

Cost Utility Analysis of Dupilumab Versus Endoscopic Sinus Surgery for Chronic Rhinosinusitis With Nasal Polyps

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Objective: Both endoscopic sinus surgery (ESS) and biologic therapies have shown effectiveness for medically-refractory chronic rhinosinusitis with nasal polyps (CRSwNP) without severe asthma. The objective was to evaluate cost-effectiveness of dupilumab versus ESS for patients with CRSwNP.

Study Design: Cohort-style Markov decision-tree economic model with a 36-year time horizon.

Methods: A cohort of 197 CRSwNP patients who underwent ESS were compared with a matched cohort of 293 CRSwNP patients from the SINUS-24 and SINUS-52 Phase 3 studies who underwent treatment with dupilumab 300 mg every 2 weeks. Utility scores were calculated from the SNOT-22 instrument in both cohorts. Decision-tree analysis and a 10-state Markov model utilized published event probabilities and primary data to calculate long-term costs and utility. The primary outcome measure was incremental cost per quality-adjusted life year (QALY), which is expressed as an Incremental Cost Effectiveness Ratio. One-way and probabilistic sensitivity analyses were performed.

Results: The ESS strategy cost \$50,436.99 and produced 9.80 QALYs. The dupilumab treatment strategy cost \$536,420.22 and produced 8.95 QALYs. Because dupilumab treatment was more costly and less effective than the ESS strategy, it is dominated by ESS in the base case. One-way sensitivity analyses showed ESS to be cost-effective versus dupilumab regardless of the frequency of revision surgery and at any yearly cost of dupilumab above \$855.

Conclusions: The ESS treatment strategy is more cost effective than dupilumab for upfront treatment of CRSwNP. More studies are needed to isolate potential phenotypes or endotypes that will benefit most from dupilumab in a cost-effective manner.

Key Words: Quality of life, cost-benefit analysis, paranasal sinuses, biologics, chronic sinusitis, nasal polyps.

Level of Evidence: 2C

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INTRODUCTION

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a condition characterized by significant declines in patient quality of life (QOL) and an economic burden to society, with a total direct and indirect cost of up to 60 billion dollars per year to the national economy.^{1–3} When

appropriate medical therapy fails, endoscopic sinus surgery (ESS) has been shown to be a cost-effective treatment option.⁴

While these data reflect the overall benefits of ESS, the reported CRSwNP surgical revision rate of 20% after 60 months demonstrates the variability in individual outcomes as well as the need for further interventions in select patients.⁵ Recent efforts to identify predictors of recurrence have focused both on phenotypes and clinical factors. Aspirin exacerbated respiratory disease (AERD) and allergic fungal rhinosinusitis (AFRS) historically have been reported to carry a risk of up to a 90% rate of recurrence,^{6–8} although a recent meta-analysis suggests this rate may be significantly lower in modern times (approximately 27–28%).⁹ Other factors, such as older age, worse SNOT-22 scores, and reduced productivity have been associated with severe disease and poorer outcomes.¹⁰

As these treatment-resistant patients have become better characterized, researchers have begun exploring the utility of monoclonal antibodies as biologic therapies to suppress the immune system and treat CRSwNP. Randomized controlled trials with mepolizumab, omalizumab, and dupilumab for CRSwNP have shown positive results in reduction of nasal polyposis and improving patient reported outcomes.^{11–13} Based on the most robust and long-term data, dupilumab was granted approval for

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horizon (36 years) for both Markov models used in the study was the difference between the average age of the study patients and the average conditional US life expectancy. Following standard guidelines, cost and utility were discounted at a rate of 3% for the base case. Half-cycle corrections were added for all initial and final reward values.²¹ The primary outcome was the cost effectiveness of dupilumab compared to surgical management with continued postoperative medical treatment for patients with CRSwNP, which is expressed as an Incremental Cost Effectiveness Ratio (ICER).²² Both one-way and probabilistic sensitivity analysis were performed.

