Real-world epidemiological outcomes of biologic therapy for chronic rhinosinusitis with nasal polyps: a big data analysis

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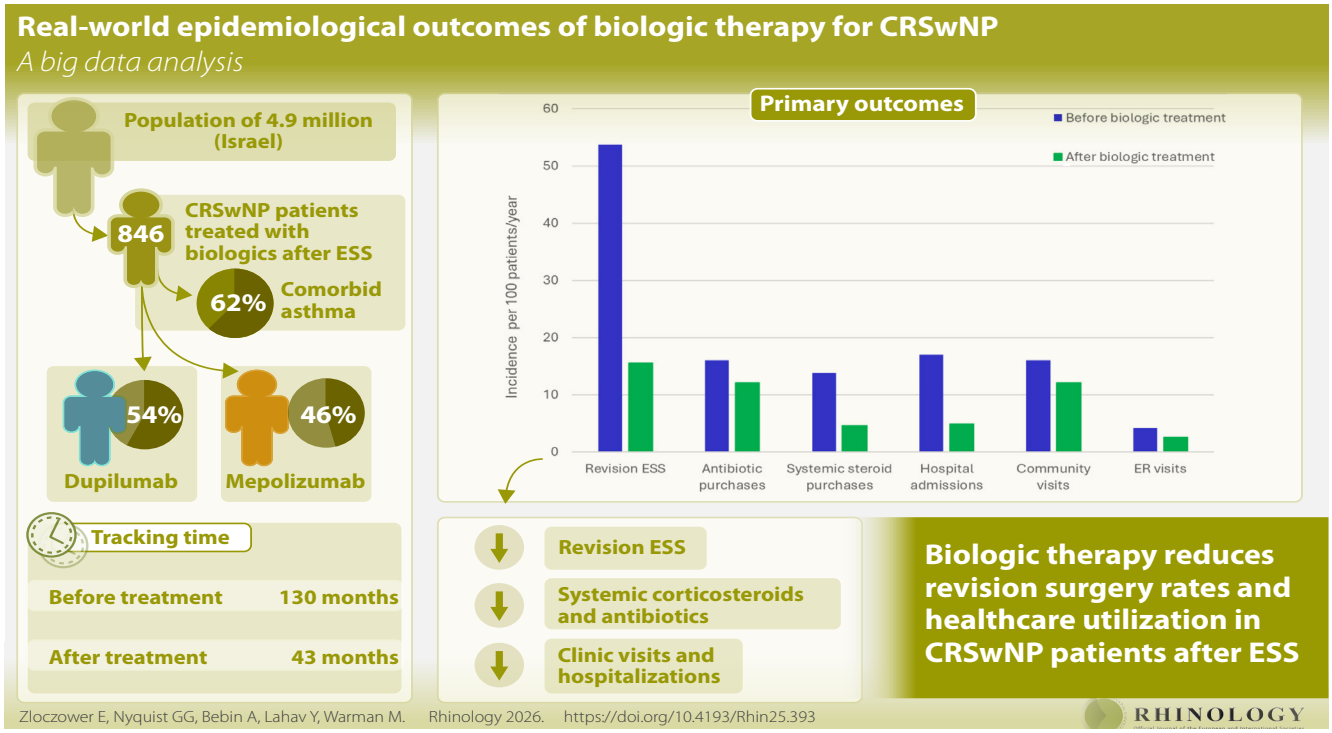

Abstract

Background: Biologic therapy has emerged as a key treatment for chronic rhinosinusitis with nasal polyps (CRSwNP), particularly in refractory cases, but its effect on healthcare utilization is not well established.

Methodology: We conducted a retrospective big-data analysis using the Clalit Health Services database, identifying all CRSwNP patients treated with dupilumab or mepolizumab following endoscopic sinus surgery (ESS) between 2010–2024. We assessed antibiotic and systemic steroid use, visits to clinics, emergency rooms (ER), hospitalizations, and repeat ESS before and after biologic initiation.

