Economic analysis of surgery and biological therapy for chronic rhinosinusitis with nasal polyps

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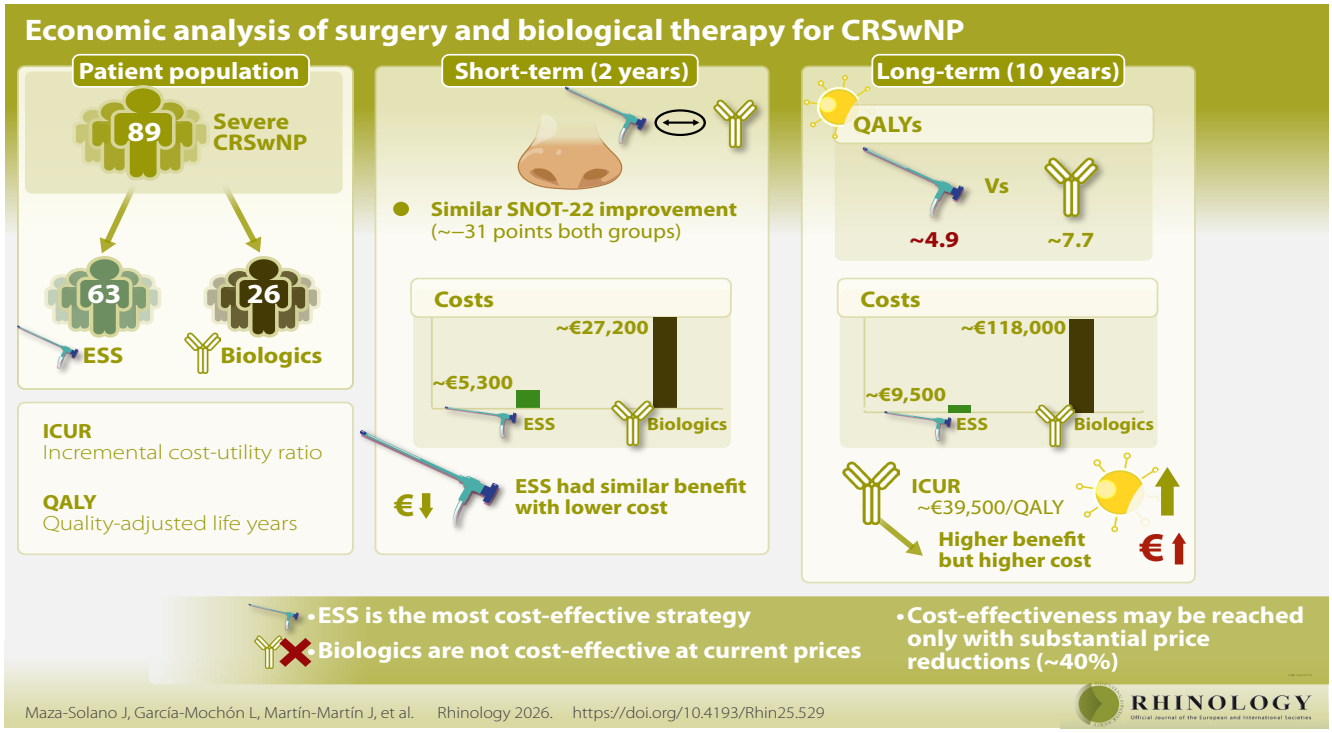

Abstract

Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) imposes major health and economic burdens. Endoscopic sinus surgery (ESS) and biologic therapy are treatment options. This study compares their effectiveness and cost-efficiency from the Spanish National Health System (NHS) perspective.

Methodology: An economic evaluation was conducted in severe CRSwNP, following Spanish-NHS guidelines. Data came from a tertiary-hospital with 10-year projections. Effectiveness was measured as reduction in the Sinonasal Outcome Test-22 (SNOT-22). Cost-utility analysis used quality-adjusted life years (QALYs). Micro-costing was applied for ESS, while annual drug costs were considered for biologics. Sensitivity analyses tested robustness.

Results: 89 patients were included (63 ESS, 26 biologics). After 2-years, both strategies achieved similar SNOT-22 improvements (-31.8 ESS, -31.0 biologics). Costs were far lower for ESS (€5,302.78) than biologics (€27,198.23), making biologics less efficient despite comparable benefit. The 2-year incremental cost-utility ratio (ICUR) for biologics was €1.2 million/QALY, above accepted thresholds. At 10-years, biologics yielded 2.75 QALYs at an incremental cost of €108,917.62 (ICUR €39,592/QALY). Sensitivity analyses showed that biologics generally remained above commonly accepted willingness-to-pay thresholds, although substantial price reductions (up to 40%) allowed ICURs to approach the upper limit of acceptability.

Conclusions: Both treatments provide meaningful improvement. ESS remained the less costly strategy and was more efficient over the short term, whereas long-term projections showed higher QALY gains with biologics at substantially greater cost. Within Spanish- NHS, biologics may approach cost-effectiveness only under favorable pricing assumptions and should be reserved for patients with contraindications or persistent disease after ESS.

Key words: antibodies, monoclonal, cost-effectiveness analysis, financing, government nasal polyps, nasal surgical procedures

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a long-standing inflammatory disorder of the nasal and paranasal mucosa, defined by symptoms persisting for at least 12 weeks, including nasal obstruction, rhinorrhea, facial pain, and olfactory dysfunction [1,2]. Its prevalence is estimated at 3-4% in Europe [3], 5% in the United States (USA) [4], and 2-4% worldwide [1]. CRSwNP is strongly associated with asthma and other type 2 (T2) inflammatory comorbidities, including aspirin-exacerbated respiratory disease (AERD), which are linked to more severe disease and higher recurrence rates after endoscopic sinus surgery (ESS) [5,6].

The health and economic burden of CRSwNP is substantial, driven by direct medical costs (outpatient care, diagnostic procedures, long-term pharmacotherapy, and surgical recurrences) and indirect costs related to reduced productivity, absenteeism, and presenteeism [7]. In Europe, direct annual healthcare costs per patient exceed €1,500 [8], nearly doubling when productivity losses are included [9]. In the USA, the total annual economic impact is estimated to surpass $10 billion [10].

Biologic therapies (BT) targeting key T2 pathways have emerged as an effective option for refractory disease [1,2]. However, high acquisition costs and the need for long-term administration raise concerns about affordability and sustainability in publicly funded healthcare systems [11,12]. ESS remains the cornerstone of treatment for most patients, although accumulated costs may arise from revision procedures and postoperative management [13].

In this context, economic evaluation can support healthcare decision-making under resource constraints. Cost-effectiveness and cost-utility analyses allow comparison of therapeutic strategies by integrating clinical outcomes and costs, particularly in chronic conditions requiring long-term assessment [14,15]. Therefore, we conducted an economic evaluation comparing ESS and BT in patients with severe CRSwNP from the perspective of the Spanish National Health System (NHS). Clinical effectiveness was assessed using changes in the Sinonasal Outcome Test-22 (SNOT-22), and efficiency was evaluated through cost-effectiveness and cost-utility analyses to provide context-specific evidence for sustainable decision-making in the NHS.

Materials and methods

Study design and population

A retrospective economic evaluation was performed comparing ESS and BT in patients with severe, uncontrolled CRSwNP. Data were obtained from the RINOBASE clinical registry of a Spanish tertiary hospital, covering patients treated between 2016-2024. Eligible patients had at least two years of follow-up after initiating either therapeutic strategy.

Patients with lower-airway comorbidities were eligible provided they did not meet the GEMA guideline criteria for BT based solely on asthma severity [16]. This ensured that treatment indication was driven exclusively by sinonasal disease, minimizing selection bias from the non-random treatment allocation. Selection followed POLINA 2.0 criteria for T2 inflammation [2], namely: blood eosinophilia >300/µL and/or >10 tissue eosinophils per high-power field (400x); nasal congestion; olfactory dysfunction; and associated respiratory comorbidities such as asthma or AERD. Baseline severity was adjusted between groups to minimize potential confounding.

Clinical and demographic variables were collected, including age, sex, comorbidities, and quality-of-life measures. Disease-specific outcomes were assessed using the SNOT-22 and visual analogue scales (VAS). Effectiveness was primarily measured as the absolute reduction in SNOT-22 score from baseline to two years. Clinically meaningful improvement was defined as a reduction of >8.9 points, corresponding to the minimal clinically important difference (MCID) [17]. Statistical analyses included normality testing (Shapiro-Wilk), non-parametric tests (Wilcoxon, Mann-Whitney U, Friedman) when appropriate, and regression modeling adjusted for baseline severity.

Health-related quality of life was assessed using quality-adjusted life years (QALYs). Utility values were derived from SNOT-22 scores using validated conversion algorithms correlating symptom improvement with the EuroQol-5 Dimensions (EQ-5D) index [18], enabling integration into the cost-utility analysis.

The study was approved by the regional Research Ethics Committee (FIS-AMYCENS-2024-03) and conducted in accordance with the Declaration of Helsinki and Spanish regulations, including Royal Decree 957/2020 and Law 3/2018 on data protection.

