Endoscopic sinus surgery versus biologic therapy for chronic rhinosinusitis with nasal polyposis: a systematic review with meta-analysis*

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Dear Editor:

Biologic therapies targeting type 2 inflammation, such as dupilumab, omalizumab, and mepolizumab, have been developed to manage chronic rhinosinusitis with nasal polyps (CRSwNP), particularly in patients with comorbid asthma or aspirin-exacerbated respiratory disease (AERD). Functional endoscopic sinus surgery (FESS) remains the mainstay of treatment in patients who are refractory to medical therapy [1,2]. However, direct comparisons between biologic therapy and FESS are limited. This systematic review and meta-analysis aimed to compare sinonasal outcomes between FESS and biologic therapy in real-world settings.

A comprehensive literature search identified 1931 articles, of which 7 met inclusion criteria for systematic review, and 6 were eligible for meta-analysis (Figure S1) [3-9]. These studies included a total of 1200 patients: 267 treated with FESS and 942 treated with biologics. Among biologics, most patients received dupilumab, while others were treated with omalizumab or mepolizumab. The studies provided short-term (3–6 months) and long-term (12 months or more) follow-up data (Table S1). Outcomes analyzed included SNOT-22 scores, Nasal Polyp Scores (NPS), Nasal Congestion Scores (NCS), and olfactory function.

The FESS and biologic groups had comparable baseline characteristics, including rates of asthma, AERD, previous sinus surgery, and CT Lund-Mackay scores (Figure S2). Results at the short term follow up (3-6 months) are provided in the supplement file.

The outcomes at 12 months follow up are presented in Figure 1. The pooled SNOT-22 scores showed no statistically significant difference between the groups (WMD 5.39, 95% -3.21, 13.98, p=0.22). Subgroup analysis showed no significant difference between dupilumab and FESS (WMD 7.56, 95% CI of -1.73, 16.84, p =0.11) and FESS over mepolizumab (WMD -4.50, 95% CI of -12.05, 3.05, p=0.24).

FESS showed significantly better outcomes in reducing NPS compared to biologics (WMD -1.93, 95% CI of -3.10, -0.77, p<0.01). This advantage was consistent when comparing FESS to both dupilumab and mepolizumab.

NCS scores were not significantly different overall (WMD -0.20, 95% -1.24, 0.83, p=0.70). FESS and dupilumab showed comparable outcomes (WMD 0.12, 95% CI -1.01, 1.26, p=0.83), but FESS outperformed mepolizumab in a single study (WMD -1.20, 95% CI -1.75, -0.65, p<0.001).

Regarding olfactory function, dupilumab was superior to FESS (Hedges's g -0.54, 95% CI of -1.09, 0.01, p =0.05).

We also performed a qualitative assessment. One study by Gilani et al. was included in the systematic review for qualitative analysis only [9]. It showed that the use of biologics was associated with a decrease in the number of ARS episodes compared to surgery; however, the use of antibiotics was not different between the two groups [9]. Subgroup qualitative analysis was performed in two studies [3,7]. One study found that dupilumab and FESS had similar efficacy in AERD patients, with FESS improving psychological symptoms more [3]. Another study showed that in patients with asthma and prior FESS, dupilumab led to better improvement in smell and SNOT-22 scores than revision surgery [7].

The strength of this meta-analysis is the inclusion of multiple biologics (dupilumab, omalizumab, mepolizumab), a mix of subjective and objective outcomes, and comparable baseline comorbidities across pooled cohorts. It provides a more comprehensive real-world comparison of FESS versus biologics than previous studies. However, limitations include reliance on non-randomized studies, small sample sizes, heterogeneity, and the potential lack of clinical significance for some statistical findings.