Effectiveness

HUVs for the dupilumab cohort were obtained from longitudinal SNOT-22 outcomes from the SINUS-24 and SINUS-52 Phase 3 studies.^{13,19,20} Using a published algorithm for the conversion of SNOT-22 scores to HUVs, baseline, 24 week, and 52 week HUVs were calculated for the dupilumab cohort.²³ Similarly, HUVs for the surgical cohort were obtained from longitudinal SNOT-22 outcomes. Baseline, 1 year, and 2 year HUVs were calculated for the surgical cohorts.^{24,25} For both cohorts, the utility value for each Markov state was set at the middle value within that state (eg, 0.95 for state 0.90–1.0).

Probabilities

All ESS perioperative complication probabilities were extracted from the following literature search on PUBMED. The terms “endoscopic sinus surgery” and “complication” produced an initial result of 3,378 studies. The search was limited to

systematic reviews or meta-analyses and yielded a total of 92 articles. Data was extracted from the five systematic reviews with the largest patient cohorts.^{26–30} All dupilumab complication probabilities were extracted from the FDA label.²⁰

Each Markov model was designed with 10 health states (0.00–0.09, 0.10–0.19, etc.) in order to capture the full spectrum of disease states.^{31–33} Entrance, first interval, and second interval transition probabilities for the surgical and dupilumab Markov models (Tables I and II) were calculated by utilizing average changes in HUV and the difference in standard deviations from each cohort's primary SNOT-22 data. The probability density function was then utilized to mathematically generate each matrix of transition probabilities from this calculated difference in probability at each treatment interval for both cohorts. Cycle 1 of the Markov model utilized first interval transition probabilities. Cycles 2 through 36 utilized second interval transition probabilities (n = 135 for ESS cohort and n = 150 for dupilumab cohort). The Chronic Rhinosinusitis Epidemiology Study reported 5-year probabilities of revision surgery of 20.6% for CRSwNP.³⁴ Assuming an exponential rate of revision surgery, a 1-year probability of revision surgery of 4.51% for CRSwNP was calculated and included in the base case of the economic model.

Cost

A systematic review reported a mean cost of uncomplicated ESS of \$8,968 (2014 USD).³⁵ Rudmik et al. calculated a cost of \$16,877 for ESS with major complication,¹⁵ which was applied to both major intraoperative and postoperative complications. The cost of revision ESS was applied yearly to each Markov cycle by multiplying the aforementioned yearly probability of revision by

TABLE I.
Transition Probabilities for the First and Second Intervals Between All Possible Markov Health States for the Biologics Cohort.

		Year 1 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
Year 0	0–0.099	0.41	0.08	0.08	0.08	0.08	0.07	0.06	0.06	0.04	0.03
	0.1–0.199	0.27	0.18	0.08	0.08	0.08	0.08	0.07	0.06	0.06	0.04
	0.2–0.299	0.20	0.06	0.22	0.08	0.08	0.08	0.08	0.07	0.06	0.06
	0.3–0.399	0.15	0.06	0.06	0.28	0.08	0.08	0.08	0.08	0.07	0.06
	0.4–0.499	0.10	0.04	0.06	0.06	0.34	0.08	0.08	0.08	0.08	0.07
	0.5–0.599	0.08	0.03	0.04	0.06	0.06	0.41	0.08	0.08	0.08	0.08
	0.6–0.699	0.05	0.03	0.03	0.04	0.06	0.06	0.48	0.08	0.08	0.08
	0.7–0.799	0.03	0.02	0.03	0.03	0.04	0.06	0.06	0.56	0.08	0.08
	0.8–0.899	0.02	0.01	0.02	0.03	0.03	0.04	0.06	0.06	0.64	0.08
	0.9–1	0.01	0.01	0.01	0.02	0.03	0.03	0.04	0.06	0.06	0.72
		Year 2 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
Year 1	0–0.099	0.49	0.11	0.10	0.09	0.07	0.05	0.04	0.03	0.01	0.01
	0.1–0.199	0.37	0.13	0.11	0.10	0.09	0.07	0.05	0.04	0.03	0.01
	0.2–0.299	0.27	0.10	0.14	0.11	0.10	0.09	0.07	0.05	0.04	0.03
	0.3–0.399	0.19	0.09	0.10	0.16	0.11	0.10	0.09	0.07	0.05	0.04
	0.4–0.499	0.13	0.07	0.09	0.10	0.20	0.11	0.10	0.09	0.07	0.05
	0.5–0.599	0.08	0.05	0.07	0.09	0.10	0.25	0.11	0.10	0.09	0.07
	0.6–0.699	0.05	0.03	0.05	0.07	0.09	0.10	0.33	0.11	0.10	0.09
	0.7–0.799	0.03	0.02	0.03	0.05	0.07	0.09	0.10	0.41	0.11	0.10
	0.8–0.899	0.01	0.01	0.02	0.03	0.05	0.07	0.09	0.10	0.51	0.11
	0.9–1	0.01	0.01	0.01	0.02	0.03	0.05	0.07	0.09	0.10	0.62