Results: Among 861 patients (54.2% on dupilumab, 45.8% on mepolizumab), 62% had asthma. Median therapy duration was 25 months. Mean follow-up was 130 ± 78 months before treatment and 43 ± 42 months after.

Biologics significantly reduced antibiotic and systemic steroid use, as well as community clinic, hospitalization, and revision ESS rates. Serum eosinophils declined from 520 ± 440 to 430 ± 460 cells/μL.

Conclusions: Post-ESS biologic therapy in CRSwNP patients is associated with reduced healthcare utilization and systemic medication use, highlighting its positive impact on disease burden and healthcare efficiency.

Key words: chronic rhinosinusitis, nasal polyps, biologic treatment

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a persistent inflammatory disease of the nasal cavity and sinuses, characterized by nasal obstruction, anosmia, and rhinorrhea, significantly affecting quality of life and imposing a substantial healthcare burden [1,2]. While first-line management includes intranasal corticosteroids and short courses of systemic corticosteroids, many patients experience refractory symptoms requiring repeated courses of systemic therapy or endoscopic sinus surgery (ESS) [3,4]. However, ESS is not always curative, and recurrence is common, particularly in patients with underlying type 2 inflammation or comorbid asthma [5].

In recent years, the emergence of biologic therapies targeting type 2 inflammatory pathways—specifically IL-4, IL-5, and IgE—has transformed the management of severe CRSwNP. Dupilumab, an IL-4 receptor α antagonist, and mepolizumab, an IL-5 antagonist, have demonstrated efficacy in reducing nasal polyp burden, improving symptom scores, and decreasing the need for systemic corticosteroids and revision surgeries in both randomized controlled trials and real-world studies [6–9]. These agents have been incorporated into international guidelines, such as EPOS 2020 and EUFOREA 2023, for patients with severe, uncontrolled CRSwNP [1,10].

Despite their proven clinical benefits, the broader real-world impact of biologics on healthcare utilization and traditional treatment metrics remains incompletely understood. Population-based studies assessing long-term outcomes—including systemic corticosteroid use, surgical intervention, and healthcare resource consumption—are lacking. In this study, we leveraged a large national healthcare database to evaluate the real-world effectiveness of biologics in patients with CRSwNP who had previously undergone ESS, focusing on clinical outcomes and healthcare utilization patterns.

Materials and methods

Ethics

The study was approved by the institutional review board and CHS National Data Use Committee (IRB approval number KMC-24-0045). All data were anonymized before analysis. Due to regulatory restrictions, data regarding specific biologic agents or comparisons between biologics were not permitted.

Study population

The initial cohort comprised all individuals insured by Clalit Health Services (CHS), as identified in the CHS database. CHS is the largest healthcare provider in Israel, covering approximately 50% of the national population—over five million individuals. Inclusion criteria included all patients diagnosed with chronic rhinosinusitis or nasal polyps between 2010 and 2024 (Table S1 for relevant ICD-9 codes). From this cohort, we included only those who received treatment with dupilumab or mepolizumab and had undergone ESS before initiating biologic therapy. We excluded individuals under 16 years of age, those who had not undergone ESS, and those treated with other biologic agents (e.g., omalizumab, benralizumab).

Data collection

This study utilized the MDClone® platform (https://www.mdclone.com), a technology tool designed to access and extract data from healthcare systems. The platform employs a longitudinal data approach, allowing for the retrieval of time-related data points for each patient. Data were extracted from the Clalit Health Services (CHS) nationwide database, which includes both hospital and community medical settings. Extracted variables included age at diagnosis of chronic rhinosinusitis (CRS) and initiation of biologic therapy, comorbid asthma and atopic dermatitis, the number of endoscopic sinus surgeries (ESS), and prescriptions for antibiotics and systemic steroids. Additionally, we reviewed data on ER visits, hospitalizations, and office visits related to CRS. For each patient, we documented the specific biologic agent used, duration of treatment, and dosing intervals.

