



Effect of Dupilumab in CRSwNP Sinonasal Outcomes from Real Life Studies: A Systematic Review with Meta-analysis

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Abstract

Purpose of Review Chronic rhinosinusitis with nasal polyps (CRSwNP) is a debilitating inflammatory condition that significantly impacts quality of life. Despite treatment advances, recurrence is common, prompting the exploration of novel therapies such as monoclonal antibodies targeting the type 2 immune response, notably dupilumab. This research aims to evaluate the real-world evidence (RWE) of dupilumab in treating severe CRSwNP, comparing sinonasal outcomes to those observed in randomized clinical trials.

Recent Findings Significant improvements were noted, with the average SNOT-22 score reduction being 37.2 points post-dupilumab treatment. The nasal polyp size (NPS) showed an average decrease of 3.6 points. The analysis highlighted the practical effectiveness of dupilumab, emphasizing its benefit over conventional therapies in reducing NPS and improving nasal symptoms.

Summary The findings advocate for the integration of dupilumab into standard treatment protocols for severe CRSwNP, providing a robust alternative that could potentially reduce the high recurrence rates associated with current management strategies. This study underscores the utility of RWE in assessing the effectiveness of new medical treatments, suggesting that dupilumab offers substantial real-world benefits for patients suffering from this challenging condition.

Keywords Biologic therapy · Chronic rhinosinusitis with nasal polyps · Dupilumab · Monoclonal antibody · Quality of life

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Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) represents a specific phenotype of chronic rhinosinusitis implying the development of inflammatory polypoid outgrowths from the nasal mucosa. It is a prevalent and debilitating disease with significant implications for public health and is estimated to affect approximately 4.2% of the general population in the United States, with approximately 0.027% facing severe uncontrolled CRSwNP [1–3]. Some recent studies have reported prevalences < 1% in Catalonia [4] and Spain [5]. Beyond its prevalence, CRSwNP exerts a substantial burden on health-related quality of life [6], affecting various aspects of quality of life (QoL), such as general health, social functioning, sleep and mental health [7], often resulting in absenteeism at work [8].

Despite standard treatment combining topical intranasal corticosteroids (INCS), systemic corticosteroids (SCS), and/or surgical interventions in the presence of severe symptoms, the recurrence rates still remain high, ranging from 40 to 80% within 3 to 12 years after surgery [9–11].

In recent years, advances in understanding the underlying inflammatory processes have paved the way for new precision medicine treatments, aimed at controlling the inflammatory cascade [12]. In approximately 80% of Caucasian patients with CRSwNP the disease is caused by type-2 inflammation [4, 13, 14]. The emergence of monoclonal antibodies (mAbs) targeting the type 2 immune response has revolutionized the treatment landscape for conditions associated with type 2 inflammation, including CRSwNP. Currently, the approved mAbs for severe CRSwNP are omalizumab (anti-IgE), dupilumab (anti-IL-4R α), and mepolizumab (anti-IL-5). Dupilumab is a fully human immunoglobulin G₄ subclass monoclonal antibody that blocks IL-4 and IL-13 signaling by specifically binding to the IL-4R α receptor subunit. Thus, it modulates cell function, cell signaling through several chemokines, and immunoglobulin E synthesis [15].

In various network meta-analyses [16–18], dupilumab has shown better effects in CRSwNP compared to other mAbs. However, these studies solely focused on comparing randomized clinical trials (RCTs), leading to certain limitations. Variations in study designs, specific characteristics of the study population and biases among trials are among these limitations. Furthermore, the controlled environments of RCTs may hinder the applicability of findings to real-world scenarios (RWE, Real World Evidence), and the short follow-up durations may restrict the assessment of long-term outcomes and safety profiles. Thus, these conditions could raise doubts about the robustness of conclusions. RWE could be an indirect way of comparing results reflecting the conditions and outcomes occurring

outside the controlled environment of clinical trials [19] and taking into account that the criteria to prescribe mAbs for CRSwNP are common to all biologics (EPOS2020 [20], POLINA [21], EPOS/EUFOREA update [22]).

The main goal of this research is to summarize in a systematic review with meta-analysis the available evidence on RWE of dupilumab in CRSwNP, and to compare the results obtained from RCTs, providing information on the possible advantages and drawbacks of employing these therapies in our daily clinical routines.

Methods

Systematic Review

The review was carried out according to the PRISMA and AMSTAR-2 guidelines. The PROSPERO protocol was published according to the NHS International Prospective Register of Systematic Reviews (Registration No. 541594).

Literature Search. Inclusion and Exclusion Criteria

The criteria for considering studies for the systematic review were based on the population, intervention, comparison, and outcome (PICOTS) framework.

Participants severe uncontrolled CRSwNP patients.

Intervention dupilumab 300 mg subcutaneously every two weeks.

Comparison pre- and posttreatment data.

Outcomes SinoNasal Outcome Test (SNOT-22), Nasal Polyp Score (NPS).

Timing and Settings included studies were published between 2022 and 2024.

Types of Studies prospective and retrospective studies published in peer-reviewed journals. Case reports and theses were not included. There were no restrictions by date or publication type, and the search was last updated in June 2024. Studies published in languages other than English, Spanish, Italian or Portuguese were excluded.

Exclusion Criteria Different studies were excluded such conference abstracts [23–35], clinical trials or studies consisting of post hoc analysis of clinical trials [36–67], studies in which dupilumab was indicated for other comorbidity different from CRSwNP [68–75], studies with population already included in other studies (duplicated) [76–80], studies in

which SNOT-22 or NPS data were not used or were published incomplete [81–93], studies where patients did not meet the inclusion criteria [94–108] and studies published in languages different from english, spanish, portuguese or italian [109–113].

Search Strategy

Five databases were explored: PubMed (Medline), EMBASE, Web Of Science, SciELO, and Trip Database. The search strategy, adapted to the syntax of each database was ((snot-22[Title/Abstract]) OR (“sinonasal outcome test”[Title/Abstract]) OR (nps[Title/Abstract]) OR (“nasal polyp score”[Title/Abstract])) AND ((dupilumab[Title/Abstract]) OR (dupixent[Title/Abstract])).

The abstracts were reviewed by two authors of the Rhinology Study Group of Young Otolaryngologists of the International Federation of Otorhinolaryngological Societies (MRI, CCH), and those that potentially met the inclusion criteria were read in full text. When differences in eligibility judgment were noted, full texts were included for the final assessment. Furthermore, the reference lists of all selected articles were manually reviewed to identify any work that may have been overlooked during the initial search.

Study Extraction and Analysis

Three authors (MRI, CCH, AGLL) analyzed and extracted data, including sample size, sex, age, type of study, comorbidities (i.e., asthma, NSAID-exacerbated respiratory disease [N-ERD], prior Endoscopic Sinus Surgery [ESS]) and main outcome variables (SNOT-22 [114] and/or NPS [115]). When data were only partially published, common variances were calculated using the formula $(\sqrt{\sigma_x^2 + \sigma_y^2}) / \sqrt{(n_x + n_y)} * 1.96$. When the main data were published expressed in median and interquartile range, the mean and standard deviation were estimated using the Wan’s method [116].

Follow-up was expressed in weeks. Data were converted assuming 1 month equaled to 4.3 weeks, and 1 year equaled to 52 weeks.

Statistical Analysis

All statistical data were analyzed using STATA for Macintosh v. 15.1 (StataCorp®). Significance was considered at a P -value < 0.05 .

Meta-analysis was conducted using rBiostatistic Web Tool (https://www.rbiostatistics.com/one_group_means). Heterogeneity among the included studies was rigorously evaluated through two established tests: the Q-test and the I^2 test. The Q-test assesses whether the observed variability in effect sizes across studies exceeds what would be expected

by chance alone, while the I^2 test quantifies the proportion of total variation attributable to heterogeneity rather than random error.

To determine the appropriate statistical model for combining study findings, the level of heterogeneity was pivotal. A fixed-effects model, predicated on the assumption of a common effect size across all studies, was employed when heterogeneity was below 50% and did not exhibit statistical significance ($p \geq 0.05$). Conversely, a random-effects model, accommodating both within-study and between-study variability, was applied when heterogeneity surpassed 50% or when the p -value was < 0.05 .

Furthermore, an assessment of publication bias was conducted to discern any potential skew in the literature towards the publication of studies with significant findings. This involved the utilization of a funnel plot, allowing visual inspection of the distribution of effect sizes, with asymmetry potentially suggestive of publication bias. Additionally, the Egger regression test was employed to formally evaluate funnel plot asymmetry, determining whether the intercept of the regression line significantly deviated from zero, thus indicating the presence of a publication bias.

Results

Search Results

The PRISMA flow chart of the search process is shown in Fig. 1. The initial search returned 404 publications. After screening, 247 duplicated records were removed. Finally, after screening and complete reading, a total of 26 studies comprising 2,183 patients met the inclusion criteria.

Thirteen authors were contacted twice by email to request missing or unpublished data [72, 76, 77, 81, 84, 88, 89, 101, 103, 117–120]. Out of those thirteen, only three answered [79, 119, 120].

Of the selected articles, 92 publications were excluded following the exclusion criteria outlined above since they consisted of post hoc analysis of clinical trials ($n = 32$), conference abstracts ($n = 13$), studies where dupilumab was indicated for other comorbidity different from CRSwNP ($n = 8$), population not meeting the inclusion criteria ($n = 15$), population already included in other studies ($n = 6$), studies where SNOT-22 or NPS data were not used or were published incomplete ($n = 13$), and papers in different language other than English/Spanish/Portuguese/Italian ($n = 5$). References of excluded papers can be found in *Supplementary Annex 1*.

Results of the Included Studies

The mean difference and standard deviation of the difference for SNOT-22 were estimated from medians and quantiles in

