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Original Research Paper

Diagnosis and therapy of adult type-2 inflammation chronic rhinosinusitis: a systematic literature review

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Abstract
Adult type-2 inflammation chronic rhinosinusitis with nasal polyp impacts quality of life. Despite diagnosis and treatment advances, recurrence is common, prompting the exploration of new diagnosis and therapies. Objectives To review the current literature for the best diagnosis and therapy of adult type-2 inflammation chronic rhinosinusitis and future research to find new specific diagnoses and therapies. We conducted a literature review of PubMed, Google Scholar, Cochrane Library and others, August, 2 - 9, 2025. The search terms included "type-2 inflammation", "chronic rhinosinusitis", and "therapy". We got 107 e-journals from: PubMed: 13, Google scholar: 11, Cochrane Library: 14, Others: 69. Type 2 inflammation is responsible for driving the disease in 80% to 90% of patients with nasal polyps (CRSwNP) and biomarkers for diagnosis include tissue/blood eosinophils, total IgE, and interleukin. Type 2 inflamation CRSwNP have high recurrence rates 38% to 60% at 12 months follow-up, and resistance to conventional medical or surgical treatment. Effectiveness of recent treatment for severe type 2 CRSwNP: corticosteroid effective for rapid reduction of inflammation, Endoscopic Sinus Surgery (ESS) is effective for restoring sinus drainage, and biological agents promosing future treatment. Future studies should investigate the optimal diagnostic techniques for individual patients based on underlying pathophysiology especially endotype and biomarker to better direct treatment and should assess the role of new therapies. The treatment of corticosteroid combine with antihistamine, new biologics agent and new surgery technic promising strategy for achieving therapeutic benefits type-2 inflammation chronic rhinosinusitis.

Keywords: chronic rhinosinusitis; therapy; type-2

1. Introduction

Chronic rhinosinusitis (CRS) is defined as a long-lasting (>12 weeks) inflammation of the nasal cavity and paranasal sinuses, characterized by symptoms of nasal blockage/congestion or nasal discharge, possibly associated with facial pain/pressure and a dysregulated sense of smell (Giunta et al., 2023). Chronic rhinosinusitis (CRS) is a common health problem, with a prevalence reaching 10.9% in Europe and between 12% to 16% in the United States (Al-Sharif et al., 2019; Kim et al., 2022; Yao et al., 2021).

Inflammation in CRS is mainly characterized by 3 endotypes based on elevation of canonical lymphocyte cytokines: 1). T1 by TH1 cytokine IFN-g; 2). T2 by TH2 cytokines IL-4, IL-5, and IL-13; 3). T3 by TH17 cytokines including IL-17 which are strongly linked to a higher rate of recurrence (Kato et al., 2022; SC, Pelletier et al., 2025; Toppila-Salmi et al., 2024).

Current treatment protocol includes saline nasal irrigation, long-term antibiotics including macrolides and doxycycline, and topical and systemic corticosteroids. Where pharmacological intervention is insufficientwith the additional addressing of comorbidities and trigger factor, endoscopic sinus surgery is performed, with the aim of widening the openings of the sinuses, removing inflammatory tissue, reducing inflammatory load, and in CRSwNP removing nasal polyps (Hildenbrand et al., 2024).

Despite these current guidelines, around 30% of CRS patients experience difficulties managing symptoms (Ahern et al, 2019; Bachert et al., 2018). CRSwNP continues to attract researchers attention in

the rhinology field because the percentage of patients with disease relapse still is considerably higher than in CRSsNP, with figures ranging from 38% to 60% at 12 months follow-up. Implementation of diagnosis and therapy requires a precise definition of indications, by defining the phenotypic and endotypic characterization of patients (Mortuaire, G., et al., 2018). New promising biologicals targting IgE are being developed with the aim of improving anti-IgE treatment (De Greeve et al., 2017).

Research on type 2 inflammation in Chronic Rhinosinusitis (CRS) primarily revolves around bridging the gap between clinical phenotypes (e.g., CRSwNP) and specific endotypes to improve personalized medicine. Key gaps include predicting patient response to biologics, standardizing non-invasive biomarkers, and addressing non-type 2 subtypes: 1. Heterogeneity and response to biologics; 2. Geographic and endotypic variations; 3. Non-Invasive biomarker standardization; 4. Non-type 2 and mixed CRS; 5. Upstream mechanisms & epithelial barrier dysfunction (Giri, Schneider, & Tan, 2022; Yang et al., 2025). While progress diagnosis and therapy is rapid, gaps remain in patient selection, long-term outcomes, and understanding non-type 2 pathways (Seccia et al., 2022). Many questions remain in suspense of biologic therapy, including new therapeutic targets, factors for success (enabling appropriate selection), optimal treatment duration, risk of failure, and development of administration routes other than subcutaneous or intravenous (Bartier, Coste, & Béquignon, 2021). This literature review aims to find the best current diagnosis and therapy as well as future therapy for type 2 chronic inflammatory rhinosinusitis.

1.1.Objective

Type-2 inflammation, especially CRSWNP recurrency is high. We review the current literature, what is the best diagnosis and therapy of adult type-2 inflammation chronic rhinosinusitis and future studies to find a specific diagnosis and therapy.

2. Research Methods

We conducted a literature review of PubMed, Google Scholar, Cochrane Library and others, August, 2 - 9, 2025. The search terms included “type-2 inflamation”, “chronic rhinosinusitis”, and “therapy”. The abstracts were reviewed by two authors of the Otolaryngologists and those that potentially met the inclusion criteria were read in full text. When diferences 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. Inclusion criteria: English version, publication period 10 years, systematic literature review, Randomized Controlled Trial, full text, DOI registered. Exclusion criteria: double literature, no data relevant, abstract only, clinical trial. Finally, we got as many as 107 e-journals from: PubMed: 13, Google scholar: 11, Cochrane Library: 14, Others: 69 for a systematic literature review (Figure 1).

