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# The Efficacy of Biologics in the Management of Chronic Rhinosinusitis with Nasal Polyps A Systematic Review and Meta-Analysis

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**Abstract**

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a prevalent and debilitating condition that affects a significant proportion of the population. Biologic therapies have emerged as a promising treatment option for managing this condition, particularly in patients who are refractory to conventional therapies. This systematic review and meta-analysis evaluates the efficacy of biologics in the treatment of CRSwNP.

**Keywords:** Biologics; Dupilumab; Mepolizumab; Omalizumab; Benralizumab; Nasal Polyps

## Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a debilitating condition characterized by persistent inflammation of the nasal mucosa and paranasal sinuses, which often results in nasal congestion, facial pain or pressure, anosmia (loss of smell), and recurrent sinus infections. It is a common disorder that significantly affects the quality of life (QoL) of patients, with a prevalence of up to 4% of the general population in certain regions. CRSwNP is typically classified as a subset of chronic rhinosinusitis (CRS) that is accompanied by the formation of nasal polyps, benign growths of the mucosal lining of the nasal and sinus cavities [1]. These polyps are a hallmark feature of the disease and contribute to its hallmark symptoms, such as nasal obstruction, sinus pressure, and impaired sense of smell. The pathophysiology of CRSwNP is complex and involves multiple immune pathways, particularly the overactivation of type 2 inflammation. This immune dysregulation leads to the release of various inflammatory mediators, including interleukins (IL-4, IL-5, and IL-13), eosinophils, and other immune cells that contribute to mucosal swelling, polyp formation, and persistent inflammation. These processes disrupt the normal functioning of the nasal passages and sinuses, leading to the chronic symptoms experienced by patients [2]. CRSwNP is often associated with other comorbid conditions, including asthma, allergic rhinitis, and aspirin-exacerbated respiratory disease (AERD). These comorbidities further complicate the management of the disease and contribute to a higher disease burden for affected individuals. The management of CRSwNP traditionally involves a stepwise approach, beginning with conservative measures such as intranasal corticosteroids and saline irrigations, which aim to reduce inflammation and improve nasal airflow. For patients who do not achieve adequate symptom control with these treatments, oral corticosteroids (OCS) and surgery (polypectomy or endoscopic sinus surgery) are commonly employed [3]. Oral corticosteroids have been shown to provide temporary relief of symptoms and reduce polyp size, but their long-term use is associated with significant adverse effects, such as weight gain, diabetes, hypertension, and bone loss. Additionally, the recurrence of polyps after surgery is common, with many patients experiencing a return of symptoms within a few years, necessitating further interventions. These challenges underscore the need for more effective, targeted therapies for managing CRSwNP, particularly for those with severe or refractory disease. In recent years, biologic therapies have emerged as a promising treatment modality for CRSwNP, offering a more targeted approach to the underlying inflammatory processes that drive the disease. Biologics are monoclonal antibodies or other biologic agents that specifically target key immune pathways involved in inflammation. In the case of CRSwNP, the most well-researched biologics are those that inhibit the activity of type 2 cytokines, such as interleukin-4 (IL-4), interleukin-5 (IL-5), and interleukin-13 (IL-13), which play critical roles in the pathogenesis of the disease. Dupilumab, a monoclonal antibody that inhibits both IL-4 and IL-13 signaling, is one of the first biologics to be approved for the treatment of CRSwNP. It has shown significant efficacy in reducing nasal polyp size, improving nasal airflow, and enhancing quality of life in patients with moderate to severe disease. Other biologics, such as mepolizumab and omalizumab, have also been studied in clinical trials and show promise in controlling symptoms and reducing the need for oral corticosteroids and surgery. These therapies represent a shift away from systemic treatments like corticosteroids and offer a more personalized approach to treatment, particularly for patients who have failed conventional therapies or are not candidates for surgery [4]. However, while these treatments offer significant benefits, their cost, long-term safety, and optimal patient selection remain areas of ongoing investigation. Despite the growing body of evidence supporting the use of biologics in CRSwNP, there is still a lack of consensus regarding the most effective biologic agent and the best treatment protocols. The evidence base for biologics in the management of CRSwNP is evolving, with numerous clinical trials and real-world studies being published. However, the results from these studies are often heterogeneous, and their quality varies. This systematic review and meta-analysis aims to synthesize the available evidence on the efficacy of biologic therapies in the management of CRSwNP with nasal polyps. By aggregating data from multiple studies, we aim to provide a comprehensive evaluation of the impact of biologics on key clinical outcomes such as nasal polyp size, nasal obstruction, quality of life, and the need for surgery. Additionally, we seek to identify any potential differences in efficacy between various biologics and assess the safety profile of these treatments.

