Long-term dupilumab therapy reduces concomitant medication use in patients with CRSwNP

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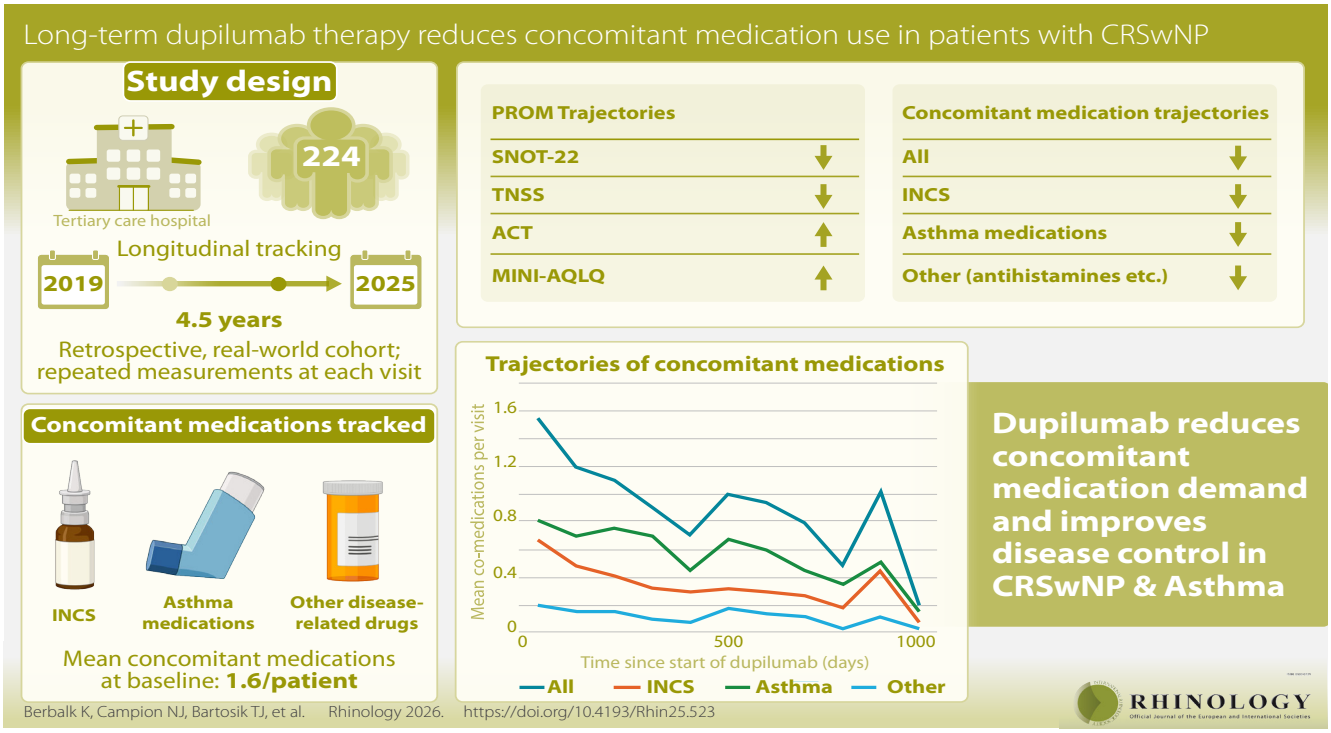

Abstract

Background: Dupilumab has demonstrated efficacy in Chronic Rhinosinusitis with Nasal Polyps. While its impact on sinonasal and asthma symptoms is well established, less is known about its effects on the demand for concomitant medications in long-term routine care.

Methodology: This retrospective longitudinal real-world study included 224 patients diagnosed with Chronic Rhinosinusitis with Nasal Polyps and treated with Dupilumab at a tertiary centre between 2019 and 2025, with a maximum follow-up of up to 4.5 years. At each visit, use of nasal sprays, asthma drugs, and other disease-related drugs was recorded. Linear mixed-effects models were fitted to assess longitudinal changes.

Results: At baseline, patients reported a mean of 1.6 concomitant medications, most commonly INCS and inhaled asthma drugs. The total number of concomitant medications, the number of nasal sprays, asthma medications, and other disease-related drugs decreased significantly over time. Parallel improvements were observed in patient-reported outcome measures (SNOT-22, TNSS, ACT, miniAQLQ).