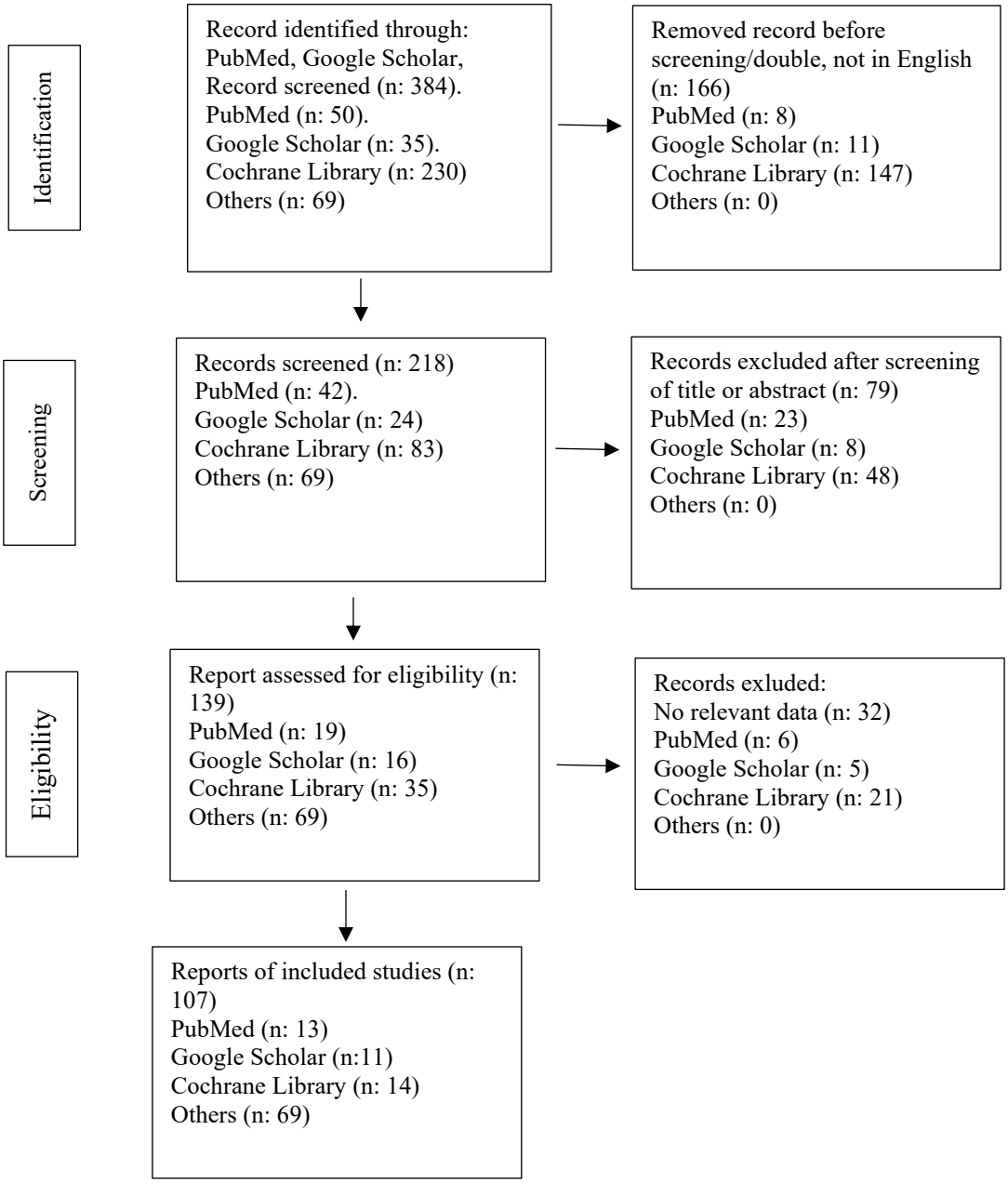

Figure 1. PRISMA Screening Flowchart

2.1.Diagnosis and Therapy

2.1.1.Definition

Chronic Rhinosinusitis in adults is characterized by the presence of two or more symptoms, such as nasal obstruction, nasal discharge, facial pressure, decreased sense of smell for a duration of more than 12 weeks (Aldajani et al., 2024). Type 2 inflammation in chronic rhinosinusitis (CRS) is an immune response characterized by the activation of type 2 cytokines like IL-4, IL-5, and IL-13, leading to eosinophil and mast cell activation, IgE production, and tissue changes such as nasal polyp formation and mucus hypersecretion (Bachert et al., 2019; Matsunaga et al., 2025).

2.1.2.Risk Factor

Risk factor of chronic rhinosinusitis is not yet fully understood. Contributing factors likely genetic predisposition, microbial pathogens, environmental factors such as air pollution, and allergy, although none of these factors appears to be solely causative (Chin et al., 2025; Leland et al., 2022). Furthermore, smoking and inadequate primary surgery increase the chance of revision surgery in case of recurrence (Sedaghat et al., 2022).

2.1.3. Epidemiology

Chronic rhinosinusitis with nasal polyps (CRSwNP) is estimated to affect up to 4% of the adult population and causes a considerable socioeconomic burden (Bachert et al., 2024; Jonstam et al., 2019). In Western countries, 80% of CRSwNP patients exhibit type 2 (T2) inflammation. In contrast, among Eastern populations such as those in China, Japan, Korea, and Malaysia, T2 inflammation is observed in only 20% - 60% of cases (Chen et al., 2025).

2.1.4. Pathophysiology

The pathogenesis of CRSwNP is closely linked to type 2 immune responses. ILC2s play a critical role in the formation of nasal polyps in patients with type 2 chronic rhinosinusitis. Recent studies highlight that the synergistic interaction between Th2 cells and ILC2s in driving local inflammation, tissue remodeling, and disease recalcitrance constitutes a core mechanism underlying CRSwNP progression (Yang et al., 2025).

