perfect health, respectively.

Previous studies have shown that disease-specific outcomes for CRS (SNOT-22, Chronic Sinusitis Survey) correlate with EQ-5D scores, establishing construct validity of the EQ-5D instrument for CRS.^{13,14} Using the published EQ-5D algorithm, baseline, 1-year and 2-year HUVs were calculated for surgical and medical cohorts.^{22,23} Each health state within the Markov model was assigned a utility value equal to the middle utility value within that state (eg, 0.65 for state 0.60 to 0.69).

Probabilities

A PubMed (<https://www.ncbi.nlm.nih.gov/pubmed>) literature search was used to determine perioperative complication rates for the model. The search terms "complication" and "endoscopic sinus surgery" yielded 3378 unique manuscripts. After limiting the search to systematic reviews and meta-analyses, 92 articles remained. The 5 manuscripts with the largest patient cohorts were utilized (Table 1).^{24–28}

The Markov model was built with 10 health states (0.00 to 0.09, 0.10 to 0.19, 0.20 to 0.29, etc.) in an attempt to capture the full range of disease severity.^{29–31} Entrance, first year, and second year transition probabilities for all cohorts were computed from the primary data of each cohort (Table 2). Cycle 1 of the Markov model utilized year 1 transition probabilities. Cycles 2 through 35 utilized year 2 transition probabilities. The Chronic Rhinosinusitis Epidemiology Study published a 5-year probability of revision surgery of 20.6% for CRSwNP.³² Assuming an exponential rate of revision surgery, a 1-year probability of revision surgery of 4.51% for CRSwNP was applied to the Markov model for both cohorts, as no difference in

revision surgery rates for asthmatics has been published to date.

Cost determinates

Mean total costs of uncomplicated and complicated ESS (\$8,968 2014 USD and \$16,877 2014 USD, respectively) have been reported.^{11,33} The cost of various postoperative complications were also obtained from the medical literature.¹¹ The cost of revision ESS for CRSwNP was incorporated yearly into each Markov cycle by multiplying the yearly probability of revision by the cost of uncomplicated ESS. In an attempt to conservatively assess the cost of medical treatment of CRS, a modest yearly cost reported for medically treated CRS of \$772³⁴ was utilized. The cost of death was equated to the cost of an average night in an intensive care unit: \$31,574.³⁵ Ranges were applied to all costs in the model based on published variability for purposes of the probabilistic sensitivity analysis (Table 1).

Studies have suggested that CRS-specific resource consumption correlates with the degree of QOL detriment^{11,36}; therefore, the cost assigned to each of the 10 Markov utility states was calculated from a linear relationship between mean utility scores and costs of pre-ESS and post-ESS states (generated from primary study data and the literature, respectively).^{33,37,38} A literature search did not reveal any previously published cost differences between treatment of CRS in patients with and without asthma.

Sensitivity analysis

A 10,000 sample, Monte Carlo microsimulation was executed. Beta, triangular, and gamma distributions were attached to all matrix probabilities, Markov HUVs, and costs, respectively.³⁹ Dirichlet distributions were utilized to ensure that all node probabilities summed to 1 during execution of the microsimulation.

ICER scatter plots and cost-effectiveness acceptability curves (CEACs) were generated from the sensitivity analysis. The ICER scatterplot displays all resultant 10,000 ICERs from the microsimulation on a cost-effectiveness plane (Fig. 2).^{20,40,41} In this representation, the overall cost effectiveness of a more costly, yet more effective, treatment option depends on the maximum ICER that a healthcare system is willing to accept.²⁰ This value is represented graphically by a line whose slope equals a society's willingness-to-pay (WTP) threshold. Alternatively, a CEAC graphically displays the probability that each treatment option is the dominant option for a range of WTP thresholds. Thus, a CEAC displays the degree of certainty when choosing between treatment strategies.^{20,42}

This CUA follows the instructions of 2013 Consolidated Health Economic Evaluation Reporting Standards⁴³ and was performed using TreeAge Pro Healthcare Module 2015 software (TreeAge Software, Inc., Williamstown, MA). Cohort matching was executed in R 3.2.0 (The R Project for Statistical Computing, Vienna, Austria;