Conclusions: In this real-world cohort, Dupilumab treatment led to a sustained overall reduction in concomitant medication use, thereby lowering pharmacological burden while improving disease control.

Key words: dupilumab, CRSwNP, asthma, N-ERD, concomitant medications

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a subtype of chronic rhinosinusitis (CRS) that features nasal obstruction, persistent sinonasal symptoms and the growth of nasal polyps. It affects approximately 0.65-2% [1,2] of the global population with higher rates in Europe. In the western world, CRSwNP is predominantly associated with type 2 inflammation with pronounced eosinophilia and dominance of interleukin (IL)-4, IL-5, and IL-13 but it can also be associated with type 1 or type 3 inflammatory responses [3,4]. Patients often suffer from comorbid conditions like asthma, non-steroidal anti-inflammatory drug (NSAID) - exacerbated respiratory disease (N-ERD), and allergic rhinitis [5]. The disease poses a significant burden on patients' quality of life [6] and has even been found to be associated with depressive symptoms [7].

First-line therapeutic options include the use of topical nasal steroid sprays, nasal douches and frequently require short cycles of systemic steroids to achieve symptom control. If non-surgical treatment options are not successful, patients often undergo endoscopic sinus surgery (ESS) [8]. In severe cases, multiple surgeries are required due to polyp recurrence [9]. However, in recent years monoclonal antibodies such as Dupilumab (anti-IL-4-receptor α chain), Mepolizumab (anti-IL-5), and Omalizumab (anti-immunoglobulin (Ig) E) have emerged as new therapeutic options for patients who previously did not respond to established treatment options. Dupilumab, a fully human monoclonal antibody targeting the IL-4-receptor α chain and thereby inhibiting the signalling of IL-4 and IL-13 in type 2 inflammation, has shown good efficacy in difficult-to-treat patients [10–12]. Due to the high costs, the new monoclonal antibodies are not used as first line and require the fulfilment of prescription criteria, which differ from country to country. Frequently, previous surgery, evidence of type 2 inflammation, and failure of non-surgical medicinal treatment are required for prescription. Previous studies have shown that Dupilumab significantly improves polyp scores, nasal congestion, sense of smell, and radiological findings with additional corticosteroid-sparing effects [12,13]. It was also found that under Dupilumab treatment the number of asthma exacerbations and the demand for inhaled and oral corticosteroids declined significantly [14,15]. Although several studies have shown that Dupilumab improves sinonasal symptoms and asthma control, its impact on the need for concomitant medications in real-world setting has not yet been comprehensively characterized.

This study aimed to assess patients diagnosed with CRSwNP and their use of disease-related concomitant medications before starting Dupilumab and with ongoing long-term treatment (up to 4.5 years) with particular focus on nasal sprays and asthma medications in a real-world setting and their longitudinal treatment response as assessed by different outcome measures.

Materials and methods

Subjects

This retrospective, longitudinal, single-centre study included patients diagnosed with CRSwNP according to EPOS criteria [8] at the Department of Otorhinolaryngology, Head and Neck Surgery at the Medical University of Vienna, between November 2019 and May 2025. The study protocol was approved by the Ethics committee of the Medical University of Vienna (EK-Nr.: 1340/2025).

Patients were followed for up to 4.5 years, with repeated visits scheduled according to clinical routine. Therefore, visits occurred at variable intervals with the first follow up intended at approximately three months and further visits at approximately 6 and 12 months. The overall observation period ranged from baseline (day 0 = before starting Dupilumab treatment) to 1661 days. Only patients treated with Dupilumab were included in this study, as it is the most frequently used biologic at our tertiary centre.

At the baseline visit, we obtained the patients' demographics, including age at the time of presentation (years), their sex (male/female), smoking-status (yes/no), asthma (yes/no), allergies (yes/no), and N-ERD (yes/no). All patients underwent thorough examination of the ears, nose, and throat, including nasal endoscopy to determine the total polyp score (TPS) and medical history was obtained. At baseline and every follow-up visit concomitant medication use (nasal sprays, asthma medications, other disease-related drugs) was documented and patients filled out a questionnaire to rate their current general health, their job-related restrictions, their leisure time related restriction, their restrictions regarding sleep, their restrictions regarding smell, the amount of nasal blockage, their sense of taste and their sinus problems on a visual analogue scale (VAS, 0=no limitation, 10=extreme limitation). The questionnaire also included patient-reported outcome measures (PROMs) like the Sino-Nasal Outcome Test - 22 (SNOT-22), the Total Nasal Symptom Score (TNSS), the Asthma Control test (ACT), and the Mini Asthma Quality of Life Questionnaire (miniAQLQ). The questionnaires were handed out routinely, but missing values occurred when patients did not complete all items. The number of available observations (N) are reported in the respective tables. Minor differences in N between variables reflect missing data for individual parameters. Whenever N is reported, it indicates the number of patients with available data for that specific variable.