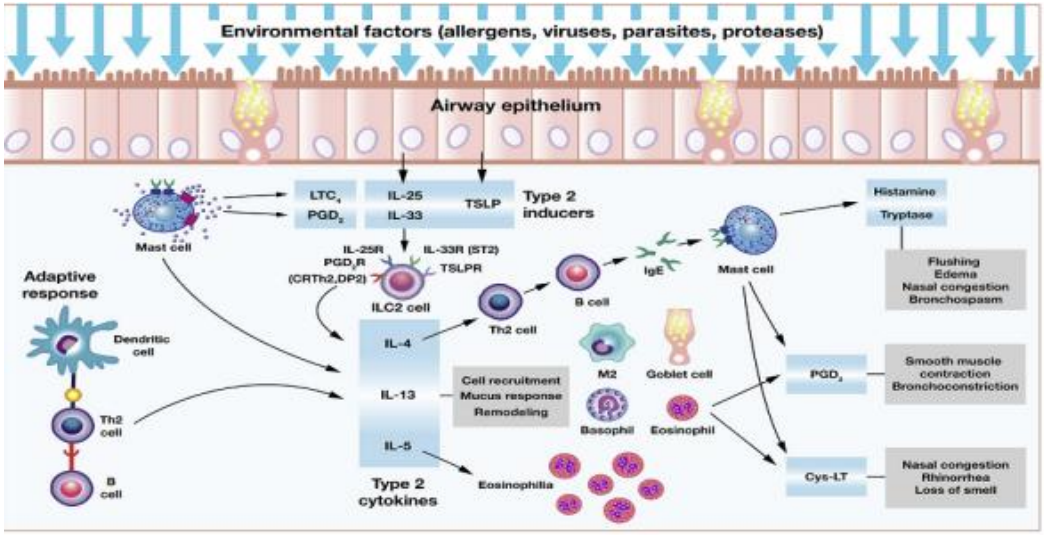

Figure 2. Type 2 inflammation pathway in upper and lower airway diseases (Laidlaw et al., 2021)

Type 2 Immune responses are defined by interleukin-4 (IL-4) IL-5,IL-9 and IL-13, which can be host protective yet, when dysregulated, have pathogenic activity. Type 2 immunity induces a complex respons involving granulocytosis (eosinophil, basophil), mastocyte, type-2 innate lymphoid cel (ILC2), IL4 and / or IL-13- conditioned macrophages and T helper 2 (Th2) cells. These cells are crucial to the pathogenesis Of CRS and related disorders and are therefore mechanism that control the intensity maintenance and resolution of type-2 immunity. They are also reasonably important regulators of disease progression and must be fully understood for therapeutic purposes (Figure 2) (Giunta et al., 2023; Laidlaw et al., 2021).

2.1.5. Classification

Inflammatory responses can be divided into three types: 1). The key cytokines involved in type 1 inflammatory responses include interferon gamma and tissue necrosis factor alpha 2). The key cytokines

involved in type 2 inflammatory responses are interleukin (IL)-4, IL-5, and IL-13. IL-4 and IL-13 are involved in polyclonal IgE formation. IL-4/IL-13 signaling drives class switching of B cells to IgE production; 3). Type 3 inflammation is primarily involved in host defense against bacterial and fungal pathogens and is mediated by Th17 cells and type 3 ILCs. The key cytokines involved in type 3 inflammatory responses are IL-17 and IL-22 (Bachert at al., 2024; Cao et al., 2019; Toppila-Salmi et al., 2024).

2.1.6. Diagnosis

Acoording to European Position Paper on Rhinosinusitis and Nasal Polyp (EPOS), diagnosis of rhinosinusitis is enforced based on symtoms, nasal endoscopy and computed tomography (CT) – Magnetic Resonance Imaging (MRI) (Dharmaputri et al., 2017).

2.1.6.1. Clinical Finding

The clinical findings of CRS type 2: 1). Nasal obstruction was the most severe symptom in non-type 2 CRSwNP, with no significant difference from type2; 2). Rhinorrhea was another severe and specific CS for endotype 2; 3). Olfactory disfunction: A test of the sense of smell is not absolutely necessary for diagnosing CRS, but it is a criterion for the success of treatment, e.g., with biologics, and it is also recommended for preoperative documentation; 4). Polyp formation, asthma comorbidity, severe disease, and recurrence after sinus surgery. 5). Patients with type 2 CRSwNP have a significantly worse SNOT-22 (Bogaert et al., 2025; Hildenbrand et al., 2024; Marin et al., 2022; Mullol et al., 2022; Pedersen et al., 2025; Zhu et al., 2025).

a. Nasal Endoscopic

Nasal endoscopy is a useful adjunctive tool in the diagnosis and management of CRS. Future studies may seek to delineate exact parameters for endoscopic diagnosis of this disease. Nasal endoscopy also has functions to asses predisposing factor and contributor of rhinosinusitis such as variation in anatomical structure and mucosal change in midle meatus and osteomeatal complex. Nasal endoscopy turned out to be a cost-efective diagnostic approach and improves the diagnostic accuracy for CRS (Dharmaputri et al., 2017; Sheikh et al., 2024; Wiederman et al., 2025).

b. X-Ray, CT-Scan and MRI

Conventional x-ray examination using the waters open mouth method featuring superposition free maxillaries, frontalis, ethmoidalis and sphenoidalis sinus results with processus alveolar and petrous ridge. CT-Scan examination is the modality with the highest sensitivity that can display the entire paranasal sinuses and surrounding anatomy with a variation in slice thickness of 1 mm. If the symptoms are typical but the endoscopic findings are normal, a CT-scan is recommended to confirm the diagnosis. MRI examination can clearly distinguish between soft tissue and fat on the body and is used to support therapy in cases of rhinosinusitis and particularly in children, because it does not expose the patient to radiation (Hildenbrand et al., 2024; Nugroho et al., 2022).

c. Laboratory finding

Laboratory finding in type2 chronic rhinosinusitis are: 1). Tissue eosinophil count >10/high-power field (HPF); 2) Serum eosinophil count >250 cells/mcL; 3). Total IgE > 100 IU/mL (Aldajani et al., 2024; Al - Fraihat et al., 2025; Bachert et al, 2019; Bogaert et al., 2025). Although numerous biomarkers have been identified for characterising endotypes, challenges persist in their application to routine clinical practice: (1) There is a lack of unanimous criteria and consensus regarding a cut-off point for biomarkers identifying T2 inflammation and neutrophilic inflammation. (2) Most biomarkers are identified through laboratory research, but non-invasive biomarkers with good clinical accessibility and simplicity are needed in real-world practice (Chen et al., 2025).