Outcome measures

Primary outcome measures included antibiotic and systemic steroid prescription (Table S2), revision ESS rates, and number of visits, ER admissions, and hospitalizations. All primary outcomes were required to be temporally associated with a concurrent CRS diagnosis, as defined by the relevant ICD-9 codes. For instance, a prescription for systemic corticosteroids was considered CRS-related only if it was linked to a CRS diagnosis recorded in the patient's medical file within 72 hours. Importantly, per CHS policy, all CRS patients considered for biologic therapy must have a verified diagnosis of nasal polyposis on physical (endoscopic) examination. Secondary outcomes included rates of conjunctivitis and arthritis, and serum hypereosinophilia (>1.5 K/μl) during the first 3 months of biologic treatment. Serum eosinophil levels were calculated as the mean value over the five years preceding biologic therapy initiation.

Biologic treatment

Dupilumab (Dupixent®, Sanofi-Regeneron) was administered subcutaneously in the dosage of 300 mg. Mepolizumab (Nucala®, GSK) was administered subcutaneously in the dosage of 100 mg.

Statistical analysis

Continuous variables were summarized using means, standard deviations, and medians, while frequencies and percentages represented categorical variables. Incidence rates per 100 person-years were calculated for various clinical outcomes before and after the initiation of biologic therapy, to account for differences in follow-up duration between the pre- and post-

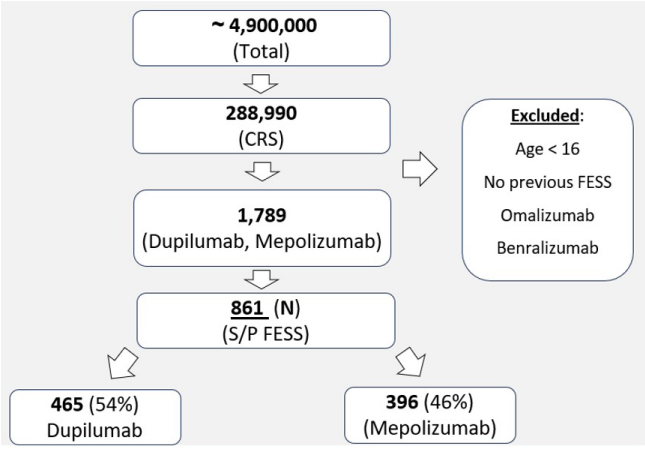

Figure 1. Study population flowchart. CRS – Chronic Rhinosinusitis; FESS – Functional Endoscopic Sinus Surgery.

treatment periods. For each clinical outcome, rate ratios (RRs) with 95% confidence intervals (CIs) and p-values were calculated using mixed-effects Poisson regression models. These models were used to compare the incidence rates before and after initiation of biologic therapy, while accounting for within-subject correlation due to repeated measures. Changes in eosinophil count and percentage before and after treatment were evaluated using mixed models. Receiver operating characteristic (ROC) analysis was conducted to assess the predictive value of pre-treatment serum eosinophil levels for revision ESS.

Results

Of the total cohort of 4.9 million individuals, 288,990 were diagnosed with chronic rhinosinusitis (CRS), and 1,789 received biologic therapy. Among them, 861 patients had undergone endoscopic sinus surgery (ESS) before initiating biologics—465 (54%) were treated with dupilumab and 396 (46%) with mepolizumab (Figure 1). Patient demographics are detailed in Table 1. The mean age at CRS diagnosis was 43 ± 14 years, and the mean age at biologic initiation was 53 ± 15 years. The sex distribution was nearly equal, with 52% female patients. The majority (N = 530, 62%) had a concurrent diagnosis of asthma.

The mean follow-up duration was 130 ± 78 months before treatment and 43 ± 42 months after biologic initiation. The average interval between biologic doses was 33 days (IQR: 29–46), and the median treatment duration was 25 months (IQR: 8–49), with a mean of 9.2 ± 4.5 biologic doses per year. Patients had a median of 4 ESS procedures (IQR: 2–7) before starting biologics. A total of 135 patients (16%) underwent revision ESS following biologic therapy, with a median interval of 7 months (IQR, 3–17) between biologic initiation and surgery.