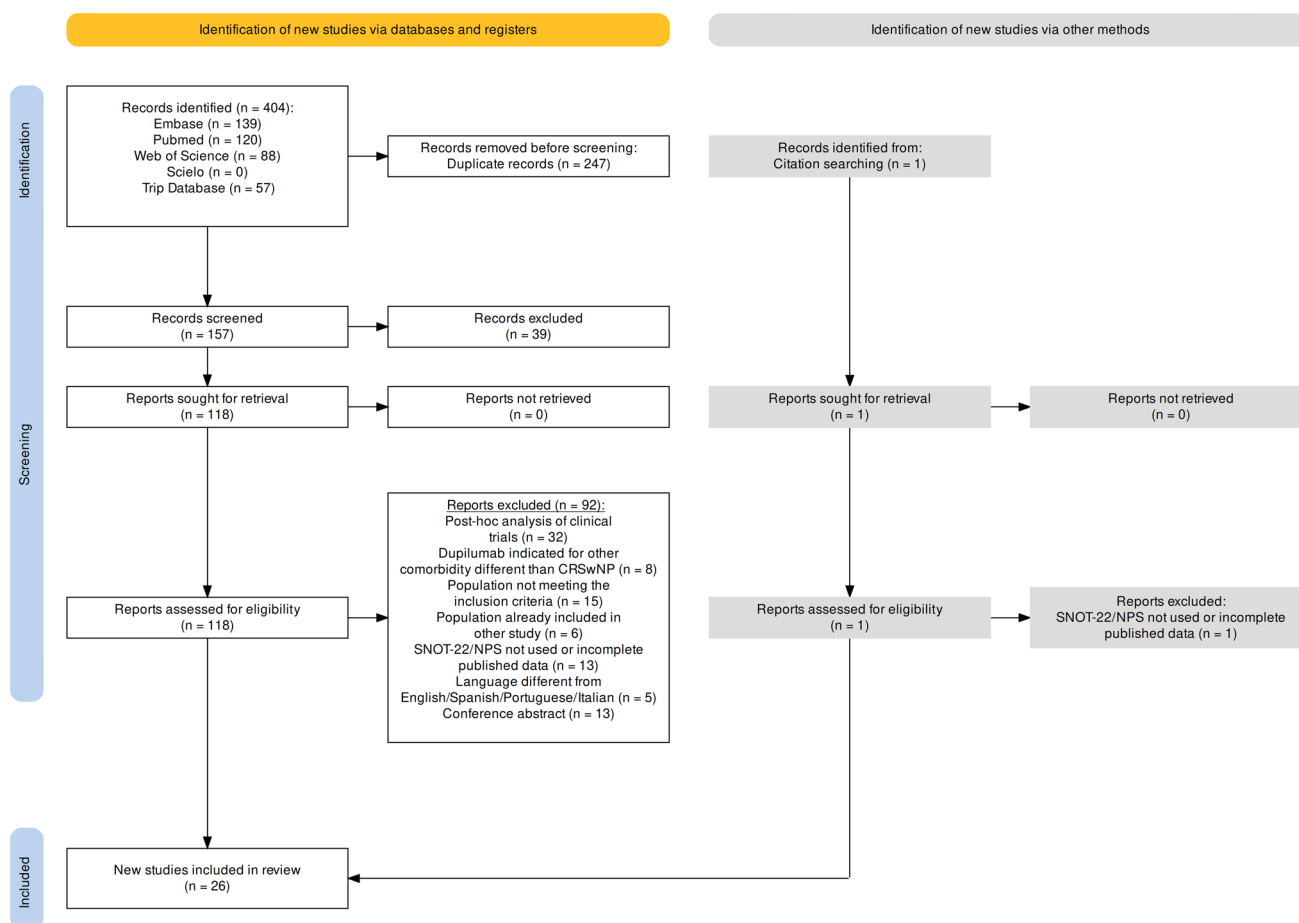


Fig. 1 PRISMA flow chart of the search process

24 studies [24, 79, 86, 108, 117–136]. The same parameters were estimated for NPS in twenty-two [24, 108, 117–120, 122–126, 128, 129, 131, 132, 134–140].

General Results

Results are summarized in Table 1. The mean and SD for sample size is 83.8 ± 125.8 among the studies. The largest sample size from a RWE was reported by De Corso et al. [118] (648 patients) and the smallest by Piazzetta et al. [125] (14 patients).

The weighted mean and SD for age was 52.6 ± 3.3 years. The lowest was reported by Grose et al. [127] (43 years) and the highest one by Piazzetta et al. [125] (60.6 years).

The weighted mean and SD for follow up time was 51.9 ± 23.2 weeks, being the lowest 4 weeks (Paoletti et al. [131]) and the highest 96 (Van der Lans et al. [128]).

The weighted mean and SD for the proportion of patients suffering from asthma was $66.7 \pm 14.5\%$, being the lowest 30.2% (Giombi et al. [132]) and the highest 100% (Garvey et al. [138]).

The weighted mean and SD for the proportion of patients suffering from N-ERD was $44.6 \pm 14.5\%$, being the lowest 11.3% (Giombi et al. [132]) and the highest 65.2% (Mocellin et al. [122]).

SNOT-22

The results are summarized in Table 1. Thirty-one observational RWE assessed SNOT-22 [24, 77, 81, 84, 88, 89, 92, 93, 108, 117–136, 138, 139].

Twenty-four of them could be included in the meta-analysis. Bellochi et al. [81], Ottaviano et al. (2022) [77], Ottaviano et al. (2023) [89] and Brkic et al. [137] could not be included because they did not provide the standard deviation (of the difference or before and after treatment). Haxel et al. [88] could not be included because they only provided the mean value at baseline. Nettis et al. [84], Ottaviano et al. (2024) [93] and Riva et al. [92] could not be included, as they provided data measured in the median and interquartile range without the necessary data (minimum and maximum

Table 1 Description of the included studies (cont)

Author (Year)	Design / Level of evidence	Sample size and sex	Age, Mean $\pm$ SD (range)	Asthma (%)	N-ERD (%)	ESS (%)	Main outcome		Follow-up (weeks)		
							Variable	T0 (mean $\pm$ SD)		T1 (mean $\pm$ SD)	Variation (mean $\pm$ SD)
Cantone (2022)	Retrospective cohort study	53 (33 M; 20 F)	53.07 $\pm$ 12.74	70	21	100	SNOT-22	55.6 $\pm$ 15	15.9 $\pm$ 9.8	39.70 $\pm$ 2.41	25.8
De Corso (2023)	Retrospective cohort study	648 (400 M; 248 F)	54 $\pm$ 13.37 **	56.5	29.5	91.4	SNOT-22	58.75 $\pm$ 3.39	12.25 $\pm$ 2.42	46.50 $\pm$ 0.16	51.6
							NPS	5.75 $\pm$ 0.16	1 $\pm$ 0.32	4.75 $\pm$ 0.01	
							Sniffin's Sticks (0–16)	4.25 $\pm$ 0.81	11.75 $\pm$ 0.81	7.50 $\pm$ 0.05	
Trimarchi (2022)	Prospective cohort study	21 (16 M; 5 F)	47 $\pm$ NR (29–84) 51.75 $\pm$ 14.75**	71.4	42.9	100	Smell VAS	8.2 $\pm$ 0.84	2.25 $\pm$ 0.81	5.95 $\pm$ 0.05	25.8
							SNOT-22	62.33 $\pm$ 20.67	15.67 $\pm$ 18.29	46.66 $\pm$ 6.01	
							NPS	5.33 $\pm$ 0.80	1.67 $\pm$ 2.39	3.66 $\pm$ 0.49	
Mocellin (2023)	Retrospective cohort study	23 (9 M; 14 F)	55.8 $\pm$ 14.8	82.6	65.2	73.9	B-SIT	3.67 $\pm$ 1.59 **	8 $\pm$ 1.99 **	4.33 $\pm$ 0.55	
							Smell VAS	0	8 $\pm$ 1.59 **	- 8 $\pm$ 0.25	
							SNOT-22	62.7 $\pm$ 18.6	29.6 $\pm$ 17.56	33.10 $\pm$ 5.33	25.8
Jansen (2023)	Retrospective cohort study	40 (18 M; 22 F)	52.7 $\pm$ 15.3 (20 – 84)	88	52.5	100	NPS	6.09 $\pm$ 1.31	2.73 $\pm$ 2.31	3.36 $\pm$ 0.53	
							Sniffin's Sticks (0–16)	4 $\pm$ 2.72	9.6 $\pm$ 3.54	3.60 $\pm$ 0.71	
							SNOT-22	60.48 $\pm$ 22.17	20.8 $\pm$ 17.7	39.68 $\pm$ 4.46	55.9
Albrecht (2023)	Prospective cohort study	68 (36 M; 32 F)	49.81 $\pm$ 12.58	77.94	44.12	100	NPS (0 – 8)	4.30 $\pm$ 1.47	1.4 $\pm$ 1.1	2.90 $\pm$ 0.29	
							Sniffin's Sticks (0–12)	3.22 $\pm$ 3.74	7.8 $\pm$ 3.5	4.58 $\pm$ 0.81	
							SNOT-22	53.74 $\pm$ 17.62	22.85 $\pm$ 16.66	30.89 $\pm$ 2.94	51.6
Piazzetta (2023)	Retrospective cohort study	14 (11 M; 3 F)	60.57 $\pm$ 12.31 (31 – 79)	57.1		92.85	NPS (0 – 8)	5.44 $\pm$ 1.79	1.41 $\pm$ 1.54	4.03 $\pm$ 0.29	24
							Sniffin's Sticks (0–12)	2.26 $\pm$ 2.72	7.82 $\pm$ 3.51	5.56 $\pm$ 0.53	
							Smell VAS	9.16 $\pm$ 1.85	3.09 $\pm$ 2.73	6.07 $\pm$ 0.39	
La Mantia (2023)	Prospective controlled study	60 (38 M; 22 F)	50.83 $\pm$ 14.10	55	20	NR	SNOT-22	53.64 $\pm$ 22.39	11.86 $\pm$ 8.73	41.78 $\pm$ 5.88	25.8
							NPS	6.36 $\pm$ 1.28	2.63 $\pm$ 1.33	3.73 $\pm$ 0.49	
							SNOT-22	59.68 $\pm$ 21.11	16.21 $\pm$ 13.77	43.47 $\pm$ 3.18	
Grose (2023)	Retrospective cohort study	27 (15 M; 12 F)	43 $\pm$ 10.9	96.3	40.7	93	NPS	5.72 $\pm$ 1.24	2.2 $\pm$ 1.91	3.52 $\pm$ 0.29	
							Sniffin's Sticks (0–16)	3.08 $\pm$ 2.63	10.23 $\pm$ 4.21	7.15 $\pm$ 0.62	
							SNOT-22	60.6 $\pm$ 18.8	26.1 $\pm$ 17.9	34.50 $\pm$ 4.99	51.6
Orlando (2023)	Prospective controlled study	26 (20 M; 6 F)	53.9 $\pm$ NR (28–75)	53.8	26.2	92.3	SNOT-22	51.12 $\pm$ 19.50	23.19 $\pm$ 18.37	27.93 $\pm$ 5.25	51.6
							NPS	4.96 $\pm$ 2.13	3.65 $\pm$ 1.71	1.31 $\pm$ 0.53	
							Sniffin's Sticks (0–16)	5.04 $\pm$ 2.94	9.59 $\pm$ 3.21	4.55 $\pm$ 0.85	

Table 1 (continued)

