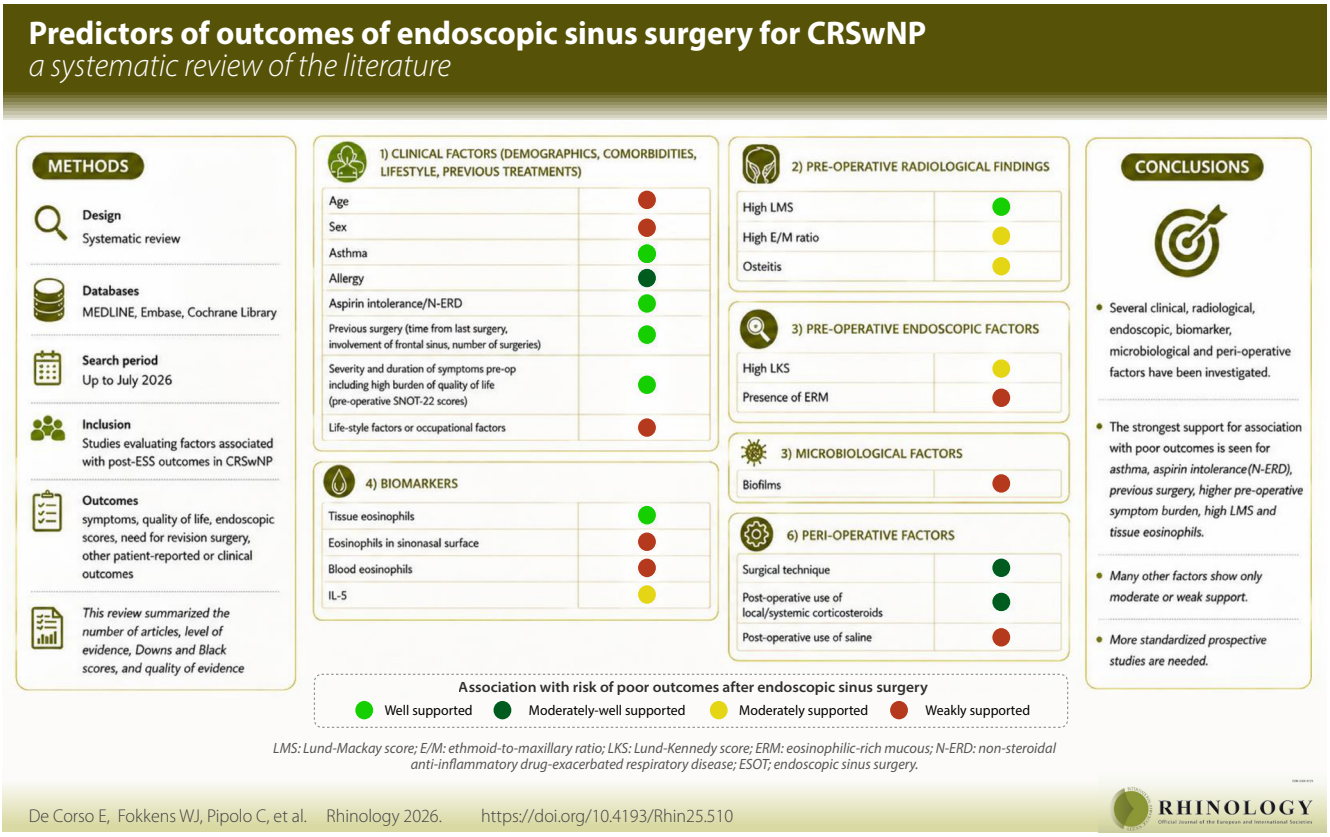
Predictors of outcomes of endoscopic sinus surgery for CRSwNP: a systematic review of the literature

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Abstract

Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) has a wide spectrum of severity and varying impact on quality of life. Endoscopic sinus surgery (ESS) is effective for symptom relief and modifying the natural history of the disease in most patients. Although there have been numerous attempts to ascertain factors predicting outcomes after ESS, there is no universally accepted model for identifying those at risk that can be applied in clinical practice.

Methodology: This systematic review aimed to identify potential pre-, peri- and post-operative factors predicting poor outcomes after ESS.

Results: A total of 152 studies were identified for inclusion, revealing a number of factors well predicting poor outcomes: asthma, non-steroidal anti-inflammatory drug-exacerbated respiratory disease, previous surgery (time from last surgery, involvement of

frontal sinus, number of surgeries), severity and duration of symptoms pre-operatively, high pre-operative Lund-Mackay score and high tissue eosinophil counts. Some evidence was also found for allergy, surgical related factors and lack of post-operative use of corticosteroids, high ethmoid-to-maxillary opacification ratios at computed tomography scan, high Lund-Kennedy endoscopic score, osteitis and interleukin-5 as biomarkers.
Conclusions: This review may assist clinicians in identifying patients at higher risk of poor outcomes after ESS, contributing to more precise and personalised medical care.

Key words: biomarkers, endoscopy, nasal polyps, recurrence, rhinosinusitis

Introduction

The clinical presentation of chronic rhinosinusitis (CRS) with nasal polyps (CRSwNP) and its natural history progression is highly heterogeneous, with a wide spectrum of severity and varying impact on quality of life (QoL) impairment [1,2]. In Europe and the United States of America (USA), more severe forms of CRSwNP are associated with a stronger eosinophilic inflammatory profile and greater olfactory dysfunction [3,4].

Until the advent of biologics, the mainstay of CRSwNP treatment has been the combination of nasal saline irrigation, intranasal (INCS) and systemic corticosteroids (SCS) and endoscopic sinus surgery (ESS) [5,6]. Surgery removes nasal polyp (NP) tissue and opens the sinus cavities, resulting in improved sinus ventilation and mucociliary clearance, reduced bacterial load within the paranasal sinuses and reduced inflammatory burden [7]. In doing so, surgery can improve access for topical therapy such as saline irrigation and INCS (spray or droplet formulation), resulting in a decreased need for systemic antibiotic and corticosteroid therapies, and preventing progressive nasal mucosa and bone remodelling [8]. As a result, ESS can expediently alleviate the cardinal symptoms of CRS, significantly improving QoL [9,10].

ESS is effective in the majority of the patients; however, the revision rate following initial surgery has been reported with considerable variability in the literature [11–15]. This variability is often due to differences in assessment time points, types of surgical procedures and degrees of extension, making precise estimation challenging [11]. Furthermore, the outcomes of ESS are influenced by a complex interplay of multiple factors, broadly categorized into disease-related, surgery-related, patient-related, and external factors. Disease-related factors such as extent of sinonasal inflammation, extent of radiological opacification of the sinuses, comorbidities (e.g., asthma, non-steroidal anti-inflammatory drug [NSAID] intolerance or NSAID-exacerbated respiratory disease [N-ERD], chronic obstructive pulmonary disease [COPD], immunodeficiency, other general diseases), osteitis, or eosinophilic burden in tissue/mucus may significantly predict post-operative trajectory [12,13]. Surgery-related factors include mainly the completeness of surgery and its extension ranging from minimal to extended/radical ESS [14]. Patient-related factors also play a key role, including adherence to the use of post-operative medical therapy such as nasal saline irrigations and INCS, patient expectations, and compliance with long-term follow-up [16]. Lund-Mackay score (LMS) and other radiological scores predict revision ESS [17]. Lastly, external influences – including environmental exposures, occupational risks, lifestyle behaviours, and substance use (e.g., intranasal cocaine abuse) – can modulate disease recurrence and overall surgical efficacy [18].

The advent of biological therapy has led to a revolution in the treatment strategy for CRSwNP, by providing another option for care in those with difficult-to-control, severe disease after ESS [19]. In most patients with severe, uncontrolled CRSwNP, it is now possible to prevent the need for multiple and repeated surgical interventions by identifying high risk patients and by weighing available therapeutic options against the risk of poor post-operative disease control [20,21].