TABLE II.
Transition Probabilities for the First and Second Intervals Between All Possible Markov Health States for the Surgical Cohort.

		Year 1 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
Year 0	0–0.099	0.45	0.08	0.08	0.08	0.07	0.07	0.06	0.05	0.04	0.04
	0.1–0.199	0.30	0.18	0.08	0.08	0.08	0.07	0.07	0.06	0.05	0.04
	0.2–0.299	0.23	0.07	0.22	0.08	0.08	0.08	0.07	0.07	0.06	0.05
	0.3–0.399	0.18	0.06	0.07	0.27	0.08	0.08	0.08	0.07	0.07	0.06
	0.4–0.499	0.13	0.05	0.06	0.07	0.34	0.08	0.08	0.08	0.07	0.07
	0.5–0.599	0.10	0.04	0.05	0.06	0.07	0.40	0.08	0.08	0.08	0.07
	0.6–0.699	0.07	0.03	0.04	0.05	0.06	0.07	0.47	0.08	0.08	0.08
	0.7–0.799	0.05	0.02	0.03	0.04	0.05	0.06	0.07	0.56	0.08	0.07
	0.8–0.899	0.03	0.02	0.02	0.03	0.04	0.05	0.06	0.07	0.62	0.08
	0.9–1	0.02	0.01	0.02	0.02	0.03	0.04	0.05	0.06	0.07	0.70
		Year 2 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
Year 1	0–0.099	0.48	0.10	0.10	0.08	0.07	0.06	0.04	0.03	0.02	0.01
	0.1–0.199	0.37	0.13	0.10	0.10	0.08	0.07	0.06	0.04	0.03	0.02
	0.2–0.299	0.28	0.09	0.15	0.10	0.10	0.08	0.07	0.06	0.04	0.03
	0.3–0.399	0.21	0.07	0.09	0.18	0.10	0.10	0.08	0.07	0.06	0.04
	0.4–0.499	0.15	0.07	0.07	0.09	0.21	0.10	0.10	0.08	0.07	0.06
	0.5–0.599	0.10	0.05	0.07	0.07	0.09	0.27	0.10	0.10	0.08	0.07
	0.6–0.699	0.06	0.04	0.05	0.07	0.07	0.09	0.35	0.10	0.10	0.08
	0.7–0.799	0.04	0.02	0.04	0.05	0.07	0.07	0.09	0.43	0.10	0.10
	0.8–0.899	0.02	0.01	0.02	0.04	0.05	0.07	0.07	0.09	0.53	0.10
	0.9–1	0.01	0.01	0.01	0.02	0.04	0.05	0.07	0.07	0.09	0.63