Economic evaluation

Cost-effectiveness and cost-utility analyses were performed following Spanish Guidelines for Economic Evaluation of Medicines [19] and the CHEERS (Consolidated Health Economic Evaluation Reporting Standards) reporting standards [20]. The analysis adopted the perspective of the Spanish-NHS, considering exclusively direct healthcare costs [19] associated with each therapeutic strategy (ESS and BT with dupilumab or mepolizumab). Omalizumab was excluded because it is not reimbursed for CRSwNP in the Spanish-NHS. This approach is consistent with methodological recommendations for evaluations supporting public funding decisions, as it objectively quantifies healthcare resource utilization while excluding indirect costs, such as productivity losses, that do not directly impact the payer.

All costs were expressed in euros and updated to 2023, based on the official salary resolution of the Andalusian Health Service (SAS). Surgical and perioperative hospital costs were estimated using a bottom-up micro-costing approach based on the clinical pathway modules of the Rhinology Unit. Each procedural stage was itemized by task and professional category (otolaryngologists, anesthesiologists, nursing staff, porters, and administrative staff). For each category, the average time allocated was multi-

Table 1. Baseline characteristics of patients in the biologic therapy and ESS treatment groups.

Variable	Biologic therapy	ESS	p-value
Total number of patients	26	63	0.584
Sex, Female (%) / Male (%)	F 13 (50.0%) / M 13 (50.0%)	F 27 (42.9%) / M 36 (57.1%)	0.702
Mean age (years)	56,65 ± 12,83	55,00 ± 13,00	0,584
Asthma comorbidity (n, %)	17 (65.4%)	46 (73.0%)	0.642
AERD comorbidity (n, %)	9 (34.6%)	17 (27.0%)	0.642
Polyp size (mean ± SD)	2.96 ± 2.14	4.89 ± 1.81	0.00024*
Endoscopic signs of active disease (n, %)	26 (100.0%)	63 (100.0%)	1.0
SNOT-22 (mean ± SD)	66.31 ± 26.21	71.06 ± 19.53	0.409
VAS – Nasal congestion (mean ± SD)	76.85 ± 30.96	83.46 ± 23.28	0.332
VAS – Olfactory dysfunction (mean ± SD)	81.92 ± 27.42	92.24 ± 15.26	0.080
VAS – General health (mean ± SD)	78.46 ± 26.65	70.24 ± 22.81	0.175
Cumulative corticosteroid dose (mean ± SD, mg)	512.87 ± 746.73	329.89 ± 263.11	0.589

ESS: Endoscopic Sinus Surgery; %: Percentage; n: Sample size; AERD: Aspirin-Exacerbated Respiratory Disease; SNOT-22: Sinonasal Outcome Test-22; SD: Standard Deviation; mg: milligrams; VAS: Visual Analogic Scale.

plied by the cost per working hour, calculated from gross annual salaries and effective working hours using SAS data. Operating room resource utilization was calculated as the sum of individual components (personnel time, anesthesia-related resources, recovery unit care, infrastructure use, and surgical consumables) rather than as a single aggregated operating room cost, as detailed in Tables S2-S5 of the Supplementary Material. Personnel costs were subsequently combined with unit costs of diagnostic tests, surgical materials, and hospital resources obtained from internal accounting modules and official tariffs (Supplementary Materials).

For the BT group, costs were estimated for two biologic drugs authorized by the Spanish Agency of Medicines and Medical Devices (AEMPS) for the indication of CRSwNP [21]. The annual acquisition cost was calculated according to official price lists, acknowledging that confidential discounts applied at hospital pharmacies may alter the real cost for the NHS. Short- and long-term adverse events related to systemic corticosteroids were not included, as the analysis focused on ESS and BT as the primary alternatives.

Cost-effectiveness analysis

The relative efficiency of both strategies was assessed through a cost-effectiveness analysis based on mean changes in SNOT-22 scores. Costs reflected the mean cumulative expenditure per patient in each group, while effectiveness was expressed as the mean reduction in SNOT-22 scores. For long-term projections, modeled absolute SNOT-22 values were first estimated for each horizon and then converted into mean reductions from baseline to ensure consistency with the 2-year cost-effectiveness analysis. Analyses were performed for two time horizons: short-term (2 years), based on observed cohort data, and long-term (10 years), using projection models. For BT, a logarithmic regression was applied to model the accrual of clinical benefit followed by a plateau over time. This approach accounts for real-world factors such as imperfect adherence, treatment interruptions, and discontinuation, which may attenuate observed effectiveness, without implying a loss of intrinsic biologic efficacy. This is consistent with clinical trial evidence showing early improvement followed by stabilization (plateau) of SNOT-22 outcomes under controlled conditions. For surgery, a dynamic model included the possibility of reinterventions (up to five surgeries), applying a 30% penalty in effectiveness for each additional procedure [22]. This approach was chosen to conservatively model progressive loss of surgical benefit over time, without assuming a complete return to preoperative SNOT-22 levels prior to each revision surgery, which could overestimate symptom volatility and does not consistently reflect real-world longitudinal outcomes in CRSwNP.

Beyond incremental cost-effectiveness ratios (ICERs), statistical analyses were performed to strengthen internal validity. Group comparisons employed Student's t-tests when normality assumptions were met, or Mann-Whitney U tests otherwise.

A linear regression model was also developed, with SNOT-22 improvement as the dependent variable and treatment type, baseline score, and other clinical factors as covariates. Results were illustrated using cost-effectiveness planes to depict the relationship between costs and clinical benefits across time horizons.

Cost-utility analysis

A cost-utility analysis was performed to assess efficiency in terms of QALYs. Utility values were derived from SNOT-22 score

Table 2. Evolution of SNOT-22 scores in patients treated with ESS or biological therapy during 2 years of follow-up. Within-group comparisons of SNOT-22 scores over time.

Table 2A. Descriptive statistics of SNOT-22 at baseline, 1 year, and 2 years

Time point	Treatment (n)	Mean	SD	Min	Max	MCID ≥ 8.9 (%)
Baseline	ESS	71.06	19.53	19	110	–
	BT	66.31	26.21	11	107	–
1 year	ESS	35.52	27.88	0	105	81.0
	BT	34.81	27.15	0	85	65.4
2 years	ESS	39.25	28.06	0	101	74.6
	BT	35.35	25.55	0	103	73.1

Table 2B. Within-group comparisons of SNOT-22

Comparison	Z statistic	Original p	Bonferroni-adjusted p
BT: Baseline vs. 1 year	28.5	0.0001	0.0002
BT: 1 year vs. 2 years	131.5	0.4041	1.0
BT: Baseline vs. 2 years	14.0	0.0001	0.0003
ESS: Baseline vs. 1 year	88.0	0.001	0.001
ESS: 1 year vs. 2 years	693.0	0.1472	0.4416
ESS: Baseline vs. 2 years	128.0	0.001	0.001

SNOT-22: Sinonasal Outcome Test-22; n: Sample size; SD: Standard Deviation; MCID: Minimum Clinically Important Difference; %: Percentage; ESS: Endoscopic Sinus Surgery; BT: Biological Therapy.

changes using a validated conversion algorithm correlating symptom improvement to the EQ-5D index [18]. QALYs were then accumulated for each treatment group and incorporated into incremental cost-utility ratios (ICURs).

As reference thresholds, the range commonly accepted in the Spanish-NHS was applied (€25,000-30,000 per QALY gained) [19]. To address uncertainty, 95% confidence intervals were estimated for the base-case ICUR at 2 years without discounting. For long-term scenarios (2 and 10 years) with 30-40% discounts, as well as the 10-year projection without discounting, deterministic analyses were applied using aggregated mean values of cost and utility, acknowledging that confidence intervals could not be estimated in these projections.

Long-term projections

Economic outcomes were projected over 2- and 10-year horizons. For ESS, a dynamic model simulated repeated interventions based on published revision intervals, with progressively shorter intervals over time (mean 4.39 years between the first and second surgery and 2.18 years thereafter) [22]. A linear function was derived to simulate reintervention timing, incorporating a 30% reduction in effectiveness with each additional surgery, thereby capturing the progressive decline in surgical benefit. Based on these values, the slope (m) was calculated as m = (2.18 - 4.39) / (4 - 1) = -0.7367, and the constant (b) as b = 4.39 - (m x 1) = 5.1267. This linear function was used to represent the temporal trend between reinterventions, enabling a dynamic and realistic simulation of cumulative costs and outcomes.

For BT, costs were projected linearly, assuming continuous treatment with full adherence, in accordance with local hospital pharmacy protocols. Full adherence was assumed throughout the projection as a conservative and transparent modeling choice from the payer perspective. Reduced real-world adherence would be expected to decrease clinical effectiveness without proportionally reducing drug acquisition costs, thereby further worsening the cost-effectiveness profile of BT. The logarithmic plateau in effectiveness reflects stabilization of clinical benefit rather than declining intrinsic efficacy or treatment discontinuation. Disease progression was modeled using logarithmic regression, capturing the typical clinical course of marked improvement during the first year followed by stabilization (plateau) without further incremental SNOT-22 reductions [23]. For the cost-effectiveness analysis, long-term modeled SNOT-22 values were converted into reductions from baseline rather than reported as absolute scores, in order to maintain consistency with the observed 2-year effectiveness metric.