Unfortunately, there is a lack of applicable, real-life predictive models to identify which patients are at high risk of CRSwNP recurrence/poor control after ESS.

The current review aims to systematically evaluate the literature on clinical predictors of poor outcomes after ESS in adults with CRSwNP, classifying the predictors and analysing the quality of the published evidence. All potential contributing factors to poor post-operative control are included in this qualitative analysis.

Materials and methods

Search strategy, study selection and evaluation of study quality

Literature search strategies and study selection criteria

This review was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) process [22] to identify published articles with data on the predictive relating factors for ESS outcomes in adults with primary CRSwNP. It should be noted that, in this analysis, we excluded cases of CRSwNP secondary to genetic disorders, such as cystic fibrosis and ciliary dysfunctions, as these conditions warrant a separate discussion due to their distinct pathophysiological mechanisms and different management requirements.

A comprehensive literature search was conducted in PubMed/

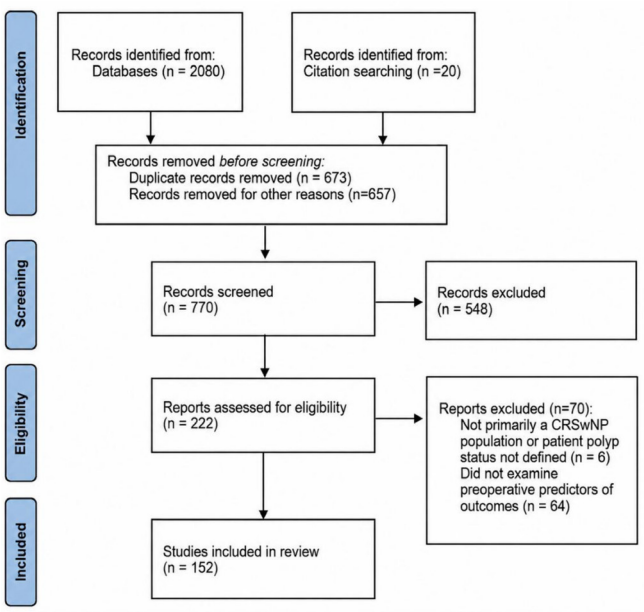


Figure 1. PRISMA flow diagram. CRSwNP, chronic rhinosinusitis with nasal polyps.

MEDLINE, Embase, and the Cochrane Library from database inception to 27 July 2026. The search combined database-specific controlled vocabulary terms with free-text terms related to CRSwNP, ESS, prognostic or predictive factors, and postoperative outcomes. The PubMed search strategy is reported in detail in Table S1. The strategy was translated and adapted for Embase and the Cochrane Library using the corresponding controlled vocabulary and database-specific syntax. The reference lists of eligible studies and relevant reviews were also screened to identify additional publications.

The search results were manually screened to identify primary research (including descriptive studies, observational studies, randomised trials, guidelines and basic science articles), published in the last 20 years, addressing the pre-operative factors influencing outcomes after ESS. We excluded secondary research studies (e.g., review articles or systematic reviews), case studies, news reports, correspondence, comments, personal narratives, consensus papers, conference reports and editorials. Additional relevant studies that were identified from the reference lists of retrieved literature were also included if they met the selection criteria. We excluded all articles that did not meet the inclusion criteria or did not directly report findings relevant to the topics investigated.

To minimize this risk of bias related to the potential overlap between study populations in the selected studies, we cross-checked included studies for overlapping recruitment periods, institutions, author groups, and cohort descriptions. When potential duplication was suspected, the most comprehensive and/or most recent dataset was retained, and smaller or overlapping reports were excluded.

Determination of study quality

Quality of the included studies was assessed using the Downs and Black checklist [23], which consists of 27 questions designed to evaluate the overall quality of reporting for both randomised and non-randomised studies. Quality levels were assigned to each included study, using the categories according to literature evidence: excellent (Downs and Black score ≥26), good (20–25), fair (15–19) and poor (≤14). The scoring methodology of the checklist was structured so that only randomised controlled trials could receive a score of 26 or greater. The level of evidence for each study was assigned using the 2011 Oxford Centre for Evidence Based Medicine classification [24]. Considering the number of articles, quality of the research, level of evidence, and the domains evaluated according to the GRADE [25] approach (study limitations, inconsistency of results, indirectness of evidence, imprecision, and reporting bias), we classified the strength of the association as follows: well supported (further research is very unlikely to change our confidence in the estimate of effect); moderately-well supported (further research may have an impact on our confidence in the estimate of effect and may change the estimate); moderately supported (further research is very likely to have an impact on our confidence in the estimate of effect and is likely to change the estimate); or weakly supported (any estimate of effect is very uncertain). Unfortunately, the heterogeneity of the data did not allow us to perform a meta-analysis.

Screening of titles/abstracts and full-text articles was performed independently by two authors (EDC and CP). Data extraction and quality assessment using the Downs and Black checklist were also conducted independently by two authors. Disagreements were resolved through discussion and, when necessary, adjudicated by a third senior author (PH).

Results

Search results and included studies

There were 2080 articles identified, of which 770 were selected for screening of abstracts. Of these, 222 articles were assessed for eligibility and examined in greater detail (Figure 1). A total of 152 studies, which have been summarised and tabulated, are included in this review.

Study categorisation and outcomes of interest

The included studies were categorised according to the type of predictive factors they examined: clinical, radiological/imaging, microbiological, inflammatory markers, experimental and factors related to ESS and pre-, peri- and post-operative treatment. In this review, we defined post-operative outcomes in patients with CRSwNP as including symptom burden, degree of nasal obstruction, endoscopic findings, radiological findings, QoL scores, olfactory function (i.e., improvement in sense of smell), and the requirement for SCS and/or revision ESS. These outcomes

were evaluated in relation to various pre-operative and intra-operative factors, with the aim of identifying potential predictors of surgical success, disease control, and long-term clinical improvement [26]. With regard to pre-operative endoscopy and radiology findings as predictive factors, we included two of the scores most commonly used in clinical practice, namely the Lund-Kennedy endoscopic score (LKS) [27] and LMS [28].
Specific attention was paid to studies that examined prognostic accuracy using area under receiver operating characteristic (AUROC) curves, and to studies providing sensitivity and specificity information. The discriminant validity of predictive factors was considered to be fair if the AUROC was between 0.7 and 0.8, good if the AUROC was 0.8 to 0.9 and excellent if the AUROC was ≥0.9 [29]. Some studies included cohorts of patients with (CRSwNP) or without (CRSsNP) NPs, hereafter referred to as mixed cohorts or mixed populations.

Clinical and demographic factors

Seventy studies examined the association between clinical factors and poor post-operative outcomes [30-99], 43 in patients with CRSwNP [30-61,88-98] and 27 in mixed cohorts [62-87, 99].

Age

The impact of age on post-operative outcomes in both patients with primary CRSwNP [32-34,37,41,42,45,49,53,55,61,74,88,91,93,94,97,98] and mixed populations [62,65-67,69,71,75,76,79,80,82-84,86] were heterogeneous as reported in Table 1.
Most of the studies did not find an association between age and post-operative outcomes in primary CRSwNP [25,26,29,44,45,47,50,52,53,56,57,58,62,67,70,74,75].
Some studies suggested younger age as an independent factor associated with poorer disease control [100] or higher rates of endoscopic recurrence of NPs [33,34,49,71] and higher LKS scores [65,73], sometimes only in subpopulations without eosinophilia [51]. On the contrary, some studies reported older age to be associated with poorer olfactory function at 3 and 6 months post-ESS [49,85].
Although the quality of the collective research on "age" was mostly fair, the results were often inconsistent and contradictory, multivariate analyses were frequently missing, the age ranges studied were different, and it was not possible to identify an age cut-off for poor surgical outcomes. For these reasons, the association between age and poor surgical outcomes in patients with CRSwNP was considered unclear.