TABLE III.
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. ³⁶
plntraOpComp	Probability of death from dupilumab Probability of intraoperative complication	0.010	0.0004	FDA label ²⁰ May et al. ²⁶ Ramakrishnan et al. ²⁹
pNoIntraOpComp	Probability of no intraoperative complication	0.990	0.0004	Ramakrishnan et al. ²⁹
pNoPostOpComp	Probability of no postoperative complication	0.827	0.0069	Dalziel et al. ²⁸ Rudmik et al. ¹⁵
pPostOpComp	Probability of postoperative complication	0.173	0.0069	Dalziel et al. ²⁸ Rudmik et al. ¹⁵
pPostOpInfection	Probability of postoperative infection (assuming a postoperative complication occurred)	0.647	0.047	Dalziel et al. ²⁸ Rudmik et al. ¹⁵
pPostOpEpistaxis	Probability of postoperative epistaxis (assuming a postoperative complication occurred)	0.352	0.047	May et al. ²⁶ May et al. ²⁶
pPostOpCSFleak	Probability of postoperative CSF leak (assuming a postoperative complication occurred)	0.001	0.0002	Stankiewicz et al. ²⁷ Ramakrishnan et al. ²⁹
pPostOpEpistaxisCons	Probability of epistaxis resolving with conservative management	0.270	0.069	Stankiewicz et al. ²⁷
pPostOpEpistaxisOR	Probability of epistaxis requiring OR management	0.730	0.069	Stankiewicz et al. ²⁷
pPostOpCSFleak Cons	Probability of CSF leak resolving with conservative management	0.190	0.054	Lindstrom et al. ³⁰
pPostOpCSFleak OR	Probability of CSF leak requiring OR management	0.810	0.054	Lindstrom et al. ³⁰
pRevESSwNP	Probability of revision ESS/year for CRSwNP	0.045	0.005	Philpott et al. ³⁴
pDupComp	Probability of complication during dupilumab treatment	0.693	n/a	Desrosier et al. ¹⁹
pDupNoComp	Probability of no complication during dupilumab treatment	0.307	n/a	Desrosier et al. ¹⁹

(Continues)

TABLE III.
Continued

Variable	Description	Mean Value	Standard Error	Source
pDupAnaph	Probability of anaphylaxis from dupilumab treatment	0.001	n/a	FDA label ²⁰
pDupHyper	Probability of hypersensitivity reaction from dupilumab treatment	0.005	n/a	FDA label ²⁰
pDupConj	Probability of conjunctivitis from dupilumab treatment	0.014	n/a	Desrosier et al. ¹⁹
pDupEGPA	Probability of EGPA from dupilumab treatment	0.015	n/a	FDA label ²⁰
pDupInjRx	Probability of injection site reaction from dupilumab treatment	0.064	n/a	Desrosier et al. ¹⁹
pDupArth	Probability of arthralgia from dupilumab treatment	0.021	n/a	FDA label ²⁰
pDupFailure	Probability of failure of dupilumab treatment	0	n/a	Assumption
Cost				
cDeath	Cost of death	\$31,574	\$42,570	Dasta et al. ³⁷
cESS	Cost of ESS	\$8,968	\$904	Smith et al. ³⁵
cDupilumab	Cost of 1 year of treatment with dupilumab	\$31,000	n/a	Tice et al. ³⁸
cESSMajorComp	Cost of major complication	\$16,877	n/a	Rudmik et al. ¹⁵
cInfection	Cost of infection	\$559	n/a	Rudmik et al. ¹⁵
cBleedCons	Cost of minor epistaxis	\$400	n/a	Rudmik et al. ¹⁵
cBleedOR	Cost of major epistaxis	\$3,500	n/a	Rudmik et al. ¹⁵
cCSFCons	Cost of self-limited CSF leak	\$13,594	n/a	Rudmik et al. ¹⁵
cCSFOR	Cost of major CSF leak	\$16,877	n/a	Rudmik et al. ¹⁵
cDupAnaph	Cost of anaphylaxis from dupilumab treatment	\$671	n/a	Patel et al. ³⁹
cDupHyper	Cost of hypersensitivity reaction from dupilumab treatment	\$279	n/a	Patel et al. ³⁹
cDupConj	Cost of conjunctivitis from dupilumab treatment	\$92	n/a	Smith et al. ⁴⁰
cDupEGPA	Cost of EGPA from dupilumab treatment	\$20,865	n/a	Bell et al. ⁴¹
cDupInjRx	Cost of injection site reaction from dupilumab treatment	\$279	n/a	Patel et al. ³⁹
cDupArth	Cost of arthralgia from dupilumab treatment	\$2,117	n/a	Murphy et al. ⁴²
cMarkov1	Cost of Markov Health State #1	\$1,167	\$1,167	
cMarkov2	Cost of Markov Health State #2	\$1,408	\$1,408	
cMarkov3	Cost of Markov Health State #3	\$1,649	\$1,649	
cMarkov4	Cost of Markov Health State #4	\$1,890	\$1,890	
cMarkov5	Cost of Markov Health State #5	\$2,131	\$2,131	
cMarkov6	Cost of Markov Health State #6	\$2,372	\$2,372	
cMarkov7	Cost of Markov Health State #7	\$2,613	\$2,613	
cMarkov8	Cost of Markov Health State #8	\$2,854	\$2,854	
cMarkov9	Cost of Markov Health State #9	\$3,095	\$3,095	
cMarkov10	Cost of Markov Health State #10	\$3,336	\$3,336	