All patients who did not report intranasal corticosteroids (INCS) at baseline had a history of failed INCS treatment and had previously discontinued such treatment due to lack of efficacy or poor tolerability. All patients were instructed to make any changes to their asthma medication only after consulting their pulmonologist and to discontinue INCS only if no additional benefit was achieved under Dupilumab therapy. Patients were explicitly asked to report any nasal sprays, asthma medications,

Table 1. Mean, standard deviation, and number of observations for disease-related limitations at baseline assessed using visual analogue scales.

	Mean	SD	N
Current general health	6.5	2.1	211
Nasal blockage	4.1	3.0	217
Job	4.5	3.5	201
Leisure-time	5.6	3.3	215
Sleep	5.9	3.4	216
Sinus problems	6.7	3.1	215
Sense of smell	2.3	3.0	218
Sense of taste	3.5	3.1	216

and "other disease related medications", which in most cases comprised allergy-related drugs (Table 2).

Statistical analysis

We performed statistical analyses and generated figures using R (The R Foundation for statistical Computing, Version 4.5.1) in the RStudio (Posit Software, Boston, MA, USA, Version 2025.05.1+513 (2025.05.1+513)) environment. Information was extracted from paper-based questionnaires and electronic patient charts, entered into an Excel database (Microsoft Excel, Microsoft Corporation, Redmond, WA, USA), and data cleaning was performed by a bioinformatician. Data processing was conducted in R using 'readxl', 'dplyr', 'tidyr', and 'stringr'.

Distribution of continuous variables was assessed using histograms and QQ-plots. Continuous variables, such as age, and PROMs were presented as mean ± standard deviation (SD). Ordinal variables like VAS symptom ratings were summarized likewise. Categorical variables such as sex, smoking status, presence of asthma, allergies, and N-ERD were presented as absolute numbers and percentages in brackets.

For each visit medications were classified into nasal sprays, asthma medications, and other disease-related concomitant medications. Row sums across the respective columns were calculated to derive category counts; empty fields were coded as "no medication". A variable for total concomitant medications was computed as the sum of all three categories. For descriptive purposes, visits were grouped into intervals (i.e., 0-3, 3-6, 6-12, 12-24, and > 24 months). Patients were classified as using concomitant medications within a given interval if at least one visit during that period was documented and included at least one concomitant medication.

To assess longitudinal changes, we fitted linear mixed-effects models using the 'lmer()' function from the 'lmerTest' package in R [16]. For concomitant medications, one model was computed to total concomitant medications and three models for the different categories (i.e., nasal sprays, asthma medication, and other disease-related concomitant medications). For each PROM a designated model was fitted. Asthma-specific models (i.e., asthma medications, ACT, and mini AQLQ) only included patients with an asthma diagnosis at baseline. Because of previous studies reporting the most significant symptom improvement within the first 6 months under Dupilumab, we used a piecewise linear mixed-effects approach with a knot at 180 days, distinguishing an early (0-180 days) and late (> 180 days) phase. Empty cells were coded as "no medication" for concomitant medication models and as "missing" for PROM models.

The dependent outcome was the number of concomitant medications or the PROMs. The fixed effect was the time since Dupilumab initiation, measured in 100-day units for numerical stability and interpretability. A random intercept for each patient (PatID) accounted for intra-individual correlation and subject-specific trajectories. Only visits with complete data for both the outcome variable and the time since starting Dupilumab treatment were included. All models were fitted using restricted maximum likelihood estimation (REML) with degrees of freedom (df) approximated using the Satterthwaite method. Regression coefficients (β) represent the estimated change per 100 days with the intercept (β_0) representing the estimated baseline value. For each model standard errors (SE) and p-values are reported with significance set at a p-value of 0.05.

Model assumptions were checked by residual diagnostics. Histograms and QQ-plots indicated approximate normality, and residuals vs. fitted plots showed no major deviation from linearity or homoscedasticity.