2.1.7. Comorbid

The Comorbid of CRSwNP are: 1). Asthma, among all patients with CRSsNP was 19.6%, with a significantly increased prevalence of asthma (P < .0001) in patients with type 2 CRSsNP (30.2%) compared with in patients with non-type 2 CRSsNP (9.8%) (Delemare et al., 2020; Hassoun et al., 2021; Laidlaw et al., 2021; Maspero et al., 2022); 2). Allergic rhinitis (17 - 76%) were the most reported comorbidities in CRSwNP patients (Gadersohi & Tan, 2017; Toppila-Salmi et al., 2024;); 3). Eosinophilic esophagitis (EoE) and chronic rhinosinusitis with nasal polyps (CRSwNP) are both immune-mediated, chronic inflammatory conditions driven by type 2 inflammation (Padia et al., 2016; Simmons et al., 2022); 4). Chronic Otitis Media (COM), CRSwNP affecting the nasal passage and eustachian tube dysfunction connect the nose and ears (Brescia et al., 2023); 5). Atopic dermatitis (eczema) and Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) frequently coexist because they are both driven by the same underlying biological mechanism: Type 2 inflammation (Hassoun et al., 2021; Mora et al., 2024; Toppila-Salmi et al., 2024); 6). Aspirin - exacerbated respiratory disease (AERD) CRSwNP are closely linked respiratory conditions. AERD is a specific, severe type of CRSwNP characterized by a clinical triad of asthma, recurrent nasal polyps, and sensitivity to aspirin and other NSAIDs (Chen et al., 2025; Studer et al., 2020).

2.1.8. Therapy

Chronic rhinosinusitis (CRS) has recently undergone a significant paradigm shift, moving from a phenotypical classification towards an “endotype-based”. This paradigm shift necessitates a multidisciplinary approach (Giombi et al., 2024). Therapies should be integrated with a personalized approach for each patient who fails first-line treatment (Weissman et al., 2025).

2.1.8.1. Allergen Avoidance

Allergen avoidance measures widely recommended as part of secondary and tertiary prevention strategies for AR, they can have a beneficial effect either at a young age or in adolescence (Tome and Lourenco, 2023; Van Boven et al., 2024).

2.1.8.2. Nasal saline irrigation

Nasal irrigation is a common auxiliary treatment method, regarded as a simple and effective of sinonasal disease. When saline nasal irrigation washes out secretions and antigens, it physiologically propels a superficial gel layer, increases hydration in the sol layer, and enhances mucociliary function (Liu et al.. 2019). A hypertonic solution with the addition of the natural minerals and oligo-elements may be associated with greater clinical benefit in terms of endoscopic scores and mucociliary clearance than isotonic solutions (Casale et al, 2018).

2.1.8.3. Anti Histamine

Antihistamines are not a primary treatment for Chronic Rhinosinusitis with Nasal Polyps (CRSwNP). Their function is limited to mitigating specific histamine-mediated allergy symptoms (e.g., sneezing, watery rhinorrhea) that often coexist with CRSwNP. They do not treat or shrink the nasal polyps themselves (Narasimhan et al., 2024). It inhibits ciliary beat, as cilia do not work effectively in dry nasal mucosa. Second-generation antihistamines do not have an anticholinergic property, and thus do not cause the aforementioned adverse effects (Seresirikachorn et al., 2017).

2.1.8.4. Decongestan

In CRSwNP, the primary function of a decongestant is to provide short-term relief from nasal obstruction. They temporarily unblock your airways by narrowing the blood vessels in your nasal mucosa,

which reduces swelling (Ghadersohi & Tan, 2017). These vasoconstrictors are not recommended for a permanent therapy with nasal polyposis since they don't reduce polyp size. Long term usage can lead to rhinitis medicamentosa and rebound swelling (Fokkens et al., 2020).

2.1.8.5. Corticosteroid

Corticosteroids are pivotal in treating CRS due to their potent anti-inflammatory effects. Both topical and systemic corticosteroids are currently indispensable for the treatment of CRS and postoperative management of endoscopic sinus surgery (ESS) (Chen et al., 2025). The injected steroids show longer effects with fewer side effects. An RCT study is needed to compare OCS and injected corticosteroids (Tamene et al., 2023).

2.1.8.6. Anti-leukotriens

The effects of leukotriene on the nasal vasculature, such as vascular permeability and vasodilation play a role in producing symptoms of the mucosal swelling (Seresirikachorn et al., 2021). Leucotriens receptor antagonist drugs, such as montelukast, zafirlukast, and pranlukast, block the effects of CysLTs, improving the symptoms of some chronic respiratory diseases, particularly bronchial asthma and allergic rhinitis (Cingi et al., 2015). Anti-leukotrienes a target for finding the new ways of treatment, nevertheless due to a low quality of evidence, EPOS 2020 steering group does not recommend Montelukast application nor independently nor with corticosteroids (Fokkens et al., 2020).

2.1.8.7. Antibiotic

A number of guidelines have been developed to rationalize antibiotic prescription for CRS, but there are practical challenges in applying treatment guidelines, including antibiotic resistance rates. Reducing inappropriate antibiotic use is critical to combating antibiotic resistance. CRS is an ideal condition to clarify the appropriateness and efficacy of antibiotic prescriptions, which is very pertinent in the context of the global crisis of resistance to antibiotics (Smith, Kim, & Douglas, 2022). Studies have shown that macrolide might be effective for CRS patients with elevated levels of IL- 8, IL- 6, and IgG4, suggesting that patients with neutrophilic inflammation who respond poorly to glucocorticoid treatment might benefit from macrolide (Chen et al., 2025).