Author (Year)	Design / Level of evidence	Sample size and sex	Age, Mean $\pm$ SD (range)	Asthma (%)	N-ERD (%)	ESS (%)	Main outcome		Follow-up (weeks)
							Variable	Variation (mean $\pm$ SD)	
Kilty (2022)	Retrospective cohort study	53 (29; 24 F)	52.94 $\pm$ 10	88.67	37.73	90.56	SNOT-22	60.56 $\pm$ 21.63 23.47 $\pm$ 17.66	28 32.85 $\pm$ 21.10
Brkic (2023)	Retrospective cohort study	65 (42 M; 23 F)	51.3 $\pm$ 12.7	63.1	49.2	100	NPS	4.3 $\pm$ 1.9 1.2 $\pm$ 1.6	25.8 3.1 $\pm$ 1.7
Tsunemi (2023)	Retrospective cohort study	20 (13 M; 7 F)	50.6 $\pm$ 14.0	90	35	100	NPS	6.0 $\pm$ 0.2 0.2 $\pm$ 0.7	78.69 5.80 $\pm$ 0.14
Van der Lans (2023)	Prospective cohort study	228 (143 M; 85 F)	51 $\pm$ NR (18–90)	80.7	40.6	99.5	SNOT-22 NPS Sniffin's Sticks (0–12)	53.6 $\pm$ 19.6 5.3 $\pm$ 1.9 3.7 $\pm$ 2.4	32.40 $\pm$ 1.65 1.31 $\pm$ 0.53 3.60 $\pm$ 0.25
Böscke (2023)	Retrospective cohort study	41 (23 M; 18 F)	52.12 $\pm$ NR (27–79)	68.3	41.5	100	SNOT-22 NPS Sniffin's Sticks (0–12)	51.59 $\pm$ 22.16 4.88 $\pm$ 2.06 2.86 $\pm$ 1.64	35.00 $\pm$ 3.76 1.52 $\pm$ 1.75 8.16 $\pm$ 2.75
Galletti (2023)	Prospective cohort study	170 (109 M; 61 F)	54 (45–63)	45.3	27.6	78.8	SNOT-22 NPS Sniffin's sticks (0–16)	65 $\pm$ 18.59 5.96 $\pm$ 1.28 2.59 $\pm$ 2.74	42.46 $\pm$ 1.76 3.79 $\pm$ 0.17 10.99 $\pm$ 4.1
Alicandri-Ciuffelli (2023)	Retrospective cohort study	145 (145 M; 89 F)	55.1 $\pm$ NR (27–86)	75.8	29.6	100	SNOT-22 NPS Sniffin's Sticks (Scale NR)	56.1 $\pm$ 18.4 5.6 $\pm$ 1.3 5.7 $\pm$ 2.7	43.60 $\pm$ 1.63 4.20 $\pm$ 0.17 5.40 $\pm$ 0.30
Ferri (2023)	Prospective cohort study	29 (13 M; 16 F)	54.0 $\pm$ 9.8	82.8	37.5	86.2	Smell VAS SNOT-22 NPS	7.4 $\pm$ 2.9 62.5 $\pm$ 17.0 6.4 $\pm$ 1.3	5.00 $\pm$ 0.33 30.30 $\pm$ 4.60 3.30 $\pm$ 0.43
Campion (2023)	Retrospective cohort study	97 (61 M; 36 F)	46.3 $\pm$ 14.2	64.9	51.5	92.8	SNOT-22 NPS Sniffin's sticks (0–12)	33.29 $\pm$ 23.04 3.86 $\pm$ 2.25 5.92 $\pm$ 4.09	19.95 $\pm$ 2.67 2.58 $\pm$ 0.28 9.61 $\pm$ 3.10
Paoletti (2023)	Prospectively cohort study	33 (13 M; 20 F)	54.2 $\pm$ 11.2	87.9	60.6	78.8	SNOT-22 NPS Smell VAS	66.8 $\pm$ 15.1 6.5 $\pm$ 1.4 9.8 $\pm$ 0.8	28.40 $\pm$ 4.12 2.20 $\pm$ 0.43 4.20 $\pm$ 0.53
Giombi (2024)	Retrospective cohort study	53 (29 M; 24 F)	54.45 $\pm$ 9.87	30.2	11.3	90.6	SNOT-22 NPS Smell VAS	63.92 $\pm$ 19.98 6.06 $\pm$ 1.51 9.48 $\pm$ 1.74	35.02 $\pm$ 21.03 3.02 $\pm$ 0.33 4.78 $\pm$ 0.50

Table 1 (continued)

Author (Year)	Design / Level of evidence	Sample size and sex	Age, Mean $\pm$ SD (range)	Asthma (%)	N-ERD (%)	ESS (%)	Main outcome		Follow-up (weeks)
							Variable	Variation (mean $\pm$ SD)	
Garvey (2024)	Retrospective cohort study	39 (14M; 25 F)	52.21 $\pm$ 15.52	100	25.6	92.3	SNOT-22	57.34 $\pm$ 22.45	51.6
Gal (2024)	Retrospective cohort study	47 (36 M; 11 F)	52.9 $\pm$ 13.5	74.5%	53.2	100	NPS	4.15 $\pm$ 2.53	51.6
							SNOT-22	52.4 $\pm$ 24.3	51.6
							NPS	6.15 $\pm$ 1.71	51.6
							Sniffin's Sticks (0 - 16)	1.6 $\pm$ 2.8	51.6
Gelardi (2024)	Retrospective cohort study	27 (19 M; 8 F)	56.37 $\pm$ 10.09	63 %	NR	NR	SNOT-22	65 $\pm$ 22.12 **	51.6
							NPS	5.67 $\pm$ 1.58 **	51.6
Sarnoch (2024)	Prospective cohort study	104 (51 M; 23 F)	50.3 $\pm$ 13.8	83 %	48	NR	SNOT-22	60.42 $\pm$ 19.36	94.6
							NPS	4.72 $\pm$ 1.60	94.6
							Sniffin's Sticks (0 - 12)	3.22 $\pm$ 3.65	94.6
De Corso (2024)	Retrospective cohort study	52 (30 M; 22 F)	50.1 $\pm$ 13.6	69.2 %	26.9	86.5	SNOT-22	58.6 $\pm$ 18.8	51.6
							SNOT-22	12.2 $\pm$ 7.9	51.6

NA (not applicable). NR (not reported). SD (standard deviation). ESS (endoscopic sinus surgery). CRSwNP (chronic rhinosinusitis with nasal polyps). N-ERD (NSAID – Non steroidal anti-inflammatory drugs – Exacerbated Respiratory Disease). SNOT-22 (SinoNasal Outcome Test – 22. Score: 0 - 110). NPS (Nasal Polyp Score. Score: 0 - 8). VAS (Visual Analogue Scale. Score: 0 - 10 cm). B-SIT (Brief Smell Identification Test. Score: 0 - 12). ** Mean and Standard Deviation estimated using Wan's method.

or first and third quartile) to estimate the mean and standard deviation following Wan's method [116].

Twenty of them originally provided their data as mean and standard deviation [24, 108, 119–133, 135, 136, 138], one author provided them under request [139] and Wan's method [116] could be applied for estimating data for three studies [117, 118, 134]. This way, changes in SNOT-22 for 2094 patients could be combined in a meta-analysis (Fig. 2).

Since the I^2 heterogeneity coefficient was 96%, a random-effects model was assumed, being the mean SNOT-22 difference after dupilumab treatment 37.2 (Fig. 2).

An Egger test was performed to investigate the possibility of publication bias, yielding a coefficient of -1.03 ($p < 0.30$). Figure 3 displays the Funnel plot for the difference in SNOT-22 scores among the published studies.

When comparing the results of the current study with the results provided by the SINUS-52 [141] (28.5 ± 2.2) clinical trial using a student T test for independent samples, statistically significant differences were found with the fixed effect model ($t = 95.3$; $p < 0.01$) as well as with random-effect model ($t = 46.7$; $p < 0.01$) favoring RWE.

Nasal Polyp Score (NPS)

The results are summarized in Table 1. Thirty observational RWE assessed NPS [24, 108, 117–120, 122–126, 128, 129, 131, 137, 139, 140].

Eight of them [77, 81, 84, 88, 89, 92, 93, 133] could not be included in the meta-analysis because of the same reasons stated above regarding SNOT-22 values.

Fifteen of them originally provided their data as mean and standard deviation [24, 108, 119–131], one author provided them on request [139] and Wan's method [116] could be applied for estimating data for three studies [117, 118, 134]. In this manner, changes in NPS for 1994 patients could be combined in a meta-analysis (Fig. 4).

The heterogeneity coefficient was 96%, suggesting the high heterogeneity of samples. The mean difference in NPS after dupilumab treatment under a random effects model was 3.6 (Fig. 4).

Comparing the results of the current study with those resulting from the SINUS-52 clinical trial [141] using a student t test for independent samples, statistically

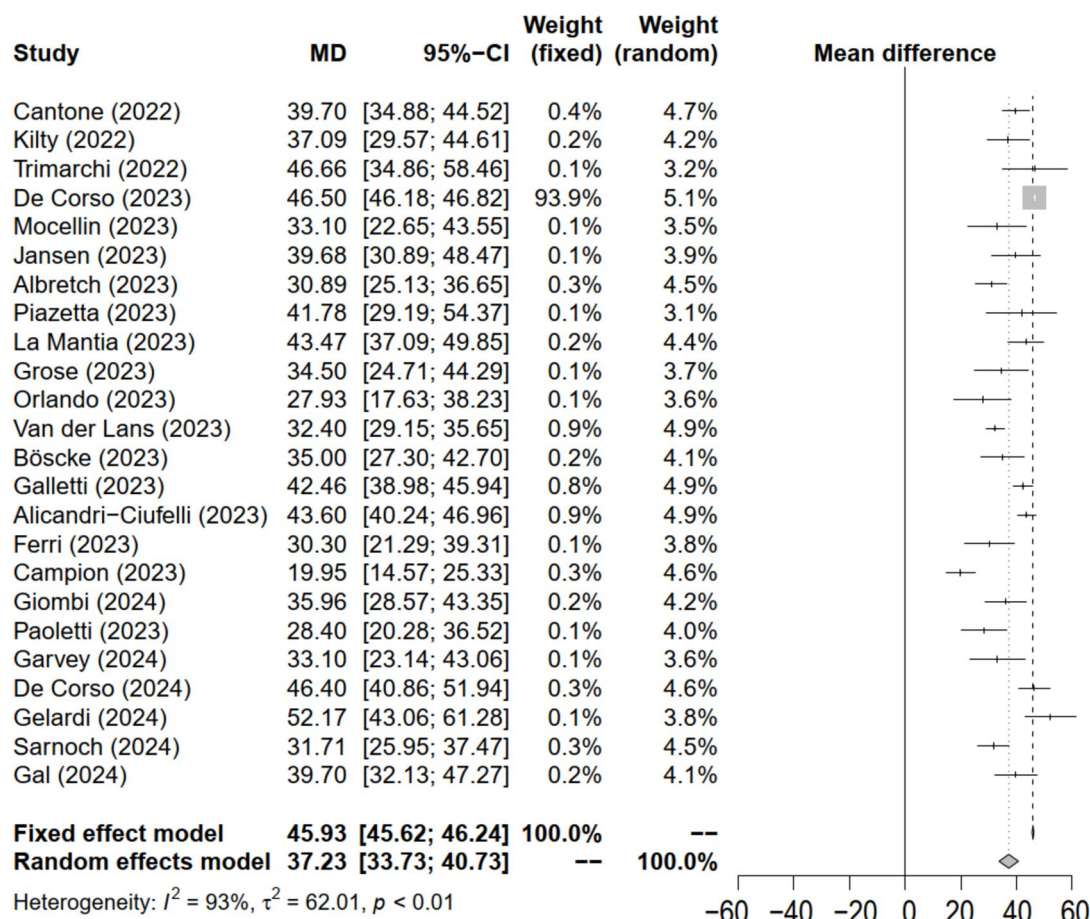


Fig. 2 Forest plot for the SNOT-22 difference after dupilumab treatment. Statistical significance was found, since the diamond did not reach the vertical discontinuous line. Taking into account the high heterogeneity observed, the random effects model was assumed

Fig. 3 Funnel plot of the SNOT-22 difference after dupilumab treatment. Most of the published studies are located on the left part of the graph bias favoring the studies with results inferior to the mean