TABLE 1. Description of model parameters used in the economic model

Variable	Description	Mean value	Standard error	Source
Probability				
pDeath	Probability of death from ESS	0.0001	0.0003	Lund et al. ¹⁵
pIntraOpComp	Probability of intraoperative complication	0.0095	0.0004	May et al. ²⁴ ; Ramakrishnan et al. ²⁷
pNoIntraOpComp	Probability of no intraoperative complication	0.9904	0.0004	Ramakrishnan et al. ²⁷
pNoPostOpComp	Probability of no postoperative complication	0.8273	0.0069	Dalziel et al. ²⁶ ; Rudmik et al. ¹¹
pPostOpComp	Probability of postoperative complication	0.1727	0.0069	Dalziel et al. ²⁶ ; Rudmik et al. ¹¹
pPostOpInfection	Probability of postoperative infection (assuming a postoperative complication occurred)	0.647	0.047	Dalziel et al. ²⁶ ; Rudmik et al. ¹¹ ; May et al. ²⁴
pPostOpEpistaxis	Probability of postoperative epistaxis (assuming a postoperative complication occurred)	0.352	0.047	May et al. ²⁴ ; Stankiewicz et al. ²⁵
pPostOpCSFleak	Probability of postoperative CSF leak (assuming a postoperative complication occurred)	0.001	0.0002	Ramakrishnan et al. ²⁷
pPostOpEpistaxisCons	Probability of epistaxis resolving with conservative management	0.27	0.069	Stankiewicz et al. ²⁵
pPostOpEpistaxisOR	Probability of epistaxis requiring OR management	0.73	0.069	Stankiewicz et al. ²⁵
pPostOpCSFleakCons	Probability of CSF leak resolving with conservative management	0.19	0.054	Lindstrom et al. ²⁸
pPostOpCSFleakOR	Probability of CSF leak requiring OR management	0.81	0.054	Lindstrom et al. ²⁸
pRevESSwNP	Probability of revision ESS/year for CRSwNP	0.0451	0.005	Philpott et al. ³²
Cost				
cDeath	Cost of death	\$31,574	\$42,570	Dasta et al. ³⁵
cESS	Cost of ESS	\$8968	\$904	Smith et al. ³³
cMedical	Cost of medical treatment for CRS	\$772	\$300	Bhattacharyya et al. ³⁸
cESSMajorComp	Cost of major complication	\$16,877		Rudmik et al. ¹¹
cInfection	Cost of infection	\$559		Rudmik et al. ¹¹
cBleedCons	Cost of minor epistaxis	\$400		Rudmik et al. ¹¹
cBleedOR	Cost of major epistaxis	\$3500		Rudmik et al. ¹¹
cCSFCons	Cost of self limited CSF leak	\$13,594		Rudmik et al. ¹¹
cCSFOR	Cost of major CSF leak	\$16,877		Rudmik et al. ¹¹
cMarkov1	Cost of Markov Health State #1	\$1167	\$1167	
cMarkov2	Cost of Markov Health State #2	\$1408	\$1408	
cMarkov3	Cost of Markov Health State #3	\$1649	\$1649	
cMarkov4	Cost of Markov Health State #4	\$1890	\$1890	
cMarkov5	Cost of Markov Health State #5	\$2131	\$2131	
cMarkov6	Cost of Markov Health State #6	\$2372	\$2372	
cMarkov7	Cost of Markov Health State #7	\$2613	\$2613	
cMarkov8	Cost of Markov Health State #8	\$2854	\$2854	
cMarkov9	Cost of Markov Health State #9	\$3095	\$3095	
cMarkov10	Cost of Markov Health State #10	\$3336	\$3336	

CRS = chronic rhinosinusitis; CRSwNP = CRS with nasal polyps; CSF = cerebrospinal fluid leak; ESS = endoscopic sinus surgery; OR = operating room.