Results

Demographics

Two hundred and twenty-four patients diagnosed with CRSwNP with a mean age of 47.9 (±14.0) years were included in this study. The study population consisted of 128 (57.1%) men and 96 (42.9%) women. Hundred and fifty-eight (70.7%) patients (N=216) also had a diagnosis of asthma, 122 (59.2%) of patients (N=206) reported allergies, and 82 (37.6%) cases (N=218) presented with N-ERD.

On average, patients had 4.57 (±2.19) visits, with a maximum of 13 visits and an average duration between first and last observation of 722 days. The longest observation time was 1661 days.

Baseline characterization of patients

At the first visit patients had mean SNOT-22-Scores of 44.5 (±24.0, N=198) and mean TNSS-Scores of 5.84 (±2.9, N=213). Patients diagnosed with asthma (n=158) had mean ACT-Scores of 19.7 (±5.0, n=140), and mini-AQLQ-Scores of 80.2 (±18.2, n=137). Patients reported their subjective limitations regarding different disease-related aspects (i.e., current general health, nasal blockage, job, leisure-time, sleep, sinus problems, sense of smell,

Table 2. Absolute numbers (N) and active pharmaceutical ingredients of concomitant medications reported at the first visit (i.e., before starting Dupilumab).

Most common concomitant medications at baseline (top 5)					
Nasal sprays	**N**	**Asthma medications**	**N**	**Other Medications**	**N**
Mometasone	89	Beclometasone/Formoterol	36	Montelukast	13
Azelastine/Fluticasone	41	Budesonide/Formoterol	26	Desloratadine	13
Decongestant sprays	8	Ipratropium/Fenoterol	19	Cetirizine	6
Fluticasone	5	Fluticasone/Salmeterol	18	Levocetirizine	4
Betamethasone	4	Salbutamol	16	Prednisolone	3

Table 3. Absolute numbers and percentages of patients reporting concomitant medications in different time intervals and for different disease sub-groups. Some patients contributed to more than one time-interval if several follow-up visits were available.

Months	Group	Number of patients (N)	Patients using concomitant meds (%)	Patients using nasal sprays (%)	Patients using asthma meds (%)
0-3	Total	224	165 (73.7%)	147 (65.6%)	115 (51.3%)
	Asthma only	73	55 (75.3%)	49 (67.1%)	45 (61.6%)
	N-ERD	82	72 (87.8%)	62 (75.6%)	60 (73.2%)
3-6	Total	129	72 (55.8%)	52 (40.3%)	53 (41.1%)
	Asthma only	41	21 (51.2%)	12 (29.3%)	16 (39.0%)
	N-ERD	53	41 (77.4%)	32 (60.4%)	34 (64.2%)
6-12	Total	139	69 (49.6%)	53 (38.1%)	46 (33.1%)
	Asthma only	40	18 (45.0%)	14 (35.0%)	14 (35.0%)
	N-ERD	56	37 (66.1%)	25 (44.6%)	30 (53.6%)
12-24	Total	117	56 (47.9%)	34 (29.1%)	39 (33.3%)
	Asthma only	36	16 (44.4%)	9 (25.0%)	13 (36.1%)
	N-ERD	47	29 (61.7%)	17 (36.2%)	23 (48.9%)
> 24	Total	95	21 (22.1%)	15 (15.8%)	13 (13.7%)
	Asthma only	21	7 (33.3%)	5 (23.8%)	3 (14.3%)
	N-ERD	51	12 (23.5%)	8 (15.7%)	10 (19.6%)

and taste) on a visual analogue scale (higher scores suggesting higher limitation on a scale from 0 to 10) before starting Dupilumab treatment as reported in Table 1.

Reduced use of concomitant medication in patients treated with Dupilumab for up to 4.5 years

All patients were asked to report any medications they used aside from Dupilumab. We then categorized all concomitant medications in one of the three following groups: nasal sprays, asthma drugs, and other disease-related drugs. At baseline, before starting Dupilumab treatment, patients reported a total of 345 different concomitant medications, comprising 149 nasal sprays, 151 asthma medications, and 46 other disease-related drugs, corresponding to an average of 1.57 (±1.35) disease-related concomitant medications (Table 2).