2.1.8.8. Imunotherapy

Allergen-specific immunotherapy (AIT) is efficacy of inoculating low-dose long-term grass pollen extract in allergic patients. AIT induces immune tolerance by increasing expression of allergen-specific activated Treg cells and by reducing differentiation into T helper 2 cells (TH2), whose cytokines (IL-4, IL-5, IL-9, IL-13) are mediators of the allergic inflammatory response. Several studies have demonstrated that both current subcutaneous (SCIT) and sublingual specific immunotherapy (SLIT) are effective in treating AR and LAR compared to placebo. The main difference between the two administration methods is the safety profile, due to the higher possible risk of side effects with SCIT (Cantone et al., 2022; Smith et al., 2022).

2.1.8.9. Biologic Therapy

Biological therapies targeting type 2 inflammatory mediators offer a promising new strategy for one step closer to precision medicine (Al-Ahmad et al., 2022; Ahern & Cervin, 2019; Chong et al., 2021; Soyka, 2021; Toppila-Salmi et al., 2024). Biologics can be effective in treating nasal polyps, with reduction in polyp size and extent of disease, and improved sense of smell and quality of life. Although no single agent was superior across all measures, these findings support the personalized use of targeted therapies (Zheng et al., 2025). The probability of the development of specific new therapies for CRS is dependent on

defining the endotypes so that the therapy can be targeted, particularly for biological agents (Lee et al, 2022; Ren et al., 2019). Discontinuation of biologics caused a slow bounce of nasal polyp scores and nasal symptoms, indicating that continued treatment is necessary to sustain positive outcomes, Table 1 (Lou & Zhang, 2022).

Table 1. Biological agents approved or in clinical trials for CRSwNP (Tai et al., 2022)

Target	Drug	Brand	Approval or Development Status for CRS	Decreased Biomarker after Treatment	Side Effects
IL-4Rα	Dupilumab	Dupixent®	FDA approved for CRSwNP	Blood thymus and activation-regulated chemokine	Injection site reaction and conjunctivitis
IgE	Omalizumab	Xolair®	FDA approved for CRSwNP	Blood Periostin	Injection site reactions
IL-5	Mepolizumab	Nucala®	FDA approved for CRSwNP	Blood Eosinophil	Headache and injection site reaction
IL-5	Reslizumab	CINQAIR®	Phase 2 trials concluded	Blood Eosinophil	Nasopharyngitis
IL-5Rα	Benralizumab	Fasenra®	Phase 3 trials concluded	Blood Eosinophil	Nasopharyngitis

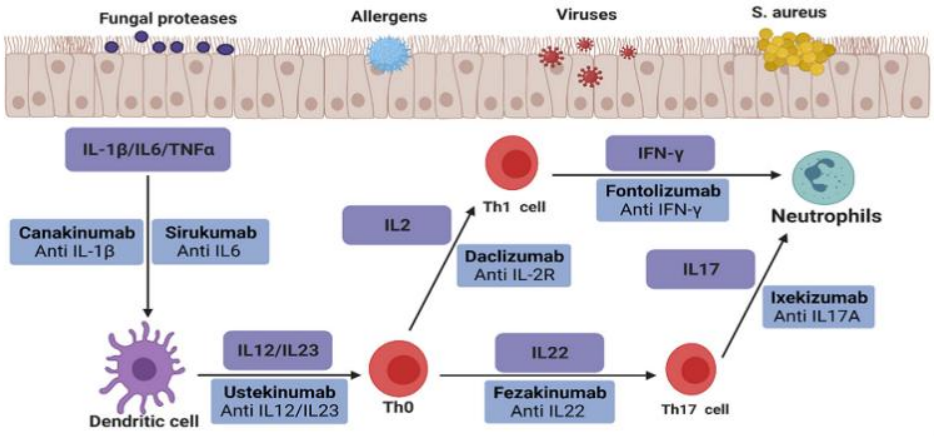

Figure 3. Possible biologics for treating CRSsN in the future (Tai et al., 2022)

A multidisciplinary approach is mandatory to find the best suitable biologic (Otten et al., 2023). Direct comparative efficacy data for biologics in chronic rhinosinusitis with nasal polyps (CRSwNP) remain limited, particularly for novel agents like tezepelumab, underscoring the need to identify optimal therapies for precision management. Treatment selection should be guided by the most dominant symptom for the patient, comorbidity patterns, and biomarker status on an individual basis (Almutairi et al., 2025). Dupilumab demonstrated the highest efficacy and safety profile (Kariyawasam, et al., 2023; Xu et al., 2025). Dupilumab shows superior efficacy for nasal polyp reduction estimated by reduced 2.44 clinical points, while mepolizumab excels in improving nasal congestion by reduced 2.64 points. Tezepelumab may offer significant quality of life improvements (27.26 - point SNOT-22 reduction) and surgery need reduction (98 % risk reduction), however validation through additional studies is required before definitive recommendations are warranted (Almutairi et al., 2025). The treatment choices also vary in cost. The financial burden faced by the patient is an important factor in treatment access especially when multiple

options are available (Ramkumar, Lal & Miglani, 2023). Recognizing the high cost of biologics forces the need for cost-effectiveness analysis, figure 3 (Kim & Naclerio, 2020; Klimek et al., 2024).