TABLE 2. Transition probabilities for the first and second postoperative years between all possible Markov Health States for the CRSwNP with asthma cohort

Year 0	Year 1									
	0.0–0.099	0.1–0.199	0.2–0.299	0.3–0.399	0.4–0.499	0.5–0.599	0.6–0.699	0.7–0.799	0.8–0.899	0.9–1.000
0.0–0.099	0	0	0	0	0	0	0	0	0	0
0.1–0.199	0	0	0	0	0	0	0	0	0	0
0.2–0.299	0	0	0	0	0	0	0	0	0	0
0.3–0.399	0	0	0	0	0	0	0	0	0	0
0.4–0.499	0	0	0	0	0	0	0	0	0	0
0.5–0.599	0	0	0	0	0	0.50	0	0	0.5	0
0.6–0.699	0	0	0	0	0	0.13	0.13	0.25	0.50	0
0.7–0.799	0	0	0	0	0	0	0.00	0.36	0.57	0.07
0.8–0.899	0	0	0	0	0	0	0	0.02	0.53	0.44
0.9–1.000	0	0	0	0	0	0	0	0.04	0.36	0.6
Year 1	Year 2									
	0.0–0.099	0.1–0.199	0.2–0.299	0.3–0.399	0.4–0.499	0.5–0.599	0.6–0.699	0.7–0.799	0.8–0.899	0.9–1.000
0.0–0.099	0	0	0	0	0	0	0	0	0	0
0.1–0.199	0	0	0	0	0	0	0	0	0	0
0.2–0.299	0	0	0	0	0	0	0	0	0	0
0.3–0.399	0	0	0	0	0	0	0	0	0	0
0.4–0.499	0	0	0	0	0	0	0	0	0	0
0.5–0.599	0	0	0	0	0	1.00	0	0	0	0
0.6–0.699	0	0	0	0	0	0	0	0	1.00	0
0.7–0.799	0	0	0	0	0	0	0.11	0.56	0.33	0
0.8–0.899	0	0	0	0	0.04	0.02	0	0.09	0.60	0.26
0.9–1.000	0	0	0	0	0	0	0	0.03	0.31	0.67

CRS = chronic rhinosinusitis; CRSwNP = CRS with nasal polyps.

<https://www.r-project.org/>) by utilizing the nearest neighbor matching principle in the MatchIt package.^{44,45}

Results

Patient characteristics

The preoperative EQ-5D (standard deviation [SD]) scores were not statistically different ($p > 0.05$) between the asthma (0.842 [0.126]) and non-asthma (0.842 [0.111]) cohorts. The baseline SNOT-22 [SD] scores were, however, statistically different ($p = 0.0009$) between the asthma cohort (55.253 [20.401]) and the cohort without asthma (45.295 [20.123]). The baseline Lund-Mackay scores (SD) were 16.4 [3.9] for the asthma cohort and 13.6 [4.7] for the cohort without asthma ($p < 0.0001$). The percentage of revision surgery was not statistically different ($p = 0.1356$) between these 2 cohorts.

Cost effectiveness

CRSwNP with asthma

With a cost and utility discount rate of 3%, the model ran a cohort of patients for 35 years and showed that the ESS treatment strategy cost \$40,102 and produced 15.16 QALYs. The medical treatment strategy cost \$27,191 and produced 14.09 QALYs. The ICER for ESS vs medical treatment alone in CRSwNP with asthma is \$12,066 per QALY.

CRSwNP without asthma

With a cost and utility discount rate of 3%, the model ran a cohort of patients for 35 years and showed that the ESS treatment strategy cost \$37,331 and produced 16.27 QALYs. The medical treatment strategy cost \$25,910 and produced 14.72 QALYs. The ICER for ESS vs medical