Throughout the observational period, the proportion of patients requiring concomitant medication declined steadily. During the first three months, almost three quarters of patients reported concomitant medications whilst after 6 months, only approximately 50% of patients required additional medication (Table 3). The strongest reductions were seen in patients requiring asthma treatment in absence of N-ERD: Whilst 61.6% (n=45) took asthma medications during the first 3 months, this dropped to 35.0% (n=14) after 12 months of Dupilumab treatment. Patients with a N-ERD comorbidity showed higher and more persistent use of both nasal sprays and asthma drugs. Taken together, Dupilumab therapy was associated with a marked and sustained reduction in the use of concomitant medications, particularly, asthma drugs in patients without N-ERD.

Linear mixed effects models confirm reduction of concomitant medication use over time

The fitted linear mixed-effects models evaluated the change in the number of concomitant medications in patients undergoing

Table 4. Estimates (β_0 Intercept (baseline) and β slope (change per 100 days)), standard errors (SE), degrees of freedom (df), and p-values for the longitudinal change in total concomitant medications, nasal sprays, asthma medications, and other disease-related medications under Dupilumab therapy.

Concomitant medications	β_0 (Intercept)	β (per 100 days)	SE	df	p-value
Total	1.33	-0.120	0.007	854	<0.001
Nasal sprays	0.55	-0.050	0.003	886	<0.001
Asthma medications (n=149)	0.82	-0.062	0.005	597	<0.001
Other disease-related concomitant medications	0.18	-0.018	0.002	876	<0.001

Table 5. Linear mixed-effects models with a knot at 180 days to describe PROMs over time. Estimates (β_0 Intercept (baseline) and β slope (change per 100 days) was calculated for the first 180 days ($\beta_{0\text{-}180}$) and the rest of the observational period (β_{180+}), and p-values for changes in SNOT-22, TNSS, ACT, and mini AQLQ scores during treatment. Asthma related scores were only calculated for patients diagnosed with asthma. All estimates are reported as $\beta\pm$standard error (SE).

Score	β_0 (Intercept)	$\beta_{0\text{-}180}$ (early, per 100 days)	p-value (early)	β_{180+} (late, per 100 days)	p-value (late)
SNOT-22 (N=220)	39.80 ± 1.31	-14.500 ± 0.78	<0.001	0.246 ± 0.17	0.147
TNSS (N=224)	5.28 ± 0.16	-1.800 ± 0.09	<0.001	0.002 ± 0.02	0.921
ACT (N=152)	20.20 ± 0.28	1.720 ± 0.17	<0.001	-0.020 ± 0.04	0.581
Mini-AQLQ (N=152)	81.70 ± 1.23	7.170 ± 0.63	<0.001	-0.038 ± 0.14	0.780

Dupilumab treatment over time. The models revealed a statistically significant overall decline in the total number of concomitant medications with increasing duration of Dupilumab therapy (Figure 1, Table 4). The number of concomitant medications per visit decreased significantly by 0.120 per 100 days of therapy (β=-0.120, p-value<0.001, Figure 1A).

In the next step we assessed the reduction of concomitant medications between groups of medications. Although concomitant medication use decreased significantly in all subgroups (Table 4, Figure 1B-D), the most pronounced reduction was observed in asthma medications. Specifically, the number of asthma medications per visit significantly decreased by 0.062 medications per 100 days of Dupilumab treatment (β=-0.062, p<0.001, Table 4, Figure 1C). For this model only patients with an asthma diagnosis at the first visit were included. Nasal sprays decreased by 0.050 (β=-0.050, p<0.001, Table 4, Figure 1B) and other disease-related concomitant medications decreased by 0.018 (β=-0.018, p-value<0.001, Table 4, Figure 1D) per 100 days. Thus, linear mixed-effects models confirmed a continuous and statistically significant decline in all categories of concomitant medications, with the strongest effect observed for asthma drugs.