Sensitivity analyses

To evaluate result robustness of the results, both probabilistic and deterministic sensitivity analyses were conducted. Probabilistic analysis employed non-parametric bootstrapping with 1,000 resampled datasets per treatment group, calculating total costs, mean SNOT-22 improvement, QALY estimates, and corresponding ICERs and ICURs. Aggregated outcomes yielded

Table 3. Cost-effectiveness and cost-utility analysis at 2 years for ESS and biological therapy, and comparative cost-effectiveness across 2 and 10 years horizons based on SNOT-22 reduction from baseline.

Table 3A. Cost-effectiveness results at 2 years

Concept	Biologic	ESS
Mean cost (SD)	€27,198.23 (823.44)	€5,302.78 (1,129.22)
Incremental cost	€21,895.45	–
Effectiveness (SNOT-22 reduction)	30.96	31.81
Incremental effectiveness (SNOT-22)	-0.85	–
ICER (€/point)	-25,759.35 €/point	–
Effectiveness (QALYs)	1.55	1.53
Incremental effectiveness (QALYs)	0.018	–
ICUR (€/QALY gained) (mean; 95% CI)	€1,216,413.89/QALY (-432,459; 334,104)	–

Table 3B. Cost-effectiveness over different time horizons

Horizon	SNOT-22 BT	SNOT-22 ESS	Cost Biologic (€)	Cost ESS (€)	ICER (€/point)	Cost per SNOT-22 point (€)
2 years	30.96	31.81	27,198.23	5,302.78	ESS dominant	BT: 878.55 ESS: 166.71
10 years	35.0	55.1	118,438.30	9,520.68	ESS dominant	BT: 3,383.95 ESS: 172.68

SNOT-22: Sinonasal Outcome Test-22; n: Sample size; SD: Standard Deviation; MCID: Minimum Clinically Important Difference; %: Percentage; ESS: Endoscopic Sinus Surgery; BT: Biological Therapy.

empirical 95% confidence intervals and were displayed on cost-effectiveness planes. Deterministic analysis applied univariate sensitivity testing to BT acquisition costs, which in Spanish hospital pharmacies are typically 30-40% below official prices due to confidential discounts. Total costs and ICURs at 2 and 10 years were recalculated under these scenarios to assess whether BT could meet accepted efficiency thresholds within the Spanish-NHS framework.

Results

Baseline characteristics

Baseline analysis showed no statistically significant differences between BT and ESS groups in most demographic or clinical variables ($p>0.05$), including age, sex, and prevalence of respiratory comorbidities such as asthma and AERD. The only significant difference was in mean nasal polyp score (NPS), which was higher in the ESS group (4.89 ±1.81) than in the BT group (2.96 ±2.14; $p=0.00024$). This difference likely reflects real-world clinical decision-making patterns, as NPS is frequently used to guide surgical indication, rather than a true difference in patient-perceived disease burden. Clinically, however, NPS does not necessarily reflect active disease, as polyp size is not a consistent marker of underlying inflammation [24]. Endoscopic evidence of active inflammation was evenly distributed between groups, confirming clinical comparability at baseline [25]. Overall, despite differences in NPS, both cohorts were considered equivalent regarding baseline severity and inflammatory activity, supporting the validity of subsequent comparative analyses (Table 1).

Health outcomes at 2 years

Mean SNOT-22 scores decreased markedly in both treatment groups after therapy initiation. In the ESS group, the baseline mean score of 71.06 (SD 19.53) declined to 35.52 at year 1 and 39.25 at year 2. In the BT group, the baseline score of 66.31 decreased to 34.81 and 35.35 at years 1 and 2, respectively. The proportion of patients achieving the MCID was high in both cohorts: 81% and 74.6% at years 1 and 2 for ESS, and 65.4% and 73.1% for BT. Within-group analyses showed statistically significant improvements from baseline to years 1 and 2 ($p<0.001$), with no significant differences between years 1 and 2, indicating stabilization of the treatment effect over time (Table 2).

Economic evaluation results

Cost-effectiveness outcomes

During the first 2 years, both strategies achieved similar clinical benefit, with mean SNOT-22 reductions of 30.96 points for BT and 31.81 points for ESS. However, BT incurred an adjusted mean cumulative cost of €27,198.23, compared with €5,302.78 for ESS, resulting in disproportionate cost-effectiveness. The cost per point of improvement was €878.55 for BT versus €166.71 for ESS (Table 3). Over a 10-year horizon, the modeled absolute SNOT-22 score was 35.0 in the BT group and 55.1 in theESS

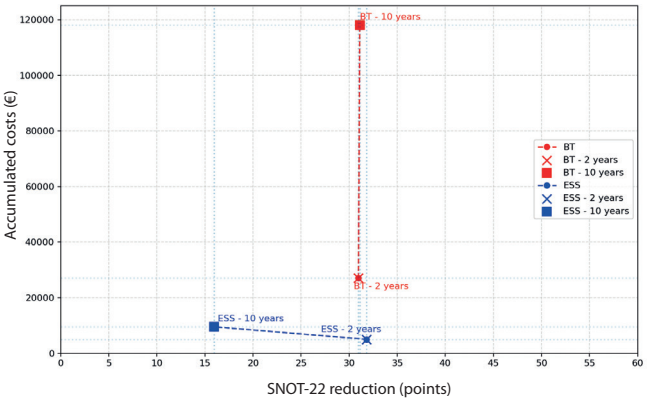

Figure 1. Cost-effectiveness plan comparing biological therapy and endoscopic sinus surgery at 2 and 10 years, using SNOT-22 reduction from baseline as the effectiveness measure. SNOT-22: Sino-Nasal Outcome Test-22; ESS: Endoscopic Sinus Surgery; BT: Biological Therapy.

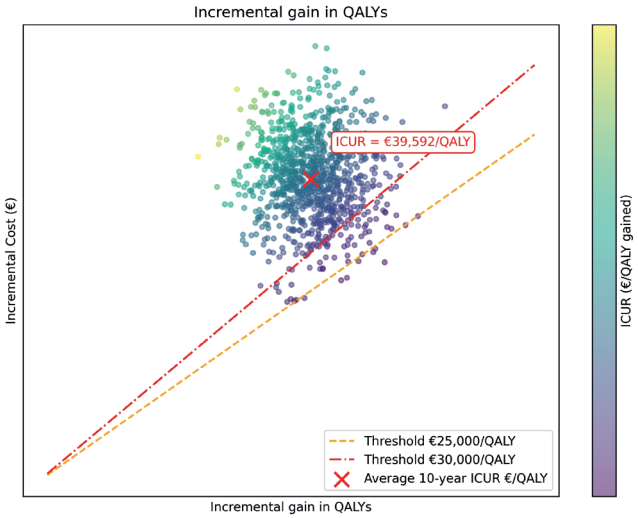

Figure 2. Probabilistic sensitivity analysis: dispersion of the incremental cost-utility ratio (ICUR) over a 10-year horizon. ICUR: Incremental Cost-Utility Ratio; QALY: Quality-Adjusted Life Year.

group. Relative to baseline, this corresponded to mean SNOT-22 reductions of 31.31 and 15.96 points, respectively. Cumulative adjusted costs were €118,438.30 for BT and €9,520.68 for ESS. Under this definition of effectiveness, BT was associated with greater clinical benefit but substantially higher cost, resulting in an ICER of €7,095.61 per additional SNOT-22 point gained. Cost-per-point analyses yielded values of €3,782.76 for BT and €596.53 for ESS at 10 years (Table 3; Figure 1). The long-term difference reflects the modeling structure: biologic therapy achieves an early improvement followed by sustained disease control, whereas ESS incorporates symptom recurrence and re-interventions over time, which reduce the net long-term SNOT-22 reduction from baseline despite partial benefit from revision procedures (Table 3; Figure 1).

Cost-utility outcomes

At 2 years, mean costs per patient were €27,198.23 for BT and €5,302.78 for ESS, yielding an incremental difference of €21,895.45. QALY gains were 1.55 for BT and 1.53 for ESS, with the marginal 0.018-QALY benefit in BT associated with substantially higher costs, yielding a cost per QALY of €1,216,413.89 (95% CI: -432,459 to 334,104), well above accepted thresholds (Table 4). At 10 years, BT utility rose from 0.85 at year 2 to 0.90 by year 7, remaining stable thereafter, while ESS utility declined due to reinterventions (0.84 initially, 0.65 at years 5-6, 0.55 at years 7-8, and 0.47 at years 9-10). Cumulative adjusted costs were €118,438.30 for BT versus €9,520.68 for ESS, an incremental difference of €108,917.60. Total QALY gains were 7.68 for BT and 4.93 for ESS, a 2.75-QALY advantage for BT at higher cost, resulting in an ICUR of €39,592 per QALY gained (Table 4).

Probabilistic sensitivity analysis results

The bootstrapping analysis, applied over a 10-year horizon, demonstrated a wide dispersion of ICUR values, with the majority of simulations remaining above the efficiency thresholds commonly accepted within the Spanish-NHS. Although a limited number of iterations approached threshold values under favorable assumptions, more than 90% of the 1,000 simulations exceeded the €30,000/QALY threshold. These findings indicate that, from a probabilistic perspective, BT has a low likelihood of being considered cost-effective compared with ESS in the context of a public payer (Figure 2).

