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Modern methods of treating chronic rhinosinusitis with nasal polyps – A review

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ABSTRACT

Chronic rhinosinusitis with nasal polyps (CRSwNP) is characterized by a long-term inflammatory process in the upper airways that is mainly driven by type-2 immune responses, including IL-4, IL-5, and IL-13. Epithelial barrier deficiency with eosinophilic inflammation contributes to chronic mucosal edema, polyp formation, and poor quality of life. It is treated with intranasal corticosteroids, saline irrigations, and short courses of oral steroids, or FESS for recalcitrant disease. But the disease relapses frequently, and control for the long term has proven difficult. Novel type 2-targeted biologics include dupilumab (anti-IL-4Rα), mepolizumab (anti-IL-5), omalizumab (anti-IgE), and benralizumab (anti-IL-5Rα), which are part of modern therapy. These treatments have also been shown to significantly reduce polyp size, nasal obstruction, and the need for surgery or steroids. The latest EPOS/EUFOREA recommendations propose the selection of biologics according to phenotype and endotype in order to be used in conjunction with surgery and topical maintenance. The barriers are high cost and lack of long-term data, even though they have been shown to be effective, with good safety. A combination of biologics, state-of-the-art topical therapy, and surgery has the greatest promise for achieving lasting remission and improved quality of life in CRSwNP.

Keywords: chronic rhinosinusitis, nasal polyps, type 2 inflammation, biologic therapy, endoscopic sinus surgery

1. INTRODUCTION

Chronic rhinosinusitis is a phenotypically diverse entity characterized by local airway inflammation. It has historically been divided into two major phenotypes: CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). CRS is one of the highly prevalent chronic inflammatory diseases with a reported incidence of approximately 10% worldwide. CRSwNP, accounting for approximately 18–20% of all CRS subtypes, is considered the more severe endophenotype. It is thought to be associated with increased morbidity and may also affect lower airway disease in adults. The prevalence of CRSwNP is reportedly 1.1% in the United States and between 2.1% and 4.4% in Europe (Laidlaw et al.,

2021). This disorder is characterized by chronic inflammation of the sinonasal cavities and upper airways that has been present for at least 12 weeks, accompanied by nasal obstruction, nasal discharge, facial pain or pressure, hypoosmia, and anosmia (Kato et al., 2022; Sedaghat, 2017), and is substantially associated with decreased quality of life. Predisposing factors for CRSwNP comprise obstruction of the sinus ostia, infection, mucosal barrier and immunologic dysfunction, ciliary abnormalities, and allergy. The second is edematous mucosa, which leads to a single or multiple nasal polyps in the nasal cavity and middle meatus of the sinuses (Hu et al., 2023).

Pathophysiology

While type 2 (T2) inflammation is historically known to be the dominant underlying biology in CRSwNP, marked variation is noted between populations. One of the central pathogenic events is epithelial barrier impairment, leading to exposure to environmental triggers, such as pathogens, allergens, and pollutants. After recognition of allergens via pattern-recognition receptors (PRRs), damaged epithelial cells release "alarmins," including thymic stromal lymphopoietin (TSLP), IL-25, and IL-33, that activate dendritic cells and group 2 innate lymphoid cells (ILC2s) to increment differentiation of Th2 lymphocytes, exposing amplification of type 2 cytokines (IL-4, IL-5, and IL-13) (Klingler et al., 2021; Striz et al., 2023). IL-4/IL-13 also promotes class-switch recombination to IgE through B cells, induces mucus hypersecretion, and contributes to the loss of epithelial integrity, whereas IL-5 is critical for eosinophil recruitment, activation, and survival (Kato et al., 2022). Eosinophils, once activated, release cytotoxic proteins, mainly lipid mediators and extracellular traps, including Charcot–Leyden crystals that directly injure sinonasal tissue and perpetuate inflammation (Chong et al., 2016). Apart from eosinophils, mast cells, basophils, and plasma cells will contribute to the inflammatory mixture by the release of histamine, leukotrienes, and locally produced IgE, often in reaction to staphylococcal superantigens (Gevaert et al., 2022). Fibroblasts and epithelial cells are involved in tissue remodelling via an IL-13- and TGF-β–dependent mechanism, resulting in stromal edema, pseudocyst formation, and glandular hyperplasia in the polypoid tissue of CRSwNP (Chong et al., 2016). Unlike CRSsNP, for which dysregulated fibrosis was reported, CRSwNP shows decreased fibrosis but increased tissue edema and remodelling. Of note in Asia, where we focus, T2 endotypes are less prevalent than they are in the West, and non-T2 disease (e.g., neutrophilic with IL-17 and IFN-γ signaling) is more common, illustrating these locally observed heterogeneities (Striz et al., 2023). The dysfunction of the interplay among the epithelial barrier, type 2 immunity, and remodeling is an orchestrator of the pathogenesis of chronic inflammation and the high recurrence of CRSwNP.