Significant improvement in symptom score trajectories during long-term Dupilumab therapy

In the piecewise linear mixed-effects model with a breakpoint at 180 days, all PROMs showed significant improvement during the first six months after starting Dupilumab, followed by a stabilization of score trajectories (Table 5). SNOT-22 decreased on average by 14.5 points per 100 days of therapy during the early phase (0-180 days, β_0=39.80, p-value<0.001) and remained stable afterwards (β_{180+}=0.25, p-value=0.147). The estimated time to reach the minimal clinically important difference (MCID) of minus 9 points was approximately 65 days, indicating a rapid improvement of symptoms. Similarly, the TNSS score significantly decreased by 1.8 points every 100 days of treatment throughout the early phase (β_0=5.28, p-value<0.001) and a stabilisation afterwards (β_{180+}=0.002, p-value=0.921). This steady reduction also suggests an improvement in nasal symptoms. In the subgroup of patients diagnosed with asthma (n=158) symptoms were assessed using the ACT score, which increased by 1.72 points per 100 days during the early phase (β_0=20.2, p-value<0.001) followed by stable trajectories (β_{180+}=-0.020, p-value=0.581), and the mini-AQLQ, which improved by 7.17 points in 100 days of the early phase (β_0=81.7, p-value<0.001), also followed by a period of stabilization (β_{180+}=-0.038, p-value=0.780), indicating a steady improvement of symptoms and Quality of Life (QoL) in asthma patients. In summary, symptom trajectories rapidly improved and stayed consistently low under Dupilumab, highlighting sustained benefits on sinonasal, asthma-related, and QoL outcomes.

Discussion

In this retrospective real-world cohort of 224 patients diagnosed with CRSwNP and undergoing Dupilumab therapy, we observed a significant and continuous reduction in the number