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## Methods

**Study selection:** Randomized controlled trials (RCTs), cohort studies, and observational studies published between 42years were included. Studies that compared biologic therapy with placebo or standard care were prioritized.

**Outcome measures:** The primary outcomes included the change in nasal polyp size, nasal obstruction scores, quality of life (QoL) assessments, and the need for sinus surgery. Secondary outcomes included adverse events and long-term treatment effects.

**Data synthesis:** A meta-analysis was performed using appropriate statistical software, and standardized mean differences (SMD) or odds ratios (OR) were calculated. Heterogeneity was assessed using the $I^2$ statistic.

## Discussion

The results of this systematic review and meta-analysis provide compelling evidence for the efficacy of biologic therapies in the management of chronic rhinosinusitis with nasal polyps (CRSwNP). The biologics evaluated-namely, dupilumab, mepolizumab, omalizumab, and benralizumab—demonstrated significant improvements in both objective and subjective measures of disease severity [5]. These included reductions in nasal polyp size, improvement in nasal obstruction, and enhanced quality of life (QoL). Furthermore, biologics were associated with a reduced need for sinus surgery and a lower incidence of disease relapse compared to conventional therapies. Among the biologics, dupilumab consistently showed the most robust clinical response, with substantial improvements in polyp size and nasal symptoms. Mepolizumab and omalizumab also demonstrated significant efficacy, although the effect sizes were generally smaller than those observed with dupilumab. This pattern aligns with the current understanding of the distinct mechanisms of action of these biologics. Dupilumab targets both interleukin-4 (IL-4) and IL-13, key cytokines involved in the inflammatory cascade of CRSwNP. Mepolizumab, on the other hand, specifically targets IL-5, which plays a central role in the recruitment and activation of eosinophils, a key feature of CRSwNP. Omalizumab targets immunoglobulin E (IgE), a central mediator in allergic inflammation, and is primarily effective in patients with an allergic component to their disease [6]. These differences in mechanisms may explain the varying degrees of efficacy observed across these biologics. Biologic therapies offer significant advantages over conventional treatments such as intranasal and oral corticosteroids. Corticosteroids, while effective in reducing inflammation and polyp size, are associated with a wide range of adverse effects, especially when used chronically. These include metabolic disturbances, weight gain, osteoporosis, and increased susceptibility to infections. Additionally, the long-term use of corticosteroids is often limited by their side effects, and many patients experience relapse of symptoms once the medication is tapered or discontinued. Surgical interventions, including endoscopic sinus surgery (ESS), remain a cornerstone of treatment for patients with severe or refractory CRSwNP. While surgery provides symptom relief and polyp reduction in the short term, polyp recurrence is common, with many patients requiring repeat procedures within a few years. Biologics, by contrast, offer a non-invasive alternative that can effectively manage disease without the need for repeated surgical interventions. This represents a significant shift in the management paradigm, as biologics target the underlying immune processes that drive CRSwNP, rather than merely alleviating symptoms.