Gender

The vast majority of studies investigating the impact of gender on outcomes in a CRSwNP population [32-35,37,38,46,49,50,52,53,55,59,61,88,91,93,94], and in a mixed population [62,65-67,71,76,79,80,83,84,86] showed no correlation between gender and outcomes especially in terms of radiological and endoscopic outcomes. Some gender differences have been observed in studies that examined PROMs; specifically, female patients were reported to have worse pre- and post-operative SNOT-22 scores [101].

Comorbidities and type 2 inflammation

Patients with CRSwNP frequently have comorbid asthma, allergic rhinitis, and/or N-ERD, alone or concomitantly. CRSwNP patients with asthma and/or N-ERD had significantly poorer ESS outcomes as reported in Table 1.
In the CRSwNP studies, asthma was the comorbidity most commonly associated with a poor outcome, and it was significantly correlated with an increased risk of endoscopic or symptomatic recurrence [33,34,40,41,43,46,52,54,58,59,61,88,90,91,92,97,98,99], the need for repeat ESS [33,36] and poor post-operative olfactory function [48]. Accordingly, Toppila-Salmi and colleagues confirmed in a very large series of patients who had undergone ESS for CRSwNP (n=3,506) that asthma was associated with higher revision rates [14]. Interestingly, Veloso-Teles and colleagues found that the presence of non-immunoglobulin (Ig)E-mediated asthma was predictive of the need for revision ESS (p=0.012), in contrast to the presence of IgE-mediated asthma [88]. In a multivariate analysis, a higher pre-operative forced expiratory volume in 1 second (FEV1) resulted in a reduced risk of CRSwNP recurrence (odds ratio [OR] 0.96; 95% confidence interval [CI] 0.92–0.99; p=0.023) [51]. Finally, in studies of mixed CRS patients, asthma was significantly associated with recurrent symptoms [66], recurrence of NPs on nasal endoscopy [80], poorer post-operative QoL [76,86], and worse olfactory function [75].
N-ERD was specifically associated with recurrence of CRSwNP [34,36,41,43,61], poor olfactory function [32], and repeat ESS [53]. Furthermore, N-ERD was associated with worse QoL as measured by the Rhinosinusitis Disability Index (RSDI) at a mean of 1.4 years after ESS [62].
Allergic status (defined based on the presence of sensitization to specific allergens, as determined by a positive skin prick test with allergen-specific IgE, and/or a positive serum-specific IgE test, and/or a positive nasal allergen provocation test) has been associated with the need for revision ESS in patients with CRSwNP [40,42,58,92,93,94]. Accordingly, in studies in mixed populations, allergy was significantly correlated with poorer QOL as measured by SNOT-22 and RSDI scores [86] 3 months after ESS.
The risk of poor outcomes was most marked in patients with more than one comorbidity [31,33,54]. For example, De Corso and colleagues found that the risk of poorer outcomes at 12 months post-ESS (defined as LKS ≥2 and SNOT-22 score ≥20) was significantly increased by at least 2-fold in patients with allergy sensitisation to aeroallergens (relative risk [RR] 2.32; 95% CI 1.01–4.94; p<0.05) or asthma (RR 2.04; 95% CI 1.05–5.08; p<0.05), but by at least 20-fold in those with asthma and N-ERD (RR 21.41; 95% CI 17.15–26.02; p<0.01) [54]. Similarly, Gelardi and colleagues reported relapse rates of 26.1% in patients with allergy, 26.1% in patients with asthma plus NSAID sensitivity, 35.7% in those with

Table 1. Clinical factors investigated in relation to post-operative outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
In patients with CRSwNP-only								
Lee 2008 [89] South Korea	125	Retrospective	Prior ESS	LMS, SNOT-20 and CRS-related medication use in the 12 months post-ESS	No significant difference in the magnitude of improvement in SNOT-20 score, LKS or need for CRS-related medication within 12 months in patients undergoing primary vs revision ESS	III	18	Fair
Danielides 2009 [30] Greece	166	Prospective, observational	Duration of olfactory deficit, previous ESS	Olfactory function using "Sniffin' Sticks" at 1, 3 and 6 months post-ESS	After adjustment for confounders, longer duration of olfactory deficit and previous ESS were significant predictors of not achieving normal olfactory function after ESS	III	15	Fair
Gelardi 2009 [31] Italy	161	Prospective, observational	Comorbidities	Need for repeat surgery within 10 years	The presence of asthma + atopy + aspirin/NSAID sensitivity moderately increased the risk for repeat ESS (OR 1.4; p=0.23), but risk was highest in patients with asthma + aspirin/NSAID sensitivity + nasal cytology with eosinophils >20% and mast cells >10% (OR 4.5; p=0.04)	IV	12	Poor
Katotomichelakis 2010 [32] Greece	116	Prospective, observational	Age, sex, comorbidities, taste dysfunction, duration of olfactory deficit, smoking	Olfactory function using "Sniffin' Sticks" at 6 months post-ESS	After adjustment for confounders, older age, longer duration of olfactory deficit, N-ERD and previous ESS were significant predictors of poor TDI score at 6 months	III	16	Fair
Mendelsohn 2011 [33] Canada	549	Retrospective cohort	Age, sex, comorbidities, medical history, smoking, fungal mucin	Recurrence of NPs, need for revision ESS in 5–10 years	Patients with N-ERD or asthma were significantly more likely to have recurrence (OR 3.7; 95% CI 2.5–5.5; p<0.01) and require repeat surgery (OR 2.7; 95% CI 1.5–3.2; p<0.01), and to experience these earlier, compared with CRSwNP patients without these comorbidities. Frontal sinus involvement also significantly increased the risk of polyp recurrence (OR 1.4; 95% CI 1.2–1.9; p<0.01) and repeat surgery (OR 1.6; 95% CI 1.2–1.8; p<0.05)	III	18	Fair
Bassiouni 2013 [34] Australia	299 (338 surgeries)	Retrospective cohort	Age, sex, medical history, smoking	Recurrent NPs on CT (LKS ≥3)	Rate of recurrence was significantly increased in patients with asthma (HR 1.71; 95% CI 1.02–2.86; p=0.041) or aspirin sensitivity (HR 1.79; 95% CI 1.10–2.93; p=0.020)	III	18	Fair
Bush 2013 [35] USA	169	Prospective, observational	Sex, race	SNOT-20 scores at 6 and 12 months post-ESS	In African-American patients with CRSwNP and asthma, SNOT-20 scores had returned to pre-operative levels at 12 months and were significantly worse vs Caucasian patients (p<0.05)	III	11	Poor
Van Zele 2014 [36] Belgium	36	Case control	Comorbidity	Need for revision surgery	Significantly more patients undergoing revision vs primary ESS had asthma (p=0.001) or aspirin intolerance (p<0.0001). The risk of revision was significantly higher in patients with asthma (OR 8.8; 95% CI 1.92–40.34) or aspirin intolerance (OR 22.8; 95% CI 2.41–216.87)	IV	15	Fair
Adnane 2015 [37] Morocco	58	Prospective, observational	Age, sex, medical history, comorbidities, LKS, LMS, surgical procedure, pre-operative RSDI score	QoL using RSDI at 12 months post-ESS	After adjustment for confounders, pre-operative RSDI score, prior ESS and aspirin/NSAID intolerance were significant predictors of QoL improvement	III	18	Fair
Brescia 2015 [38] Italy	179	Prospective observational	Age, sex	Endoscopic evidence of grade ≥1 NPs during median of 36 months after ESS	After adjustment for confounders, age and sex were not significant predictors of recurrence. A panel of 3 variables (age <65 years, serum basophil percentage and eosinophilic pathology) had AUROC of 0.7028, sensitivity 41.7%, specificity 88.4%, PPV 35.7% and NPV 90.7%	III	19	Fair
Nguyen 2015 [39] France	96	Prospective, observational	Medical history, symptom severity	Olfactory function using "Sniffin' Sticks" at 6 weeks post-ESS	After adjustment for confounders, any previous history of ESS was a significant predictor of poor olfactory outcomes (OR 4.14; 95% CI 1.29–13.32; p=0.017); the more previous ESS a patient had undergone, the lower the chance of olfactory function recovery after ESS (p=0.024)	III	18	Fair
Nikakhlagh 2015 [40] Iran	93	Prospective, observational	Medical history	Recurrence based on symptoms and endoscopy	History of allergy and asthma was a significant predictor of recurrence (p=0.0002)	II	17	Fair