the cost of ESS. Costs for postoperative complications as well as complications related to treatment with dupilumab were obtained from the literature (Table III).

A review of costs and incremental cost effectiveness ratios for biologic treatments for asthma reported a conservative yearly cost of \$31,000 for dupilumab.³⁸ Despite published costs exceeding this figure, it was chosen as an attempt to conservatively evaluate the cost of dupilumab treatment. The model assumed that dupilumab would need to be taken indefinitely to achieve a sustained effect. The cost of death in this economic model for both cohorts was equated to an average intensive care unit stay: \$31,574.³⁷

To calculate cost for each Markov utility state per cycle, the mean utility levels of pre- and post-treatment states (from primary data) and the mean costs of pre- and post-treatment states (from available literature)^{35,43,44} were used to generate a linear relationship between average cost and HUVs, as CRS-specific health care resource consumption is correlated to the severity of QOL reductions.^{15,45}

Sensitivity Analysis

One-way sensitivity analyses were performed to evaluate the effect of varying the price of dupilumab and probability of revision surgery. A Monte Carlo microsimulation with 10,000 samples was performed. Beta, gamma, and triangular distributions were used for matrix probabilities, costs, and Markov utilities, respectively. Dirichlet distributions were used to ensure that chance node probabilities summed to 1 during simulation. All parameters (probabilities, costs, and utilities) were assigned distributions based on published sample sizes for sensitivity analysis.⁴⁶

ICER scatter plots were used to graphically present all ICERs generated from the Monte Carlo simulation onto the cost-effectiveness plane (Fig. 2).^{21,47,48} The decision to accept a more expensive intervention depended on the maximum ICER which policy makers are willing to accept,²¹ which is represented graphically as a line whose slope is the willingness-to-pay (WTP) threshold.

ICER Results (Dupilumab v. Surgery)

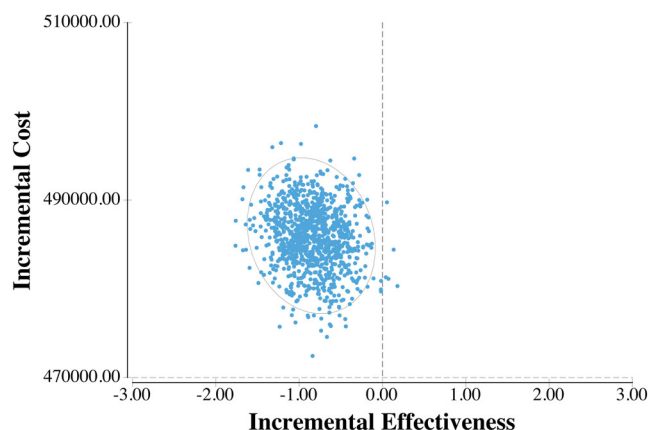


Fig. 2. The ICER Scatter Plots depict all ICERs generated from the Monte Carlo simulation onto the cost-effectiveness plane for the dupilumab versus surgical cohorts. 100% of individual ICER outcomes (dots) favored ESS when compared to dupilumab at a willingness-to-pay threshold of \$100,000-per-QALY. ESS = endoscopic sinus surgery; QALY = quality adjusted life year.