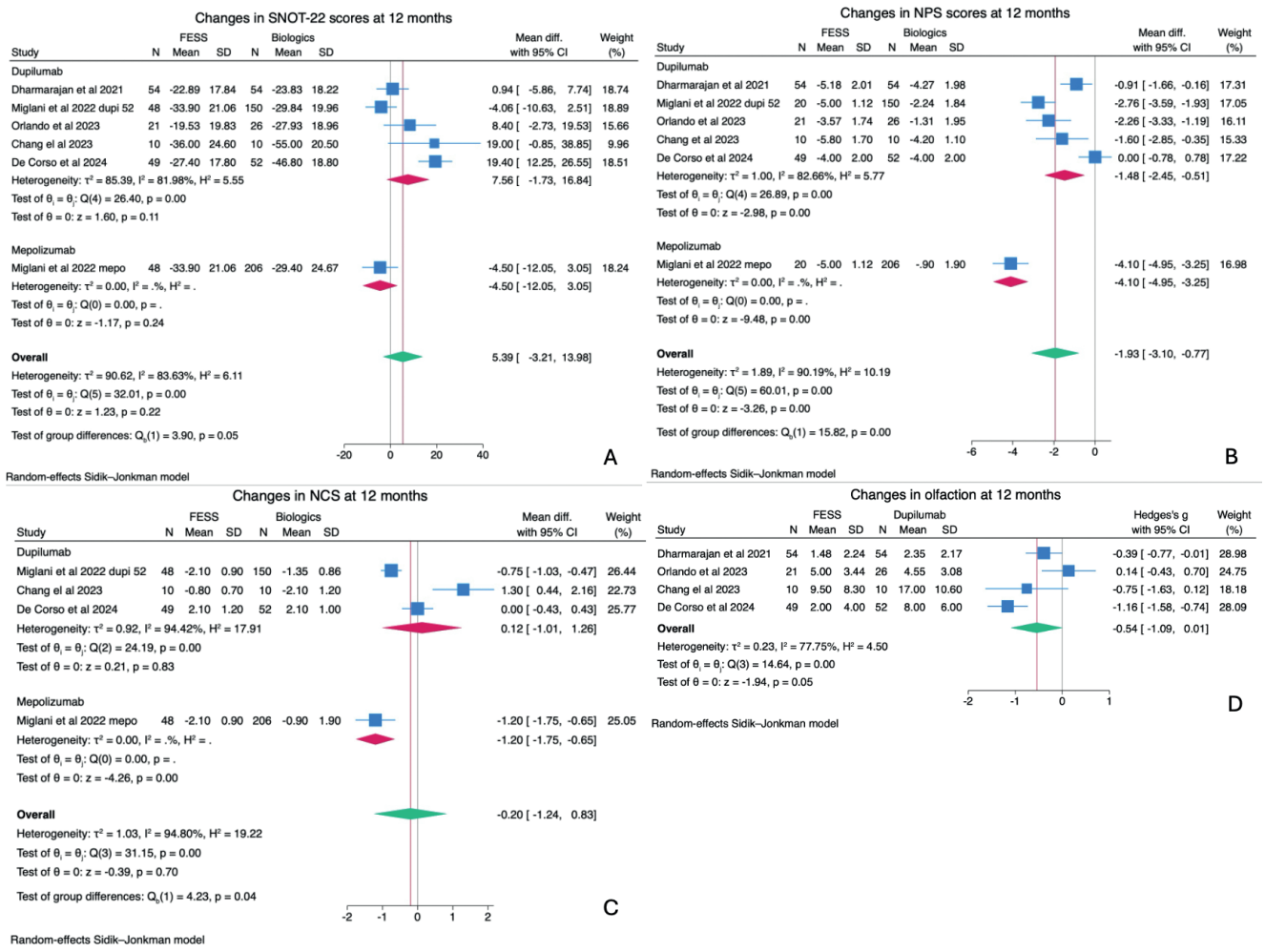

Figure 1. Forest plots comparing the change in SNOT-22 scores (A), Nasal polyposis scores (NPS) (B), Nasal congestion scores (NCS) (C), the change in olfaction scores (D) between FESS and biologics groups at 12 months follow-up. Subgroup analysis based on type of biologics is also shown.

In conclusion, this study suggests that while FESS is more effective in reducing polyp burden, dupilumab offers greater improvement in olfactory function. No significant differences were found in overall quality-of-life scores. The findings underscore the importance of individualized treatment selection based on patient priorities and comorbidities. Further research is needed, particularly randomized trials and longer-term outcome studies, to define the role of biologics in CRSwNP management. Cost-effectiveness and adverse event profiles should also be considered when choosing between surgery and biologic therapy.

Authorship contribution

HM contributed to the conceptualization, methodology, validation, investigation, data curation, visualization, project administration, writing – original draft, writing – review & editing; ZM contributed to the conceptualization, methodology, validation, investigation, data curation, visualization, project administration, writing – original draft, writing – review & editing. OGA contributed to the supervision, conceptualization, methodology, validation, writing – review & editing. MT contributed to the supervision, conceptualization, methodology, validation, writing – review & editing. GAK contributed to data curation, visualization, project administration, writing – original draft, writing – review & editing; JL contributed to the supervision, conceptualization, methodology, validation, writing – review & editing. HHR contributed to the supervision, conceptualization, methodology, validation, writing – review & editing. CAM contributed to the supervision, conceptualization, methodology, validation, writing – review & editing.