Table 1 *continued.* Clinical factors investigated in relation to post-operative outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Brescia 2016 [41] Italy	114	Retrospective	Age, medical history	Recurrent polyposis of grade ≥1 on endoscopy	Age 20–40 years was associated with a significantly higher rate of recurrence compared with age ≥65 years (p=0.05). Asthma and aspirin intolerance were significant risk factors for recurrence in both age groups	III	18	Fair
Brescia 2016 [42] Italy	143	Prospective, observational	Age, medical history, comorbidity	Recurrent polyposis of grade ≥1 on endoscopy	Significantly higher rates of recurrence were seen in patients aged <53 years (median) vs ≥53 years (OR 2.94; 95% CI 1.00–7.84; p=0.035), those with vs without allergy (OR 3.22; 95% CI 1.11–9.32; p=0.014), and those with vs without EGPA (OR 20.2; 95% CI 1.47–10.66; p=0.01), but were not significant after multivariate adjustment	III	20	Good
Brescia 2017 [43] Italy	280	Retrospective	Comorbidities	Endoscopic evidence of grade ≥1 polyposis during median of 30 months after ESS	Recurrence rates were significantly higher in patients with vs without allergy (p=0.0002), asthma (p<0.0001) or aspirin intolerance (p<0.0001)	III	16	Fair
DeConde 2017 [44] USA	363	Multicentre, prospective, observational	Study site, medical history	Post-operative nasal polyposis and oedema on endoscopy (LKS >0)	After adjustment for confounders, previous ESS was a significant predictor of recurrent post-operative polyposis (OR 2.60; 95% CI 1.50–4.60; p=0.001) and oedema (OR 4.50; 95% CI 2.10–9.80; p<0.001)	III	18	Fair
Veloso-Teles 2017 [88] Portugal	85	Retrospective	Age, sex, comorbidities, smoking, occupational dust exposure	Recurrent NPs on endoscopy 9–108 (median 27) months post-ESS	After adjustment for confounders, significant predictors of recurrent NPs were occupational dust exposure (p=0.001) and non-IgE-mediated asthma (p=0.012)	III	18	Fair
Khairuddin 2018 [45] Malaysia	70	Prospective, observational	Eosinophilic phenotype (serum eosinophilia, atopy, extensive disease)	Recurrent NPs on endoscopy	Rate of recurrent NPs was significantly higher in patients with eosinophilic CRSwNP than those with non-eosinophilic CRSwNP (63% vs 30%; p<0.016)	III	11	Poor
Kim 2019 [46] South Korea	134	Retrospective	Age, sex, symptom duration, olfactory function, comorbidities, smoking, alcohol intake, BMI	Complete disease control according to EPOS 2012 criteria	In multivariate analysis, younger age was associated with worse disease control (p=0.015)	III	17	Fair
Kim 2019 [47] South Korea	375	Retrospective, cluster analysis	Age, asthma, eosinophilia, blood eosinophil levels, E/M ratio, LKS	Revision surgery within 4 years	Revision-free rates were lower in 3 clusters characterised by (1) asthma + eosinophilic NPs (66.7%; p=0.013), (2) no asthma + eosinophilic NPs + higher E/M ratio (66.7%; p=0.017) or (3) no asthma + non-eosinophilic NPs + age <35 years (70.9%; p=0.001) compared with cluster characterised by no asthma + non-eosinophilic NPs + age ≥35 years (98.0%)	III	19	Fair
Rives 2019 [48] France	119	Prospective, observational	Age, duration of olfactory impairment, comorbid asthma	Recovery of olfactory function (≥50% on a VAS from 0 to 100%) at 1-year post-ESS	Age >65 years, olfactory impairment for >5 years and asthma were not associated with recovery of olfactory function at 1 year	III	16	Fair
Akiyama 2020 [49] Japan	84 + 17 controls	Retrospective	Age, sex, medical history, smoking, olfactory cleft lesions, baseline olfaction, WBC, eosinophils, IgE	T&T score at 3 months post-ESS	Negative pre-operative intravenous olfaction test (p=0.011), male sex (p=0.03) and age ≥45 years (p=0.004) were negatively associated with 3-month T&T score	III	18	Fair
Loftus 2020 [50] USA	536	Retrospective	Age, sex, race, comorbidities, CRSwNP subtype, patient history, smoking	Revision surgery ≥6 months after ESS (mean 52.9 months of follow-up)	After adjustment for confounders, factors associated with an increased risk of revision were younger age (OR 1.06; 95% CI 1.04–1.08; p<0.0001), longer follow-up time (OR 1.12; 95% CI 1.02–1.25; p=0.024), and previous surgery (OR 3.28; 95% CI 1.68–6.39; p<0.0001). Younger age was also a significant predictor in subgroups of patients with comorbid AFRS or N-ERD, and CRSwNP without comorbid AFRS or N-ERD	III	20	Good
Nakamaru 2020 [51] Japan	69	Retrospective	Pulmonary function (spirometry)	Recurrent CRSwNP during 9–114 (median 62) months	After adjustment for confounders, pre-operative FEV1 (% predicted) was a significant predictor of not getting a recurrence (OR for recurrence 0.96; 95% CI 0.92–0.99; p=0.023)	III	16	Fair