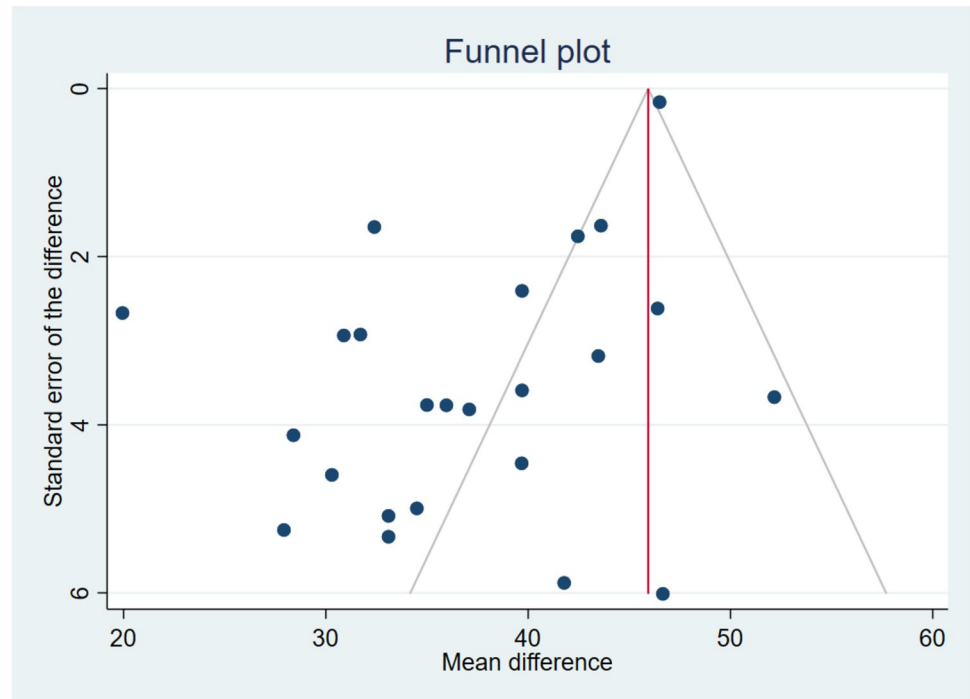
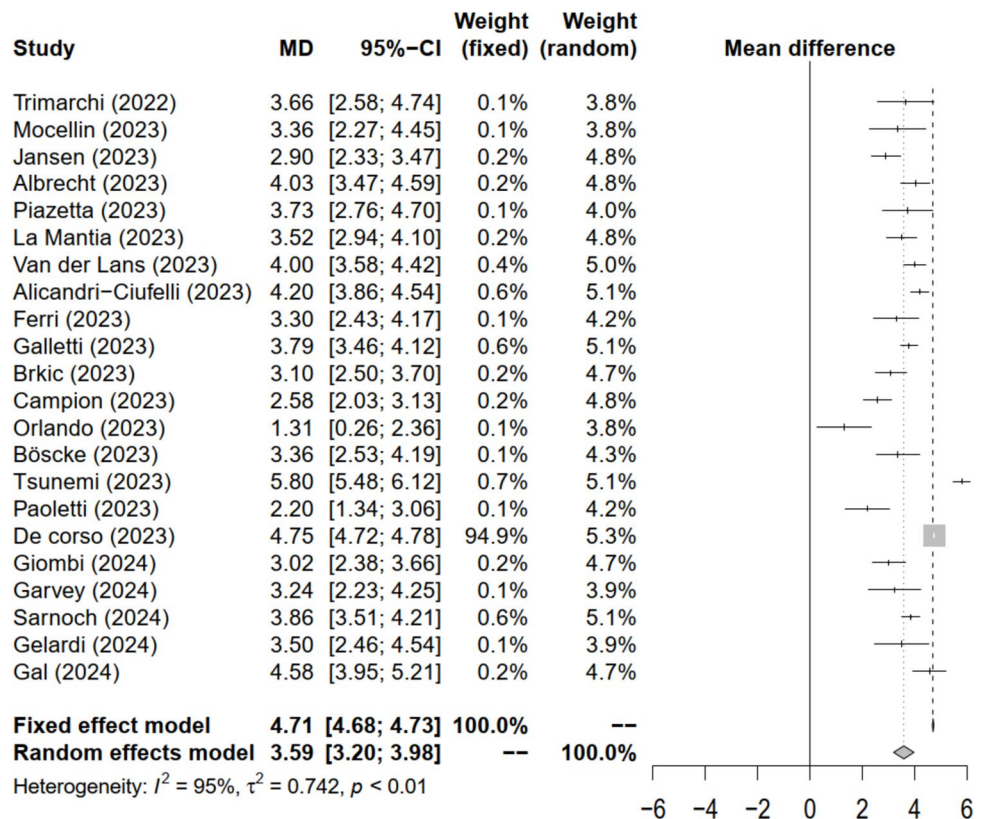


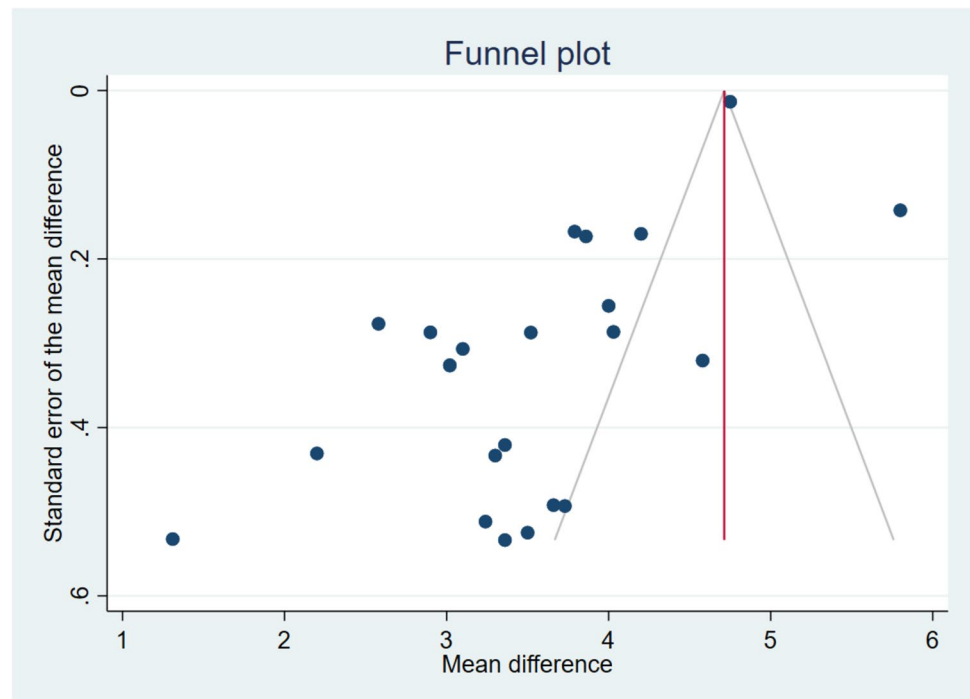
Fig. 4 Forest plot for the difference in Nasal Polyp Size (NPS) after dupilumab treatment. Statistical significance was found, since the diamond did not reach the vertical discontinuous line. Taking into account the high heterogeneity observed, the random effects model was assumed



significant differences were found with the fixed-effects model ($t = 146.9$; $p < 0.01$) as well as with the random-effects model ($t = 75.6$; $p < 0.01$).

An Egger test was performed to investigate the possibility of publication bias, yielding a coefficient of -3.35 ($p < 0.001$). Figure 5 displays the Funnel plot

Fig. 5 Funnel plot of the Nasal Polyp Size (NPS) difference after dupilumab treatment. Most of the published studies are located on the left part of the graph bias favoring the studies with results inferior to the mean



for the difference in NPS scores among the published studies.

Discussion

To the best of our knowledge, this is the first meta-analysis evaluating nasal variables improvement after dupilumab treatment in RWE performed on patients where the indication for treatment was severe CRSwNP. This review concludes that dupilumab is a promising therapy for patients with CRSwNP, with results in real life that outweigh those reported in clinical trials.

Several published studies have measured the nasal effects of dupilumab in patients with CRSwNP. However, only in a small fraction of these studies, severe CRSwNP has been the indication for the biologic therapy, as in the vast majority it has been indicated for other conditions such as severe asthma, or eosinophilic esophagitis, among others. As mentioned above, these studies were excluded in our review (*Supplementary Annex 1*).

The goals of CRSwNP treatment are to achieve effective and sustained symptom control, minimize polyp recurrence, and control of comorbid lower airway disease while minimizing the risk of side-effects associated with systemic corticosteroid use and revision ESS [20]. In our research, we decided to focus on quantifying the variability in nasal symptoms using the SNOT-22 questionnaire as our primary target. A total of 24 studies could finally be combined in a meta-analysis in which the main result

to highlight is that RWE have shown satisfactory results in nasal symptoms, better than those reported in the SINUS-52 RCT [141]. SINUS-52 obtained a decrease of 28.5 points on the SNOT-22 in the treatment cohort, whereas our meta-analysis obtained 37.2 points of decrease under a random effects model. It represents an improvement of 4.18 times the minimal clinically importance difference (MCID), which was established at 8.9 points for SNOT-22 [49]. In SINUS-52 it was 3.2 times the MCID [141].

Our second endpoint was the NPS. The meta-analysis suggests better outcomes in terms of NPS decrease for RWE compared to the SINUS-52 clinical trial [141]. SINUS-52 obtained a decrease of 2.3 ± 0.2 points in the NPS in the treatment cohort, while the present meta-analysis obtained 3.6 ± 0.2 points of decrease. These results could be interpreted as the SINUS-52 clinical trial does not have adequate external validity, with better results in real-life practice. External validity is a problem for several RCT as they try to achieve an accurate and homogeneous patient selection (internal validity), which does not usually correlate with real practice (external validity) [142].

It is important to highlight the analysis regarding the bias of publication performed in this study. In relation to SNOT-22, the graphic representation (with funnel plot) could suggest that a publication bias exists. Nevertheless, when performing the Egger regression to estimate it, a $p > 0.3$ is obtained, indicating that there is not a publication bias. On the other hand, a publication bias exists in relation to NPS. However, it is also of interest to consider that this is a negative publication bias. As observed in the funnel plot, it is

likely that there are yet-to-be-published articles in which a greater reduction in NPS could be found, indicating that the difference posttreatment is probably underestimated. In this case, RWE is better than the reported in the SINUS-52 clinical trial [141]. However, being scientifically prudent, both cohorts should not be fully compared, as they encompass different types of patients. In the SINUS-52 RCT cohort, the mean was 50.2 points for baseline SNOT-22 and 6.1 for baseline NPS, while the weighted mean in our meta-analysis was 57.3 points for baseline SNOT-22 and 5.5 for baseline NPS.

In relation to the comorbidities, proportions are different as well. In the SINUS-52 RCT [141], 57% and 23% of the patients suffered from asthma and N-ERD, respectively. The weighted mean for the proportion of asthmatic patients in the studies included in our meta-analysis was 66.7% for asthma and 44.6% for N-ERD. This relationship may be highly relevant when evaluating the response to treatment. Patients diagnosed with CRSwNP and concurrent asthma, with or without N-ERD, experience a more severe form of the disease. This is characterized by an elevated nasal polyp growth, higher rate of recurrence after surgery, frequent reliance on systemic corticosteroids, inadequate asthma control, and increased healthcare costs and resource utilization [143]. Even so, it should be mentioned that asthma control appears to be improved, as some studies found a statistically significant improvement in the Asthma Control Test after 1 and 3 months post-treatment [108, 131]. Following this point, an additional potential confounding factor is the prevalence of severe asthma; although most authors provide the prevalence of asthma, they do not specify the severity of the disease or its control degree.