2.1.8.10. Surgery

a. Endoscopic Sinus Surgery (ESS)

For CRS patients unresponsive to comprehensive medical therapy, endoscopic sinus surgery (ESS) remains the primary intervention to restore sinus ventilation, drainage, removal of nasal polyps (Chen et al., 2025; Fokkens et al., 2020). ESS, a minimally invasive procedure, is a gold standard in treating CRS. This type of surgery lowers the symptoms and improves the quality of life in CRS (Hopkins et al., 2006). However, reoperation is needed in 4% of patients which 88% have CRSwNP (Miglani et al., 2018). Veloso-Teles, et al. (2018) reported that after 1 year of surgery 3,5% patients wih CRSwNP required revision ESS while only 1,6% in CRS group. Most mentioned complication of ESS are epistaxis, injury of the lamina papyracea and periorbital ecchymosis (Benninger et al., 2015; Fokkens et al., 2020; Orlando et al., 2024). Corticosteroids are used before, during and after the surgery to reduce bleeding and surgical field is more apparent, therefore duration of the procedure decreases (Albu, 2010).

b. Reboot Surgery

The Reboot technique should be considered for patients with severe and uncontrolled chronic rhinosinusitis with nasal polyposis (CRSwNP), especially when previous classical endoscopic sinus surgery (ESS) has failed to maintain adequate olfactory function and polyp-free status. It is indicated for patients at higher risk of polyp recurrence, especially those with associated asthma (Smith et al., 2025). Using bilateral endonasal mucoplasty as a complementary technique to reboot surgery is a suitable technical choice that has improved short- and medium-term QoL (Martin-Jimenez et al., 2023). Reboot surgery significantly improved olfaction, reduced recurrence rates (from 40% - 50% to < 15%), and decreased oral steroid dependency (Chen et al., 2025). Reboot surgery is an innovative procedure that may be considered a valid alternative to mAbs, especially in younger patients, considering costs of medication and long- term safety (Pirola et al., 2025).

c. Turbinectomy

Turbinate enlargement usually bilateral and is caused by thickening of mucosa with or without hypertrophy of the underlying structures. Many patients are refractory to medical treatment and nasal obstruction prevails due to dilatation of venous sinuses or fibrosis. In such cases surgical approach is recommended (Park et al., 2022; Thomas et al., 2019). The goal of turbinate surgery is to improve nasal patency by minimizing complications such us postoperative hemorrhage, crusting, foul odor, and the “empty nose syndrome”. Turbinectomy is a safe and reliable technique for patients with chronic inferior turbinate hypertrophy refractory to medical management, and has a very low complication rate. There is a variety of turbinate procedures, but there is a lack of consensus about which technique is the best. Several surgeries like partial or total inferior turbinectomy, submucosal resection, submucosal diathermy, inferior turbinoplasty, laser turbinectomy and radiofrequency ablation have been widely used (Neri et al., 2019; Park et al., 2022; Thomas et al., 2019).

d. Vidian Neurectomy and Posterior Nasal Neurectomy

Vidian neurectomy was first described in the early 1960s using a transantral approach. Since then, other surgical techniques have been implemented, including transpalatal, transseptal and transnasal approaches. Despite its original popularity, vidian neurectomy was almost completely

abandoned because of side effects and the lack of long-term effectiveness. Recently published studies have demonstrated the efficacy of vidian neurectomy in treating patients with persistent non-allergic rhinitis and allergic rhinitis. Improved endoscopic visualisation and a better comprehension of the anatomy has significantly improved the capability of the surgeon to locate and precisely resect the vidian nerve (Marshak et al., 2016). Compared to standard treatment, vidian neurectomy has advantages in terms of cost and treatment effectiveness, making it a suitable treatment option for moderate to severe allergic rhinitis and vasomotor rhinitis (Sun et al., 2024).

Posterior nasal neurectomy effectively alleviates rhinorrhea, nasal obstruction, nasal itching and sneezing in patients with allergic rhinitis, and improves quality of life, demonstrating favorable short-term post-operative efficacy (Hu et al., 2025), without significant adverse effects (Kim, Stybayeva & Hwang, 2025). Several surgical procedures for posterior nasal neurectomy have been reported, but no conclusion has been reached about which procedure is best (Chen et al., 2021; Makihara et al., 2021).

2.1.8.11. Combination Therapy

A significant reduction for all important parameters such as SNOT-22, NPS, VAS CRS, and NCS in patients with large polyps (NPS 6–8), when combining biologics with FESS compared with biologics only (Homøe et al., 2025). ESS removes polyps and widens sinus pathways, while targeted biologics (e.g., Dupilumab) suppress type 2 inflammation to prevent polyp regrowth and reduce the need for repeat surgery (Cai et al., 2025). Currently approved biologics for combination with INCS in uncontrolled CRSwNP comprise dupilumab, omalizumab, and mepolizumab (Barroso et al., 2023).

2.1.8.12. Remission

Remission as a treatment goal in chronic inflammatory NCDs was first introduced in RA, and then adopted in other non-type 2 inflammatory diseases. Among diseases with type 2 Inflammation, this concept is novel and currently most advanced in asthma. Aiming at remission in type 2 inflammatory diseases offers many opportunities in the future. However, much more clinical and mechanistic insight has to be gained until this concept can be fully established, Table 2 (Fokkens et al., 2020; Lommatzsch et al., 2024).

Table 2. Assesment of current clinical control of CRS (Fokkens et al., 2020)

EPOS 2020: Assessment of current clinical control of CRS (in the last month)

	Controlled (all of the following)	**Partly controlled** (at least 1 present)	**Uncontrolled** (3 or more present)
Nasal blockage[1]	Not present or not bothersome[2]	Present on most days of the week[3]	Present on most days of the week[3]
Rhinorrhoea / Postnasal drip[1]	Little and mucous[2]	Mucopurulent on most days of the week[3]	Mucopurulent on most days of the week[3]
Facial pain / Pressure[1]	Not present or not bothersome[2]	Present on most days of the week[3]	Present on most days of the week[3]
Smell[1]	Normal or only slightly impaired[2]	Impaired[3]	Impaired[3]
Sleep disturbance or fatigue[1]	Not present[2]	Present[3]	Present[3]
Nasal endoscopy (if available)	Healthy or almost healthy mucosa	Diseased mucosa[4]	Diseased mucosa[4]
Rescue treatment (in last 6 months)	Not needed	Need of 1 course of rescue treatment	Symptoms (as above) persist despite rescue treatment(s)

[1] Symptoms of CRS; [2] For research VAS ≤ 5; [3] For research VAS > 5; [4] Showing nasal polyps, mucopurulent secretions or inflamed mucosa

2.1.8.13. Recurency

CRSwNP continues to attract researchers attention in the rhinology field because the percentage of patients with disease relapse still is considerably higher than in CRSsNP, with figures ranging from 38% to 60% at 12 months follow-up (Al-Sharif et al., 2019). The factors such as bronchial asthma, eosinophilia, aspirin-exacerbated respiratory disease (AERD), atopy were found to be the most important clinical risk factors, viral or bacterial infections, fungal infections and sinonasal abnormalities, but the clinical backdrop

is often more complex, smoking habits and less extensive primary surgery are associated with the likelihood of needing revision surgery in cases of recurrence (Fageeh et al., 2023; Toppila-Salmi et al., 2024).