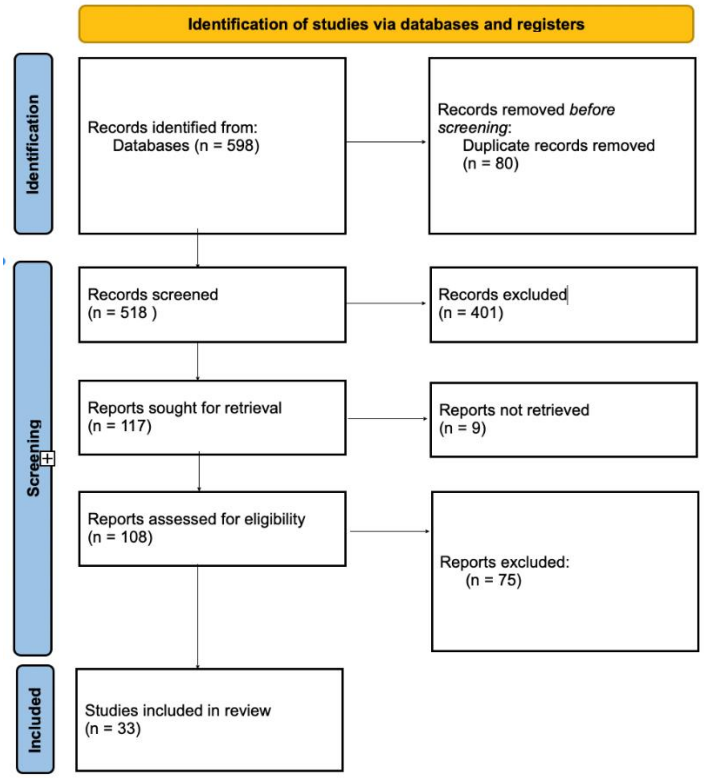

Figure 1. Prisma flow diagram detailing the screening process.

2. REVIEW METHODS

This review was based on a systematic search of the published literature on CRSwNP. A review of PubMed and Scopus was conducted that retrieved English-language articles published between January 2015 and June 2025 with terms including "CRSwNP", "type-2 inflammation", "biologic therapy", and "endoscopic sinus surgery". Preferential consideration was given to randomised controlled trials, systematic reviews, and international consensus statements (EPOS, EUFOREA). Other relevant publications referred to in the papers were also reviewed. The aim was to provide a state-of-the-art review of existing evidence and emerging therapeutic approaches in CRSwNP treatment. The entire selection process is presented in the PRISMA flow diagram (Figure 1).

3. RESULTS & DISCUSSION

Topical steroids

Inhaled corticosteroids (ICS) and intranasal corticosteroids (INCS) are first-line treatments for chronic rhinosinusitis, including CRSwNP. Nasal obstruction, disease-specific quality of life, and endoscopic scores improved relative to placebo. Rapid local side effects are generally mild (e.g., epistaxis, dryness) (Wise et al., 2024). Delivery to the sinuses with traditional sprays is inconsistent, which partially accounts for the heterogeneity of response (Tait et al., 2018). This, in turn, is supported by evidence that there are more effective ways to deliver therapy: high-volume corticosteroid irrigations (e.g., budesonide + saline) can enhance positive symptoms & endoscopic findings (> all post-FESS at least); & do so with an acceptable safety profile. Exhalation-delivery fluticasone (EDS-FLU) has reduced symptoms, intrasinus opacification, and acute exacerbations in two randomised parallel trials (Fokkens et al., 2020). However, non-response is widespread among those who are non-compliant or have inadequate technique, and long-term control usually requires ongoing treatment (Head et al., 2016).

Oral corticosteroids

Short bursts of oral corticosteroids (OCS) reduce polyp burden and disease impact in CRSwNP, but benefits wane by 3–6 months with recurrent use, leading to systemic risk exposure (e.g., metabolic, psychiatric, bone, and adrenal effects). Current recommendations are that OCS should be reserved for liberation or short induction in uncontrolled disease, and that the majority of patients use ≤1–2 courses annually when combined with maintenance INCS. Randomized data are limited in non-CRSwNP and not sustained in efficacy. The use of perioperative OCS may reduce short-term tissue inflammation with no clear effect on quality of life (Head et al., 2016; Orlandi et al., 2021).