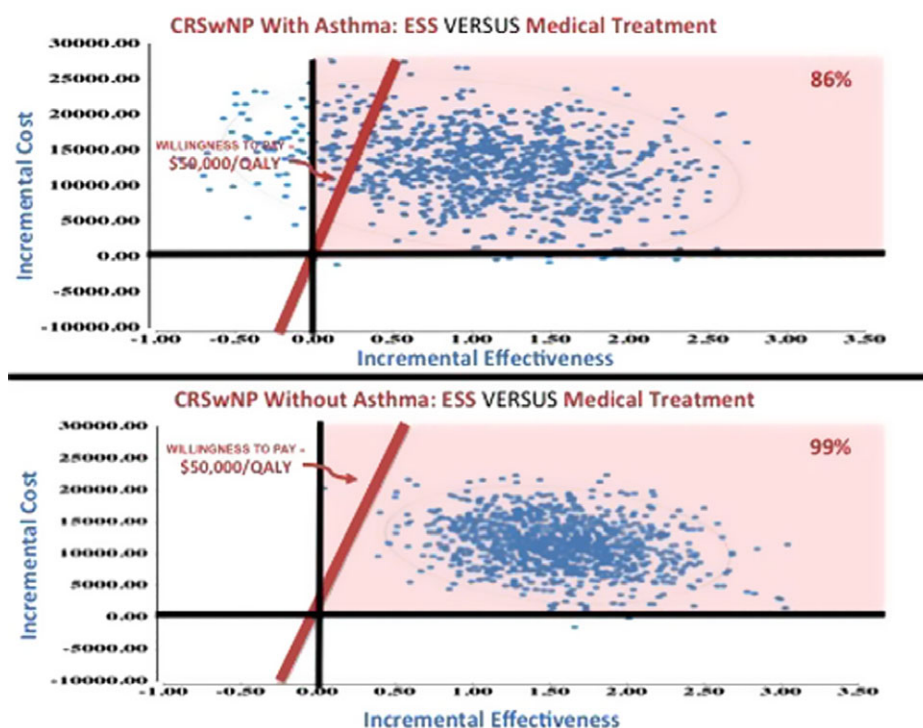


FIGURE 2. The ICER scatter plots depict all ICER results generated from the microsimulation onto the cost-effectiveness plane. For CRSwNP with asthma, 86% of individual ICER outcomes favored ESS when compared to medical management while also falling below the \$50,000-per-QALY threshold. In comparison, for CRSwNP without asthma, 99% of ICER outcomes favored ESS when compared medical management at the same WTP threshold. CRSwNP = chronic rhinosinusitis with nasal polyps; ESS = endoscopic sinus surgery; ICER = incremental cost effectiveness ratio; QALY = quality adjusted life year; WTP = willingness-to-pay.

treatment alone in CRSwNP without asthma is \$7369 per QALY.

Sensitivity analysis: probabilistic sensitivity analysis

ICER scatter plot analysis (Fig. 2) demonstrates that, at a WTP threshold of \$50,000 per QALY, in 99% of individual ICER outcomes, ESS for CRSwNP without asthma was more cost-effective than medical treatment. Similarly, in 86% of individual ICER outcomes, ESS for CRSwNP with asthma was more cost-effective. Figure 3 displays 2 CEACs. The non-asthma CEAC demonstrates an extremely favorable threshold of \$50,000 per QALY, above which there is $\geq 99\%$ certainty that ESS remains the most cost effective treatment option. The asthma CEAC demonstrates that 95% certainty is not achieved within the accepted WTP threshold of \$50,000 to \$100,000 per QALY. However, at the upper limit of acceptability (\$100,000 per QALY), there is $\geq 90\%$ certainty that ESS remains the most cost effective treatment option for asthma patients.

Statistical analysis

As the ICER results of the asthma and non-asthma CUAs were not normally distributed, a Kruskal-Wallis test was performed. The calculated *p* value was 0.494. Figure 4 depicts complete overlap of 95% confidence ellipses between ICER results of both surgical cohorts.

Discussion

CRS is a disease that encompasses heterogeneous patient populations making prognostication of ESS outcomes challenging.^{13,46,47} The goal of otolaryngologists is to differentiate these populations, so as to provide appropriate counsel, including choice of therapeutic options, to their CRS patients. Asthma represents a common comorbidity in CRS patients that has been of particular relevance to the field since description of the unified airway hypothesis.⁴⁸ Previous studies have reported relatively poor outcomes for asthmatics with CRSwNP who undergo ESS compared to patients without asthma.^{5,6,49}

Recent legislation aimed at our resource-constrained healthcare system has emphasized the importance of the overall utility and cost of various treatment options, especially for non-terminal conditions.^{50,51} Our study represents a robust CUA examining the impact of asthma on the overall cost effectiveness of ESS compared to medical treatment for CRSwNP. The CRSwNP subtype was chosen because of the known association between nasal polypsis and the comorbid diagnosis of asthma.⁷

Economic evaluation yielded ICERs of \$12,066 per QALY and \$7369 per QALY for asthma and non-asthma cohorts, respectively. Both ICERs fell well below the acceptable WTP threshold in the United States: \$50,000 to 100,000 per QALY.^{52–55} In comparison, a recent CUA of ESS vs medical therapy for a general CRS population