3. Results and Discussion

3.1.Result

Type 2 inflammation in the airways and lungs is inflammation induced by type 2 cytokines such as IL-4, IL-5, and IL-13, produced primarily by type 2 helper T cells and type 2 innate lymphoid cells, and causes changes in the physiology and structure of the airways. Type 2 inflammation is currently in the spotlight because of its direct link to the treatment of several airway and lung diseases (Matsunaga et al., 2025).

Diagnosis: Clinical findings: persistent congestion, loss of smell, and the presence of bilateral polyps, endoscopic: typically reveal bilateral, pale, translucent, or edematous polypoid tissue originating from the middle meatus, X-Ray: Higher Lund-Mackay scores**:** Indicates more extensive sinonasal disease, CT-Scan and MRI: typically display extensive bilateral disease, specifically with ethmoid sinus dominance, often characterized by high Lund-Mackay scores and olfactory cleft opacification, Laboratory finding: characterized by a "Type 2-high" endotype, often driven by interleukin-4 (IL-4), interleukin-5 (IL-5), and interleukin-13 (IL-13) (Canevari et al, 2023).

Therapy: Allergen avoidance is a cornerstone of managing allergic rhinitis (AR), aiming to reduce exposure to triggers like pollen, dust mites, and pet dander to alleviate symptoms. Key strategies include using HEPA filters, limiting outdoor time during high pollen counts, and keeping windows closed. While a multifaceted approach is most effective, it should supplement, not replace, medical treatment (Narasimhan et al., 2024). Nasal saline irrigations is safe, effective, non-pharmacological, and low-cost complementary therapy for relieving allergic rhinitis symptoms in both adults and children (Park et al., 2024). Anti histamine Second-generation antihistamines are the first-line, non-drowsy treatment for allergic rhinitis, effectively reducing sneezing, itching, and runny nose by blocking histamine-induced inflammation. Top choices include cetirizine (10 mg), loratadine (10 mg). fexofenadine (120 mg) and rupatadine (10-20 mg) often chosen for their long-lasting effects without significant sedation (Wallace, 2024). Decongestan (both oral and nasal) are effective for fast relief of severe congestion caused by allergic rhinitis by shrinking swollen nasal vessels. Common options include pseudoephedrine and oxymetazoline, with combinations like Allegra-D or Claritin-D often used for comprehensive symptom management. Use nasal sprays for no more than 3 days to avoid rebound congestion. Long-term use of decongestant nasal sprays can actually worsen congestion (rebound congestion) (Khalaf, Jumaah, & Hadeed, 2025). Corticosteroid: Intranasal corticosteroids (INCS) are the most effective first-line therapy for moderate-to-severe allergic rhinitis, reducing inflammation, nasal congestion, sneezing, and itching (Mawkili et al., 2025). Anti-leukotriens specifically montelukast, are effective oral medications for treating allergic rhinitis by blocking inflammatory chemicals (leukotrienes) that cause nasal congestion and airway resistance as add-on therapy with antihistamines or for patients with concurrent asthma, although they are generally less potent than intranasal corticosteroids (Feng et al., 2021; Wallace, 2024). The only RCTs for systemic antibiotics have evaluated doxycycline or macrolides, antibiotics with anti-inflammatory properties. Short-course doxycycline appears to have some benefit in patients with polyps, although study follow up was <3 months (Barshak & Durand, 2017).

SCIT combined with nasal irrigation can improve the patients' symptoms and quality of life, promote the epithelialization of the mucosa in the surgical cavity, regulate the local immune response of the nasal cavity; thus improve the prognosis of patients with ESS after 1 year (Li et al., 2021). The use of HDM immunotherapy for 14 weeks is proven to be able to improve the health status of children with CRA cause by HDM: decreased serum-specific IgE, decreased sleep disturbances, and improved quality of life for children with CRA caused by HDM (Putera et al., 2021).

Surgery is standard of care when medical treatment has not led to adequate control of symptoms. Surgery is carried out according to the needs of each patient: Endoscopic Sinus Surgery (ESS), Reboot

surgery, Turbinectomy, Vidian neurectomy and posterior nasal neurectomy (Chen et al., 2025; Fokkens et al., 2020; Park et al., 2022; Thomas et al., 2019; Smith et al., 2025).

Biologic therapies are highly effective, targeted treatments for severe chronic rhinosinusitis with nasal polyps (CRSwNP) that have not responded to standard care (steroids, surgery). They address underlying Type 2 inflammation, reducing polyp size and improving quality of life, particularly in patients with asthma. Dupilumab is the primary FDA-approved option (Kratchmarov, Dharia, & Bucheit, 2025; Patel & Peters, 2021). Personalized care grounded on endotypic and phenotypic profiles is gradually replacing one-size-fits-all strategies particularly in CRSwNP, where biologics have shown meaningful clinical impact (Nappi et al., 2025).

3.2.Discussion

3.2.1.Type 2 Inflamation CRSWNP

Research on type 2 inflammation in Chronic Rhinosinusitis (CRS) primarily revolves around bridging the gap between clinical phenotypes (e.g., CRSwNP) and specific endotypes to improve personalized medicine. Key gaps include predicting patient response to biologics, standardizing non-invasive biomarkers, and addressing non-type 2 subtypes: 1. Heterogeneity and Response to Biologics; 2. Geographic and Endotypic Variations; 3. Non-Invasive Biomarker Standardization; 4. Non-Type 2 and Mixed CRS; 5. Upstream Mechanisms & Epithelial Barrier Dysfunction. Because type 2 inflammation is a complex, overlapping immune response rather than a single disease pathway, study constraints often restrict the clinical application and generalizability of findings (Ahern & Cervin, 2019).