Conflict of interest

Masayoshi Takashima is a consultant for Neurent Medical and Medtronic ENT. Omar G. Ahmed is a consultant for Aerin Medical and Medtronic ENT. The rest of authors have no funding, financial relationships, or conflicts of interest to disclose.

Funding

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References

1. Orlandi RR, Kingdom TT, Smith TL, et al. International consensus statement on allergy and rhinology: rhinosinusitis 2021. Int Forum Allergy Rhinol. Mar 2021;11(3):213-739.
2. Fokkens WJ, Lund VJ, Hopkins C, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology. Feb 20 2020;58(Suppl S29):1-464.
3. 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. Aug 2022;12(8):986-995.
4. Miglani A, Soler ZM, Smith TL, Mace JC, Schlosser RJ. A comparative analysis of endoscopic sinus surgery versus biologics for treatment of chronic rhinosinusitis with nasal polyposis. Int Forum Allergy Rhinol. Feb 2023;13(2):116-128.
5. 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. Mar 2024;281(3):1317-1324.
6. Sima Y, Zhang J, Zheng M, Zhao Y, Wang X, Zhang L. Revision surgery versus biologic treatment with omalizumab in recurrent chronic rhinosinusitis with nasal polyps: An analysis of cost-utility and clinical outcomes. World Allergy Organ J. Dec 2023;16(12):100846.
7. Chang E NN, Samargandy S, Odisho NL, Shroff P, Carr T, Le C. A pilot prospective longitudinal study comparing dupilumab to surgery in CRSwNP. Authorea. June 02, 2023.
8. 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. Jul 2024;49(4):481-489.
9. Gilani S, Bhattacharyya N. Biologics versus endoscopic sinus surgery: Acute rhinosinusitis episodes and antibiotic use in chronic rhinosinusitis. Am J Otolaryngol. Jul-Aug 2024;45(4):104368.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Materials and Methods

This study was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines [1].

Eligibility criteria

Study designs that directly compared FESS (irrespective of the extent of surgery) to a biologic therapy (dupilumab, mepolizumab, omalizumab, or benralizumab) for CRSwNP were considered, including randomised controlled trials (RCT), cohort studies (prospective and retrospective) and case-control studies. Studies were included without language restrictions. Only adult patients (18 years of age or older) were included. The primary subjective outcome was the change in the SNOT-22 score while the primary objective outcome was the change in the Nasal Polyp Score (NPS). Secondary outcomes included the change in the Nasal Congestion Score (NCS) as well as any olfactory outcome test; Smell Identification Test (SIT), Sniffin' Sticks test, Visual Analog Score (VAS).

Search strategy

A systematic review of the literature was conducted by two authors (CAM and HM). PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) databases were queried from inception to September 2024. Search terms used in PubMed as well as all other databases were as follows: (biologic* OR dupilumab OR mepolizumab OR omalizumab OR benralizumab) AND (surgery*) AND (chronic rhinosinusitis OR nasal polyps). A similar strategy, adapted to the requirements of the other databases, was used for all other searches. Patients with asthma, aspirin exacerbated respiratory disease (AERD), and allergic rhinitis were included if they also had diagnosed CRSwNP. Case reports, narrative commentaries, and reviews were excluded. Studies unavailable as full-text articles or irrelevant content were also excluded. The bibliography of the included articles was manually reviewed to ensure no further relevant articles were missed. Preprints and conference proceedings were included when complete data was available. A systematic review of the literature was conducted by two authors (CAM and HM) to identify and consolidate results of head-to-head comparisons of the effectiveness of biologic therapy versus FESS for CRSwNP. PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) databases were queried with the help of a librarian for studies comparing the effectiveness of biologics against that of FESS for the treatment of CRSwNP from inception to September 2024.

Data screening and abstraction

Two independent authors (CAM and HM), working independently, conducted title and abstract screening of articles imported from the search using Rayyan [1]. Any conflicts between the two reviewers were resolved after consulting a third reviewer (HHR). If data was missing or incomplete, the original authors of the included studies were contacted for the necessary information. In the case of no response from the original authors, missing values were imputed based on appropriate formulas.