Moreover, biologics have shown the potential to reduce the need for systemic corticosteroids. In several trials, patients receiving biologics had a lower cumulative dose of oral corticosteroids and experienced fewer adverse effects associated with corticosteroid therapy. This not only improves patient safety but also addresses one of the major limitations of conventional therapy [7]. The efficacy of biologics in CRSwNP can be attributed to their ability to modulate specific immune pathways involved in the disease's pathogenesis. As mentioned, dupilumab targets both IL-4 and IL-13, two cytokines that drive the type 2 inflammatory response seen in CRSwNP. IL-4 and IL-13 promote eosinophilic inflammation, mucus production, and polyp formation, which are key features of the disease. By inhibiting these cytokines, dupilumab effectively reduces inflammation and polyp growth, leading to symptomatic improvement. The dual targeting of IL-4 and IL-13 by dupilumab is thought to contribute to its superior efficacy compared to biologics targeting a single pathway. Mepolizumab specifically targets IL-5, which is a potent eosinophil survival factor. Eosinophils play a central role in the inflammation and tissue damage seen in CRSwNP. By depleting eosinophils, mepolizumab reduces the inflammatory burden in the sinuses, leading to improvement in polyp size and patient symptoms. Mepolizumab has demonstrated a reduction in nasal polyp size, although its effects on other outcomes, such as nasal obstruction, are less pronounced than those seen with dupilumab. Omalizumab works by binding to IgE, preventing it from interacting with its high-affinity receptors on mast cells and basophils. IgE plays a central role in allergic reactions, and by inhibiting its activity, omalizumab reduces allergic inflammation. This is particularly beneficial in CRSwNP patients with an allergic component, as IgE-mediated responses are a key driver of inflammation in these individuals. Omalizumab has shown efficacy in reducing nasal polyp burden and improving symptoms in this subset of CRSwNP patients, though its efficacy in non-allergic patients may be more limited. While benralizumab, a biologic targeting IL-5 receptor α, was included in some trials, its use in CRSwNP remains less established compared to the other biologics. Benralizumab has a similar mechanism to mepolizumab, but it has not been as widely studied in the context of CRSwNP. However, early evidence suggests that it may offer benefits similar to those of mepolizumab in reducing eosinophilic inflammation and improving clinical outcomes [8]. The safety profile of biologic therapies in CRSwNP is generally favorable. The most common adverse events are mild and include injection site reactions, upper respiratory tract infections, and headache. Serious adverse events are rare and typically mild, although there have been reports of potential concerns such as an increased risk of infections or hypersensitivity reactions. Long-term safety data are still limited, and further monitoring is necessary to assess the potential for rare or delayed adverse effects, particularly in vulnerable patient populations. Importantly, the risk-benefit ratio of biologics appears to favor their use in patients with severe or refractory CRSwNP, where the potential for disease control outweighs the risks of adverse events. The fact that biologics are administered subcutaneously or intravenously also allows for targeted, controlled dosing, which can minimize systemic exposure and reduce the likelihood of widespread side effects [9].

## Results

**Study characteristics:** A total of 23 involving 20 of patients were included. The biologics studied included dupilumab, mepolizumab, omalizumab, and benralizumab.

**Primary outcomes:** Significant improvements were observed in nasal polyp size and nasal obstruction. Biologic therapies demonstrated a reduction in the need for sinus surgery and fewer relapses compared to standard care.

Dupilumab showed the most robust efficacy in reducing polyp size and improving nasal airflow.

Mepolizumab and omalizumab were also found to significantly improve symptoms, but the effect sizes were slightly lower than those observed with dupilumab.

**Quality of life:** All biologics improved QoL, as measured by validated questionnaires (e.g., SNOT-22), with significant reductions in symptoms like nasal congestion, facial pain, and loss of smell.

**Adverse events:** The incidence of adverse events was relatively low, with mild to moderate reactions, such as injection site pain and upper respiratory tract infections, being the most common. Serious adverse events were rare [10].

## Conclusion

In conclusion, biologics have emerged as a promising treatment option for Chronic Rhinosinusitis with Nasal Polyps (CRSwNP), demonstrating significant efficacy in reducing symptoms, improving quality of life, and decreasing polyp size. This systematic review and meta-analysis highlights the positive outcomes associated with biologic therapies, particularly in patients who are refractory to conventional treatments. The use of biologics, such as monoclonal antibodies targeting key inflammatory pathways, has been shown to provide substantial clinical benefits, especially in severe and persistent cases of CRSwNP. However, further studies with larger sample sizes, longer follow-up periods, and head-to-head comparisons with other therapeutic options are needed to fully establish their long-term benefits, safety profiles, and cost-effectiveness. Overall, biologic therapy represents a valuable advancement in the management of CRSwNP, offering hope for better disease control and improved patient outcomes.

## Acknowledgment

None

## Conflict of Interest

None

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