The loss of smell, which is one of the most challenging symptoms for patients with severe CRSwNP, is associated with both the severity and recurrence of the disease significantly affecting their QoL [127, 128]. Its recovery is one of the first signs of treatment efficacy that patients experience once dupilumab therapy is started [24]. There is a lack of information on whether a history of previous surgery influences the speed of recovery. Among the studies included in the revision, seventeen of them measured smell function [24, 79, 117–120, 122–124, 126, 128, 129, 132, 133, 135, 136]. Furthermore, the wide variety of methods used to measure olfactory impairment (Sniffin' Sticks – 16 [79, 118, 120, 122, 126, 133, 136], Sniffin' Sticks–12 [24, 119, 123, 124, 128, 135], Visual Analog Scale [117, 118, 124, 129, 131–133], Brief Smell Identification Test [117]) makes it difficult to obtain comparable data. A post hoc analysis of SINUS-24 and SINUS-52 cohorts, found that patients with three or more previous ESS at baseline, exhibited the worst results regarding olfaction [49]. However, they showed similar improvement during the follow-up period regardless of the number of prior ESS without reporting any significant

correlation between the results and the number of previous ESS. In this regard, De Corso et al. claimed that olfaction improved faster in patients without previous surgeries, but that difference was not clinically relevant [118].

Another factor to be considered is the history of previous surgery, as it could interfere with the speed of improvement. In the ESS sinus surgery at the beginning of the study. The weighted mean with previous surgeries among the patients included in our meta-analysis is 77.8%, being the range from 56.5 to 100% in eight studies [24, 117, 121, 123, 124, 129, 137, 140]. In this sense, some studies phrased that SNOT-22 and NPS showed a faster decrease in patients who had undergone previous surgery [118, 122]. Although most of the reviewed studies did not analyze this factor in RWE, a post hoc analysis described how a short onset of biological treatment (<3 years since the last ESS) correlated with greater improvements in endoscopic findings [49], highlighting the importance of timing in combined treatment. In addition to the surgical history, it would also be necessary to include the type of surgery performed, since extensive surgeries appear to achieve better results regarding illness control [118, 122, 144]. The majority of authors utilized different systems to classify the surgeries performed, making comparisons of the surgery-related outcomes challenging. Nevertheless, a more comprehensive surgical analysis is necessary in this fast-moving field.

Although the results found in this study seem to be better than those obtained in RCT, there are several limitations that should be considered. The first limitation is the novelty of this treatment. In medicine, first reports tend to be the most notable, whereas subsequent studies, as enthusiasm decreases, tend to diminish. As all included studies were published between 2022 and 2023, we cannot know if we are seeing these first results. At present, the cumulative meta-analysis does not suggest a latency in published results, but future research including new studies is highly recommended to study this phenomenon. Another limitation lies in the variability of the follow-up times. Although it may not be the best option to merge studies with such marked variability in follow-up time in a meta-analysis, it should be taken into account that the most significant reduction was observed in the initial weeks, with a slow and gradual improvement afterwards, particularly for subjective parameters such as SNOT-22, VAS scores for loss of smell and nasal obstruction. For this reason, and given the available evidence at this moment, it seems reasonable to combine the results. A stratified analysis by subgroups should be performed in future studies as more samples become available.

Despite this systematic review with meta-analysis follows rigorous guidelines to evaluate the efficacy of dupilumab therapy, there are limitations. Strict inclusion criteria, which exclude small sample sizes, certain specific study designs and those studies where dupilumab was indicated for other

conditions (*Supplementary Annex 1*), may have led to omitted data. In addition, methodological difficulties in estimating the mean and standard deviation from partially published or median-based data, as well as the conversion of follow-up periods into weeks, introduce uncertainties. Thus, although these inherent limitations of the review are attempted to be controlled by a meticulous statistical analysis process, controlling for heterogeneity and publication biases of the included articles, cautious interpretation and further research are warranted to validate the findings.

Despite the limitations discussed above, it should be kept in mind that we are currently dealing with a new line of treatment. Therefore, it is to be expected that the available evidence presents these types of limitations. This kind of systematic review, which gathers all the available evidence, helps to shed some light and limit the potential distortion of the results generated by small observational studies. It also highlights pitfalls and knowledge gaps to guide future studies.

Conclusion

The available evidence is limited by the observational design of the included studies, and any results should be carefully managed. The available evidence appears to favor dupilumab RWE studies compared with the previous dupilumab RCT (SINUS-52), with a better response regarding NPS and SNOT-22.

Key References

- De Corso E, Pasquini E, Trimarchi M, et al. (2023) Dupilumab in the treatment of severe uncontrolled chronic rhinosinusitis with nasal polyps (CRSwNP): A multicentric observational Phase IV real-life study (DUPIREAL). *Allergy* 78:2669–2683. <https://doi.org/10.1111/all.15772>.

COMMENT: This RWE study has the biggest sample size among the included into the meta-analysis.

- Alobid I, Colás C, Castillo J, et al. (2023) Spanish Consensus on the Management of Chronic Rhinosinusitis With Nasal Polyps (POLIposis NAsal/POLINA 2.0). *J Investig Allergol Clin Immunol* 33:317–331. <https://doi.org/10.18176/jiaci.0910>.

COMMENT: The POLINA consensus provides new definitions of control, therapeutic management (including surgery and evaluation of severity), indications for use of biologics, and response.

- Fokkens WJ, Viskens A-S, Backer V, et al. (2023) EPOS/ EUFOREA update on indication and evaluation of Biologics in Chronic Rhinosinusitis with Nasal Polyps 2023. *Rhinology* 61:194–202. <https://doi.org/10.4193/Rhin22.489>.

COMMENT: Criteria for the selection of patients who would benefit from biologics were updated.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Ethical Approval This article does not contain any studies with human participants performed by any of the authors.

Competing Interests The authors declare no competing interests.

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References

- Bachert C, Han JK, Wagenmann M, et al. EUFOREA expert board meeting on uncontrolled severe chronic rhinosinusitis with nasal polyps (CRSwNP) and biologics: definitions and management. *J Allergy Clin Immunol*. 2021;147:29–36. <https://doi.org/10.1016/j.jaci.2020.11.013>.
- Settipane GA, Chafee FH. Nasal polyps in asthma and rhinitis. A review of 6,037 patients. *J Allergy Clin Immunol*. 1977;59:17–21. [https://doi.org/10.1016/0091-6749\(77\)90171-3](https://doi.org/10.1016/0091-6749(77)90171-3).
- Hedman J, Kaprio J, Poussa T, Nieminen MM. Prevalence of asthma, aspirin intolerance, nasal polyposis and chronic obstructive pulmonary disease in a population-based study. *Int*

- J Epidemiol. 1999;28:717–22. <https://doi.org/10.1093/ije/28.4.717>.
4. Sanchez-Collado I, Mora T, Munoz-Cano R, et al. Prevalence of chronic rhinosinusitis with nasal polyps in Catalonia (Spain): a retrospective, large-scale population-based study. *Rhinology*. 2022;0:0–0. <https://doi.org/10.4193/Rhin21.364>.
5. Mullol J, Sastre J, Domínguez-Ortega J, et al. Prevalence of chronic rhinosinusitis without/with nasal polyps according to severity in Spain. *Rhinology*. 2024;0:0–0. <https://doi.org/10.4193/Rhin23.341>.
6. Gliklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otolaryngologic care. *Otolaryngol Head Neck Surg*. 1995;113:104–9. <https://doi.org/10.1016/S0194-59989570152-4>.
7. Alobid I, Benítez P, Bernal-Sprekelsen M, et al. Nasal polyposis and its impact on quality of life: comparison between the effects of medical and surgical treatments. *Allergy*. 2005;60:452–8. <https://doi.org/10.1111/j.1398-9995.2005.00725.x>.
8. Sahlstrand-Johnson P, Ohlsson B, Von Buchwald C, et al. A multi-centre study on quality of life and absenteeism in patients with CRS referred for endoscopic surgery. *Rhinology*. 2011;49:420–8. <https://doi.org/10.4193/Rhino11.101>.
9. DeConde AS, Mace JC, Levy JM, et al. Prevalence of polyp recurrence after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. *Laryngoscope*. 2017;127:550–5. <https://doi.org/10.1002/lary.26391>.
10. Rosati D, Rosato C, Pagliuca G, et al. Predictive markers of long-term recurrence in chronic rhinosinusitis with nasal polyps. *Am J Otolaryngol*. 2020;41. <https://doi.org/10.1016/j.amjoto.2019.102286>.
11. Arancibia C, Langdon C, Mullol J, Alobid I. Twelve-year long-term postoperative outcomes in patients with chronic rhinosinusitis with nasal polyps. *Rhinology*. 2022;60:261–9. <https://doi.org/10.4193/Rhin21.148>.
12. Tomassen P, Vandeplas G, Van Zele T, et al. Inflammatory endotypes of chronic rhinosinusitis based on cluster analysis of biomarkers. *J Allergy Clin Immunol*. 2016;137:1449–e14564. <https://doi.org/10.1016/j.jaci.2015.12.1324>.
13. Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. *Am J Rhinol Allergy*. 2013;27:473–8. <https://doi.org/10.2500/ajra.2013.27.3981>.
14. Bachert C, Zhang N, Hellings PW, Bousquet J. Endotype-driven care pathways in patients with chronic rhinosinusitis. *J Allergy Clin Immunol*. 2018;141:1543–51. <https://doi.org/10.1016/j.jaci.2018.03.004>.
15. Shirley M. Dupilumab: first global approval. *Drugs*. 2017;77:1115–21. <https://doi.org/10.1007/s40265-017-0768-3>.
16. Wu Q, Zhang Y, Kong W, et al. Which is the best biologic for nasal polyps: dupilumab, omalizumab, or Mepolizumab? A network meta-analysis. *Int Arch Allergy Immunol*. 2022;183:279–88. <https://doi.org/10.1159/000519228>.
17. Boechat JL, Silva D, Sousa-Pinto B, Delgado L. Comparing biologicals for severe chronic rhinosinusitis with nasal polyps: a network meta-analysis. *Allergy Eur J Allergy Clin Immunol*. 2022;77:1299–306. <https://doi.org/10.1111/all.15205>.
18. Oykhman P, Paramo FA, Bousquet J, et al. Comparative efficacy and safety of monoclonal antibodies and aspirin desensitization for chronic rhinosinusitis with nasal polyposis: a systematic review and network meta-analysis. *J Allergy Clin Immunol*. 2022;149:1286–95. <https://doi.org/10.1016/j.jaci.2021.09.009>.
19. Sherman RE, Anderson SA, Dal Pan GJ, et al. Real-world evidence — what is it and what can it tell us? *N Engl J Med*. 2016;375:2293–7. <https://doi.org/10.1056/NEJMs1609216>.
20. Fokkens WJ, Lund VJ, Hopkins C, et al. European position paper on rhinosinusitis and nasal polyps 2020. *Rhinology*. 2020;58:1–464. <https://doi.org/10.4193/Rhin20.600>.
21. Alobid I, Colás C, Castillo J, et al. Spanish consensus on the management of chronic rhinosinusitis with nasal polyps (POLIPOLIS Nasal/POLINA 2.0). *J Investig Allergol Clin Immunol*. 2023;33:317–31. <https://doi.org/10.18176/jiaci.0910>.
22. Fokkens WJ, Viskens A-S, Backer V, et al. EPOS/EUFOREA update on indication and evaluation of biologics in chronic rhinosinusitis with nasal polyps 2023. *Rhinology*. 2023;61:194–202. <https://doi.org/10.4193/Rhin22.489>.
23. Bachert C, Mannent L, Naclerio RM, et al. Dupilumab in chronic sinusitis with nasal polyposis, with and without asthma. *Allergy Eur J Allergy Clin Immunol*. 2015;70:107. <https://doi.org/10.1111/all.12715>.
24. Boscke R, Bruchhage KL. Real-life data on the effectiveness and safety of dupilumab in adult patients with uncontrolled chronic rhinosinusitis with nasal polyps (CRSwNP). *Laryngo-Rhino-Otol*. 2021;100:S278–9. <https://doi.org/10.1055/s-0041-1728626>.
25. Cipolla F, La Mantia I. Chronic rhinosinusitis with nasal polyps and dupilumab: results after six months of treatment. *Allergy Eur J Allergy Clin Immunol*. 2023;78:421–2. <https://doi.org/10.1111/all.15616>.
26. De Prado Gomez L, Khan AH, Peters A, et al. Evaluating treatment Responses of dupilumab versus omalizumab in type 2 patients: the EVEREST trial. *Allergy Eur J Allergy Clin Immunol*. 2023;78:616–7. <https://doi.org/10.1111/all.15616>.
27. Dennis SK, Martin L, Marc D, et al. CRSwNP and dupilumab-experiences after one year of clinical use at a university ENT clinic. *Laryngo-Rhino-Otol*. 2022;101:S329. <https://doi.org/10.1055/s-0042-1747025>.
28. Mathias H, Robert B, Marius T, et al. Dupilumab-treatment for uncontrolled CRSwNP: real-life 15-months follow-up data. *Laryngo-Rhino-Otol*. 2022;101:S332. <https://doi.org/10.1055/s-0042-1747000>.
29. Schmale I, Poulakis A, Abend A, et al. Real-world outcomes of dupilumab therapy for nasal polyposis in patients with aspirin-exacerbated respiratory disease. *J Allergy Clin Immunol*. 2023;151:AB218. <https://doi.org/10.1016/j.jaci.2022.12.680>.
30. Hoffmann AS, Eden J, Jansen F, et al. Efficacy of dupilumab (Dupixent) in the treatment of chronic rhinosinusitis with nasal polyps: first results from Hamburg. *Laryngo-Rhino-Otol*. 2021;100:S284–5. <https://doi.org/10.1055/s-0041-1728858>.
31. Sophie HA, Florian J, Benjamin B, et al. Real world data on the effectiveness and safety of dupilumab in adult patients with uncontrolled severe chronic rhinosinusitis with nasal polyps (CRSwNP). *Laryngo-Rhino-Otol*. 2022;101:S328. <https://doi.org/10.1055/s-0042-1747020>.
32. Ferreira Gom MP, Ferreira S, Gomes Rosa JP, et al. Chronic rhinosinusitis with nasal polyposis: Portuguese experience with dupilumab in two centers. *J Allergy Clin Immunol*. 2024;153:AB214. <https://doi.org/10.1016/j.jaci.2023.11.691>.
33. Juarez C, Eusebio I, Viciano MG, et al. Dupilumab effectiveness in chronic rhinosinusitis with nasal polyps and asthma in real-life conditions. *J Allergy Clin Immunol*. 2024;153:AB103. <https://doi.org/10.1016/j.jaci.2023.11.337>.
34. Lanz M, Eisenlohr C, Chartrand E, Herrera L. Early clinical improvement of anosmia and sinus nitric oxide in CRSwNP subjects treated with Dupilumab. *J Allergy Clin Immunol*. 2024;153:AB210. <https://doi.org/10.1016/j.jaci.2023.11.677>.
35. Peters A, Han J, Goeckner B, et al. Efficacy of Biologics in patients with moderate-to-severe, uncontrolled asthma and nasal polyps. *J Allergy Clin Immunol*. 2024;153:AB100. <https://doi.org/10.1016/j.jaci.2023.11.329>.
36. Laidlaw TM, Bachert C, Amin N, et al. Dupilumab improves upper and lower airway disease control in chronic rhinosinusitis with nasal polyps and asthma. *Ann Allergy Asthma*