Table 1 *continued*. Clinical factors investigated in relation to post-operative outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Wang 2020 [52] China	346	Prospective cohort	Age, sex, comorbidities	Presence of CRS symptoms and/or NPs, and management with intranasal CS and ≤2 short courses of antibiotics or systemic CS within 24 months of ESS	After adjustment for confounders, asthma history was associated with a significantly increased risk of recurrence (OR 2.06; 95% CI 1.78–2.32; p<0.001)	III	18	Fair
Wu 2020 [53] Taiwan	107	Prospective cohort	Age, sex, smoking, comorbidity, pre-operative symptom severity	Revision surgery for 5 years post-ESS	After adjustment for confounders, nasal allergy was a significant independent risk factor for revision surgery (OR 9.29; 95% CI 1.675–51.50; p=0.011)	III	18	Fair
De Corso 2021 [54] Italy	80	Prospective, observational	Comorbidity	Disease control (LKS ≥2 and SNOT-22 score ≥20) at 12 months post-ESS	On univariate analysis, the risk of poor disease control at 12 months was increased in patients with allergy (RR 2.32; 95% CI 1.01–4.94; p<0.05), asthma (RR 2.04; 95% CI 1.05–5.08; p<0.05), and aspirin intolerance triad (RR 21.41; 95% CI 17.15–26.02; p<0.01)	III	16	Fair
Gan 2021 [55] China	77	Prospective, observational	Age, sex, comorbidity, symptom severity (VAS)	Endoscopic recurrence of NP during 1-year post-ESS	Patients with recurrent NP had a significantly higher mean pre-operative symptom score than patients who did not develop recurrence (p<0.0001)	III	16	Fair
Hopkins 2021 [56] UK	980	Prospective, observational	History and timing of previous sinus surgery	Need for revision surgery within 5 years of index ESS	Patients who had a history of prior surgery had a 5-year revision rate of 20.2% vs 9.8% in those with no history of surgery. After adjustment for confounders, time between previous surgery and index surgery was a significant predictor of need for revision surgery (longer time since surgery reduced risk of revision; p=0.005). Patients presenting with a symptomatic recurrence within 3 years of surgery have a high risk of treatment failure, defined as the need for further surgery	III	20	Good
Kuan 2021 [57] USA	47	Retrospective	Symptom severity using SNOT-22	SNOT-22 post-surgery but pre-AD and at <2 months and >6 months after surgery + AD	In patients with aspirin-exacerbated CRSwNP, pre-operative SNOT-22 score was positively correlated with change in SNOT-22 score post-surgery but pre-AD (p<0.001) and with SNOT-22 score <2 months post-AD (p<0.001), but not >6 months post-AD	III	17	Fair
Vlaminck 2021 [58] Belgium	133	Prospective observational	Age, comorbidity and prior surgery	Endoscopic evidence of recurrence + ≥3 symptoms lasting ≥1 month during 11–17 (mean 13.5) years post-ESS	Age at surgery was significantly lower in patients who developed recurrence vs those who did not (mean 47.7 vs 52.6 years; p=0.014), and significantly more patients who developed recurrence had pre-operative asthma (36.6% vs 13.7%; p=0.001), allergy (42.7% vs 15.7%; p=0.001), or prior surgery (29.3% vs 11.8%) compared with patients who did not develop recurrence. Asthma was significantly associated with risk of recurrence over time (p<0.001 vs no asthma; Kaplan-Meier analysis)	III	19	Fair
Bai 2022 [59] USA	94	Prospective, observational, incorporated machine learning	Age, sex, medical history	Recurrent NPs on endoscopy within 2–5 years after ESS	Asthma was predictive of polyp recurrence (p<0.01)	III	15	Fair
Kim 2022 [60] South Korea	334 + 13 controls	Retrospective	Age	LKS at 3, 6 and 12 months post-ESS	Age had no impact on outcomes in patients with eosinophilic NPs, but in the group with non-eosinophilic CRSwNP, LKS at 3 and 6 months post-ESS were significantly higher in patients aged <35 years vs ≥35 years	III	18	Fair
Riva 2022 [61] Italy	61	Retrospective	Age, sex, medical history, comorbidities	Endoscopic evidence of CRSwNP recurrence, revision surgery	Median number of recurrences per year were significantly predicted by presence of asthma (p=0.045) or N-ERD (p=0.035)	III	19	Fair
Canakci 2025 [90] Turkey	102	Retrospective	Asthma and ASA sensitivity	Endoscopic recurrence within 3 years after ESS	Asthma was independently associated with recurrence in multivariable logistic regression. ASA sensitivity was evaluated but was not identified as an independent predictor.	III	16	Fair

Table 1 *continued.* Clinical factors investigated in relation to post-operative outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Kirtsreesakul 2026 [91] Thailand	437	Retrospective	Age, sex, smoking status, asthma, NSAID hypersensitivity and symptom duration	Time to postoperative CRSwNP recurrence	Age, asthma, NSAID hypersensitivity and longer symptom duration were retained in the LASSO-penalised Cox recurrence model; sex and smoking were not retained.	III	18	Fair
Liu 2025 [92] China	185	Retrospective	Comorbid asthma and allergic rhinitis, evaluated separately and in combination	Disease-control status, SNOT-22 and postoperative endoscopic score at 12 months after ESS	Patients with asthma, either alone or combined with allergic rhinitis, had higher rates of uncontrolled disease than patients without either comorbidity. Asthma was independently associated with uncontrolled CRS in multivariable logistic regression, whereas allergic rhinitis was not. Patients with asthma also had higher postoperative SNOT-22 and worse endoscopic scores than patients without asthma or allergic rhinitis.	III	17	Fair
Zhong 2026 [93] China	603	Retrospective	Allergic rhinitis, asthma, previous sinus surgery, age, sex, BMI and disease duration	Time to postoperative CRSwNP recurrence over ≥3 years after FESS	Recurrence occurred in 48.0% of patients with allergic rhinitis and 28.4% of those without allergic rhinitis. Allergic rhinitis remained independently associated with shorter recurrence-free survival after adjustment for clinical, eosinophilic and radiological variables (adjusted HR 1.550; 95% CI 1.141–2.104; p=0.005). Previous surgery and asthma were not independently associated with recurrence in the fully adjusted analysis.	III	17	Fair
Ji 2026 [94] China	152	Retrospective	Age, sex, asthma or allergic rhinitis, hypertension, diabetes	Clinically confirmed recurrence during 6–36 months after ESS	Comorbid asthma or allergic rhinitis was independently associated with recurrence (OR 2.74; 95% CI 1.31–5.74; p=0.007). Age, sex, hypertension and diabetes were not associated with recurrence	III	16	Fair
Zhang 2025 [95] China	102	Prospective	Preoperative CRS-PRO, SNOT-22 and EQ-5D-VAS scores; individual CRS-PRO and SNOT-22 items	EPOS 2020-defined disease control at a median of 21 months after FESS; partly controlled and uncontrolled disease classified as suboptimal control	Patients with suboptimal disease control had higher preoperative CRS-PRO and SNOT-22 scores than controlled patients. A logistic regression model combining individual CRS-PRO items with selected objective clinical variables showed the best predictive performance for suboptimal control.	III	18	Fair
Zhang 2026 [96] China	178	Retrospective	History of previous/revision ESS and asthma	Recurrence within 24 months	Previous/revision surgery was independently associated with recurrence (OR 6.963; 95% CI 2.275–21.313). Asthma was associated with recurrence in univariate analysis but was not retained as an independent factor.	III	17	Fair
Zhang 2026 [97] China	312	Retrospective	Clinical data and preoperative serum levels of inflammatory markers (eotaxin-1, periostin, IL-5, total IgE)	Recurrence after ESS	During a minimum of 2-year follow-up, recurrence occurred in 38.5% of the total cohort. LASSO and multivariate analyses identified five independent predictors: history of asthma (odds ratio [OR] = 3.45), revision surgery (OR = 2.12), Lund-Mackay score (OR = 1.15), serum eotaxin-1 level (OR = 1.02 per pg/mL), and serum periostin level (OR = 1.04 per ng/mL).	III	18	Fair
Dharia 2026 [98] USA	325	Retrospective	ACT and SNOT-22, use of OCS in the past 12 months, data on lung function, BMI, and absolute eosinophil count.	Patient-reported timing and associated symptoms of CRSwNP recurrence after ESS, as well difference of current disease burden based on prior recurrence timing	Impact of severe CRSwNP in patients with NSAID-ERD, with rapid recurrence following ESS leading to impairment in QoL, as evidenced by higher SNOT-22 and lower ACT scores. There is no significant difference in age of onset of CRSwNP or asthma between the groups; however, patients in the fast recurrence group were younger and had a shorter lifetime duration of CRSwNP at registry enrollment.	III	18	Fair
In a mixed population of patients with CRSwNP/CRSsNP								
Smith 2005 [62] USA	119	Prospective, observational	Age, sex, medical history, comorbidities, smoking	Endoscopic LKS, QoL using RSDI and CSS at ≥1 year (mean 1.4) post-ESS	After adjustment for confounders, aspirin intolerance significantly predicted less improvement in endoscopy score (p=0.037) and RSDI (p=0.012) and depression significantly predicted less improvement in RSDI (p=0.030)	III	18	Fair
Litvak 2007 [64] USA	167	Prospective, observational	Prior ESS	Endoscopic LKS, QoL using RSDI and CSS at 6–39 months (mean 16.4) post-ESS	NPs and prior ESS were predictive of post-operative endoscopic score, but in patients with NPs, prior ESS was not predictive of improvement in post-operative endoscopic scores (OR 0.48; 95% CI 0.15–1.59; p=0.23). NPs and prior ESS were not significantly predictive of post-operative QoL on CSS or RSDI	III	17	Fair