This manuscript follows the 2013 Consolidated Health Economic Evaluation Reporting Standards guidelines.⁴⁹ Cost-effectiveness analysis was performed using TreeAge Pro Healthcare Module 2015 software (TreeAge Software, Inc., Williamstown, MA, USA). Matching of cohorts was performed using propensity score matching in SPSS version 25.^{50,51}

RESULTS

Patient Characteristics and SNOT-22 Outcomes

Demographics and comorbidities of both study cohorts are shown in Table IV. The baseline SNOT-22 (SE) of the ESS cohort was 49.68 (1.40). The baseline SNOT-22 (SE) of the dupilumab cohort was 48.00 (1.69). Average SNOT-22 (SE) after first and second treatment intervals were 24.26 (1.39) and 20.09 (1.72), respectively, for the ESS cohort. Average SNOT-22 (SE) after first and second treatment intervals were 18.58 (1.25) and 16.51 (1.63), respectively, for the dupilumab cohort.

TABLE IV.
Patient Demographics and Clinical Characteristics for ESS and Dupilumab 300 mg Every 2 Weeks.

	ESS Cohort (N = 197)	Dupilumab Cohort (N = 293)
Age (SD)	50 (14)	51 (9)
Sex	52% Male	63% Male
Race	92% White	89% White
Smoking	5% Smokers	10% Smokers
Asthma	50%	57%
Previous surgery	66%	64%
AERD	20%	28%

AERD = aspirin exacerbated respiratory disease; ESS = endoscopic sinus surgery.

Cost Effectiveness

CRSwNP. With costs and utilities discounted at 3%, the model managed a cohort of patients for 36 years and demonstrated that the ESS strategy cost a total of \$50,436.99 and produced a total of 9.80 QALYs. The dupilumab treatment strategy cost a total of \$536,420.22 and produced a total of 8.95 QALYs. Because dupilumab treatment was more costly and less effective than the ESS strategy, it is dominated by ESS in the base case.

Sensitivity Analysis: One-Way Sensitivity Analysis: Cost of Dupilumab

A one-way sensitivity analysis was conducted on the cost of dupilumab, which was varied from \$0 to \$31,000. The results demonstrate that the dupilumab treatment option is dominated by ESS until the yearly cost of dupilumab reaches \$855 or below.

Sensitivity Analysis: One-Way Sensitivity Analysis: Probability of Revision Surgery

A one-way sensitivity analysis was performed on the yearly probability of revision ESS, which was varied from 1% to 100%. The results demonstrated lower cost and higher utility gained for the ESS cohort regardless of the rate of revision surgery.

Sensitivity Analysis: Probabilistic Sensitivity Analysis

The ICER scatter plot (Fig. 2) demonstrates that, at a WTP threshold of \$100,000/QALY, in 100% of the 10,000 ICER outcomes of the economic model, ESS treatment for CRSwNP was more cost-effective than dupilumab treatment.

DISCUSSION

CRSwNP is a chronic disease that encompasses heterogeneous patient populations. Until endotypes of this disease are better characterized and linked to clinical outcomes, prognostication and selection of treatment options will remain challenging. The cost-effectiveness of various interventions, therefore, is critical in a resource constrained health care system.

The current study showed that ESS offers greater cost effectiveness than dupilumab for upfront management of CRSwNP. The cohort of patients who underwent ESS with postoperative medical therapy generated less cost and more utility than those who were treated with dupilumab alone. The ESS strategy cost a total of \$50,436.99 and produced a total of 9.80 QALYs, whereas the dupilumab treatment strategy cost a total of \$536,420.22 and produced a total of 8.95 QALYs. Given the superior cost effectiveness profile for ESS regardless of prior surgical status, a trial of at least one ESS appears to be the preferred treatment option for a non-operated CRSwNP patient who fails appropriate medical therapy.