Effect measures

The primary and secondary outcome measures for the meta-analysis are reported as the weighted mean differences (WMD) when the results are reported using the same scale, and as the standardised mean differences (SMD) using Hedge's g when results were reported in different scales. Results were aggregated at baseline, early follow-up (around 6 months), and late follow-up (approximately 12 months) periods. Baseline differences in comorbidities (AERD, asthma, CT Lund Mackay scores, history of FESS) were examined using risk differences. The random effects restricted maximum likelihood (REML) model with Sidik-Jonkman adjustment was used to pool results. This model was chosen since heterogeneity between studies was expected. A p-value of <0.05 and non-overlapping 95% confidence intervals (CI) were considered statistically significant. Heterogeneity was examined using the Cochran Q statistic while inconsistency was examined using I-squared (I^2). Small-study effects (publication bias, etc.) were examined using the funnel plot and Egger's regression-intercept test if there were at least 10 effect publications [1]. Data analyses were conducted using Stata (version 18) and all statistical tests were two-tailed.

Risk of bias

The risk of bias was assessed using the Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I) instrument for cohort studies [2]. Two independent reviewers (CAM, HM) determined the risk of bias using ROBINS-I. A third reviewer (HHR) was consulted in the event of any discrepancies.

Ethics

This review was exempt from institutional review board approval as it involves data extraction from existing published studies.

Results

The initial text search identified 1931 articles, of which 730 duplicates were removed. A total of 1201 articles were screened based on the title and abstract, and 15 proceeded to full-text review. After excluding for wrong study type, wrong comparison,

or wrong outcome, and after adding an additional article found through cross-referencing, 7 articles representing 1422 patients met full eligibility criteria (Figure S1) [1-7]. For the Orlando et al. and Sima et al. studies, authors were contacted for missing information and data was received from both studies [8,9]. Meta-analysis could be performed on 6 of the included studies representing 1200 patients, 267 in the FESS group and 942 in the biologics group [1-3,5-7]. Four of the 6 studies compared FESS to dupilumab, 1 study compared FESS to omalizubmab, and 1 study compared a cohort of FESS patients to 2 cohorts of dupilumab, 2 cohorts of omalizumab, and 1 cohort of mepolizumab. For the last study, the biologics cohorts were combined based on the type of biologics as well as follow up duration. All studies provided follow up at 3-6 months and at 12 or more months after either treatment. The main characteristics for the included studies are shown in Table S1.

Assessment of baseline differences

Overall, the FESS and biologics groups had similar baseline characteristics in the prevalence of AERD, prevalence of asthma, prior sinus surgery, and CT LM scores (Figure S2). For the one mepolizumab study, all patients in the mepolizumab group had a history of prior sinus surgery (Risk difference of -0.41, 95% CI of -0.50, -0.31) but significantly more patients had comorbid AERD in the FESS group (Risk difference of 0.11, 95% CI of 0.01, 0.22) (2).

Outcomes at 3-6 months (Figure S3)

Four of the 6 studies included in the meta-analysis reported outcomes at 6 months [2,3,5,7]. One study, Orlando et al. 2023, reported their early outcome at 3 months [6]. This was included in the early follow up (3-6 months) meta-analysis. The study by Dharmarajan et al. reported their mean follow up to be at 17.9 months for the dupilumab group and 12.2 months for the FESS group.1 This study was included in the late (12 months) follow up meta-analysis.

The pooled SNOT-22 scores showed no statistically significant difference between the groups (WMD -5.01, 95% CI of -10.33, 0.31, p = 0.06). Subgroup analysis showed no difference between FESS and dupilumab (WMD -1.25, 95% CI of -7.46, 4.96, p = 0.69), In contrast, FESS was superior to omalizumab (WMD -10.47, 95% CI of -17.54, -6.63, p <0.001).

FESS showed significantly better outcomes in reducing NPS compared to biologics (WMD -3.15, 95% CI of -4.15, -2.15, p <0.001). This advantage was consistent when comparing FESS to both dupilumab and mepolizumab.

Overall, NCS scores results favored FESS (WMD -0.53, 95% CI -1.01, -0.05, p = 0.03) over biologics. Subgroup analysis showed that FESS and dupilumab showed comparable outcomes (WMD -0.23, 95% CI -0.70, 0.23, p = 0.32) but FESS was superior to omalizumab (WMD -1.10, 95% CI -1.32, -0.88, p<0.001).

In terms of olfactory function, no statistically significant differences were observed between the FESS and biologics group (Hedges's g -0.03, 95% CI of -0.44, 0.39, p=0.90). However, subgroup analysis showed that dupilumab was superior to FESS (Hedges's g -0.34, 95% CI of -0.65, -0.03, p=0.03), and FESS was superior to omalizumab (Hedges's g 0.65, 95% CI of 0.36, 0.94, p<0.001)

Outcomes at 12 months (Figure 1)

Five of the 6 studies included in the meta-analysis reported outcomes at 12 or more months [1-3,6,7]. See main manuscript for details of the results.