Clinical outcomes before and after biologic therapy are summarized in Table 2 and Figure 2. Statistically significant reductions were observed in the use of antibiotics and systemic corticosteroids following biologic initiation (relative risk (RR) = 1.66 (1.46-1.89) and 4.59 ((3.8-5.56), respectively; both P < 0.001). Revision ESS rates also declined significantly (RR = 5.13 (4.65-5.66), P < 0.001). Healthcare utilization decreased across several domains, including community clinic visits (RR = 1.67 (1.47-1.9)), ER admissions (RR = 2.83 (2.18-3.67)), and hospitalizations (RR = 5.72 (4.79-6.84)), all with P < 0.001.

Serum eosinophil levels declined significantly following treatment, from a median of 0.44 K/μL (IQR: 0.31–0.63) to 0.30 K/μL (IQR: 0.11–0.60) (P < 0.001). Hypereosinophilia occurred in 19 patients (2.2%) within the first three months of therapy. Trends in biologic use over time are illustrated in Figure 3. No significant increases were observed in the rates of conjunctivitis or arthritis post-treatment.

Table 1. Patient demographics and characteristics.

Characteristic	Patients N = 861
Age at diagnosis, years	
Mean ± SD	43 ± 14
Median (IQR)	42 (32, 53)
Age at initiation of biologic therapy, years	
Mean ± SD	53 ± 15
Median (IQR)	53 (42, 65)
Sex, n (%)	
Male	409 (48)
Female	452 (52)
Comorbidities, n (%)	
Atopic dermatitis	40 (5)
Asthma	530 (62)
Biologic therapy dosing interval, days	
Mean ± SD	46 ± 60
Median (IQR)	33 (29, 46)
Duration of biologic therapy, months	
Mean ± SD	35 ± 36
Median (IQR)	25 (8, 49)
Number of biologic purchases per person per year	
Mean ± SD	9.2 ± 4.5
Median (IQR)	10 (6, 12.5)
Median (IQR)	4 (2, 7)
Blood eosinophil count before biologic Tx, K/μl	0.51 ± 0.41
Mean ± SD	0.44 (0.3, 0.62)
Median (IQR)	
Hypereosinophilia (>1.5) during the first 3 months of biologic Tx, n (%)	19 (2.2)
Patients who did not receive biologic therapy within the last 6 months	170 (20)
Patients who did not receive biologic therapy within the last 12 months	124 (14)
Patients who needed revision surgery after biologic therapy initiation, n (%)	135 (16)
Time to first revision surgery after biologic therapy initiation, months	
Mean ± SD	14 ± 17
Median (IQR)	7 (3, 17)

Table 2. Clinical outcomes before and after biologic treatment.

Clinical parameter	Before treatment	After treatment	RR* (95% CI, p-value)
Tracking time, months (mean ± SD)	130 ± 78	43 ± 42	
Functional endoscopic sinus surgery Incidence per 100/year (95% CI)	53.78 (52.31-55.3)	15.64 (14.3-17.11)	5.13 (4.65-5.66, <0.001)
Antibiotic purchases Incidence per 100/year (95% CI)	16.09 (15.29-16.93)	12.17 (10.99-13.47)	1.66 (1.46-1.89, <0.001)
Systemic steroid purchases Incidence per 100/year (95% CI)	13.83 (13.09-14.61)	4.65 (3.94-5.48)	4.59 (3.8-5.56, <0.001)
Emergency department visits Incidence per 100/year (95% CI)	4.25 (3.85-4.69)	2.62 (2.1-3.26)	2.83 (2,18-3.67, <0.001)
Community clinic visits Incidence per 100/year (95% CI)	16.11 (15.31-16.95)	12.11 (10.93-13.4)	1.67 (1.47-1.9, <0.001)
Hospital admissions Incidence per 100/year (95% CI)	17.05 (16.23-17.92)	4.97 (4.24-5.83)	5.72 (4.79-6.84, <0.001)
Conjunctivitis diagnosis Incidence per 100/year (95% CI)	5.38 (4.93-5.88)	4.55 (3.85-5.37)	1.18 (0.98-1.43, 0.08)
Arthritis diagnosis Incidence per 100/year (95% CI)	0.69 (0.54-0.89)	0.43 (0.25-0.73)	2.08 (1.07-4.03, 0.03)
Eosinophil count, K/µl			<0.001
Mean ± SD	0.52 ± 0.44	0.43 ± 0.46	
Median (IQR)	0.44 (0.31, 0.63)	0.3 (0.11, 0.6)	