Table 1 *continued.* Clinical factors investigated in relation to post-operative outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Li 2008 [65] China	254	Retrospective	Age, sex, phenotype, anatomical features, medical history	Complete or partial improvement, no change or deterioration within 24 months post-ESS	After adjustment for confounders, significant predictors of a poor outcome (no improvement, i.e. no change or deterioration) were allergy (p=0.0002), NPs (p=0.0007) and previous ESS (p<0.0001)	III	16	Fair
Matsuwaki 2008 [66] Japan	56	Prospective, cohort	Age, sex, history of asthma and/or allergic rhinitis	Recurrence of symptoms or need for revision surgery within 5 years of ESS	After adjustment for confounders, the presence of asthma significantly predicted increased risk of recurrence (OR 1.806; p=0.045)	III	17	Fair
Minovi 2008 [67] Germany	64	Prospective, cohort	Age, sex, medical history, comorbidities	Olfactory function at 6 months post-ESS	Significant predictors of improved olfactory scores were presence of NPs (p<0.001), aspirin intolerance (p=0.007) and female sex (p<0.03)	IV	13	Poor
Psaltis 2008 [68] Australia	40	Prospective, observational	Previous sinus surgery	Presence of any ongoing symptoms or any mucosal abnormality for 8 months post-ESS	Patients who had undergone previous ESS were more likely to have ongoing post-operative symptoms (OR 30.00; 95% CI 3.339–269.50; p=0.0002) or ongoing mucosal inflammation (OR 7.29; 95% CI 1.737–30.57; p=0.009)	III	17	Fair
Busaba 2013 [69] USA	514a	Prospective, observational	Age	Symptoms at 3 months post-ESS	Patients aged ≥60 years had significantly higher rates of improvement in rhinorrhoea (93.3%) compared with other age groups (18–39 years: 85.5%; 40–59 years: 85.3%) whereas patients aged 18–39 years had significantly higher rates of improvement in olfactory function (85.5%) compared with other age groups (40–59 years: 71.1%; ≥60 years: 71.4%)	IV	14	Poor
Murthy 2013 [70] UK	81	Prospective, observational	Symptom severity on VAS	Symptom severity on VAS at 12 months post-ESS	Patients with high pre-operative scores for nasal discharge and olfactory disturbance showed the least improvement in post-operative symptoms (p<0.001)	III	16	Fair
Katotomichelakis 2014 [71] Greece	111 + 48 controls	Prospective, observational	Age, sex, socioeconomic status, NPs, medical history, smoking, baseline olfactory function	QoL, using QOD, BDI and SF-36 at 12 months post-ESS	After adjustment, smoking was associated with a lower likelihood of achieving improvement in BDI (OR 0.41; 95% CI 0.17–0.98; p=0.046) [b]	III	17	Fair
Hopkins 2015 [72] UK	2534	Retrospective case-control	Pre-operative symptom duration	CRS-related healthcare visits, prescriptions and reoperations in 5 years post-ESS	After matching, patients who had been experiencing symptoms for >60 months prior to ESS had more CRS-related healthcare visits (p<0.0001) and prescriptions (p<0.0001) in 5 years post-ESS compared with patients experiencing symptoms for <12 months, but reoperation rates were similar (11.52% vs 11.86%, respectively)	IV	18	Fair
Hopkins 2015 [73] UK	1493	Prospective, observational	Pre-operative symptom duration	SNOT-22 scores at 3, 12 and 60 months post-ESS	At 5 years post-ESS, the proportion of patients with SNOT-22 remaining below the MCID was significantly lower in patients who had been experiencing symptoms for 12–60 months (57.3%) or >60 months (53.0%) vs those who had symptoms for <12 months (71.5%; p=0.028). After adjustment for confounders, duration of symptoms was a significant predictor of SNOT-22 scores at 60 months post-ESS (p=0.05)	III	20	Good
Hopkins 2015 [87] UK	2263	Prospective, observational	Pre-operative symptom severity on SNOT-22	SNOT-22 score at 3 months post-ESS; revision ESS at 5 years	Pre-operative SNOT-22 score was a significant predictor of achieving MCID in SNOT-22 at 3 months (p<0.001) and of needing revision ESS at 5 years (p<0.001)	III	20	Good
Kim 2016 [74] South Korea	133 + 20 controls	Retrospective	Age	LKS at 12 months post-ESS	In patients with non-eosinophilic CRSwNP, post-operative LKS were significantly correlated with age (r= –0.5550; p<0.05), with significantly lower scores in patients aged 60–81 years vs those aged 18–39 or 40–59 years (p<0.01), and this effect was attributed to an age-related decline in neutrophils	III	15	Fair
Levy 2016 [75] USA	122	Prospective, cohort	Baseline olfactory function, polyposis, comorbidities	BSIT at 6,12 and 18 months post-ESS	After initial improvement, olfactory function significantly worsened between 6 and 18 months in patients with NPs (p=0.033) or comorbid asthma (p=0.010), but remained stable in other patient groups	III	17	Fair

Table 1 *continued*. Clinical factors investigated in relation to post-operative outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Adnane 2017 [76] Morocco	113	Prospective, observational	Age, sex, medical history, time to ESS, SNOT-22 score	SNOT-22 score at 1-year post-ESS	Presence of asthma, prior ESS and NPs had a significant negative impact on extent of SNOT-22 improvement	III	18	Fair
Liao 2018 [77] China	246	Prospective, observational	28 clinical variables and 39 cellular and molecular variables	Difficult to treat CRS (symptoms despite intranasal CS and ≤2 short courses of antibiotics and systemic CS) within 12 months of ESS	Three clusters of Chinese patients were identified with poor outcomes at 12 months after ESS: (1) eosinophilic CRSwNP with severe pre-operative symptoms; (2) CRS with neutrophilic inflammation; and (3) CRSwNP with long disease duration, high rate of prior ESS and moderate neutrophilic inflammation	III	19	Fair
Miglani 2018 [78] USA								
Stein 2018 [79] USA	61,339	Retrospective database analysis	Age, sex, presence of NPs, income, insurance status, hospital setting, ethnicity	Revision ESS within 5 years	After adjustment for confounders, the risk of revision ESS was significantly associated with diagnosis of NPs (OR 1.20; 95% CI 1.11–1.29; p<0.001), female sex (OR 1.10; 95% CI 1.11–1.29; p<0.001) and public insurance (OR 1.10; 95% CI 1.00–1.21; p=0.048)	III	21	Good
Tsuzuki 2019 [80] Japan	281	Retrospective	Age, sex, comorbidities, NPs, viscous secretions, baseline olfactory function	Endoscopic score at 12–24 (mean 16.4) months post-ESS	After adjustment for confounders, younger age (p=0.0003), comorbid asthma (p=0.0464) and the presence of NPs in the frontal sinus (p=0.0498) were significant predictors of poor endoscopic scores	III	19	Fair
Wang 2019 [81] China	88	Retrospective	Serum vitamin D status	SNOT-22 score at 6 months post-ESS	93% of patients with CRSwNP had vitamin D deficiency. In patients with CRSwNP, serum levels of 25-hydroxy vitamin D3 were significantly correlated with improvement in SNOT-22 score (p<0.001)	III	18	Fair
Holmes 2020 [82] USA	431	Retrospective	Age	SNOT-22 score and LKS at 0.5, 1, 1.5, 2 and 3 years post-ESS	Post-operative SNOT-22 scores were similar at all timepoints in patients aged 18–39, 40–64 or ≥65 years. LKS score at 1-year post-ESS was significantly higher in those aged 18–39 years vs other age groups	III	15	Fair
Al Sharhan 2021 [83] Saudi Arabia	68	Prospective cohort	Age, sex, medical history, smoking, culture positivity	SNOT-22 score at 6 months post-ESS	Allergic rhinitis (compared with non-allergic rhinitis) significantly predicted a worse SNOT-22 score at 6 months (p=0.035)	III	18	Fair
Guo 2021 [84] China	189	Prospective, observational	Age, sex, comorbidities, symptom severity	Uncontrolled CRS (presence of ≥3 symptoms + need for antibiotics or systemic CS within previous 3 months)	Severity of hyposmia (on VAS) and allergic rhinitis were significant predictors of uncontrolled CRS within 12 months of ESS	III	19	Fair
Anne 2022 [86] India	100	Prospective, observational	Age, sex, comorbidities, smoking, symptom severity	QoL using RSDI and SNOT-22 at 3 months post-FESS	Younger age (p=0.039) was associated with better improvement in SNOT-22, while allergy (p=0.001), smoking (p=0.002) and asthma (p=0.001) correlated with poorer improvement in SNOT-22, as well as poorer improvement in RSDI: allergy (p=0.0001), smoking (p=0.001) and asthma (p=0.001)	III	16	Fair
Kim 2007 [63] USA	208	Retrospective	Samter's triad [c]	Symptoms and endoscopic NP recurrence at 6 months post-ESS	Patients with vs without Samter's triad had a significantly higher rate of recurrent NPs (50.0% vs 89.5%; p<0.001), nasal obstruction (17.5% vs 7.9%; p<0.005), facial pain (28.1% vs 6.9%; p<0.05), post-nasal drip (40.0% vs 4.5%; p<0.05) and anosmia (20.1% vs 3.9%; p<0.05)	III	15	Fair
Huang 2022 [85] USA	205	Retrospective	Comorbidity burden (CCI)	SNOT-22 score at 3 months post-ESS	After adjustment for potential confounders, CCI was not a significant predictor of change from baseline in SNOT-22 scores at 3 months or in the odds of achieving MCID in SNOT-22 score	III	18	Fair
Joustra 2025 [99] The Netherlands	123	Retrospective	CRS phenotype, asthma, allergic rhinitis, N-ERD and smoking	Clinical control according to updated EPOS criteria and HRQoL using the EES-Q at 6–8 years after surgery	CRSwNP was associated with partly controlled (p=0.024) and uncontrolled disease (p=0.027). Asthma was associated with partly controlled disease (p=0.024); allergic rhinitis with partly controlled (p=0.001) and uncontrolled disease (p<0.001); N-ERD with partly controlled (p=0.003) and uncontrolled disease (p<0.001); and smoking with uncontrolled disease (p<0.001).	III	16	Fair