Qualitative assessment

One study was included in the systematic review for qualitative analysis only [4]. The study by Gilani et al. examined the number of acute rhinosinusitis episodes and its associated use of antibiotics in CRSwNP patients who had surgery vs dupilumab or mepolizumab [4]. The use of biologics was associated with a decrease in the number of ARS episodes compared to surgery; however, the use of antibiotics was not different between the two groups [7].

Risk of bias

Each article included in the study was assessed for risk of bias using the ROBINS-I instrument. Moderate risk of bias was observed for all studies (Figure S4). It is also important to note that we were unable to examine for small-study effects (publication bias, etc.) for any of our outcomes because the number of effect sizes was less than 10 for all.

References

1. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. Dec 5 2016;5(1):210.
2. Sterne JA, Sutton AJ, Ioannidis JP, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ. Jul 22 2011;343:d4002.
3. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. Oct 12 2016;355:i4919.
4. 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. Aug 2022;12(8):986-995.
5. Miglani A, Soler ZM, Smith TL, Mace JC, Schlosser RJ. A comparative analysis of endoscopic sinus surgery versus biologics for treatment of chronic rhinosinusitis with nasal polyposis. Int Forum Allergy Rhinol. Feb 2023;13(2):116-128.
6. 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. Jul 2024;49(4):481-489.
7. Gilani S, Bhattacharyya N. Biologics versus endoscopic sinus surgery: Acute rhinosinusitis episodes and antibiotic use in chronic rhinosinusitis. Am J Otolaryngol. Jul-Aug 2024;45(4):104368.
8. Sima Y, Zhang J, Zheng M, Zhao Y, Wang XD, Zhang L. Revision surgery versus biologic treatment with omalizumab in recurrent chronic rhinosinusitis with nasal polyps: An analysis of cost-utility and clinical outcomes. World Allergy Organ J. 2023 Nov 29;16(12):100846.
9. 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. Mar 2024;281(3):1317-1324.
10. Chang E NN, Samargandy S, Odisho NL, Shroff P, Carr T, Le C. A pilot prospective longitudinal study comparing dupilumab to surgery in CRSwNP. Authorea. June 02, 2023.

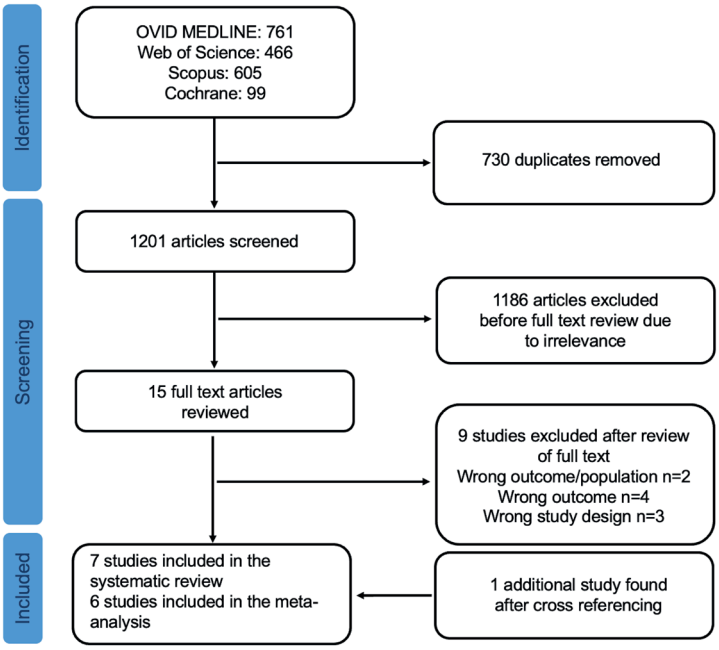

Figure S1. PRISMA flow diagram.