Functional endoscopic sinus surgery (FESS)

FESS is indicated in patients who are symptomatic despite adequate medical treatment (saline irrigations and INCS alone, with or without a trial of short-term OCS), or active disease in those who fail early management for specific complications (e.g., obstructing mucoceles, fungal balls). When combined with postoperative topical treatment, endoscopic sinus surgery reduces symptoms and improves endoscopy and radiology results, but recurrence (especially polyps in CRSwNP) remains frequent and often necessitates reintervention during long-term follow-up (Calus et al., 2019). Recurrence and revision rates reported depend on phenotype, extent of surgery, an overall comorbid burden but are approximately one third at 3-5 years and over 75% within a decade in CRSwNP cohort (Rodriguez-Van Strahlen et al., 2024; Martin-Jimenez et al., 2024). Expanded approaches may provide better results than limited FESS, although long-term control still relies on continuous medical follow-up (Seys et al., 2025). Key characteristics and limitations of conventional medical and surgical therapies for CRSwNP are summarized in Table 1.

Table 1. Conventional therapies for CRSwNP

Therapy	Main benefit	Key limitation	Role in management
Intranasal corticosteroids (INCS)	Improve nasal obstruction, endoscopic scores and quality of life	Limited sinus deposition; response depends on adherence and technique	First-line and long-term maintenance therapy
Optimized topical delivery (steroid irrigations, EDS-FLU)	Enhanced symptom and endoscopic improvement, especially post-FESS	Requires training and sustained adherence	Augments topical control and postoperative outcomes

Oral corticosteroids (OCS)	Rapid, short-term reduction in polyp size and symptoms	Transient benefit; cumulative systemic adverse effects	Reserved for exacerbations or short induction courses
Functional endoscopic sinus surgery (FESS)	Improves symptoms and facilitates topical drug delivery	High long-term recurrence and revision rates in CRSwNP	Adjunct to medical therapy, not disease-modifying

New methods of treatment

Contemporary biologic therapy for chronic rhinosinusitis with nasal polyps (CRSwNP) is focused on type 2-based pathways and has become a core option in the management of patients whose disease remains uncontrolled despite topical corticosteroid therapy and who have often already undergone surgery. The fully human monoclonal antibody directed against the IL-4 receptor-α, dupilumab, which inhibits signaling of both IL-4 and IL-13, resulted in clinically significant and statistically superior improvements in coprimary (endoscopic nasal polyp score, nasal congestion) and key secondary endpoints (sense of smell, SNOT-22; reduced systemic steroids/surgery) in the phase 3 LIBERTY NP SINUS-24 and SINUS-52 trials with sustained effects over time with continued dosing. Subsequent post-hoc analysis shows dupilumab efficacy irrespective of biomarker strata and treatable traits characteristic of type-2 disease, for example, differing blood eosinophil levels, and comorbid asthma, or NSAID-exacerbated respiratory disease, consistent with the upstream blockade of IL4/IL13 signaling (Papacharalampous et al., 2024; Fokkens et al., 2023).

Concurrently, anti-IL-5 therapies suppress eosinophil-mediated inflammation. Mepolizumab 100 mg s.c. was also investigated in the phase 3 SYNAPSE study. Every 4 weeks for up to 52 weeks was associated with reduced polyp size and nasal obstruction in comparison to placebo, an acceptable side-effect profile, and it reduced the risk of requiring endoscopic sinus surgery across all subgroups studied (stratified by baseline eosinophil count or surgical history) (Han et al., 2021; Damask et al., 2022). By targeting IgE, omalizumab (dose adjusted for weight and pre-treatment IgE) was proven to significantly improve both endoscopically-assessed and patient-reported outcomes in the duplicate phase 3 POLYP-1 and POLYP-2 trials (including notably NPS, nasal congestion, and SNOT-22) with consistent treatment responses across prespecified subgroups according to eosinophil count, prior surgery history, concomitant asthma status, or aspirin sensitivity (Gevaert et al., 2020; Bachert et al., 2022). The phase 3 OSTRO trial demonstrated that benralizumab (an afucosylated anti-IL-5Rα that targets an IL-R isoform to deplete eosinophils) significantly reduced polyp burden and nasal obstruction among anti-IL-5 receptor strategies. Numerical differences, but not all reaching uniform statistical significance for some secondary variables, highlighting heterogeneity of response in this category (Lipworth et al., 2025).