- Immunol. 2021;126:584–e5921. <https://doi.org/10.1016/j.anai.2021.01.012>.
37. Boguniewicz M, Beck LA, Sher L, et al. Dupilumab improves asthma and sinonasal outcomes in adults with moderate to severe atopic dermatitis. *J Allergy Clin Immunol Pract*. 2021;9:1212–e12236. <https://doi.org/10.1016/j.jaip.2020.12.059>.
 38. Miglani A, Soler ZM, Smith TL, et al. A comparative analysis of endoscopic sinus surgery versus biologics for treatment of chronic rhinosinusitis with nasal polyposis. *Int Forum Allergy Rhinol*. 2023;13:116–28. <https://doi.org/10.1002/alr.23059>.
 39. Khan AH, Reaney M, Guillemin I, et al. Development of sinonasal outcome test (SNOT-22) domains in chronic Rhinosinusitis with nasal polyps. *Laryngoscope*. 2022;132:933–41. <https://doi.org/10.1002/lary.29766>.
 40. Busse WW, Wellman A, Diamant Z, et al. Impact of dupilumab on SNOT-22 sleep and function scores in CRSwNP. *J Allergy Clin Immunol Pract*. 2022;10:2479–e24823. <https://doi.org/10.1016/j.jaip.2022.05.013>.
 41. Weinstein SF, Katial R, Jayawardena S, et al. Efficacy and safety of dupilumab in perennial allergic rhinitis and comorbid asthma. *J Allergy Clin Immunol*. 2018;142:171–e1771. <https://doi.org/10.1016/j.jaci.2017.11.051>.
 42. Mullol J, Laidlaw TM, Bachert C, et al. Efficacy and safety of dupilumab in patients with uncontrolled severe chronic rhinosinusitis with nasal polyps and a clinical diagnosis of NSAID-ERD: results from two randomized placebo-controlled phase 3 trials. *Allergy*. 2022;77:1231–44. <https://doi.org/10.1111/all.15067>.
 43. Bachert C, Zinreich SJ, Hellings PW, et al. Dupilumab reduces opacification across all sinuses and related symptoms in patients with CRSwNP. *Rhinology*. 2020;58:10–7. <https://doi.org/10.4193/Rhin18.282>.
 44. Busse WW, Pavord ID, Siddiqui S, et al. Dupilumab improves outcomes in patients with chronic rhinosinusitis with nasal polyps and coexisting asthma irrespective of baseline asthma characteristics. *J Asthma Allergy*. 2023;16:411–9. <https://doi.org/10.2147/JAA.S391896>.
 45. Desrosiers M, Mannent LP, Amin N, et al. Dupilumab reduces systemic corticosteroid use and sinonasal surgery rate in CRSwNP. *Rhinology*. 2021;59:301–11. <https://doi.org/10.4193/Rhin20.415>.
 46. Bachert C, Khan AH, Hopkins C, et al. Rapid and Continuing improvements in nasal symptoms with dupilumab in patients with severe CRSwNP. *J Asthma Allergy*. 2022;15:557–63. <https://doi.org/10.2147/JAA.S355391>.
 47. Fujieda S, Matsune S, Takeno S, et al. The effect of dupilumab on intractable chronic rhinosinusitis with nasal polyps in Japan. *Laryngoscope*. 2021;131:E1770–1777. <https://doi.org/10.1002/lary.29230>.
 48. Lee SE, Amin N, Mannent LP, et al. The relationship of sinus opacification, olfaction and dupilumab efficacy in patients with CRSwNP. *Rhinology*. 2023;61:531–40. <https://doi.org/10.4193/Rhin22.220>.
 49. Hopkins C, Wagenmann M, Bachert C, et al. Efficacy of dupilumab in patients with a history of prior sinus surgery for chronic rhinosinusitis with nasal polyps. *Int Forum Allergy Rhinol*. 2021;11:1087–101. <https://doi.org/10.1002/alr.22780>.
 50. Mullol J, Bachert C, Amin N, et al. Olfactory outcomes with dupilumab in chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol Pract*. 2022;10:1086–e10955. <https://doi.org/10.1016/j.jaip.2021.09.037>.
 51. Canonica GW, Bourdin A, Peters AT, et al. Dupilumab demonstrates rapid onset of response across three type 2 inflammatory diseases. *J Allergy Clin Immunol Pract*. 2022;10:1515–26. <https://doi.org/10.1016/j.jaip.2022.02.026>.
 52. Chuang C-C, Guillemin I, Bachert C, et al. Dupilumab in CRSwNP: responder analysis using clinically meaningful efficacy outcome thresholds. *Laryngoscope*. 2022;132:259–64. <https://doi.org/10.1002/lary.29911>.
 53. Peters AT, Wagenmann M, Bernstein JA, et al. Dupilumab efficacy in patients with chronic rhinosinusitis with nasal polyps with and without allergic rhinitis. *Allergy Asthma Proc*. 2023;44:265–74. <https://doi.org/10.2500/aap.2023.44.230015>.
 54. Gevaert P, Lee SE, Settipane RA, et al. Dupilumab provides early and durable improvement of symptoms in patients with chronic rhinosinusitis with nasal polyps. *Clin Transl Immunol*. 2023;12. <https://doi.org/10.1002/cti2.1433>.
 55. Bachert C, Khan AH, Lee SE, et al. Prevalence of type 2 inflammatory signatures and efficacy of dupilumab in patients with chronic rhinosinusitis with nasal polyps from two phase 3 clinical trials: SINUS-24 and SINUS-52. *Int Forum Allergy Rhinol*. 2023. <https://doi.org/10.1002/alr.23249>.
 56. Hellings PW, Peters A, Chaker AM et al (2021) Rapid and sustained effects of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps: analysis of the sinus-24 and sinus-52 phase 3 trials. *Am J Respir Crit Care Med* 203. https://doi.org/10.1164/ajrccm-conference.2021.203.1_MeetingAbstracts.A1345
 57. Bachert C, Khan A, Fokkens W, et al. Onset, maintenance, and durability of response with dupilumab in chronic rhinosinusitis with nasal polyps. *Eur Respir J*. 2022;60:60. <https://doi.org/10.1183/13993003.congress-2022.1711>.
 58. Bachert C, Khan A, Lee S, et al. Dupilumab improves chronic rhinosinusitis with nasal polyps disease outcomes irrespective of type 2 signature definition. *Ann Allergy Asthma Immunol*. 2022;129:S72–3. <https://doi.org/10.1016/j.anai.2022.08.710>.
 59. Bachert C, Peters AT, Heffler E, et al. A responder analysis to demonstrate dupilumab treatment effect across objective and patient-reported endpoints for patients with severe chronic rhinosinusitis with nasal polyps (CRSwNP). *Clin Exp Allergy*. 2021;51:1665–6. <https://doi.org/10.1111/cea.14044>.
 60. Busse W, Pavord I, Siddiqui S, et al. Dupilumab improves crswnp/asthma outcomes in patients with crswnp and comorbid asthma irrespective of asthma characteristics. *Ann Allergy Asthma Immunol*. 2021;127:S52–3. <https://doi.org/10.1016/j.anai.2021.08.158>.
 61. Laidlaw TM, Mullol J, Fan C, et al. Dupilumab improves nasal polyp burden and asthma control in patients with CRSwNP and AERD. *J Allergy Clin Immunol Pract*. 2019;7:2462–e24651. <https://doi.org/10.1016/j.jaip.2019.03.044>.
 62. Lane A, Mullol J, Hopkins C, et al. Dupilumab leads to reduction of anosmia in patients with severe chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol*. 2022;149:AB144. <https://doi.org/10.1016/j.jaci.2021.12.486>.
 63. Peters A, Wagenmann M, Bernstein JA, et al. Efficacy of dupilumab in patients with chronic rhinosinusitis with nasal polyps and allergic rhinitis. *Am J Respir Crit Care Med*. 2021;203:203. https://doi.org/10.1164/ajrccm-conference.2021.203.1_MeetingAbstracts.A1340.
 64. Soler Z, Lane A, Patel Z, et al. Association between smell loss, disease burden, and dupilumab efficacy in chronic rhinosinusitis with nasal polyps. *Ann Allergy Asthma Immunol*. 2022;129:S72. <https://doi.org/10.1016/j.anai.2022.08.709>.
 65. Hellings P, Bachert C, Mullol J, et al. Dupilumab improves ACQ-5 items in CRSwNP patients with comorbid asthma. *Respirology*. 2018;23:153. <https://doi.org/10.1111/resp.13268>.
 66. Hopkins C, Mullol J, Khan AH, et al. Impact of dupilumab on sinonasal symptoms and outcomes in severe chronic rhinosinusitis with nasal polyps. *Otolaryngol Head Neck Surg*. 2024;170:1173–82. <https://doi.org/10.1002/ohn.627>.