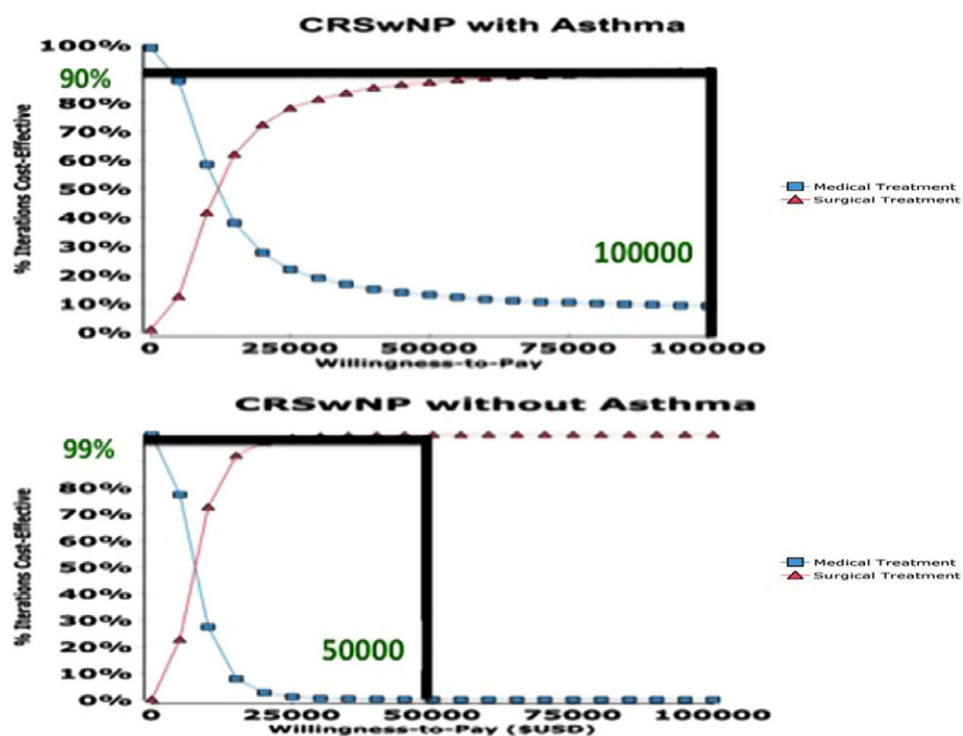


FIGURE 3. The CEAC shows the degree of certainty that ESS is the most cost-effective option. For CRSwNP with asthma, at a threshold of \$100,000 per QALY, ESS is more cost effective than medical management with 90% certainty. For CRSwNP without asthma, 95% confidence for ESS is achieved at a threshold of \$50,000 per QALY. CEAC = cost-effectiveness acceptability curve; CRSwNP = chronic rhinosinusitis with nasal polyps; ESS = endoscopic sinus surgery; QALY = quality adjusted life year.



FIGURE 4. The ICER scatter plot depicts all ICER results from both surgical cohorts generated from the microsimulation and the resultant 95% confidence ellipses, which are completely overlapping. A Kruskal-Wallis test yielded a p value of 0.494. ICER = incremental cost effectiveness ratio.

TABLE 3. Assumptions

Assumption	Source
Surgical complication rates and cost of surgical treatment between CRSwNP patients with and without asthma were assumed to be equal.	Smith et al. ³³ ; Bhattacharyya et al. ³⁸
The 5-year rate of revision surgery was assumed to be 20.6% for CRSwNP.	Philpott et al. ³²
Markov transition probabilities in the surgical cohort, which were calculated from changes in the first and second year post-ESS, were assumed to accurately represent long-term yearly transition probabilities for CRS patients post-ESS.	Remenschneider et al. ¹⁴ ; Rudmik et al. ⁵⁷
The diagnosis of CRS in the MEPS cohort, which was self reported, was assumed to be accurate.	Bairdain and Samnaliev ⁵⁸ ; Ozieh et al. ⁵⁹ ; Agarwal and Sambamoorthi ⁶⁰ ; AHRQ ⁶¹ ; Fu et al. ⁶² ; Tomassen et al. ⁶³
MEPS patients were assumed to report any history of previous sinonasal surgery.	Zuvekas et al. ⁶⁴
All medical treatments of CRS were assumed to proceed without complication.	Liu et al. ⁶⁵
A linear relationship between health utility value and average cost of yearly care was assumed.	Rudmik et al. ¹¹ ; Wang et al. ³⁶