* Rate Ratio represents the incidence rate before treatment relative to after treatment, estimated using mixed-effects Poisson regression. Values >1 indicate higher incidence before treatment.

Table 3 presents outcomes stratified by asthma status. Both patients with and without asthma experienced significant improvements across all clinical and healthcare utilization measures (P < 0.001). The reduction in systemic corticosteroid use was more pronounced among patients with asthma (RR = 5.46 (4.32-6.9), P<0.001) compared to those without asthma (RR = 3.12 (2.26-4.31), P<0.001). Similarly, revision ESS rates declined more substantially in the asthma group (RR = 5.52 (4.87-6.25)) than in the non-asthma group (RR = 4.48 (3.82-5.26)) (both P < 0.001). Outcome trends stratified by asthma status are shown in Figure 3 (D).

Receiver operating characteristic (ROC) analysis demonstrated limited discriminatory ability of baseline eosinophil counts for predicting revision ESS within 24 months (AUC = 0.554; 95% CI, 0.483–0.625). The optimal threshold of 0.404 K/µL yielded a sensitivity of 0.53 and a specificity of 0.61, indicating a very weak predictive association (Table S3 and Figure S1).

Discussion

In this cross-sectional, population-based study, we used big data analysis to evaluate the impact of biologic therapies on patients with CRSwNP. Our findings demonstrate that biologics significantly reduced the rates of antibiotic and systemic corticosteroid purchases, revision endoscopic sinus surgery (ESS), community clinic visits, emergency room admissions, and hospitalizations. In addition, serum eosinophil levels declined significantly following the initiation of biologic therapy, with only 2.2% of patients developing hypereosinophilia within the first 3 months of treatment. These results are consistent with previously published randomized controlled trials (RCTs) and real-world data supporting the efficacy of biologics in CRSwNP.

Biologic treatments for CRSwNP were introduced in Israel beginning in 2018 with dupilumab, followed by mepolizumab in 2019. In our healthcare system, eligibility criteria for biologic therapy vary across health maintenance organizations (HMOs), and co-payment is typically required. In Clalit Health Services (CHS), the criteria for biologics in CRS include: 1) Evidence of nasal polyps 2) chronic use of intranasal corticosteroids for more than 3 months, and 3) at least two courses of systemic corticosteroids in the preceding year (each consisting of prednisone 40 mg daily for 5 days). Notably, CHS does not require previous ESS as a prerequisite for biologic therapy. However, to align our cohort with EPOS 2020/EUFOREA 2023 guidelines [1,10], we included only patients who had undergone ESS before initiating biologic treatment. The median number of ESS procedures per patient was four, in line with previous reports [11,12]. The efficacy of dupilumab for CRSwNP has been well established in double-blind RCTs [3,13]. In a multicenter, prospective trial, Bachert et al. demonstrated that dupilumab reduced the need for systemic corticosteroids and revision ESS. More recently, accumulating real-world evidence has supported these findings, with follow-up periods of one [14-16], two [11,17], three [18], and four [19] years showing sustained

Table 3. Clinical outcomes before and after biologic treatment, stratified by concurrent asthma diagnosis.