67. Bachert C, Khan AH, Lee SE, et al. Prevalence of type 2 inflammatory signatures and efficacy of dupilumab in patients with chronic rhinosinusitis with nasal polyps from two phase 3 clinical trials: SINUS-24 and SINUS-52. *Int Forum Allergy Rhinol.* 2023. <https://doi.org/10.1002/alr.23249>.
68. Mustafa SS, Vadmalai K, Scott B, Ramsey A. Dupilumab as add-on therapy for chronic rhinosinusitis with nasal polyposis in aspirin exacerbated respiratory disease. *Am J Rhinol Allergy.* 2021;35:399–407. <https://doi.org/10.1177/1945892420961969>.
69. Napolitano M, Maffei M, Patruno C, et al. Dupilumab effectiveness for the treatment of patients with concomitant atopic dermatitis and chronic rhinosinusitis with nasal polyposis. *Dermatol Ther.* 2021;34. <https://doi.org/10.1111/dth.15120>.
70. Lyly A, Genberg E, Kauppi P, et al. Real-life experience of biologic treatment for asthma on chronic rhinosinusitis: a Finnish cohort. *Int Arch Allergy Immunol.* 2023;184:149–60. <https://doi.org/10.1159/000526365>.
71. Nolasco S, Campisi R, Cipolla A, et al. Dupilumab effectiveness in patients with type 2-high severe asthma and chronic rhinosinusitis with nasal polyps. *Eur Respir J.* 2022;60. <https://doi.org/10.1183/13993003.congress-2022.3319>.
72. Förster-Ruhrmann U, Stergioudi D, Szczepek AJ, et al. A real-life comparison of pulmonary and nasal outcomes in patients with severe asthma and nasal polyposis treated with T2-biologics. *World Allergy Organ J.* 2023;16. <https://doi.org/10.1016/j.waojou.2023.100746>.
73. Pelaia C, Lombardo N, Busceti MT, et al. Short-term evaluation of dupilumab effects in patients with severe asthma and nasal polyposis. *J Asthma Allergy.* 2021;14:1165–72. <https://doi.org/10.2147/JAA.S328988>.
74. Berger P, Menzies-Gow A, Peters AT, et al. Long-term efficacy of dupilumab in asthma with or without chronic rhinosinusitis and nasal polyps. *Ann Allergy Asthma Immunol.* 2023;130:215–24. <https://doi.org/10.1016/j.anai.2022.11.006>.
75. Caminati M, Maule M, Benoni R, et al. Dupilumab efficacy on asthma functional, inflammatory, and patient-reported outcomes across different disease phenotypes and severity: a real-life perspective. *Biomedicines.* 2024;12. <https://doi.org/10.3390/biomedicines12020390>.
76. Ottaviano G, De Corso E, Saccardo T, et al. Effectiveness of dupilumab in the treatment of adult and older adult patients with severe, uncontrolled CRSwNP. *JPM.* 2023;13. <https://doi.org/10.3390/jpm13081241>.
77. Ottaviano G, Saccardo T, Rocuzzo G, et al. Effectiveness of dupilumab in the treatment of patients with uncontrolled severe CRSwNP: a real-life Observational Study in Naïve and Post-surgical patients. *JPM.* 2022;12(1526). <https://doi.org/10.3390/jpm12091526>.
78. Torretta S, De Corso E, Nava N, et al. Proposal for a structured outpatient clinic for dupilumab treatment in chronic rhinosinusitis with nasal polyps in the first year of treatment. *J Pers Med.* 2022;12:1734. <https://doi.org/10.3390/jpm12101734>.
79. Galletti C, Barbieri MA, Ciodaro F, et al. Effectiveness and safety profile of dupilumab in chronic rhinosinusitis with nasal polyps: real-Life Data in Tertiary Care. *Pharmaceuticals (Basel).* 2023;16. <https://doi.org/10.3390/ph16040630>.
80. van der Lans RJL, Fokkens WJ, Adriaansen GFJPM, et al. Real-life observational cohort verifies high efficacy of dupilumab for chronic rhinosinusitis with nasal polyps. *Allergy.* 2022;77:670–4. <https://doi.org/10.1111/all.15134>.
81. Bellocchi G, Loperfido A, Passali FM, et al. Biologics in severe uncontrolled chronic rhinosinusitis with nasal polyps: a bicentric experience. *Acta Biomed.* 2023;94:e2023227. <https://doi.org/10.23750/abm.v94i5.14745>.
82. Al-Ahmad M, Ali A, Khalaf M, et al. Comorbid asthma in patients with chronic rhinosinusitis with nasal polyps: did dupilumab make a difference? *BMC Pulm Med.* 2023;23:266. <https://doi.org/10.1186/s12890-023-02556-8>.
83. Danisman Z, Linxweiler M, Kühn JP, et al. Differential nasal swab cytology represents a valuable tool for therapy monitoring but not prediction of therapy response in chronic rhinosinusitis with nasal polyps treated with dupilumab. *Front Immunol.* 2023;14. <https://doi.org/10.3389/fimmu.2023.1127576>.
84. Nettis E, Brussino L, Patella V, et al. Effectiveness and safety of dupilumab in patients with chronic rhinosinusitis with nasal polyps and associated comorbidities: a multicentric prospective study in real life. *Clin Mol Allergy.* 2022;20:6. <https://doi.org/10.1186/s12948-022-00171-2>.
85. Minagawa S, Araya J, Watanabe N, et al. Real-life effectiveness of dupilumab in patients with mild to moderate bronchial asthma comorbid with CRSwNP. *BMC Pulm Med.* 2022;22:258. <https://doi.org/10.1186/s12890-022-02046-3>.
86. Garvey E, Naimi B, Duffy A, et al. Optimizing the timing of biologic and surgical therapy for patients with refractory chronic rhinosinusitis with nasal polyposis (CRSwNP). *Int Forum Allergy Rhinol.* 2024;14:651–9. <https://doi.org/10.1002/alr.23246>.
87. Suzuki I, Maruyama Y, Kamimura S, et al. Residual nasal polyp tissue following dupilumab therapy is associated with periostin-associated fibrosis. *Eur Arch Oto-Rhino-Laryngol.* 2024;281:1807–17. <https://doi.org/10.1007/s00405-023-08336-8>.
88. Haxel BR, Hummel T, Fruth K, et al. Real-world-effectiveness of biological treatment for severe chronic rhinosinusitis with nasal polyps. *Rhin.* 2022;6:435–43. <https://doi.org/10.4193/Rhin22.129>.
89. Ottaviano G, De Corso E, Cantone E, et al. Measuring nasal patency and the sense of Smell in CRSwNP patients treated with dupilumab. *J Pers Med.* 2023;13. <https://doi.org/10.3390/jpm13020234>.
90. Schmale IL, Poulakis A, Abend A, et al. Chronic rhinosinusitis with nasal polyposis treated with dupilumab: real-world use and outcomes. *J Allergy Clin Immunol Pract.* 2023;11:3203–10. <https://doi.org/10.1016/j.jaip.2023.07.038>.
91. Newshean S, Darveaux JJ. Dupilumab in the treatment of nasal polyposis: a retrospective, real-world study. *Ann Allergy Asthma Immunol.* 2021;127:386–7. <https://doi.org/10.1016/j.anai.2021.05.018>.
92. Riva G, Garetto M, Borgione M, et al. Dupilumab improves sleep quality in chronic rhinosinusitis with nasal polyps. *Am J Otolaryngol.* 2024;45. <https://doi.org/10.1016/j.amjoto.2024.104310>.
93. Ottaviano G, Rocuzzo G, Lora L, et al. The impact of dupilumab on work productivity and emotional health in CRSwNP: a multicentric study in Northeast Italy. *J Pers Med.* 2024;14. <https://doi.org/10.3390/jpm14050468>.
94. Pecorari G, Piazza F, Borgione M, et al. The role of intranasal corticosteroids in chronic rhinosinusitis with nasal polyposis treated with dupilumab. *Am J Otolaryngol.* 2023;44:103927. <https://doi.org/10.1016/j.amjoto.2023.103927>.
95. Pelaia C, Benfante A, Busceti MT, et al. Real-life effects of dupilumab in patients with severe type 2 asthma, according to atopic trait and presence of chronic rhinosinusitis with nasal polyps. *Front Immunol.* 2023;14. <https://doi.org/10.3389/fimmu.2023.1121237>.
96. Gerstacker K, Ketterer MC, Jakob TF, Hildenbrand T. Real life observational study of treatment success of monoclonal antibodies for refractory chronic rhinosinusitis with nasal polyps. *J Clin Med.* 2023;12. <https://doi.org/10.3390/jcm12134374>.
97. Brkic FF, Liu DT, Klimbacher R, et al. Efficacy and safety of switching between biologics in chronic rhinosinusitis with nasal