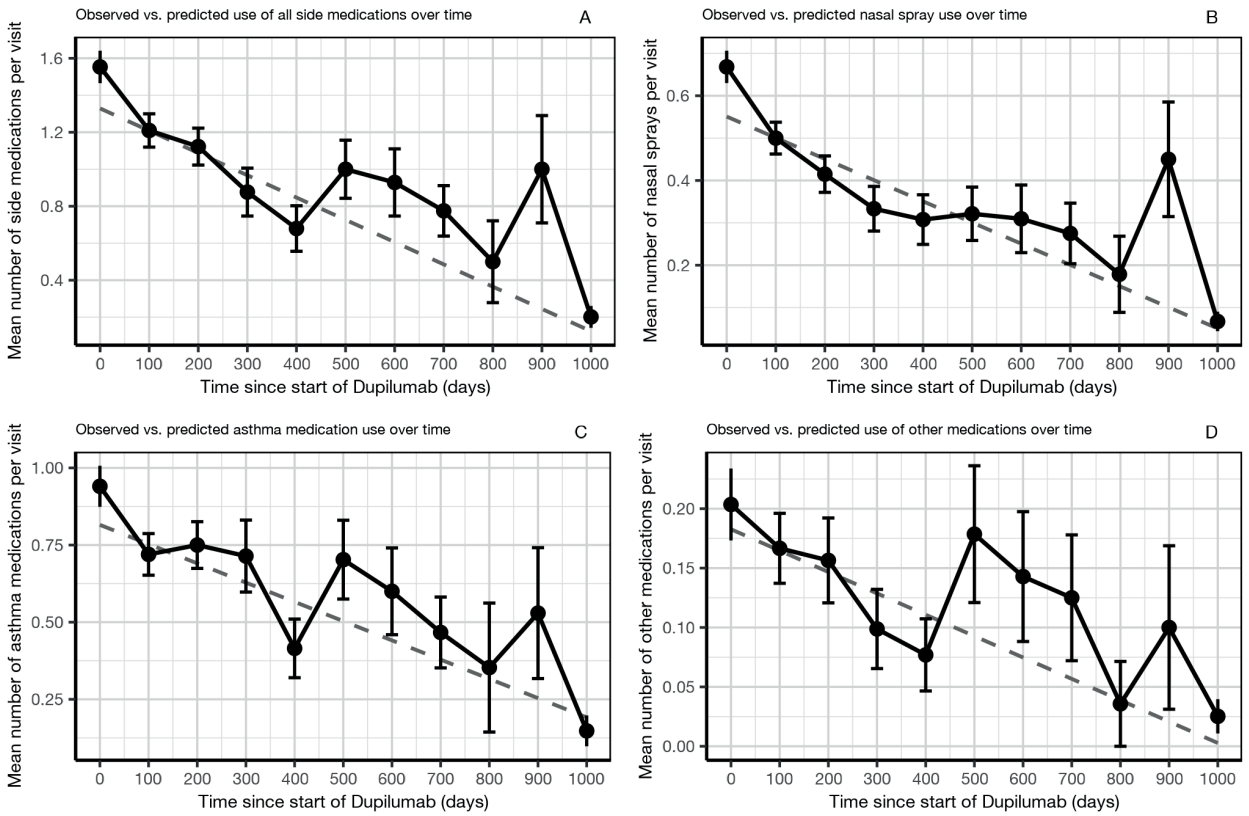

Figure 1. Observed and predicted use of concomitant medications during Dupilumab therapy. Data was grouped into 100-day intervals as follows: baseline = day 0 (n=224), 1-100 days = 100 (n=184), 101-200 days = 200 (n=146), 201-300 days = 300 (n=79), 301-400 = 400 (n=78), 401-500 = 500 (n=55), 501-600 = 600 (n=43), 601-700 = 700 (n=40), 701-800 = 800 (n=31), 801-900 = 900 (n=20), 901-1000 = 1000 (n=26). Black lines with points represent the mean number of concomitant medications per visit (± standard error), and dashed lines represent the predicted trend from the linear mixed-effects models. Results are shown for all concomitant medications (A), nasal sprays only (B), asthma medications only (C), and other disease-related concomitant medications (D) separately.

of disease-related concomitant medication during the 4.5-year observational period with nearly one hundred patients being under therapy for more than 24 months. Using linear mixed-effects modelling, we demonstrated a significant decrease of 0.120 medications per 100 days of Dupilumab treatment with the strongest effects observed in asthma medications (-0.062/100days), followed by nasal sprays (-0.050/100days). Simultaneously, we also observed significant symptom improvement as measured by patient-reported outcome measures to assess sinonasal symptoms and asthma control.

One of the key strengths of this study lies in the application of linear mixed effects models to assess changes in concomitant medication use and symptom scores over time. This statistical approach is particularly well suited for our dataset with repeated measurements per patient, as it accommodates both fixed effects (i.e., duration of therapy) and patient-specific random effects (i.e., individual intercepts), thereby capturing both individual trajectories and population-level trends [17]. Unlike traditional linear regression, the mixed effects model accounts for the correlation of within-subject observations and is robust to unbalanced longitudinal data, which is often the case in real-world clinical follow-ups, where patients do not always adhere to strict or identical observation intervals [18]. For optimal assessment of PROM trajectories, which typically follow a non-linear course with rapid early improvement, followed by a plateau, we applied a piecewise linear mixed-effects model with a breakpoint at 180 days to distinguish between early and late treatment response. By using this model, we were able to capture population trends and individual trajectories alike [19].

CRSwNP has traditionally been managed with intranasal corticosteroids, repeated courses of systemic corticosteroids and, in refractory cases, surgery [20]. The phase-3 SINUS-24 and SINUS-52 trials showed that adding Dupilumab to intranasal Mometasone drastically reduced the need for systemic steroids and surgery [12], establishing Dupilumab as an effective steroid-sparing therapy. However, previous studies assessed the combined efficacy of Dupilumab and add-on therapies, most commonly Mometasone, together [21]. Only one small real-life study specifically investigated intranasal corticosteroid adherence and observed no significant differences in clinical outcomes between regular

and irregular use of Mometasone nasal spray under Dupilumab [22]. Importantly to the best of our knowledge no published study to date has quantified changes in concomitant medications such as inhaled asthma therapies or nasal sprays. Our study is therefore the first to systematically evaluate how Dupilumab affects the need for disease-related concomitant medications in CRSwNP. While previous trials demonstrated a reduction in systemic steroid use and demand for surgery, they mandated continued intranasal steroid therapy or did not report on other medications [12]. Our data shows a significant decrease not only in systemic steroids but also in intranasal corticosteroids and asthma medications after initiation of Dupilumab over an extended follow-up period of up to 4.5 years, suggesting that the biological effect of Dupilumab itself may be sufficient to achieve disease control. The transient increase around 900 days most likely reflects increased variability due to the small number of observations, combined with short-term clinical and seasonal fluctuations in concomitant medication use, most prominently in the use of allergy drugs, which may coincide with the pollen season or occasional higher demand for allergy medications. Simultaneously, our findings are in accordance with previous studies which demonstrated the efficacy of Dupilumab in improving nasal symptoms as assessed by SNOT-22 [23] and reducing nasal polyp burden [24] even with reduced use of disease-related concomitant medications. This observation challenges the prevailing assumption that maximal benefit requires adherence to nasal spray therapy and provides new evidence that Dupilumab alone may substantially reduce the need for concomitant medications.