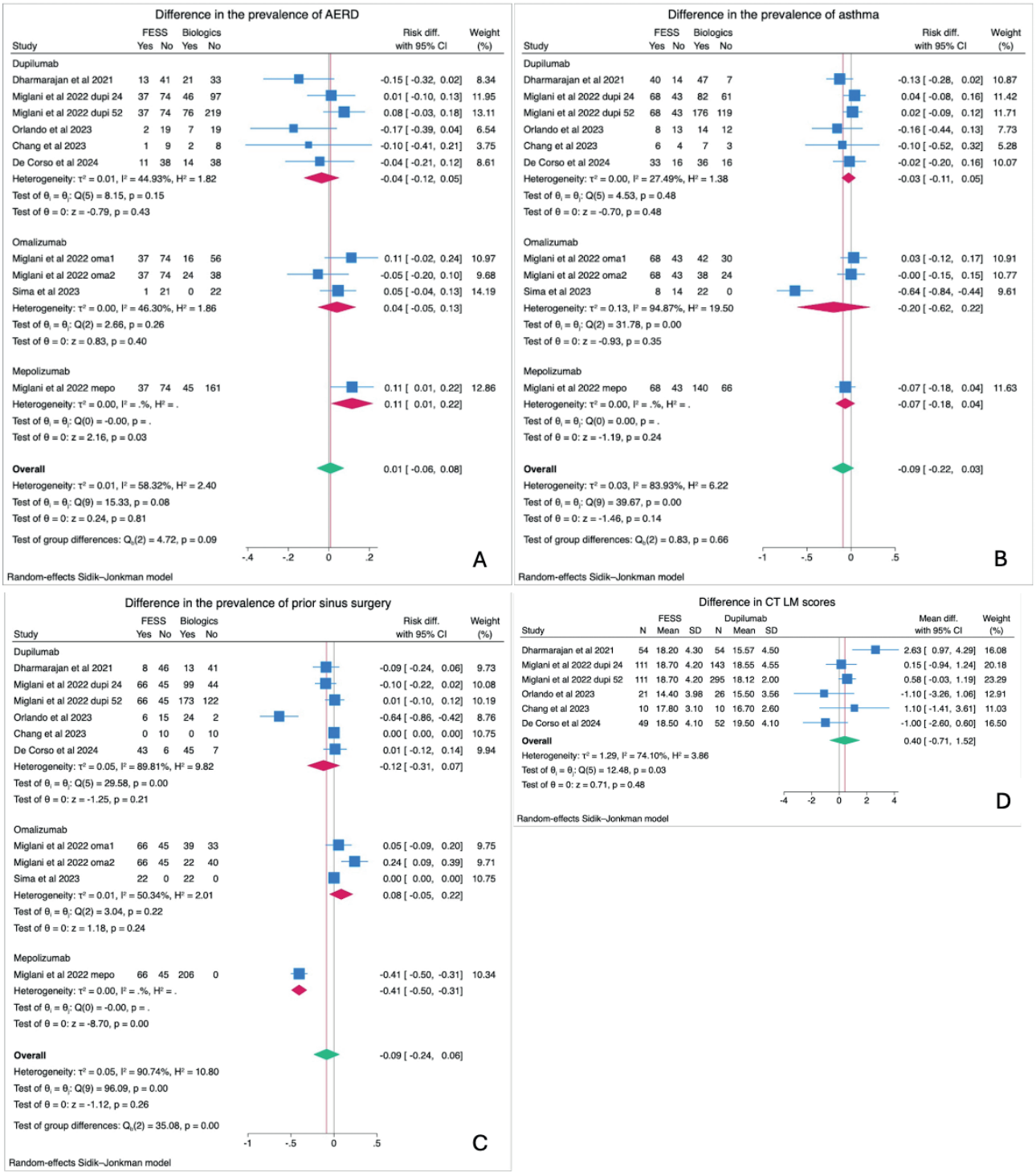

Figure S2. Forest plots comparing the prevalence of AERD (A), asthma (B), prevalence of prior history of sinus surgery (C) and the difference in CT Lund-Mackay scores (D) between FESS and biologics groups.