- polyps or N-ERD. *Rhinology*. 2023;61:320–7. <https://doi.org/10.4193/Rhin22.408>.
98. Book R, Eligal S, Tal Y, Eliashar R. Biological treatment for uncontrolled chronic rhinosinusitis with nasal polyps: preliminary real-world results from a tertiary medical center. *J Clin Med*. 2023;12:12. <https://doi.org/10.3390/jcm12113671>.
 99. De Corso E, Montuori C, Settini S, et al. Efficacy of biologics on refractory eosinophilic otitis media associated with bronchial asthma or severe uncontrolled CRSwNP. *J Clin Med*. 2022;11:11. <https://doi.org/10.3390/jcm11040926>.
 100. Mümmeler C, Dünzelmann K, Kneidinger N, et al. Real-life effectiveness of biological therapies on symptoms in severe asthma with comorbid CRSwNP. *Clin Transl Allergy*. 2021;11. <https://doi.org/10.1002/ctlt2.12049>.
 101. Dharmarajan H, Falade O, Lee SE, Wang EW. Outcomes of dupilumab treatment versus endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps. *Int Forum Allergy Rhinol*. 2022;12:986–95. <https://doi.org/10.1002/alr.22951>.
 102. Hopkins C, Buchheit KM, Heffler E, et al. Improvement in health-related quality of life with dupilumab in patients with moderate-to-severe asthma with comorbid chronic rhinosinusitis with/without nasal polyps: an analysis of the QUEST study. *J Asthma Allergy*. 2022;15:767–73. <https://doi.org/10.2147/JAA.S363527>.
 103. Ryser FS, Yalamanoglu A, Valaperti A, et al. Dupilumab-induced eosinophilia in patients with diffuse type 2 chronic rhinosinusitis. *Allergy*. 2023;78:2712–23. <https://doi.org/10.1111/all.15844>.
 104. Bertlich M, Ihler F, Bertlich I, et al. Management of chronic rhinosinusitis with nasal polyps in Samter triad by low-dose ASA desensitization or dupilumab. *Med (Baltim)*. 2021;100. <https://doi.org/10.1097/MD.00000000000027471>.
 105. Bajpai S, Marino MJ, Rank MA, et al. Benefits of biologic therapy administered for asthma on co-existent chronic rhinosinusitis: a real-world study. *Int Forum Allergy Rhinol*. 2021;11:1152–61. <https://doi.org/10.1002/alr.22774>.
 106. Soyka MB, Ryser FS, Brühlmann C, et al. Predicting dupilumab treatment outcome in patients with primary diffuse type 2 chronic rhinosinusitis. *Allergy*. 2023;78:1036–46. <https://doi.org/10.1111/all.15532>.
 107. Rosso C, De Corso E, Conti V, et al. Switching of biological therapy to dupilumab in comorbid patients with severe asthma and CRSwNP. *Eur Arch Oto-Rhino-Laryngol*. 2024;281:3017–23. <https://doi.org/10.1007/s00405-024-08461-y>.
 108. Ferri S, Montagna C, Casini M, et al. Sleep quality burden in chronic rhinosinusitis with nasal polyps and its modulation by dupilumab. *Ann Allergy Asthma Immunol S*. 2023. <https://doi.org/10.1016/j.anai.2023.08.594>.
 109. Boiko NV, Stagnieva IV, Lodochnikina OE, Kurbatova NV. [Experience with dupilumab in the treatment of chronic rhinosinusitis with nasal polyps]. *Vestn Otorinolaringol*. 2023;88:46–53. <https://doi.org/10.17116/otorino20228804146>.
 110. Larin RA, Mokeeva PP, Grishin AS. [Experience of biological therapy in severe forms of chronic rhinosinusitis with nasal polyps in the conditions of regional healthcare]. *Vestn Otorinolaringol*. 2023;88:51–8. <https://doi.org/10.17116/otorino20228802151>.
 111. Knizek Z. Efficacy of dupilumab in patients with chronic rhinosinusitis with nasal polyps with comorbid allergic rhinitis. *Alergie*. 2023;2023:187–91.
 112. Appel HM, Lochbaum R, Hoffmann TK, Hahn J. Chronic rhinosinusitis with nasal polyps-extension of dupilumab treatment intervals. *HNO*. 2024. <https://doi.org/10.1007/s00106-024-01487-y>.
 113. Staufenberg A-R, Frankenberger HK, Förster-Ruhrmann U, et al. Biologic therapy in patients with severe NSAID-exacerbated respiratory disease and previous aspirin desensitization : results of a multicentric study. *HNO*. 2024. <https://doi.org/10.1007/s00106-024-01433-y>.
 114. Hopkins C, Gillett S, Slack R, et al. Psychometric validity of the 22-item sinonasal outcome test. *Clin Otolaryngol*. 2009;34:447–54. <https://doi.org/10.1111/j.1749-4486.2009.01995.x>.
 115. Gevaert P, De Craemer J, Bachert C, et al. European academy of allergy and clinical immunology position paper on endoscopic scoring of nasal polyposis. *Allergy*. 2023;78:912–22. <https://doi.org/10.1111/all.15650>.
 116. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14:135. <https://doi.org/10.1186/1471-2288-14-135>.
 117. Trimarchi M, Vinciguerra A, Rampi A, et al. A prospective study on the efficacy of dupilumab in chronic rhinosinusitis with type 2 inflammation. *Acta Otorhinolaryngol Ital*. 2022;42:538–44. <https://doi.org/10.14639/0392-100X-N2156>.
 118. De Corso E, Pasquini E, Trimarchi M, et al. Dupilumab in the treatment of severe uncontrolled chronic rhinosinusitis with nasal polyps (CRSwNP): a multicentric observational phase IV real-life study (DUPIREAL). *Allergy*. 2023;78:2669–83. <https://doi.org/10.1111/all.15772>.
 119. Campion NJ, Brugger J, Tu A, et al. The real life efficacy of dupilumab is independent of initial polyp size and concomitant steroids in CRSwNP. *J Otolaryngol - Head Neck Surg*. 2023;52:56. <https://doi.org/10.1186/s40463-023-00663-4>.
 120. Orlando P, Licci G, Kuitche D, et al. Effectiveness of dupilumab versus endoscopic sinus surgery for the treatment of type-2 chronic rhinosinusitis with nasal polyps: a preliminary report. *Eur Arch Otorhinolaryngol*. 2024;281:1317–24. <https://doi.org/10.1007/s00405-023-08309-x>.
 121. Cantone E, De Corso E, Ricciardiello F, et al. Olfaction recovery following dupilumab is independent of nasal polyp reduction in CRSwNP. *J Pers Med*. 2022;12:12. <https://doi.org/10.3390/jpm12081215>.
 122. Mocellin D, Ioppi A, Gaglio G, et al. Severe chronic rhinosinusitis treated with dupilumab, a real-life analysis of early effectiveness. *Eur Rev Med Pharmacol Sci*. 2023;27:7324–36. https://doi.org/10.26355/eurev_202308_33304.
 123. Jansen F, Becker B, Eden JK, et al. Dupilumab (Dupixent) tends to be an effective therapy for uncontrolled severe chronic rhinosinusitis with nasal polyps: real data of a single-centered, retrospective single-arm longitudinal study from a university hospital in Germany. *Eur Arch Oto-Rhino-Laryngol*. 2023;280:1741–55. <https://doi.org/10.1007/s00405-022-07679-y>.
 124. Albrecht T, Sailer MM, Capitani F, et al. Real-world evidence for the effectiveness and safety of dupilumab in patients with CRSwNP after 1 year of therapy. *World Allergy Organ J*. 2023;16. <https://doi.org/10.1016/j.waojou.2023.100780>.
 125. Piazzetta GL, Lobello N, Chiarella E, et al. Targeting IL-4 and IL-13 receptors on eosinophils in CRSwNP patients: the clinical efficacy of dupilumab. *J Pers Med*. 2023;13:13. <https://doi.org/10.3390/jpm13091404>.
 126. La Mantia I, Grigaliute E, Ragusa M, et al. Effectiveness and rapidity on olfactory function recovery in CRS patients treated with dupilumab: a real life prospective controlled study. *Eur Arch Otorhinolaryngol*. 2024;281:219–26. <https://doi.org/10.1007/s00405-023-08184-6>.
 127. Grose E, Li AY, Lee JM. Clinical outcomes of dupilumab therapy in chronic rhinosinusitis with nasal polyps in a Canadian tertiary care rhinology practice. *Allergy Asthma Clin Immunol*. 2023;19:26. <https://doi.org/10.1186/s13223-023-00782-7>.
 128. van der Lans RJL, Otten JJ, Adriaansen GFJPM, et al. Two-year results of tapered dupilumab for CRSwNP demonstrates

- enduring efficacy established in the first 6 months. *Allergy*. 2023;78:2684–97. <https://doi.org/10.1111/all.15796>.
129. Alicandri-Ciufelli M, Marchioni D, Pipolo C, et al. Influence of prior endoscopic sinus surgery extent on dupilumab effectiveness in CRSwNP patients. *Laryngoscope*. 2023. <https://doi.org/10.1002/lary.30983>.
 130. Kilty SJ, Lasso A. Canadian real-world study of access and clinical results using dupilumab for chronic rhinosinusitis with polyps. *J Otolaryngol - Head Neck Surg*. 2022;51:17. <https://doi.org/10.1186/s40463-022-00570-0>.
 131. Paoletti G, Casini M, Malvezzi L, et al. Very rapid improvement in extended nitric oxide parameters is associated with clinical and functional improvement in patients with chronic Rhinosinusitis with nasal polyps treated with Dupilumab. *J Investig Allergol Clin Immunol*. 2023;33:457–63. <https://doi.org/10.18176/jiaci.0851>.
 132. Giombi F, Pace GM, Nappi E, et al. Radiological versus clinical 1-year outcomes of dupilumab in refractory CRSwNP: a real-life study. *Laryngoscope*. 2024;134:2626–33. <https://doi.org/10.1002/lary.31238>.
 133. De Corso E, Porru DP, Corbò M, et al. Comparative real-world outcomes of dupilumab versus endoscopic sinus surgery in the treatment of severe CRSwNP patients. *Clin Otolaryngol*. 2024. <https://doi.org/10.1111/coa.14172>.
 134. Gelardi M, Giancaspro R, Quaranta VN, et al. Dupilumab's impact on nasal cytology: real life experience after 1 year of treatment. *Am J Otolaryngol*. 2024;45. <https://doi.org/10.1016/j.amjoto.2024.104275>.
 135. Sarnoch SO, Pepić A, Schmitz L, et al. The value of biomarkers in the therapy of CRSwNP with biologicals—a long-term follow-up of dupilumab therapy. *Eur Arch Otorhinolaryngol*. 2024. <https://doi.org/10.1007/s00405-024-08574-4>.
 136. Gal A, Gravier-Dumoncau R, Penicaud M, et al. Efficacy of dupilumab in real-life settings: a STROBE study. 2024;281:4781–4788. <https://doi.org/10.1007/s00405-024-08553-9>.
 137. Brkic FF, Liu DT, Rücklinger I, et al. Platelet-to-lymphocyte ratio might predict the response to dupilumab treatment for patients with nasal polyposis. *J Otolaryngol Head Neck Surg*. 2023;52:75. <https://doi.org/10.1186/s40463-023-00660-7>.
 138. Garvey E, Naimi B, Duffy A, et al. Medication utilization for patients with chronic rhinosinusitis with nasal polyposis and asthma in 12 months pre- and post-dupilumab initiation. *Int Forum Allergy Rhinol*. 2024;14:1399–401. <https://doi.org/10.1002/alr.23340>.
 139. Galletti C, Ragusa M, Sireci F, et al. Dupilumab in chronic rhinosinusitis with nasal polyps: real life data in a multicentric sicilian experience. *Am J Otolaryngol Head Neck Med Surg*. 2024;45:104106. <https://doi.org/10.1016/j.amjoto.2023.104106>.
 140. Tsunemi Y, Nakayama T, Kashiwagi T, et al. Long-term efficacy of dupilumab for eosinophilic chronic rhinosinusitis. *Am J Rhinol Allergy*. 2024;38:14–22. <https://doi.org/10.1177/19458924231204128>.
 141. Bachert C, Desrosiers M, Mullol J, et al. A randomized phase 3 study, Sinus-52, evaluating the efficacy and safety of Dupilumab in patients with severe chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol*. 2019;143:AB433. <https://doi.org/10.1016/j.jaci.2018.12.980>.
 142. Rothwell PM. Factors that can affect the external validity of randomised controlled trials. *PLOS Clin Trial*. 2006;1. <https://doi.org/10.1371/journal.pctr.0010009>.
 143. Bhattacharyya N, Villeneuve S, Joish VN, et al. Cost burden and resource utilization in patients with chronic rhinosinusitis and nasal polyps. *Laryngoscope*. 2019;129:1969–75. <https://doi.org/10.1002/lary.27852>.
 144. Martin-Jimenez DI, Moreno-Luna R, Callejon-Leblic A, et al. Improved quality of life in patients with chronic rhinosinusitis with nasal polyps associated with expanded types of endoscopic sinus surgery: a 2-year retrospective study. *Int Forum Allergy Rhinol*. 2024;14:1119–22. <https://doi.org/10.1002/alr.23321>.

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