Results of the univariate deterministic sensitivity analysis

Assuming 30-40% reductions in biologic acquisition costs, ICURs decreased, particularly over the 10-year horizon. At 2 years, the ICUR decreased to €763,110.06/QALY with a 30% reduction and to €612,008.78/QALY with a 40% reduction. At 10 years, ICURs further decreased to €32,885.28/QALY and €27,692.63/QALY, respectively (Table 4). Despite these reductions, values close to commonly accepted cost-effectiveness thresholds were observed only under the most favorable long-term pricing assumptions.

Discussion

Before the introduction of BT, CRSwNP management followed a stepwise approach based on appropriate medical therapy (AMT) and, in refractory cases, ESS. Patel et al. demonstrated that ESS after AMT failure led to significant improvements in quality of life, endoscopic outcomes, and work productivity, supporting surgery as a cost-effective intervention prior to the availability of biologics [26].

The economic burden of CRSwNP has been evaluated across different healthcare systems, consistently demonstrating substantial costs, although with marked heterogeneity driven

Table 4. Comparative cost-utility analysis of biological therapy and ESS at 2 and 10 years. Impact of biological price discounts on economic efficiency: deterministic sensitivity analysis.

Time Horizon	Applied Discount	BT Cost (€)	ESS Cost (€)	Incremental Cost (€)	BT QALYs	ESS QALYs	Incremental QALYs	ICUR (€/QALY gained)
2 years	Without	27,198.23	5,302.78	21,895.45	1.55	1.53	0.018	1,216,413.89
2 years	30%	19,038.76	5,302.78	13,735.98	1.551	1.533	0.018	763,110.06
2 years	40%	16,318.94	5,302.78	11,016.16	1.551	1.533	0.018	612,008.78
10 years	Without	118,438.30	9,520.68	108,917.62	7.68	4.929	2.751	39592.33
10 years	30%	99,921.60	9,520.68	90,400.92	7.684	4.935	2.749	32885.28
10 years	40%	85,647.10	9,520.68	76,126.42	7.684	4.935	2.749	27692.63

ESS: Endoscopic Sinus Surgery; QALY: Quality-Adjusted Life Year; ICUR: Incremental Cost-Utility Ratio; %: Percentage; BT: Biological Therapy

by healthcare organization and analytic perspective. In the USA, incremental annual costs increase notably in surgically treated patients and in those with asthma comorbidity [27,28], with population-level estimates exceeding $60 billion annually [29]. In Canada, patients with CRSwNP have been reported to incur considerable out-of-pocket expenses and productivity losses [30], while disease recurrence and nasal polyposis have been associated with increased need for revision surgery and systemic corticosteroids, leading to higher costs and reduced quality of life [31,32]. In Europe, Clarke et al. estimated a mean cost of £2,173 per patient in the year of surgery [33], while a USA study by Lerner et al. identified surgical time and intraoperative supplies as key drivers of ESS-related costs, with mean expenditures approaching $9,000 per procedure [34].

Cross-country comparisons remain challenging due to differences in healthcare financing and cost-reporting methodologies. In the USA, private insurance systems allow detailed capture of direct and indirect costs, often resulting in higher reported expenditures [35,36], whereas public healthcare systems rely mainly on standardized cost-utility analyses with limited inclusion of indirect costs [37,38]. In Spain, economic evaluations are typically restricted to direct healthcare costs calculated through clinical tariffs and hospital micro-costing, with productivity losses poorly captured [19,39,40]. As illustrated in the Netherlands, where indirect costs accounted for most of the total burden (€5,659 annually versus €1,501 in direct healthcare costs) [8], this perspective may underestimate the overall socioeconomic impact of CRSwNP. Within this context, and from the perspective of the Spanish-NHS, our results demonstrate substantially higher cumulative 10-year expenditures for biologic therapy than for endoscopic sinus surgery (€118,438.30 versus €9,520.68), corresponding to €3,782.76 versus €596.53 per SNOT-22 point gained, respectively.

BT have represented a significant advance in the management of refractory CRSwNP but are associated with high long-term costs. In our analysis, the mean annual cost per patient was €14,274.52, remaining substantially higher than surgical management and showing effectiveness that tends to plateau over time. Importantly, the Spanish healthcare system is highly decentralized, and biologic acquisition costs may vary considerably across autonomous communities depending on local procurement agreements and reimbursement policies [41]. In this context, Mora et al. reported lower annual costs of approximately €10,000-12,000 in Catalonia [42], reflecting region-specific pricing rather than standardized national estimates [41,42]. Even so, these figures remain lower than the $30,000-40,000 per year commonly reported in the USA [43,44], where different financing and pricing mechanisms apply. Moreover, Codispoti and Mahdavinia have highlighted that widespread use of biologics without rigorous patient selection may pose significant challenges to healthcare sustainability [45].

Our findings are consistent with international economic models showing greater cost-effectiveness of ESS compared with biologics. At two years, ESS achieved a mean reduction of 31.81 SNOT-22 points at a cost of €166.71 per point, compared with €878.55 per point for biologics, resulting in a negative ICER (-€25,759.35 per point) and indicating dominance of surgery. However, this dominance applied only to the 2-year cost-effectiveness analysis based on observed SNOT-22 reduction. Over the 10-year horizon, when effectiveness was expressed as modeled SNOT-22 reduction from baseline, biologic therapy showed greater clinical benefit (31.31 vs 15.96 points) at substantially higher cost, yielding an ICER of €7,095.61 per additional SNOT-22 point gained rather than ESS dominance. Previous studies support these findings: Parasher et al. reported an ICUR of $691,691/QALY for dupilumab versus ESS [46]; Scangas et al. found that surgery generated more QALYs at lower cost over a long-term horizon [47]; and Álvarez et al. concluded that ESS clearly dominated, reserving biologics for selected patients [48]. In our analysis, the base-case ICUR for biologics at 10 years was €39,592/QALY, remaining above commonly accepted willingness-to-pay thresholds within the Spanish-NHS and approaching these thres-

holds only under highly favorable pricing assumptions explored in sensitivity analyses. These results align with the budget impact analysis by Fieux et al., which showed that first-line use of biologics substantially increased direct costs compared with ESS [49]. While surgery remains the most cost-effective option for the majority of patients within the Spanish-NHS, some authors have suggested that biologics may offer added value in specific subgroups, such as patients with highly inflammatory T2 phenotypes, corticosteroid dependence, or multiple surgical recurrences [33,47]. However, even in these settings, associated costs often exceed efficiency thresholds, underscoring the importance of careful patient stratification. Overall, these results indicate that ESS should remain the preferred strategy in most cases, with biologics reserved for well-defined clinical scenarios and reimbursement decisions informed primarily by sensitivity analyses rather than list-price base-case estimates.

Probabilistic sensitivity analysis confirmed the robustness of our findings, with most simulations exceeding the €30,000/QALY threshold, indicating a low overall probability of BT being cost-effective compared with ESS within the Spanish-NHS. While some iterations approached lower ICUR values, the majority remained above commonly accepted willingness-to-pay thresholds. Deterministic sensitivity analyses showed that a 30% reduction in biologic acquisition costs resulted in a 10-year ICUR that remained slightly above the threshold, whereas a 40% price reduction yielded an ICUR within the accepted range (€27,693/QALY); however, probabilistic analysis indicated that this favorable scenario represented only a minority of simulations. Importantly, this result reflects optimistic pricing assumptions rather than the base-case analysis, which remained above thresholds (€39,592/QALY). These findings suggest that biologics may approach cost-effectiveness only under substantial price reductions, while ESS remains cost-effective across all modeled scenarios, reinforcing concerns about the long-term sustainability of biologic therapy in publicly funded healthcare systems [50].

Several limitations should be acknowledged. This was a single-center study, which may limit generalizability. Cost estimates were derived from local micro-costing data and may not fully reflect other institutional or regional settings. The assumption of full adherence to BT over a 10-year horizon may overestimate both costs and effectiveness, although this approach was intentionally conservative from a payer perspective. Not all BT approved internationally for CRSwNP were included. In particular, omalizumab was excluded because it lacks price and reimbursement approval for this indication within the Spanish-NHS. Indirect costs were not considered, as the analysis was conducted strictly from the Spanish-NHS perspective, likely underestimating the broader socioeconomic burden of CRSwNP. Finally, the analysis reflects current biologic market prices. While patent expiration and biosimilar entry may reduce costs in the future, the magnitude and timing of such reductions remain uncertain. To address this uncertainty, deterministic sensitivity analyses applying 30-40% price reductions were conducted.

Conclusions

Both ESS and BT provide significant symptom relief in patients with severe uncontrolled CRSwNP. However, within the Spanish-NHS context, ESS remains substantially more cost-effective, while biologics entail high costs with limited likelihood of being cost-effective at current prices. In this context, biologics should be reserved for patients in whom surgery is contraindicated or insufficient. Moreover, their potential role as disease-modifying agents and as part of combined strategies should be further investigated in future studies.