In this study, the number of prior sinus surgeries in the ESS cohort did not impact the results of the CUA. These findings suggest that revision ESS should be the preferred option for patients whose polyps and symptoms recur. When considering treatment options for the patient with recurrent symptoms after ESS, however, additional factors need to be considered that are difficult to quantify and incorporate into such an economic model. For example, multiple surgeries involve multiple recovery periods and repeated exposure to the potential negative effects of general anesthesia.⁵² In addition, revision ESS can also prove more hazardous with distorted surgical anatomy and increased risk of complications.⁵³

A substantial subset of patients with CRSwNP would prefer non-surgical intervention for management of their chronic disease due to associated risks and personal preference.⁵⁴ Recent studies have demonstrated the clinical efficacy of biologics in the treatment of patients with nasal polyps. In a randomized, controlled study of patients with severe CRSwNP, Bachert et al. found that only 1.2% of surgically naive CRSwNP patients taking dupilumab plus mometasone spray progressed to ESS after 1 year compared to 10.2% of subjects receiving only mometasone spray in the same timeframe. In study subjects with a history of prior ESS, only 1.5% of patients in the dupilumab group progressed to surgery, compared to 11.4% in the mometasone only group.^{13,55} In addition, Bachert et al. reported a modest, yet significant, 2-point reduction (0–8 scale) in bilateral nasal polyp score in both the SINUS-24 and SINUS-52 Phase 3 studies.¹³ This reduction in the need for ESS, as well as improvement in outcome measures, suggest an important role of biologic therapy in the treatment of CRSwNP patients.

Dupilumab was chosen as the comparison biologic in the current study, as it has recently gained FDA approval as a stand-alone treatment option for patients with CRSwNP. A European consensus statement identified five important factors to consider in decision making for initiating monoclonal biologic therapy in CRSwNP patients: 1) evidence of type 2 inflammation (biological biomarker), 2) need for systemic corticosteroids in the past 2 years, 3) significant quality of life impairment, 4) significant loss of smell, and 5) diagnosis of comorbid asthma. The panel concluded that biologics should be recommended for patients who have undergone prior ESS if three or more factors are present and for those patients who have not undergone prior ESS if four or more factors are present.⁵⁶

The total utility generated in the ESS cohort (9.80 QALYs) exceeded that of the dupilumab cohort (8.95 QALYs) despite assumptions made in favor of dupilumab treatment. First, the model did not incorporate rates of dupilumab treatment failure or patient dropout. Second, the model did not incorporate potential long-term complications from dupilumab therapy, such as malignancy and helminth infections, which have yet to be fully characterized. Despite these exclusions from the current model, dupilumab was found to be less cost-effective than ESS at any yearly cost of dupilumab above \$855.

In this study, several inherent limitations merit attention. HUV transition probabilities in the Markov

model for both the dupilumab and ESS cohorts were presumed to accurately represent long-term outcomes in the treatment of CRSwNP. With respect to ESS, 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.^{4,57} With respect to dupilumab, long-term HUVs and efficacy have not yet been reported. In addition, this model assumed that dupilumab would need to be taken indefinitely to achieve a sustained effect. An additional limitation was the non-randomization of cohorts. While patients were matched based on relevant demographic factors and comparable disease burden, the patients in the ESS arm ultimately chose surgical treatment demonstrating a potential selection bias.

CONCLUSION

Cost utility analysis demonstrates both primary and revision ESS to be a more cost-effective treatment option compared to dupilumab for CRSwNP patients. While the role of monoclonal biologics remains promising in the treatment of this heterogeneous disease, these findings emphasize the need for proper patient selection when considering costly interventions. Additional studies are needed to identify subsets of CRSwNP patients that will benefit most from biologic treatments in a cost-effective manner.

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