More recently, upstream epithelial alarmin blockade has extended the armamentarium: in WAYPOINT (phase 3), tezepelumab, an anti-TSLP antibody, reduced polyp size and nasal congestion, decreased systemic corticosteroid use and surgery up to 52 weeks, and lowered risk of polyp recurrence at 52 weeks versus placebo (Lelegren et al., 2022). Phase 3 data have led to U.S. FDA approval for dupilumab, mepolizumab, and omalizumab in CRSwNP, while the three agents are also approved for use in the European Union, which emphasizes their established efficacy in patients with severe, uncontrolled disease (Favier et al., 2024; Oykhman et al., 2022). There are no direct comparative trials, yet network meta-analysis suggests that all approved biologics improve patient-important outcomes, with dupilumab generally ranking among the most beneficial treatment options across several endpoints (e.g., SNOT-22, surgery rescue), followed by omalizumab and mepolizumab, which also offer significant benefits. It is also worth mentioning that an integrated approach in CRSwNP pairs surgery (endoscopic sinus surgery) to debulk polyps and re-establish ventilation, with biologic therapy targeting residual type-2 inflammation. ESS also significantly facilitates the penetration of high-volume topical corticosteroid irrigations into the sinuses, thereby enhancing postoperative medical management.

Evidence for the biologics of significant reductions in total NP score, congestion, CT opacification, and decreased requirement for systemic glucocorticoids and sinus surgery is found over 24/52 weeks (LIBERTY NP SINUS-24/52) (Bachert et al., 2019). This approach has been recently adopted by the current EPOS 2020 and will be embraced once again by EPOS/EUFOREA 2023 guidelines offer biologics to adults with bilateral CRSwNP associated with type-2 inflammation, not controlled under optimized IN therapy (often after ESS), personalize the agent (anti-Il4Rα/anti-IgE or anti-IL5/5R) according to biomarkers and co-morbidities (asthma, AERD) and strict monitoring at month 4–6 and year one. Current principles highlight structured eligibility and evaluation of the response. EPOS 2020, as well as the EPOS/EUFOREA updates and beyond, suggest that biologics should be taken into consideration in adult patients with bilateral CRSwNP and type-2 inflammation who have failed to be controlled. Uncontrolled sinonasal disease despite use of intranasal corticosteroids (typically following prior surgery) whose choice has generally been directed by a composite of criteria including type-2

inflammation biomarkers (tissue eosinophils and/or elevated blood or total IgE), high symptom burden and impact on quality-of-life due to antibiotic resistant infection (elevated SNOT-22), anosmia, frequent courses of systemic corticosteroids over the previous year, history or anticipation of future surgery.

The EUFOREA consensus first defined these as fulfilling ≥3 of 5 criteria in previously operated patients (more stringent in prior non-surgery) (Head et al., 2016; Fokkens et al., 2019). The 2023–2024 EPOS/EUFOREA recommendations also more closely standardise indication, timing and metrics of biologic response, usually at 16–24 weeks and then after one year by using binary composite outcomes averaged from symptom scores with other outcome metrics including endoscopy, olfaction, systemic corticosteroid use or surgery as agreed definitions of control, remission or recurrence (Fokkens et al., 2023).

The safety profile across programs has been positive overall. Trials and real-world studies of dupilumab have described a rate of an elevation in blood eosinophils that can be occasionally observed, but is generally transient, which requires monitoring within context but rarely treatment discontinuation (Boscke et al., 2023). Taken together, these data support a precision-medicine model in CRSwNP in which the treatment decision between IL-4Rα, anti-IL-5/IL-5Rα, anti-IgE or anti-TSLP biologics is individualized to endotype, comorbid asthma or NSAID-exacerbated respiratory disease (NERD), biomarker profile, prior surgery and patient-reported priorities within evidence-driven selection and monitoring frameworks. A comparative summary of pivotal phase 3 trials and real-world evidence supporting biologic therapy in CRSwNP is presented in Table 2.