Author contributions

Conception: JMS, SSG. Design: JMS, LGM. Supervision: LGM, JMM. Resource: JMS, LGM, SSG. Materials: JMS, SSG. Data collection and/or processing: JMS, SSG. Analysis and/or interpretation: JMS, LGM, JMM. Literature search: JMS. Writing: JMS, LGM, PH. Critical reviews: JMS, LGM, JMM, PH.

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Conflict of interest

JMS has received honoraria for consultancy, projects, advisory boards and talks from Astra Zeneca, GlaxoSmithKline, MSD, Novartis and Sanofi/Regeneron; LGM declares that it has no conflict of interest; JMM declares that it has no conflict of interest; PH has received grants and/or speaking/advisory fees from Sanofi/Regeneron, Astra Zeneca, and GSK; SSG has received grants and/or speaking/advisory fees from Sanofi/Regeneron, Astra Zeneca, Medtronic and GSK.

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SUPPLEMENTARY MATERIAL

Table S1. Clinical Pathway of the Sinonasal Inflammation Unit, Clinical Management Unit of Otorhinolaryngology and Head and Neck Surgery, Virgen Macarena University Hospital, Seville, Spain.

1. Candidate eligibility assessment stage					
WHEN? Phase of the process	**WHAT? Activity**	**WHO? Professional**	**WHERE? Healthcare center**	**HOW? Quality criteria**	**USING WHAT? Resources**

1	ENT Assessment: targeted rhinological evaluation.	ENT.	Rhinology Clinic.	• Anamnesis.
				• Personal and family medical history.
				• Comorbidities.
				• Nasofibroscopy.
				• Comprehensive ENT examination.
				• Exclusion of alternative forms of non-polypoid chronic rhinosinusitis.
				• Phenotypic assessment during consultation:
				  • High Power Field (HPF) sampling.
				  • Request for type 2 inflammation (T2) biomarker panel.
				• Administration of disease-specific quality-of-life questionnaires and Visual Analogue Scales (VAS) for severity assessment.
				• Radiological evaluation (CT scan).
				• Specialist referrals (interconsultations)
					• DIRAYA Electronic Medical Record.
					• Rhinoscope.
					• Nasofibroscopy.
					• POLINA 2.0 Guideline: Consensus Document on CRSwNP (SEORL-CCC).
					• Diagnostic management protocol for patients with inflammatory sinonasal disease of the ENT Clinical Management Unit (2.1.1. UINS).
					• Patient information leaflet on CRSwNP.

2	Diagnosis of olfactory dysfunction.	ENT. Nurse. Nursing Care Assistant.	Rhinology Clinic.	• Olfactometry.	• DIRAYA Electronic Medical Record + RINOBASE. • BOT-8 diagnostic olfactory test.
3	Radiological evaluation.	Radiologist.	Radiology Department.	• Anatomical diagnosis. • Pathological diagnosis.	• DIRAYA Electronic Medical Record + RINOBASE. • CT scan protocols.

4	Evaluation of individual, family, social, and environmental needs.	Nurse.	ENT Clinical Management Unit (Nurse-led Counseling Clinic).	• Clinical Nursing Diagnoses.
				• Nursing Needs Diagnoses.
				• Pre-therapeutic quality of life assessment (medical or surgical).
					• DIRAYA Electronic Medical Record + RINOBASE.
					• Specific questionnaires."
					  • SNOT-22.
					  • VAS.
					  • ACT (Asthma Control Test).
					  • A14 Adherence Questionnaire

5	Therapeutic decision.	ENT.	Rhinology Clinic.	• Results review consultation.
				• Enrollment in ADM (Assisted Demand Management, Andalusian Health Service).
					• DIRAYA Electronic Medical Record.
					• POLINA 2.0 Guideline: Consensus Document on CRSwNP (SEORL-CCC).
					• Appropriate medical treatment (AMT).
					• ESS treatment.
					  • Informed consent.
					  • Surgical Demand Registry.
					• Revision ESS.
					  • Informed consent.
					  • Surgical Demand Registry.
					• Biological treatment.
					  • Informed consent.
					  • Biological drugs committee for CRSwNP

2.1. Endoscopic Sinus Surgery (ESS) stage					
WHEN? Phase of the process	**WHAT? Activity**	**WHO? Professional**	**WHERE? Healthcare center**	**HOW? Quality criteria**	**USING WHAT? Resources**
1	Surgical procedure planning.	• ENT. • Administrative staff.	ENT Department (Management Area)	• Virtual surgery. • Surgical simulation.	• DICOM image processing software (Osirix, Horos) • Rendering software (Blender).
2	Surgical scheduling.	• ENT. • Administrative staff.	ENT Department (Management Area)	• Criteria for outpatient major surgery (OMS). • Morning or afternoon surgical sessions. • Preoperative assessment. • Instructions.	• Surgical waiting list. • Patient prioritization list. • Telephone call.
3	Preoperative assessment	• Nurse. • Laboratory technician. • Radiology technician. • Radiologist. • Anaesthetist.	• Surgical Block Clinical Management Unit. • Laboratory. • Radiology.	• Blood sample collection. • ECG (Electrocardiogram). • Biometry. • Hematological analysis. • Radiological study. • Pre-anesthetic assessment.	• Sample collection material. • Scale. • Stadiometer. • Laboratory equipment. • Radiology equipment.
4	Surgical procedure	• ENT surgeon. • Radiologist. • Nurse. • Nursing Care Assistant. • Orderly.	Operating room.	• Surgical procedure. • Neuronavigation. • Intraoperative phenotyping.	• Endoscopy tower. • Optics. • Microdebrider and drilling equipment. • Sample collection (HPF). • Recording hardware and software. • Neuronavigator. • Endonasal hemostatic agents and packing.
5	Immediate postoperative care	• Nurse. • Nursing Care Assistant. • Anaesthetist.	Surgical Block Clinical Management Unit.	• Monitoring of vital signs. • Analgesia control. • Assessment of post-anesthesia recovery.	• Patient monitoring equipment.
6	Postoperative assessment	• ENT.	ENT inpatient ward	• At 6 hours post-surgery in OMS. • Within 24 hours in hospitalized patients.	• Clinical Pathway and written protocol of Precision and Personalized Medicine for the indication and surgical planning of functional and extensive endoscopic surgeries based on phenotypes of the ENT Clinical Management Unit (UGC-ORL, 2.3.1 UINS). • Hospitalization protocols of the ENT Clinical Management Unit.
7	Hospital discharge	• ENT. • Nurse. • Nursing Care Assistant. • Care coordinator. • Operations coordinator.	ENT inpatient ward	• Medical discharge report. • Nursing continuity of care report. • Planning of wound care in the Day Unit and by outpatient clinical nurses of the ENT Clinical Management Unit. • Notification to the patient's primary healthcare professionals regarding the surgical procedure performed (if applicable). • Follow-up consultation planning.	• Clinical Pathway and written protocol of Precision and Personalized Medicine for the indication and surgical planning of functional and extensive endoscopic surgeries based on phenotypes of the ENT Clinical Management Unit (UGC-ORL, 2.3.1 UINS). • Hospitalization protocols of the ENT Clinical Management Unit.
8	Assessment of personal, family, social, and environmental needs	• Nurse	ENT Clinical Management Unit (Nursing Advisory Service)	• Clinical Nursing Diagnoses. • Nursing Needs Diagnoses.	• DIRAYA Electronic Medical Record + RINOBASE. • Monitoring for postoperative complications.

2.2.- Follow-up stage (indefinite six-monthly monitoring/assessment					
WHEN? Phase of the process	**WHAT? Activity**	**WHO? Professional**	**WHERE? Healthcare center**	**HOW? Quality criteria**	**USING WHAT? Resources**
1	• ENT follow-up: targeted rhinological evaluation. • Biannual review.	ENT.	ENT Department	• Anamnesis. • Personal and family medical history. • Comorbidities. • Nasofibroscopy. • Comprehensive ENT examination. • Exclusion of alternative forms of non-polypoid chronic rhinosinusitis. • Phenotypic assessment during consultation: • High Power Field (HPF) sampling. • Request for type 2 inflammation (T2) biomarker panel. • Administration of disease-specific quality-of-life questionnaires and Visual Analogue Scales (VAS) for severity assessment. • Radiological evaluation (CT scan). • Specialist referrals (interconsultations).	• DIRAYA Electronic Medical Record. • Rhinoscope. • Nasofibroscopy. • POLINA 2.0 Guideline: Consensus Document on CRSwNP (SEORL-CCC). • Diagnostic management protocol for patients with inflammatory sinonasal disease of the ENT Clinical Management Unit (2.1.1. UINS). • Patient information leaflet on CRSwNP.
2	• Assessment of personal, family, social, and environmental needs. • Biannual review.	Nurse.	ENT Clinical Management Unit (Nursing Advisory Service)	• Clinical Nursing Diagnoses. • Nursing Needs Diagnoses. • Assessment of pre-therapeutic quality of life (medical or surgical). • Olfactory evaluation: olfactometry.	• DIRAYA Electronic Medical Record + RINOBASE. • Specific questionnaires." • SNOT-22. • VAS. • ACT (Asthma Control Test). • A14 Adherence Questionnaire.