Legend Table 1. [a] 202 patients with CRSwNP underwent surgery. [b] Factors associated with significantly increased likelihood of improvement in QoL were pre-operative anosmia, pre-operative hyposmia, NPs and medium/high social status. [c] Samter's triad includes asthma, recurrent nasal polyps, and NSAID sensitivity.

AD, aspirin desensitisation; AFRS, allergic fungal rhinosinusitis; AUROC, area under the receiver operating characteristic curve; BDI, Beck Depression Inventory; BMI, body mass index; BSIT, Brief Smell Identification Test; CCI, Charlson Comorbidity Index; CI, confidence interval; CRS, chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; CS, corticosteroids; CSS, Chronic Sinusitis Survey; CT, computed tomography; E/M, ethmoid-to-maxillary; EGPA, eosinophilic granulomatosis with polyangiitis; EPOS, European Position Paper on Rhinosinusitis and Nasal Polyps; ESS, endoscopic sinus surgery; FESS, functional endoscopic sinus surgery; FEV1, forced expiratory volume in 1 second; GPA, granulomatosis with polyangiitis; HR, hazard ratio; Ig, immunoglobulin; LKS, Lund-Kennedy score; LMS, Lund-Mackay score; MCID, minimal clinically important difference; N-ERD, non-steroidal anti-inflammatory drug-exacerbated respiratory disease; NP(s), nasal polyp(s); NPV, negative predictive value; NSAID, non-steroidal anti-inflammatory drug; OR, odds ratio; PPV, positive predictive value; QoL, quality of life; QOD, questionnaire of olfactory deficits; RR, relative risk; RSDI, Rhinosinusitis Disability Index; SF-36, 36-item Short Form health survey; SNOT-20 or -22, 20-item or 22-item SinoNasal Outcome Test; T&T, Toyota & Takagi; TDI, Threshold-Discrimination-Identification (composite); VAS, Visual Analogue Scale; vs, versus; WBC, white blood cell count.

asthma plus allergy and 42.9% in those with all three of these comorbidities [31]. The overall burden of comorbidities (indicated by the Charlson Comorbidity Index) was also found to be a significant independent predictor of worse early (3-month) SNOT-22 scores and of achieving a minimal clinically important difference in SNOT-22 score at this time in a mixed cohort, after adjustment for confounders [85].

Several authors observed an even stronger association with poor outcomes after ESS when combining the presence of comorbidities and inflammatory biomarkers, especially when markers of type 2 inflammation were included [47,85]. These authors specifically investigated the predictive value of clustering comorbidities with the type 2 signature [45]. For example, a cluster analysis by Kim and colleagues found that patients with asthma and eosinophilic NPs (cluster 1) or with no asthma but eosinophilic NPs and a high ethmoid-to-maxillary (E/M) opacification ratio (cluster 2) were more likely to need revision ESS compared with patients who had no asthma, no eosinophilic NPs and were aged ≥35 years (cluster 4) [47].

In summary, results of many studies indicate a clear and significant association between comorbidities, especially asthma and N-ERD, and poorer post-operative outcomes; the quality of the studies was mainly fair (level of evidence III/IV). This association is even stronger in the presence of type 2 biomarkers or in the case of a greater number of comorbidities.

History of previous ESS in CRSwNP

Outcomes after revision ESS were worse than after primary surgery [30,32,37,44,50], with poorer endoscopic outcomes [44], an increased need for revision ESS [50,56], poorer QoL (determined using the RSDI) [37] and worse olfactory function [30,32,39].

Patients who had undergone more prior ESS procedures were less likely to experience olfactory recovery than patients with fewer surgeries [39]. In a large observational study (n=980), the 5-year rate of revision ESS was almost 10% in patients who underwent primary ESS compared with 20% in those with a history of prior ESS [56]. In addition, the time elapsed since the previous ESS was a predictor of the need for repeat surgery; the more recent the ESS, the more likely the patient would require revision surgery. Indeed, patients who lost disease control within three years were particularly likely to require further surgical intervention in a shorter timeframe [56]. Only one study found no differences in outcomes between patients undergoing primary ESS or revision ESS [89].

Frontal sinus involvement has been shown to be a significant independent predictor of disease recurrence (OR 1.40; 95% CI 1.20–1.90; p<0.01) and revision ESS (OR 1.60; 95% CI 1.20–1.80; p<0.05) in the 5–10 years after ESS in patients with CRSwNP (33). Considering the quality of the papers (fair/good; level of evidence III/IV) and consistency of the results, the evidence in the literature appears to support the association between previous ESS, the time from the last ESS (especially within 3 years), number of previous surgeries and frontal recess involvement with poorer post-operative outcomes.

Pre-operative symptoms and the burden of disease

The extent and duration of pre-operative CRSwNP symptoms were associated with poor post-operative outcomes [22,24,29,31,38,45,47,48,61,63,64,78,75,77,93]. Two studies demonstrated that the duration olfactory deficit before ESS [30,32] was predictive of the poor olfactory recovery post-ESS in patients with CRSwNP. However, one study found that olfactory impairment for >5 years was not predictive of olfactory recovery at 1 year post-ESS [48].