AHRQ = Agency for Healthcare Research and Quality; CRS = chronic rhinosinusitis; CRSwNP = CRS with nasal polyps; ESS = endoscopic sinus surgery; MEPS = Medical Expenditures Survey Panel.

yielded an ICER of \$13,851.26 per QALY.⁵⁶ Probabilistic sensitivity analysis in the current study yielded ICER scatter plots that show that at WTP threshold of \$50,000 per QALY, there is 86% and 99% certainty that ESS is cost effective for asthma and non-asthma cohorts, respectively (Fig. 2).

While the ICER for patients with asthma was inferior compared to non-asthma patients, the overall cost effectiveness of ESS was not statistically different between cohorts ($p = 0.494$). Over the 35-year time horizon of the economic analysis, there was a minor increase in overall cost associated with asthma (+\$2,771). The main driver of the difference in ICERs was the decreased utility gained by asthmatics compared to non-asthmatics (−1.11 QALYs). This finding is consistent with prior studies showing relatively poor outcomes for asthmatics with CRSwNP after ESS.^{5,6,49} The lack of statistical difference when comparing the cost effectiveness of ESS for asthma and non-asthma cohorts could have been influenced by confounding factors. While baseline HUV scores were not statistically different between cohorts, the asthma cohort had significantly worse SNOT-22 scores. Thus, a potential higher baseline burden of disease in the asthma cohort could explain decreased overall gains in utility at a similar cost. Conversely, as has been described in prior publications, the possibility of a ceiling effect should also be considered.⁹ Namely, a higher burden of disease in the asthma cohort could present an opportunity for greater net improvement post-ESS.

Interestingly, a prospective study by Schlosser et al.⁹ recently identified 3 independent factors that may predict improvement in asthma-specific QOL post-ESS: preoperative steroid dependence, improvement in SNOT-22 scores, and the comorbidity of obstructive sleep apnea (OSA).⁹ While data on oral or inhalational steroid dependence was unavailable for review, the asthma cohort's degree of

improvement in SNOT-22 scores and incidence of OSA were not statistically different ($p = 0.16$ and $p = 0.62$, respectively) than the non-asthma cohort. Thus, aside from the unknown impact of preoperative steroid dependence, it does not appear that the difference in utility was influenced by an increased change in disease-specific outcomes or incidence of OSA. Overall, thorough sensitivity analysis on the results indicates that the cost effectiveness of ESS, which remains robust in both cohorts, does not appear to be influenced by asthma status.

In this study, several inherent limitations merit attention (Table 3). First, the nature of our study did not allow for assessment of the preoperative or postoperative degree of asthma burden. In addition, the diagnosis of asthma was made by previous physicians, and as such, it remains possible that patients could have been misdiagnosed. Next, HUV transition probabilities in the Markov model for both the asthma and non-asthma cohorts were presumed to accurately represent long-term values for CRSwNP. This assumption of longevity was based on prior publications showing long-term improvements in HUVs following ESS and has been used in prior published CUAs.^{13,56,57} An additional limitation was the nonrandomization of cohorts. While patients were matched based on relevant demographic factors, the patients in each surgical arm ultimately chose surgical treatment. Finally, the medically treated asthma cohort consisted of a small number of patients ($n = 10$). While these patients were matched to all cohorts, the possibility of sampling error exists. Ultimately, the conclusion that ESS remains a cost-effective treatment for CRSwNP patients with and without asthma should be interpreted with the caveat that CRSwNP remains a patient-centered disease. The individualization of treatment plans for CRS based on patients' disease status, in conjunction with their inclinations and input, should remain at the forefront of the surgeon's thought process.

Conclusion

ESS remains cost effective compared to medical therapy for patients both with and without asthma. While the

comorbidity of asthma results in an inferior ICER result, it does not result in a statistically significant negative impact on the overall cost effectiveness of ESS. 

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