Clinical parameter	Before treatment	After treatment	RR* (95% CI, p-value)
Functional endoscopic sinus surgery, incidence per 100 patients/year (95% CI)			
With prior asthma	50.37 (48.56-52.25)	13.98 (12.5-15.62)	5.52 (4.87-6.25, <0.001)
Without prior asthma	59.35 (56.85-61.96)	19.98 (17.19-23.24)	4.48 (3.82-5.26, <0.001)
Antibiotic purchases, incidence per 100 patients/year (95% CI)			
With prior asthma	16.17 (15.16-17.24)	11.53 (10.2-13.04)	1.78 (1.52-2.09, <0.001)
Without prior asthma	15.96 (14.69-17.34)	13.84 (11.54-16.58)	1.44 (1.16-1.79, 0.001)
Systemic steroid purchases, incidence per 100 patients/year (95% CI)			
With prior asthma	14.99 (14.02)	4.34 (3.55-5.3)	5.46 (4.32-6.9, <0.001)
Without prior asthma	11.93 (10.84-13.13)	5.44 (4.07-7.26)	3.12 (2.26-4.31, <0.001)
Emergency department visits, incidence per 100 patients/year (95% CI)			
With prior asthma	3.85 (3.37-4.39)	1.76 (1.29-2.41)	3.55 (2.47-5.1, <0.001)
Without prior asthma	4.91 (4.23-5.7)	4.85 (3.57-6.58)	2.14 (1.46-3.13, <0.001)
Community visits, incidence per 100 patients/year (95% CI)			
With prior asthma	16.17 (15.16-17.24)	11.53 (10.2-13.04)	1.78 (1.52-2.09, <0.001)
Without prior asthma	16.01 (14.74-17.4)	13.6 (11.33-16.33)	1.47 (1.19-1.83, <0.001
Hospital admissions, incidence per 100 patients/year (95% CI)			
With prior asthma	17.32 (16.28-18.43)	4.75 (3.92-5.75)	6.23 (5.01-7.75, <0.001)
Without prior asthma	16.61 (15.32-18.02)	5.56 (4.18-7.4)	4.75 (3.48-6.48, <0.001)

* Rate Ratio represents the incidence rate before treatment relative to after treatment, estimated using mixed-effects Poisson regression. Values >1 indicate higher incidence before treatment.

improvements in patient-reported outcome measures (PROMs) such as SNOT-22 scores after 6 months of treatment. Objective improvements, including reductions in nasal polyp scores, were observed after 12–24 months. These studies also reported decreased need for systemic corticosteroids and revision ESS following initiation of dupilumab.

Mepolizumab has also shown efficacy in CRSwNP, although its effect appears milder than that of dupilumab. A double-blind RCT demonstrated that mepolizumab reduced revision ESS rates in refractory CRSwNP [10] and decreased systemic corticosteroid use compared to placebo [20]. Consistently, our findings show a significant reduction in both revision ESS and systemic corticosteroid use following treatment with dupilumab or mepolizumab. The maximal reduction in ESS rates occurred after two years of treatment and remained stable thereafter, while reductions in corticosteroid use were more gradual and sustained throughout the study period.

When examining trends over time, we observed that peak rates of revision ESS and serum eosinophil levels occurred approximately one year before the initiation of biologic therapy. This likely reflects the lag between the clinical decision to pursue biologics and the actual purchase date, primarily due to regulatory procedures and HMO insurance approval. In parallel, we noted a rise in systemic steroid prescriptions during the year preceding biologic initiation. This is consistent with HMO coverage requirements, which mandate documentation of at least two courses of systemic steroids per year. These findings offer real-world evidence of how administrative and reimbursement policies shape treatment patterns in clinical practice.