In this context, it should be emphasized that INCS remain a cornerstone of standard therapy in CRSwNP and are often required for reimbursement of biologic treatments. In many healthcare systems, including Austria, discontinuation of INCS is only acceptable in cases of documented intolerance or lack of additional clinical benefit. In our cohort, all patients who reduced or discontinued INCS during therapy did so because of a lack of additional clinical benefit or intolerance, with all treatment modifications performed under specialist supervision. Importantly, our findings should not be interpreted as discouraging guideline-recommended INCS use, but rather reflect real-world, treatment adjustments.

The most prominent reduction was observed in patients diagnosed with CRSwNP and asthma, which suggests significant control of lower airway inflammation. This finding is also supported by a significant improvement of ACT and mini-AQLQ scores over time with ongoing treatment duration suggesting a sustained improvement of asthma symptoms. These results align with phase III trials demonstrating reduced steroid dependence and exacerbation rates [25], as well as long-term data showing durable improvement of lung function and asthma control [26]. Regarding nasal symptoms we found a significant improvement of sinonasal symptoms as assessed by SNOT-22 and TNSS scores, which is in accordance with previous studies on the effects of Dupilumab [23,27,28]. This study also found that the number of nasal sprays declined significantly with ongoing Dupilumab treatment, while simultaneously sinonasal symptoms improved, suggesting better overall sinonasal disease control even without continued use of nasal sprays [7].

International guidelines often provide eligibility criteria for treatment with biologics, due to the high costs with often different national indications to balance medical and financial considerations [8]. Previous studies have shown that even after multiple revision surgeries, a surgical approach is still far more cost-effective than treatment with biologics [29]. However, the time between revision surgeries is in many patient cases characterized by severe symptoms, which is highly burdensome for many patients [30]. Furthermore, surgeries can also be associated with complications and some patients may not able to undergo surgery due to other diseases [31]. Better disease control, fewer side effects, better improvement of sense of smell [32] and the steady reduction in adjuvant medication use may partially contribute to offset the high costs, particularly as disease control also translates to fewer healthcare visits, fewer asthma exacerbations with hospitalizations, and avoidance of revision surgery.

This study, nevertheless, also has some limitations. Firstly, the retrospective study design may introduce a reporting bias, particularly in the documentation of concomitant medications, although all patients were explicitly asked to report any concomitant medications, specifically nasal sprays and asthma medications at every visit. Secondly, our study was performed at a single tertiary centre which may limit generalizability to broader populations. Thirdly, although we observed significant longitudinal improvements, we cannot fully exclude the influence of confounding variables, such as seasonal variation, adherence, or comorbid treatments. Finally, no placebo or control group was included, therefore causality cannot be established.

Despite these limitations, the strengths of our study lie in the large sample size, long follow-up duration, statistical methodology, and detailed documentation of both medication use and patient-reported outcome measures. To our knowledge, this is the first study to systematically model the longitudinal reduction in disease-related concomitant medications under Dupilumab treatment using mixed-effects modelling in a real-world setting.

Conclusion

Our real-world data demonstrated that Dupilumab treatment in patients with CRSwNP not only leads to a significant symptom improvement as measured by patient-reported outcome measures, but also to a significant reduction of the number of disease-related concomitant medications, including nasal sprays, asthma medication, and other adjunctive therapies.

Our findings support the sustained effectiveness of Dupilumab beyond the controlled environment of clinical trials and its potential to reduce pharmacological treatment extent in long-term application. Further prospective studies are warranted to fully understand this impact.

Author contributions

KB, SS, JED, NJC contributed to the design and methodology of this study. KB, NJC, CM, AT, LL, MP, TJB, VS curated and verified the data. KB performed the statistical analysis and drafted the manuscript. SS, JED supervised the study and contributed to the interpretation of results. All authors acquired data, reviewed and interpreted results, provided feedback on manuscript development, and approved the final version for submission.

Conflict of interest

KB, NJC, TJB, LL, MP, CM, VS SS has served as a speaker for Sanofi, GSK and AstraZeneca; is an advisory board member for Sanofi, GSK and AstraZeneca; and is an investigator for Sanofi, GSK, Novartis and AstraZeneca (grants paid to his institution). JED has served as a speaker, consultant, advisory board member, and investigator for Sanofi, AstraZeneca and GSK (grants paid to her institution). SST served as a consultant and advisory board member for AstraZeneca, Sanofi, GSK, Insmed and received fees outside the submitted work.

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