3.2.2.Diagnosis of Type 2 Inflamation CRSWNP

Diagnosis approaches, current medical technologies have achieved substantial breakthroughs in the precision diagnosis of T2 inflamation CRSwNP. The integration of non-invasive liquid biopsy, bioinformatics analysis, and ML has provided novel insights into molecular endotyping, therapeutic response prediction, and personalized interventions for CRSwNP. Moreover, current models predominantly rely on single-center cohorts, limiting their generalizability owing to racial, geographic, and phenotypic heterogeneity among populations. To address these limitations, systematic strategies including multimodal data calibration and dynamic model optimization must be implemented. Through continuous technologic refinement, such non-invasive diagnostic frameworks may achieve widespread clinical practice, enabling earlier and more precise identification of patients with T2 inflamation CRSwNP (Qi & Feng, 2025).

3.2.3.Therapy of Type 2 Inflammation CRWNNP

Therapy for type 2 chronic rhinosinusitis (often with nasal polyps) focuses on suppressing eosinophilic inflammation using saline irrigations, intranasal corticosteroids, oral corticosteroids for short-term control of severe inflammation, though long-term use is avoided due to side effects, endoscopic sinus surgery (ESS), targeted biologic agents for severe or recurrent cases. Research into Type 2 (T2) inflammation therapies such as biologics targeting IL-4, IL-5, IL-13, and IgE faces several key limitations. These include high costs, primary resistance in some patients, the risk of infection and side effects, and an inability to reverse irreversible airway remodeling: 1). Primary non-response and loss of efficacy: Up to 30% 40% of patients fail to respond to initial biologic treatments (primary non-response), and a subset experiences secondary loss of response over time, 2). Irreversible tissue remodeling, 3). Immune system redundancy, 4). High costs and accessibility barriers: Biological therapies require long-term, sometimes lifelong, administration and are associated with significant financial burdens, making access and consistent insurance coverage major obstacles for many patients, 5). Infection risk and adverse events: broadly inhibiting immune pathways or cells can increase susceptibility to certain infections (viral or parasitic). Characteristic side effects include injection site reactions, conjunctivitis (common in atopic dermatitis

therapies), and transient eosinophilia, 6). Uncertainty regarding remission: while researchers are shifting treatment goals from symptom control to clinical remission, long-term studies regarding whether these targeted therapies can permanently "reprogram" the immune system to achieve sustained drug-free remission are still lacking (Sahnoon et al., 2025).

There is still debate about which biologic agent is best for treating type 2 inflammatory disease (CRWNP). Each biologic agent has its own advantages and disadvantages. Therapy is tailored to each individual patient's needs. Treatment selection should be guided by the most dominant symptom for the patient, comorbidity patterns, and biomarker status on an individual basis. For polyp-predominant disease, dupilumab offers the best benefit; for congestion-predominant presentations, mepolizumab may be preferred; when quality of life impact is severe, tezepelumab shows promise for greatest improvement; and when safety concerns predominate, omalizumab presents the most favorable risk-benefit profile (Almutairi et al., 2025).

Endoscopic Sinus Surgery (ESS): Indicated for patients refractory to medical management, often to remove polyps and improve the delivery of topical medications. Adjuvant treatments: high-volume saline irrigation is strongly recommended to remove mucus and allergens.

Current clinical studies are focusing on developing: 1). Biomarker monitoring**:** Finding dynamic biomarkers to better predict which patients will respond to specific biologics, 2). Bispecific/multispecific antibodies**:** Drugs designed to hit multiple T2 inflammatory targets simultaneously to overcome immune redundancy, 3). Oral therapies**:** The development of more convenient, once-daily oral targeted therapies to ease treatment burdens. The treatment plans focus on long-term management and personalized focus on precision medicine (Giunta et al. 2023: Topila-Salmi et al., 2024).

3.2.4. Clinical Implementation

Clinical implementation of T2 inflamation especially endotype-driven care for Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) faces challenges because direct endotyping often requires tissue biopsies or complex laboratory analyses. Instead of waiting for advanced testing, clinicians use phenotype-based surrogates (like comorbid asthma) and accessible biomarkers (blood eosinophils, IgE) to tailor treatments in daily practice. Because distinct biological mechanisms (endotypes) dictate a patient's response to different treatments, managing CRSwNP has evolved toward a more personalized approach: 1). Surrogates for endotyping in routine practice, 2). Implementation of endotype-driven treatments, 3). Targeted biologics in clinical practice, 4). Patient Selection and shared decision-making

4. Conclusion

Type-2 chronic rhinosinusitis, drives the majority of chronic rhinosinusitis with nasal polyps (CRSwNP) cases, marked by elevated cytokines like IL-4, IL-5, and IL-13 is a common inflammatory condition with serious effects on individual functioning and quality of life. Diagnosis is clinical and depends on subjective symptoms and objective findings on physical examination, imaging and biomarker. First line treatment involves saline irrigation, topical and systemic steroid with consideration of endoscopic sinus surgery when necessary. The best surgical approach is a matter of debate. The currently favored procedure aims at removing inflamed sinus tissue and bony septae between the nasal and sinus cavities, as well as within the sinus cavities. Up to 85% of patients report subjective benefit from surgery, with outcomes depending on surgical skills, pre-operative findings, and postoperative care. Patients with chronic rhinosinusitis with polyps who do not achieve symptomatic relief with standard medical and surgical therapy FESS - ESS and posterior nasal neurectomy, biologics agent a promising new strategy for achieving therapeutic benefits, although the long-term effects of these agents are unknown. Future studies should investigate the optimal diagnostic techniques for individual patients based on underlying pathophysiology especially endotype and biomarker to better direct treatment and should assess the role of new therapies.

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