A concurrent diagnosis of asthma was present in most of our cohort, which is consistent with its known association with type 2 inflammation and the concept of a unified airway disease [21]. Asthma, especially the eosinophilic subtype, is a recognized risk factor for revision ESS in patients with CRSwNP, as these cases tend to be more challenging to manage [22–24]. Interestingly, our findings revealed that non-asthmatic patients underwent more revision surgeries, both before and after the initiation of biologic therapy, compared to those with asthma. This discrepancy may reflect differing indications for initiating biologics: in asthmatic patients, biologic treatment may have been driven primarily by poorly controlled lower airway disease rather than by sinonasal symptoms, potentially resulting in fewer surgical interventions. A review of the literature did not identify prior studies comparing revision ESS rates after biologic therapy in CRSwNP patients stratified by asthma status. Our findings suggest that biologics may confer a more pronounced benefit in patients with comorbid asthma, possibly due to broader systemic modulation of type 2 inflammatory pathways [25, 26]. Nonetheless, it is important

to underscore that a marked reduction in all measured outcomes was observed across the entire cohort, irrespective of asthma status.

High serum eosinophil levels are among the key criteria for initiating biologic therapy in CRSwNP [1, 10, 27]. However, their predictive value for treatment success remains uncertain. In patients with severe asthma treated with mepolizumab, elevated serum eosinophil counts have been associated with fewer respiratory exacerbations [28]. In contrast, data in CRSwNP are conflicting. A study by Png et al. reported that low tissue eosinophil levels and high serum neutrophil counts were linked to poor biologic response, while serum eosinophil counts themselves had no predictive value [29], consistent with our findings. Conversely, a recent large real-world study demonstrated that higher baseline serum eosinophil levels were strongly correlated with a favorable response to biologic therapy in CRSwNP patients [30].

On average, patients in our cohort received approximately 10 biologic doses per year, with an inter-dose interval of 33 days, longer than the recommended intervals for dupilumab (every 2 weeks) and mepolizumab (every 4 weeks). This suggests that, in real-world settings, patients and/or physicians tend to extend dosing intervals. A recent German study by Appel et al. [31] found that extending dupilumab dosing to every 4 or even 6 weeks maintained disease control in a cohort of 29 patients with CRSwNP. However, other studies have shown that prolonged cessation of biologics, such as a 24-week discontinuation of mepolizumab after one year of treatment, can lead to loss of efficacy [32]. As CRSwNP is a chronic condition requiring long-term treatment, and given the high cost of biologics, increasing dosing intervals may be a practical consideration. For example, a recent real-world study using South Korea's national health insurance database demonstrated that treatment intervals with dupilumab tend to lengthen as therapy progresses [33]. According to Han et al., by week 12 of treatment, 53.8% of patients were receiving dupilumab at intervals of four weeks or longer. Further research, particularly using big data, is needed to better understand optimal dosing strategies in real-world populations.

Biologic therapies are generally considered safe, with most adverse reactions being mild and localized, such as injection-site erythema and swelling [34,35]. Less common side effects include conjunctivitis, arthralgia, and psoriasis-like dermatitis [36, 37]. Dupilumab is known to cause transient hypereosinophilia (>1.5 K/μL) [38], typically peaking three months after treatment initiation [39,40], though this rarely necessitates discontinuation or switching of therapy [41]. In our cohort, only 19 patients (2.2%) developed hypereosinophilia, a lower rate than expected, possibly reflecting the fact that only half the cohort was treated with dupilumab. Additionally, our data did not show an increase in conjunctivitis or arthritis rates during biologic therapy.

To the best of our knowledge, this is the first study to examine the epidemiologic and healthcare utilization outcomes of CRSwNP patients treated with biologics using big data analysis. While most existing studies focus on patient-reported outcomes (PROMs) and objective clinical metrics, our study assessed the impact of biologics on healthcare utilization and traditional treatment burden (e.g., systemic corticosteroids, revision ESS). Our results suggest that biologic therapy significantly reduces the overall healthcare burden in CRSwNP and may decrease the need for further surgical intervention and systemic medication.

Limitations

The main limitation of this study is its reliance on big data analysis, which precludes access to individual-level clinical data, such as PROMs (e.g., SNOT-22) or physical examination findings (e.g., nasal polyp score, UPSIT). Consequently, we were unable to assess the type 2 inflammation status of patients in our cohort. In addition, due to regulatory constraints, we could not perform a full analysis on a specific biologic agent nor conduct a head-to-head comparison of dupilumab and mepolizumab.