3.1. Biologic therapy stage					
WHEN? Phase of the process	**WHAT? Activity**	**WHO? Professional**	**WHERE? Healthcare center**	**HOW? Quality criteria**	**USING WHAT? Resources**
1	ENT Assessment: targeted rhinological evaluation.	• ENT. • Hospital Pharmacist.	Rhinology Clinic. Hospital Pharmacy Department.	• Anamnesis. • Personal and family medical history. • Comorbidities. • Nasofibroscopy. • Comprehensive ENT examination. • Exclusion of alternative forms of non-polypoid chronic rhinosinusitis. • Phenotypic assessment during consultation: • High Power Field (HPF) sampling. • Request for type 2 inflammation (T2) biomarker panel. • Administration of disease-specific quality-of-life questionnaires and Visual Analogue Scales (VAS) for severity assessment. • Radiological evaluation (CT scan). • Specialist referrals (interconsultations).	• DIRAYA Electronic Medical Record. • Rhinoscope. • Nasofibroscopy. • POLINA 2.0 Guideline: Consensus Document on CRSwNP (SEORL-CCC). • Diagnostic management protocol for patients with inflammatory sinonasal disease of the ENT Clinical Management Unit (2.1.1. UINS). • Patient information leaflet on CRSwNP.
2	Therapeutic Planning.	• ENT. • Administrative staff.	ENT Department (Management Area)	• Day Hospital criterio. • Morning or afternoon sessions. • Instructions.	• Patient Prioritization List. • Phone Call.
3	Assessment of personal, family, social, and environmental needs.	Nurse.	ENT Clinical Management Unit (Nursing Advisory Service)	• Clinical Nursing Diagnoses. • Nursing Needs Diagnoses. • Pre-therapeutic medical quality of life assessment. • Olfactory evaluation.	• DIRAYA Electronic Medical Record + RINOBASE. • Specific questionnaires. o SNOT-22. o VAS. o ACT (Asthma Control Test). o A14 Adherence Questionnaire. • BOT-8 diagnostic olfactory test

3.1. Biologic therapy stage					
WHEN? Phase of the process	**WHAT? Activity**	**WHO? Professional**	**WHERE? Healthcare center**	**HOW? Quality criteria**	**USING WHAT? Resources**
4	Medical intervention: First injection • Mepolizumab. • Dupilumab.	• ENT. • Nurse. • Nursing Care Assistant. • Orderly.	ENT Department (Management Area)	• Vital signs monitoring. • Observation for 1 hour.	• Diagnostic management protocol for patients with inflammatory sinonasal disease of the ENT Clinical Management Unit (2.1.1. UINS). • Vital signs monitoring equipment. • DIRAYA Electronic Medical Record + RINOBASE.
5	Assessment of personal, family, social, and environmental needs.	• Nurse.	ENT Clinical Management Unit (Nursing Advisory Service)	• Clinical Nursing Diagnoses. • Nursing Needs Diagnoses.	• DIRAYA Electronic Medical Record + RINOBASE. • Adverse event detection.

3.2.- Follow-up stage (Six-month review and subsequently annual review).					
WHEN? Phase of the process	**WHAT? Activity**	**WHO? Professional**	**WHERE? Healthcare center**	**HOW? Quality criteria**	**USING WHAT? Resources**
1	• ENT follow-up: targeted rhinological evaluation. • Biannual review	• ENT.	ENT Department	• Anamnesis. • Personal and family medical history. • Comorbidities. • Nasofibroscopy. • Comprehensive ENT examination. • Exclusion of alternative forms of non-polypoid chronic rhinosinusitis. • Phenotypic assessment during consultation: • High Power Field (HPF) sampling. • Request for type 2 inflammation (T2) biomarker panel. • Administration of disease-specific quality-of-life questionnaires and Visual Analogue Scales (VAS) for severity assessment. • Radiological evaluation (CT scan). • Specialist referrals (interconsultations).	• DIRAYA Electronic Medical Record. • Rhinoscope. • Nasofibroscopy. • POLINA 2.0 Guideline: Consensus Document on CRSwNP (SEORL-CCC). • Diagnostic management protocol for patients with inflammatory sinonasal disease of the ENT Clinical Management Unit (2.1.1. UINS). • Patient information leaflet on CRSwNP.
2	• Assessment of personal, family, social, and environmental needs. • Biannual review.	• Nurse.	ENT Clinical Management Unit (Nursing Advisory Service)	• Nursing Needs Diagnoses. • Pre-therapeutic medical quality of life assessment. • Olfactory evaluation.	• DIRAYA Electronic Medical Record + RINOBASE. • Specific questionnaires. o SNOT-22. o VAS. o ACT (Asthma Control Test). o A14 Adherence Questionnaire. • BOT-8 diagnostic olfactory test

Table S2. Salary costs (€ 2023) of public healthcare personnel involved in the direct care of patients with CRSwNP, categorized by professional groups and job positions. Source: Resolution 0003/2023 on Healthcare Personnel Remuneration for the fiscal year 2023, Directorate-General of Human Resources, Andalusian Health Service.

				Specific Allowance									TOTAL COST
Job position	Sub-group	Level	Salary (x 12)	Position-based Allowance (x12)	HIA (x 12)	PRF (x 12)	Monthly Total	Additional Pay (June–December)	Extra (x 2)	Annual Total	PPS	TOTAL	Additional 28%*
ENT	A1	N.24	1.294,59	680,45	912,34	790,73	3.678,11	1.703,07	1.479,33	50.502,12	6.712,23	57.214,35	73.233,37
Hospital Pharmacist	A1	N.24	1.294,59	680,45	912,34	790,73	3678,11	1.703,07	1.479,33	50.502,13	6.712,23	57.214,35	73.233,37
Nurse	A2	N.21	1.119,41	552,57	0,00	625,25	2.297,23	625,25	1.368,98	31.555,22	2.691,18	34.246,40	43.835,39
Nursing Care Assistant	C2	N.16	699,53	408,50	0,00	387,46	1.495,49	387,46	1.101,64	20.924,08	730,83	21.654,91	27.719,29
Administrative staff	C1	N.17	840,49	434,65	0,00	401,43	1.676,57	401,43	1.161,09	23.243,88	1.286,08	24.529,96	31.398,35
Orderly	E	N.14	640,25	371,01	0,00	373,58	1.384,84	373,58	1.011,26	19.387,76	614,45	20.002,21	25.602,83

HIA = Healthcare Institutions Allowance; PRF = Personnel Remuneration Fund; PPS = Professional Performance Supplement; * Percentage that reflects the social security cost incurred by the Andalusian Health Service.

Table S3. Estimated staff cost per unit of working time by category.

Job position	Annual working hours	Total annual remuneration (€)	TOTAL COST (€) Additional 28%*	60-minute cost (€)	30-minute cost (€)	15-minute cost (€)	5-minute cost. (€)
ENT	1.540	57.214,35	73.233,37	47,55	23,78	11,89	3,97
Hospital Pharmacist	1.540	57.214,35	73.233,37	47,55	23,78	11,89	3,97
Nurse	1.540	34.246,40	43.835,39	28,46	14,23	7,12	2,37
Nursing Care Assistant	1.540	21.654,91	27.719,29	17,99	8,99	34,5	1,5
Administrative staff	1.540	24.529,96	31.398,35	20,39	10,19	5,1	1,7
Orderly	1.540	20.002,21	25.602,83	16,63	8,3	4,15	1,38

* Percentage that reflects the social security cost incurred by the Andalusian Health Service.

Table S4. Estimated total personnel cost for nasal polyposis throughout the entire time horizon according to the clinical pathway, under what is considered standard care.