Table 2. Summary of pivotal phase 3 trials and real-world evidence of biologic therapies in CRSwNP

Biologic (target)	Key phase 3 trials / studies	Main efficacy outcomes	Additional clinically relevant findings
Dupilumab (IL-4Rα; IL-4/IL-13 blockade)	LIBERTY NP SINUS-24, SINUS-52	Significant reductions in nasal polyp score (NPS), nasal congestion, and CT opacification; marked improvement in SNOT-22 and sense of smell	Reduced need for systemic corticosteroids and sinus surgery; efficacy consistent across biomarker strata (blood eosinophils, asthma, AERD); durable response with continued treatment
Mepolizumab (anti-IL-5)	SYNAPSE (phase 3)	Significant reduction in polyp size and nasal obstruction vs placebo	Decreased need for endoscopic sinus surgery across baseline eosinophil levels and surgical histories; acceptable safety profile
Omalizumab (anti-IgE)	POLYP-1, POLYP-2	Improvements in NPS, nasal congestion, and SNOT-22	Benefits consistent across subgroups defined by eosinophil counts, asthma, aspirin sensitivity, and prior surgery
Benralizumab (anti-IL-5Rα)	OSTRO (phase 3)	Significant reductions in nasal polyp burden and nasal obstruction	Variable effects on some secondary endpoints, highlighting heterogeneity of response among eosinophil-depleting strategies
Tezepelumab (anti-TSLP)	WAYPOINT (phase 3)	Reduction in polyp size and nasal congestion vs placebo	Lower systemic corticosteroid exposure and reduced need for sinus surgery over 52 weeks

Challenges and perspectives

Biologic treatment for CRSwNP, despite a strong clinical efficacy signal, is fraught with multiple system and evidentiary challenges. First, there are difficult value judgments due to high direct costs. From the economic perspective, it has been shown that dupilumab may be considered cost-effective as an add-on to best supportive care in a few assumptions, but overall costs still remain high and need to be counterbalanced against surgical and medical comparators (De Corso et al., 2022). Secondly, access and reimbursement differ widely between health care systems, with survey data and national practice reports describing heterogeneous prescribing pathways as well as differences in access limitation by country and payer (Favier et al., 2024). Thirdly, long-term safety, duration of response, and ideal duration of drug treatment are not clearly established. Pivotal trials are typically 1 year long, and modern reviews identify the absence of clear stopping rules and the scarcity of multiyear outcome data; optimistic real-world signals exist (Cai et al., 2025). Last but far from least is the need to develop and operationalize standardized eligibility/monitoring algorithms based on phenotype/endotype

and objective response parameters to inform initiation, switching, and discontinuation. Prospective validation and biomarker-guided stratification are targets for the next phase of treatment.

4. CONCLUSION

CRSwNP is a complex inflammatory disease characterized by hemo- and eosinophilic, type-2 (IL-4/IL-13, IL-5 IgE) dependent inflammation and epithelial barrier dysfunction that result in sustained symptoms, tissue remodeling, and recurrence. Treatment with standard of care, intranasal corticosteroids, and conservative short courses of oral steroids is able to achieve control but not often remission. ESS reestablishes ventilation and access to topical therapy, but ongoing medical management is necessary. Agents targeting IL-4Rα, IgE, and IL-5 significantly reduce polyp burden, symptoms, and SSS requirements and are now part of the armamentarium for patients failing conventional therapy. Most notably in the case of type-2–high endotypes with associated comorbidities (asthma, AERD). The best route is multifaceted and person-specific. ESS and biologics are not mutually exclusive but complementary, while treatment should be phenotype/endotype-directed and guided by a treat-to-target concept (symptoms, endoscopy, smell, QoL, need for OCS/surgery). Safety profiles have been generally excellent, though vigilance (e.g., for transient eosinophilia) is warranted. Barriers include cost, wide variation in reimbursement, and limited geographical availability. Insufficient multi-year data to identify best duration, switch, and stop rules also warrant further investigations.

Prospective evaluation of pragmatic eligibility algorithms, predictive biomarker development, and head-to-head sequencing versus surgery studies (and affordability) are a priority to make this feasible for everyone in the community. In combination, the above concepts of state-of-the-art care, including optimized topical therapy, quality surgery, and a biologic targeting the dominant inflammatory pathway, represent the best opportunity to avoid systemic steroids and revision surgery while improving olfaction and QoL.

Author's Contributions

Maciej Świerczyna- Conceptualization, review and editing, investigation, methodology; Agata Olecka - Methodology, investigation, visualization; Filip Gałązka - Conceptualization, visualization, resources; Fryderyka Orawczak - Review, data curation, investigation; Jakub Majcherek - Resources, writing - rough preparation, data curation; Tomasz Karwowski - Visualization, data curation, investigation; Mikołaj Kotusiewicz - Review, visualization, formal analis; Mateusz Mazurek - Supervision, writing - rough preparation, data curation; Julia Gałązka - Review and editing, formal analis, supervision; Zuzanna Czuba - Resources, writing- rough preparation, formal analis. All authors have read and agreed to the published version of the manuscript.

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Informed consent

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Ethical approval

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Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on reasonable request to the Corresponding Author.

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