Another potential limitation is the possibility that some patients received biologic therapy primarily for uncontrolled asthma rather than CRSwNP. To minimize this confounding, we included only patients diagnosed with CRSwNP who had undergone ESS before biologic treatment. For this reason, we did not include omalizumab, which was primarily indicated in severe asthma and only was also later indicated for CRSwNP, and benralizumab which is currently indicated only for asthma. Nonetheless, we acknowledge that a subset of our cohort likely had comorbid asthma, and in some cases, asthma may have been the primary indication for biologic therapy.

Additionally, we were unable to accurately identify patients who switched biologic agents or received dual biologic therapy ("double biologics") and therefore analyzed all patients according to the first biologic they received.

Conclusions

This large-scale, population-based study demonstrates that biologic therapies, specifically dupilumab and mepolizumab, significantly reduce healthcare utilization, systemic corticosteroid use, and revision sinus surgery rates in patients with CRSwNP who previously underwent ESS. These findings align with existing clinical trials and real-world evidence, highlighting the effectiveness and safety of biologics in managing CRSwNP. Our results underscore the substantial impact of biologics on reducing disease burden and suggest a growing role for these therapies in long-term CRS management.

Author contributions

EZ: Investigation, writing – original draft. GN: Investigation, review & editing. AB: Statistical analysis. YL: Conceptualization, supervisor, review & editing, MW: Conceptualization, methodology, writing – review & editing.

Conflict of interest

Senior author MW has participated in clinical trials with Sanofi® and AstraZeneca®.

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SUPPLEMENTARY MATERIAL

Table S1. ICD-9 codes included in the study.

ICD-9 code	Description
473	Chronic sinusitis
437.8	Other chronic sinusitis
473.9	Unspecified sinusitis (chronic)
471	Nasal polyps
471.9	Unspecified nasal polyp

Table S2. Antibiotic and systemic steroid agents included in the study

Antibiotics	Systemic steroids (administration method)
Amoxicillin	Prednisone (PO)
Amoxicillin-Clavulanic Acid	Methylprednisolone (IV/IM)
Doxycycline	Betamethasone Dipropionate (IM)
Ciprofloxacin	
Clindamycin	
Cefuroxime	
Azythromycin	
Trimethoprim-Sulfamethoxazole	
Levofloxacin	

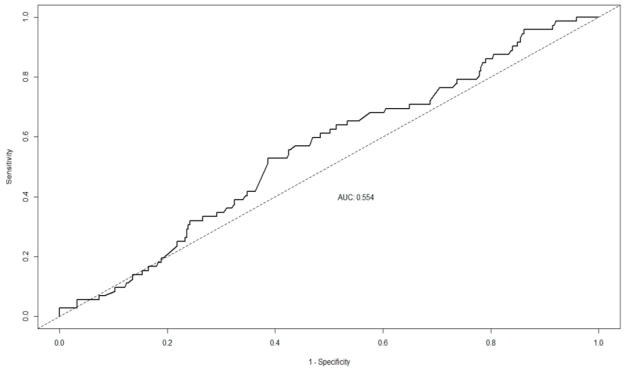

Figure S1. Receiver-operating characteristics (ROC) curve of baseline serum eosiuophil counts (K/µl) for patients with chronic rhinosinusitis with nasal polyps (CRSwNP) who were treated with biologics and needed a revision endoscopic sinus surgery (ESS) within 24 months of treatment. The area under the curve (AUC) was calculated to assess the discriminative ability of eosinophil levels to predict the likelihood of requiring revision ESS.

Table S3. Predictive value of baseline serum eosinophil counts (K/µL) for revision surgery.

Metric	Estimate	95% CI
AUC	0.554	0.483-0.625
Optimal cut-off (K/µL)	0.404	
Sensitivity at cut-off	0.528	
Specificity at cut-off	0.614	