Step	Profesional	Activity	Total duration	Cost (€)
Surgical Candidate Selection Phase				**245, 31**
1	Administrative staff	ENT consultation appointment	5 minutes	1,7
2	ENT	Otorhinolaryngology consultation	45 minutes	35,67
3	Nurse	Performance of olfactory tests	60 minutes	28,46
4	Nursing Care Assistant	Performance of olfactory tests	60 minutes	17,99
5	Administrative staff	Radiology appointment	5 minutes	1,7
6	Radiologist	Performance of CT scan	60 minutes	47,55
7	Administrative staff	Laboratory test appointment	5 minutes	1,7
8	Laboratory nurse	Performance of T2 blood test	30 minutes	14,23
9	Clinical laboratory specialist	T2 report	15 minutes	11,89
10	Administrative staff	Appointment for histological tests (HPF)	5 minutes	1,7
11	Histopathology technician	Sample preparation	30 minutes	8,99
12	Pathologist	HPF report with cell count	30 minutes	23,78
13	ENT	ENT consultation for interpretation of radiological and olfactory tests	45 minutes	35,67
14	Nurse	Nursing diagnoses of needs and assessment of quality of life	30 minutes	14,23
Surgical Phase (ESS) for CRSwNP (excluding the cost of the surgical procedure: €3095.47; (Chapter 2)				**870,79**
1	Administrative staff	Appointment for pre-anesthesia consultation and preoperative tests	10 minutes	3,4
2	Laboratory nurse	Performance of preoperative study	30 minutes	14,23
3	Clinical laboratory specialist	Preoperative report	15 minutes	11,89
4	Pre-anesthesia Nurse	Performance of preoperative study	30 minutes	14,23
5	Anaesthetist	Preoperative evaluation	30 minutes	23,78
6	Administrative staff	Appointment for hospital admission	5 minutes	1,7
7	Administrative staff	Registration of hospital admission	15 minutes	1,7
8	Orderly	Transfer to hospitalization unit	15 minutes	4,16
9	Hospitalization Nurse	Admission to hospitalization unit	30 minutes	14,23
10	Nursing Care Assistant	Preparation and hygiene	15 minutes	4,5
11	Hospitalization Nurse	Management of transfer to operating room	5 minutes	2,37
12	Orderly	Transfer to operating room	15 minutes	4,16
13	Operating Room Nurse (x2)	Surgical procedure	150 minutes	14,23
14	Nursing Care Assistant (x2)	Surgical procedure	150 minutes	90,01
15	ENT (x2)	Surgical procedure	150 minutes	237,77
16	Anaesthetist	Surgical procedure	150 minutes	118,89
17	Anaesthetist	Post-surgical care	30 minutes	23,78
18	Post-surgical Care Nurse	Post-surgical care	60 minutes	28,46
19	Nursing Care Assistant	Post-surgical care	60 minutes	17,99
20	Orderly	Transfer to hospitalization unit	15 minutes	4,16
21	Hospitalization Nurse	Post-surgical care	240 minutes	113,87
22	Nursing Care Assistant	Post-surgical care	240 minutes	71,99
23	ENT	Post-surgical hospital care	60 minutes	47,55
24	Administrative staff	Appointment for follow-up consultation	5 minutes	1,7
Post-surgical follow-up phase each year (*biannual check-ups)				**495,32 (*247,66)**
26	Administrative staff (x2)	ENT consultation appointment	5 minutes	3,4
27	ENT (x2)	Otorhinolaryngology consultation	45 minutes	71,35
28	Nurse	Performance of olfactory tests	60 minutes	28,46

Step	Profesional	Activity	Total duration	Cost (€)
29	Nursing Care Assistant	Performance of olfactory tests	60 minutes	17,99
30	Administrative staff	Laboratory test appointment	5 minutes	1,7
31	Laboratory nurse	Performance of T2 blood test	30 minutes	14,23
32	Clinical laboratory specialist	T2 report	15 minutes	11,89
33	Administrative staff	Appointment for histological tests (HPF)	5 minutes	1,7
34	Histopathology technician	Sample preparation	30 minutes	8,99
35	Pathologist	HPF report with cell count	30 minutes	23,79
36	ENT	ENT consultation for interpretation of radiological and olfactory tests	45 minutes	35,67
37	Nurse (x2)	Nursing diagnoses of needs and assessment of quality of life	30 minutes	28,46
Phase of medical treatment with a biologic drug				**14.365,51**
1	Administrative staff	Appointment for biologic drugs consultation	5 minutes	1,7
2	ENT	Otorhinolaryngology consultation	45 minutes	35,67
3	Hospital Pharmacist	Hospital Pharmacy Consultation	30 minutes	23,1
4	Nurse	Biologic Therapy Injectable	5 minutes	2,37
5	Annual cost of biological drugs	Average between Dupilumab and Mepolizumab	5 minutes	14274,52
6	Nurse for care after first injection	Care after the first injection and home-based patient education	60 minutes	28,46
7	Nursing Care Assistant for care after first injection	Care after the first injection and home-based patient education	60 minutes	17,99
8	Administrative staff	Appointment for follow-up visit	5 minutes	1,7
Follow-up phase during the first year after biological therapy				**247,66**
9	Administrative staff (x2)	ENT consultation appointment	5 minutes	3,4
10	ENT (x2)	Otorhinolaryngology consultation	45 minutes	71,35
11	Nurse	Performance of olfactory tests	60 minutes	28,46
12	Nursing Care Assistant	Performance of olfactory tests	60 minutes	17,99
13	Administrative staff	Laboratory test appointment	5 minutes	1,7
14	Laboratory nurse	Performance of T2 blood test	30 minutes	14,23
15	Clinical laboratory specialist	T2 report	15 minutes	11,89
16	Administrative staff	Appointment for histological tests (HPF)	5 minutes	1,7
17	Histopathology technician	Sample preparation	30 minutes	8,99
18	Pathologist	HPF report with cell count	30 minutes	23,78
19	ENT	ENT consultation for interpretation of radiological and olfactory tests	45 minutes	35,67
20	Nurse (x2)	Nursing diagnoses of needs and assessment of quality of life	30 minutes	28,46
Follow-up phase during the second year after biological therapy				**14.400,83**
21	Administrative staff	ENT consultation appointment	5 minutes	1,7
22	ENT	Otorhinolaryngology consultation	45 minutes	35,67
23	Annual cost of biological drugs	Media entre Dupilumab y Mepolizumab	5 minutes	14274,52
24	Nurse	Performance of olfactory tests	60 minutes	28,46
25	Nursing Care Assistant	Performance of olfactory tests	60 minutes	17,99
26	Administrative staff	Laboratory test appointment	5 minutes	1,7
27	Laboratory nurse	Performance of T2 blood test	30 minutes	14,23
28	Clinical laboratory specialist	T2 report	15 minutes	11,89
29	Administrative staff	Appointment for histological tests (HPF)	5 minutes	1,7
30	Histopathology technician	Sample preparation	30 minutes	8,99
31	Pathologist	HPF report with cell count	30 minutes	23,78
32	ENT	ENT consultation for interpretation of radiological and olfactory tests	45 minutes	35,67
33	Nurse	Nursing diagnoses of needs and assessment of quality of life	30 minutes	14,23

S5. Details of consumables used from January to December 2023 during endoscopic sinonasal surgeries in Otorhinolaryngology (000195)

CAT_SEGMEN	CAT_D_LEVEL06	CAT_D_GENERIC	2.023	Dif	Var	
313 Disposable Medical Supplies. Specific Material for Videosurgery and Endoscopy	Videosurgery: Electrosurgical Forceps and Scissors	Bipolar and Ultrasonic Forceps 5 mm Ø - Length: [20-30)	E59941	2.481	0	0,0%
		Bipolar and Ultrasonic Forceps 5 mm Ø - Length: [30-45)	E59943	0	-2.481	-100,0%
	Miscellaneous (01.13)	Sheath for Fiberscope - Diameter: [3.4-3.4]; Angle: 0º	B42121	0	0	'-
		Protective Cleaning Sheath for Optics - Diameter: [4-4]; Angle: 0º;	C28530	3.174	-338	-9,6%
		Protective Cleaning Sheath for Optics - Diameter: [4-4]; Angle: 30º	C34074	2.728	-811	-22,9%
		Adapter for Working Channel - Lateral Suction Tube: NO; Diameter: [15-15]; Angle: 0º	E38723	0	-56	-100,0%
314 Disposable Medical Supplies. Specific Operating Room Materials	Disposable Surgical Clothing for Personnel	Plastic Surgical Shoe Covers – GC	B38265	4	-15	-76,7%
		Female Surgical Cap – GC	B38343	37	-94	-71,9%
		Surgical Protective Glasses, Field 3 – GC	B39356	6	-23	-78,6%
		High-Risk Surgical Cap – GC	B40561	85	5	5,7%
		Surgical Mask EFB 95% – Fastening System: Elastic Bands; Shape: Rectangular	B40804	0	0	'-
		Surgical Mask EFB 98% Splash-Resistant – Fastening System: Elastic Bands; Shape: Rectangular	E81289	893	-856	-48,9%
	Disposable Surgical Drapes	Fenestrated Surgical Drape with Adhesive / Medium – Minor Dimension Range: 50–100; Major Dimension Range: 50–100	B41889	1.343	205	18,0%
		Surgical Drape / Medium – Minor Dimension Range: 50–100; Major Dimension Range: 35–100	C27066	0	0	'-
		Surgical Drape / Medium – Minor Dimension Range: 35–100; Major Dimension Range: 50–100	F73607	204	21	11,7%
	Surgical Gloves	Sterile Surgical Glove – Glove Size:6.0;	B40853	0	-33	-100,0%
		Sterile Surgical Glove – Glove Size:6.5;	B40854	8	-57	-88,2%
		Sterile Surgical Glove – Glove Size:7.0;	B40855	8	-46	-85,7%
		Sterile Surgical Glove – Glove Size:7.5;	B40856	8	-44	-85,1%
		Sterile Surgical Glove – Glove Size:8.0;	B40857	10	-13	-56,1%
	Manual Cutting and Incision Instruments	Scalpel Blade – Blade Number:[11-11];	B38135	6	6	'-
		Scalpel Blade – Blade Number:[15-15];	B38298	15	-3	-18,2%
		Scalpel Blade – Blade Number:[12-12];	B40216	16	2	11,5%
		Scalpel Blade – Blade Number:[21-21];	B46855	15	-7	-33,1%
		NEEDLE ELECTRODE TIP / Tungsten - Terminal Type: straight; Shaft Length: (5–7]	D82357	1.046	1.046	'-
		ELECTROSURGICAL UNIT: SUCTION COAGULATOR WITH FLEXIBLE TIP – Length: (15–20); Diameter: [8–8]	E17199	847	847	'-
		NEEDLE ELECTRODE TIP / Tungsten – Tip Type: Straight; Shaft Length: (2–3]	E66082	1.713	-471	-21,6%
		NEEDLE ELECTRODE TIP / Tungsten – Tip Type: Straight; Shaft Length: [0–2] cm	E66083	2.251	-1.004	-30,8%
			F71338	4.880	4.880	'-
	Miscellaneous (01.11)	INSTRUMENT CLEANING BRUSH – GC	B37379	230	39	20,7%
		IRRIGATION SOLUTION NaCl 0.9% – CAPACITY: [150–250]; Outer sterile bag: Nº	D61235	301	95	45,8%
	Surgical Hygiene	STERILE SURGICAL HAND SCRUB BRUSH – GC	B40985	8	4	88,1%
		SURGICAL SCRUB LIQUID SOAP – 2; Capacity: (20–500] ml; Composition with %: Chlorhexidine 4%	E85822	241	0	0,0%
		SURGICAL SCRUB LIQUID SOAP – 2; Capacity: (0–20] ml; Composition with %: Chlorhexidine 4%	F40773	219	107	95,0%