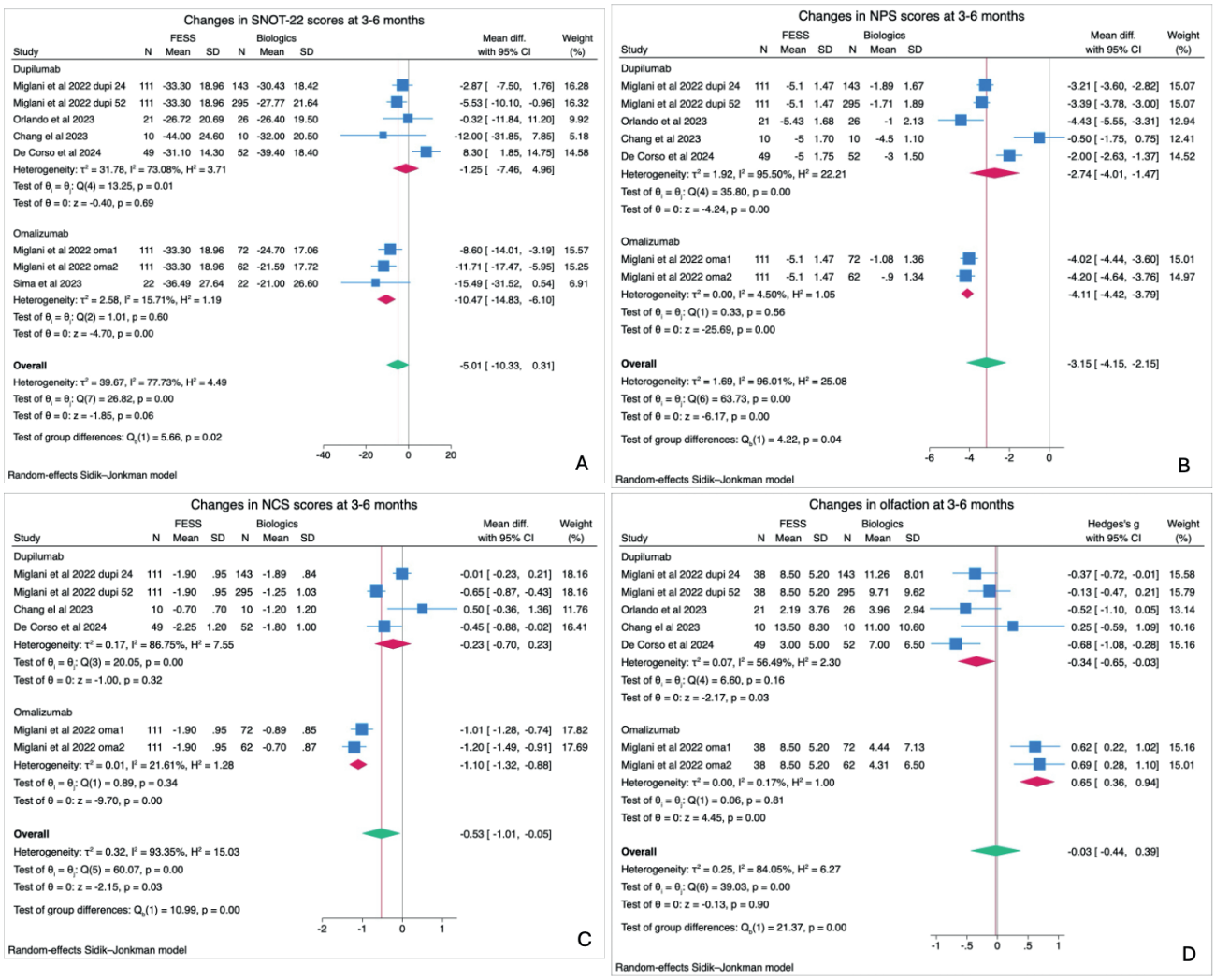

Figure S3. Forest plots comparing the change in SNOT-22 scores (A), Nasal polyposis scores (NPS) (B), Nasal congestion scores (NCS) (C), the change in olfaction scores (D) between FESS and biologics groups at 3-6 months follow-up. Subgroup analysis based on type of biologics is also shown.