CAT_SEGMEN	CAT_D_LEVEL06	CAT_D_GENERIC	2.023	Dif	Var	
316 Disposable Medical Supplies. Specific Material for Ventilation and Monitoring	Ventilotherapy and Aerosol Therapy	Oxygen Extension Tube – Length: [0–600) cm	B38895	18	1	6,1%
		Oxygen Mask with Reservoir / Adults – GC	B39361	9	-60	-87,5%
		Nasal Oxygen Cannula, Glasses Type / Adults – Distal connection: luer; Extension length: [0–300) cm	B39513	44	5	12,6%
		Variable Concentration Oxygen Mask / Adults – Max. FiO_2: [50–50]%	B39661	74	-18	-19,8%
		Inhalation Aerosol Spacer Chamber with Mask / neonates - GC	B40124	169	85	100,0%
		Nebulizer with Mask / adults - GC	B41690	0	-21	-100,0%
		Spacer Chamber for Aerosol Inhalation with Mask / adults - GC	B44298	733	321	78,2%
		Nebulizer for Environmental Contamination Prevention - GC	B51062	392	7	1,8%
		Variable Concentration Oxygen Mask / Adults – Max FiO_2: [60-60]	B59584	0	0	'-
		Pulse Oximetry Sensor, Adhesive Strip Type, Digital / Neonate – Compatible Equipment: Nellcor Technology	D40942	966	-648	-40,2%
	Electrodes for Monitoring	Monitoring Electrode Short / Adults – Size: Adult; Radiotransparent: No; Electrode Connection Type: Snap	B40767	64	4	6,3%
		Monitoring Electrode Short / Pediatric – Size: Neonate; Radiotransparent: No; Electrode Connection Type: Snap	C26276	2.377	609	34,5%
	Miscellaneous (01.10)	Adapter for Sterile Water Reservoir - GC	B38446	0	0	'-
		Conductive Gel 250 ml – Volume: [250–250]; Indications: ECG	B43078	0	0	'-
		Sterile Water Reservoir for Humidification with Connector – Volume: [500–1000)	D78112	571	370	183,9%
			D80617	0	-5	-100,0%
322 Disposable Medical Supplies. Specific Material for Otolaryngology	Surgical drills	Ethmoid Irrigating Blade Tip – Length: [0–15) mm; Diameter: [0.40–0.42) mm; Tip type: convex; Angulation: [0–15)°; Blade type	E84096	42.488	6.420	17,8%
		Ethmoid Irrigating Blade Tip – Length: [0–15) mm; Diameter: [0.29–0.32) mm; Tip type: convex; Angulation: [0–15)°; Blade type	E84094	2.348	0	0,0%
		Irrigation/Aspiration Burr Tip – Tip type: Bullet; Burr type: Curved; Burr diameter-1: (0.2–0.3] mm; Tip surface: Diamond-coated	E84199	47.835	5.792	13,8%
		Irrigation/Aspiration Burr Tip – Tip type: Round; Burr type: Curved; Burr diameter-1: (0.42–0.45] mm; Tip surface: Diamond-coated	E84197	64.032	13.390	26,4%
		Ethmoid Irrigation Blade Tip – Length: 0–15 mm; Diameter: 0.40–0.42 mm; Tip type: Concave; Angulation: 0–15°; Blade type:	E84266	0	-1.614	-100,0%
		Irrigation/Aspiration Burr Tip – Tip type: Oval; Burr type: Curved; Burr diameter-1: (0.40–0.42] mm; Tip surface: Cutting	E85070	36.047	4.736	15,1%
		Ethmoid Irrigator Blade Tip – Length: [0–15) mm; Diameter: [0.42–0.48] mm; Tip type: Concave; Angle range: [0–15)°; Blade type:	E85463	2.706	-5.412	-66,7%
		Drill Bit Tip with Irrigation/Aspiration – Tip type: Bullet; Burr type: Curved; Burr diameter-1: 0.2–0.3 mm; Tip surface: Diamond-coated	E85661	35.338	7.730	28,0%
		Drill Bit Tip with Irrigation/Aspiration – Tip type: Bullet; Burr type: Curved; Burr diameter-1: 0.3–0.4 mm; Tip surface: Diamond-coated	E85826	40.733	-11.039	-21,3%

CAT_SEGMEN	CAT_D_LEVEL06	CAT_D_GENERIC	2.023	Dif	Var	
		Drill Bit Tip with Irrigation/Aspiration – Tip type: Bullet; Burr type: Curved; Burr diameter-1: 0.3–0.4 mm; Tip surface: Diamond-coated	E85857	57.844	5.919	11,4%
		Etmoid Irrigator Blade Tip – Length: 0–15 mm; Diameter: 0.20–0.29 mm; Tip type: Concave; Angle: 0–15°; Blade type:	E86551	3.683	107	3,0%
		Coagulation Electrode Tip – Length: 25–50 mm.	D47819	0	-4.612	-100,0%
	Surgical material for rhinology.	Adjustable Septal Plug – Diameter: 32 mm.	B38623	231	0	0,0%
		Straight Nasal Packing with Cannula and Balloon – Length: [0–30); Width: [75–100]	B39818	0	0	'-
		Straight Nasal Plug with Thread 66–100 mm – Length: [55–100]; Width: [10–25)	B41995	882	882	'-
		Straight Nasal Plug with Thread and Gel 30–65 mm – Length: [0–30); Width: [0–10)	B51469	10.000	3.750	60,0%
		Nasal Speculum – Blade length: [30–40]; Size: medium	B85158	1.271	508	66,7%
		Hyaluronic Acid Sheet – Larger dimension of sheet: [25–50]; Smaller dimension of sheet: [25–35)	C23761	0	-819	-100,0%
		Straight Nasal Pack with Thread and Gel 30–65 mm – Length: [45–55); Width: [10–25)	D69855	10.696	2.880	36,8%
		Straight Nasal Tamponade with Cannula and Balloon – Length: [55–100]; Width: [10–25)	E03560	0	-1.071	-100,0%
		Pressure Gauge for Sinusplasty Balloon – Maximum Pressure: [20–20]	E65766	198	0	0,0%
		Intranasal Splint – Major Length: [50–100); Minor Length: [50–75); Thickness: [0.50–0.50]	E76463	1.488	1.022	219,5%
		Intranasal Splint – Major Length: [50–100); Minor Length: [50–75); Thickness: [1.0–1.0]	E80292	5.805	2.468	73,9%
		Epistaxis Catheter – Length: [95–95]; Diameter: 15	E94021	4.149	2.806	209,0%
		Intranasal Splint – Major length: [50–100); Minor length: [50–75); Thickness: [1.5–1.5]	E96753	250	-705	-73,9%
		Straight Nasal Plug with Thread and Gel 66–100 mm – Length: [55–100]; Width: [10–25)	F22710	5.965	0	0,0%
		Anatomical Nasal Plug without Thread 66–100 mm – Length: [55–100]; Width: [10–25)	D46162	227	-398	-63,6%
Total				**402.412**	**568.912**	**13,9%**

Number of surgeries: 130

Total cost of consumables (fungibles): €402,412

Cost per surgery: €3,095.47**

Table S6. Annual cost comparison of surgical and biologic treatment in patients with CRSwNP (€ 2023)

	Cost (€2023)
Primary Surgical Intervention	
Candidate selection phase	245.31
ESS surgical phase for CRSwNP	870.79
Surgical procedure	3095.47
Total cost of primary surgical intervention	4,211.57
Follow-up of surgical patients without revision surgery	
Semi-annual follow-up	247.66
Annual follow-up (247.66 x2)	495.32
Biologic therapy (first injection)	
Medical treatment, including annual biological drug cost (14,274.52€)	14,365.51
Follow-up during the first year after biological therapy	247.66
Total annual cost of first biological injection	14,613.17
Follow-up cost of patients on biological therapy without surgical review (from the second year onward)	14,400.83