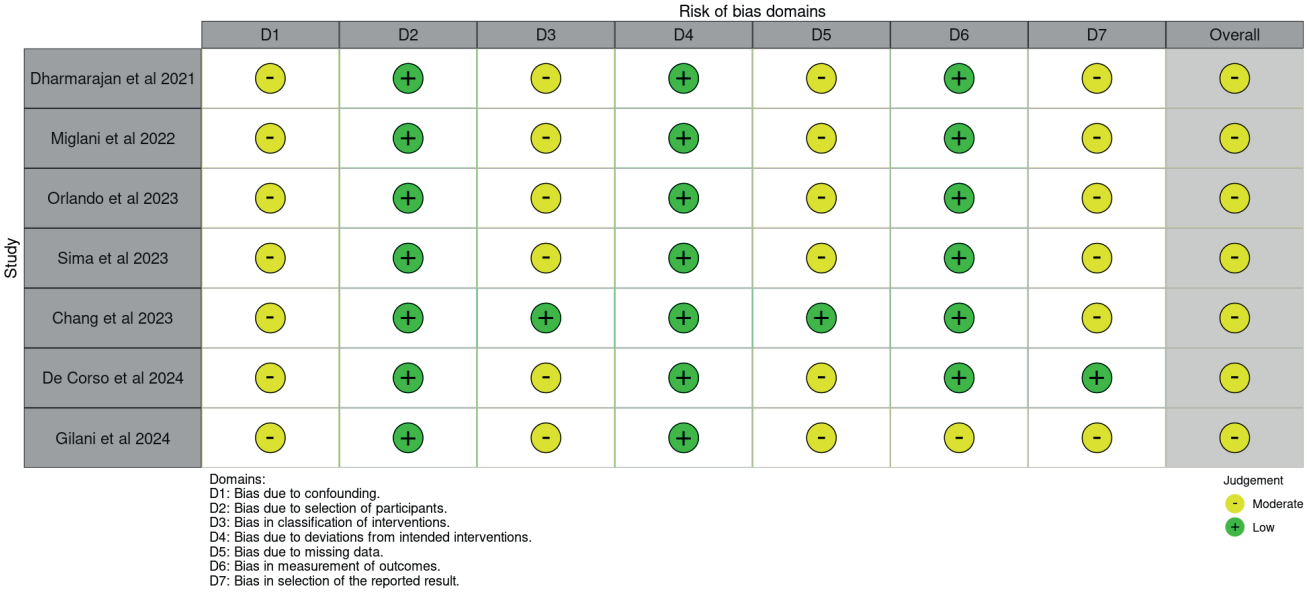

Figure S4. Risk of bias assessment of the included studies using ROBINS-I protocol.

Table S1. Summary of all the included studies.

Authors/ year	Country	Study Type	Comparison	N		Age (mean or median, SD or IQR)		Female (%)		Follow up (months)		Outcomes measures	Summary of the results
				FESS	Biologic	FESS	Biologic	FESS	Biologic	FESS	Biologic		
Dharmarajan et al. 2021	USA	retrospective cohort	Dupilumab vs FESS	54	54	53.3 (14.0)	52.4 (15.8)	50.0	44.4	17.9 (±15.80)	12.2 (±5.9)	SNOT-22 (total and subdomains), olfaction domain of SNOT-22, NPS	Equivalence in SNOT-22, Dupilumab superior in olfaction, FESS superior in NPS reduction
Miglani et al. 2022	USA	retrospective cohort	Dupilumab 24 vs FESS	111	143	51.9 (15.8)	52 (39-61)	46.8	38.0	6		SNOT-22, NPS, NCS, LK-NP, SIT-40, Sniffin's Sticks, loss of smell score	**Compared to dupilumab:** Equivalence in SNOT-22 and NCS at 24 and 52 weeks, equivalence in olfaction at 24 weeks, FESS superior in NPS reduction. **Compared to omalizumab and mepolizumab**: FESS superior in all measures
			Dupilumab 52 vs FESS	111	295	51.9 (15.8)	52 (42-63)	46.8	37.6	13			
			Omalizumab 1 vs FESS	111	72	51.9 (15.8)	50 (14.5)	46.8	34.7	6			
			Omalizumab 2 vs FESS	111	62	51.9 (15.8)	49 (11.9)	46.8	37.1	6			
			Mepolizumab vs FESS	111	206	51.9 (15.8)	48.6 (13.6)	46.8	33.0	13			
Orlando et al. 2023	Italy	prospective cohort	Dupilumab vs FESS	21	26	53.9 (-)	53.9 (-)	28.6	30.0	3 and 12		SNOT-22, NPS, mLKS, Sniffin' Sticks	Equivalence in SNOT-22 and olfaction, FESS superior in NPS reduction
Sima et al. 2023	China	prospective cohort	Omalizumab vs FESS	22	22	44.2 (10.8)	46.5 (12.1)	50.0	50.0	6		SNOT-22 (total and subdomains), VAS (0-10) for various symptoms, SF-36	FESS is superior in SNOT-22, nasal congestion, and olfaction
Chang et al. 2023	USA	prospective cohort	Dupilumab vs FESS	10	10	54.3 (14.5)	59.5 (11.2)	60.0	60.0	3, 6, 9, and 12		SNOT-22, SIT-40, Anosmia, NPS, ACQ	Dupilumab is superior in patients with history of asthma or prior sinus surgery
De Corso et al. 2024	Italy	retrospective cohort	Dupilumab vs FESS	49	52	43.3 (-)	50.1 (-)	38.8	57.7	1, 3, 6, 9, and 12		SNOT-22, Sniffin' Sticks, cycles of OCS needed	Dupilumab superior for SNOT-22 and olfaction
Gilani et al. 2024	USA	retrospective cohort	Dupilumab or mepolizumab vs FESS	-	-	57.6	57.2	50.2	50.2	12		Number of ARS episodes and associated antibiotic prescription	Dupilumab or mepolizumab superior in reduction of ARS episodes