More severe pre-operative symptoms were also associated with poorer post-operative outcomes in studies in mixed patient populations. Pre-operative symptom scores for nasal discharge or olfactory dysfunction were predictive of less improvement of post-operative symptom scores in one study [70] and higher pre-operative SNOT-22 scores were predictive of the 5-year revision ESS rate in another study [87]. Two large-scale analyses of sepa-

rate cohorts in the United Kingdom showed that the duration of pre-operative CRS symptoms was predictive of higher post-operative SNOT-22 scores [73], increased CRS-related healthcare visits, greater prescription use, higher likelihood of repeat surgeries and a higher prevalence of asthma [72].
In conclusion, an association between severity and duration of pre-operative symptoms and poorer post-operative results are well supported by the evidence, especially in relation to the pre-operative SNOT-22 score (quality of the papers are fair/good; level of evidence III).

Factors related to lifestyle or occupation
Although the negative impact of smoking on CRS pathophysiology is well known, its association with poor post-operative outcomes in patients with CRSwNP is weak. Among the 12 studies reviewed [32-34,46,49,50,53,62,71,83,86,88], only two [71,86] reported a link between smoking and post-operative outcomes, both in mixed populations (Table 1). Anne and colleagues found that smoking was associated with poorer SNOT-22 improvements at 3 months post-ESS (86), while Katotomichelakis and colleagues identified smoking as a predictor of smaller Beck Depression Inventory score improvement at 12 months [71]. There is a need for further research using larger, well-controlled studies to evaluate smoking as a predictor of outcomes post-ESS.
There are growing insights into the mechanisms by which environmental factors trigger innate and adaptive immune pathways in the sinonasal mucosa [102]. Notably, occupational exposure to airborne particulates may play a role in poorer post-operative outcomes in CRSwNP [103,104]. Nevertheless, the association between lifestyle and/or occupational exposure and poor post-operative outcomes was weak, and based on limited, moderate-quality evidence.

Radiological or endoscopic pre-operative findings
Twenty-eight articles examined the relationship between radiographic disease severity on computed tomography (CT) imaging and outcomes (Table 2) [8,44,46,51,53-55,59,68,80,91,93,94,96,97,105-117]; 22 were in patients with CRSwNP [44,46,51,53-55,59,91,93,94,96,97,105-112,114,117] and six were in mixed populations [8,68,80,113,115,116].

CT imaging
In studies including patients with CRSwNP alone, pre-operative LMS was the most common parameter investigated (Table 2). Several studies demonstrated that higher pre-operative LMS was associated with an increased rate of endoscopic recurrence/poor control after ESS [55,59,105,111,112] and a multivariate analysis revealed that specifically high pre-operative LMS was a significant independent predictor of revision ESS within 5 years (OR 1.29; 95% CI 1.08–1.54; p=0.06) [53]. A high pre-operative LMS was also correlated with SNOT-22 scores at 2 years after ESS in a multivariate regression analysis (p=0.003) [108], and with poor olfactory function recovery at 3 months (p=0.011) and 6 months (p=0.024) after ESS [117]. Furthermore, it was demonstrated that the degree of opacification in the anterior olfactory cleft was predictive of a reduced likelihood of improvement in olfactory function or of achieving normosmia (normal olfactory function) 6 months after ESS [110].
Another radiological parameter investigated in the literature was the E/M opacification ratio [107,112], where a higher ratio indicates a greater likelihood of poor outcomes after surgery or medical treatment. A higher E/M opacification ratio was predictive of poor olfactory function post-operatively [107] and of recurrence of symptoms within 3 years of ESS, with high statistical accuracy in receiver operating characteristic (ROC) analyses (AUROC 0.947) [112]. In fact, higher pre-operative E/M opacification ratios also had high sensitivity (95.8%) and specificity (91.1%) for predicting the recurrence of NPs [112].
The results of studies in mixed populations were consistent with those of CRSwNP-only populations. Higher pre-operative LMS was significantly associated with persistent symptoms post-ESS [68,116], the need for consecutive courses of rescue medication [115] and worse endoscopic scores [80] post-operatively.
In addition to LMS, the effect of pre-operative osteitis has also been evaluated previously [8,46]. The presence of pre-operative osteitis was a significant predictor of worse post-operative QoL in a multivariate analysis, where patients without osteitis had a >3-fold likelihood of achieving an improvement in QoL compared with those who had osteitis (OR 3.85; p=0.011) [8]. However, another study found that the global osteitis score was predictive of poor post-operative disease control only in univariate analyses, but not in multivariate analyses [46].
A real-world study of patients with CRS who underwent ESS (n=408) showed that a higher pre-operative sinonasal radiological score, along with higher LMS, predicted the need for revision surgery [17]. In multivariable analysis, elevated sinonasal radiological score and the presence of asthma and/or N-ERD were independent risk factors for revision ESS [17].
These analyses appear to support roles of LMS and radiological findings (E/M opacification ratio and osteitis) as predictive factors for poorer symptom control post- ESS (level of evidence III/IV).

Endoscopic findings
Ten studies examined the relationship between pre-operative endoscopic scores and post-operative outcomes in CRSwNP (Table 2) [44,51, 91,93,94,96,97,111,112,114]. Two studies [44,112] found that higher pre-operative LKS predicted endoscopic recurrence, with one study showing an increased risk of post-operative NP recurrence based on multivariate analysis (OR 1.40; 95% CI 1.10–1.80; p=0.016) [44], while the other indicated a risk of recurrence within 3 years post-ESS (AUROC 0.762), although LKS was less accurate than the E/M opacification ratio on pre-operative CT [112]. Two

Table 2. Anatomical features on CT imaging or endoscopy that were investigated for an association with surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
In patients with CRSwNP-only								
Akhtar 2010 [105] Pakistan	192	Retrospective	LMS	Endoscopic evidence of recurrent NPs of grade ≥2	Mean CT score was significantly higher in patients who developed recurrence within 24 months vs those who did not (mean 22.78 vs 13.25; p<0.001)	III	15	Fair
Kim 2011 [110] South Korea	52	Prospective, observational	Total, anterior and posterior OCS	Olfactory function (BTT, CCSIT) at 6 months post-ESS	Anterior OCS was a significant predictor of olfactory results (≤0.001), with more severe opacification predictive of lower likelihood of improvement or normosmia (p≤0.011)	IV	13	Poor
Lee 2014 [111] South Korea	71	Retrospective	LMS and endoscopic polyp grade	Presence of pathological secretions and/or polypoid mucosa on endoscopy at 6 months post-ESS	There was no difference in the proportion of patients with mild-moderate or severe disease using LMS or between those with Grade I, II or III polyposis on endoscopy between patients with a good vs poor surgical outcome	III	17	Fair
Grgić 2015 [108] Croatia	30	Prospective, observational	LMS	Symptoms and function (modified SNOT-22)	On multiple linear regression analysis, pre-operative CT score was the only factor significantly predictive of subjective score after 24 months (p=0.003)	IV	14	Poor
Olivier 2015 [114] Switzerland	33	Retrospective	Endoscopic polyposis score on a 0 to 4 scale	Symptom severity >6 on a 10-point VAS at last follow-up 1.2–20 (mean 11.6) years post-ESS	In this cohort of patients with Samter's triad, those with severe symptoms (VAS >6) at follow-up were significantly more likely to have had grade 3 or 4 polyposis, compared with patients who had moderate symptoms at follow-up (1/24 [4%])	IV	14	Poor
Vandenhende-Szymanski 2015 [117] France	30	Prospective, observational	LMS	Olfactory function (ETOC)	Pre-operative LMS was significantly predictive of poor olfactory recovery at 3 and 6 months post-operatively (p=0.011 and p=0.024, respectively)	III	17	Fair
DeConde 2017 [44] USA	363	Multicentre, prospective, observational	Bilateral LKS	Post-operative nasal polyposis and oedema on endoscopy (LKS >0)	After adjustment for confounders, pre-operative bilateral LKS was associated with post-operative polyp recurrence (OR 1.4; 95% CI 1.1–1.8; p=0.016)	III	18	Fair
Amali 2018 [106] Iran	138	Prospective, cohort	Polypoid changes on the anterior free border of the middle turbinate	NPs present on endoscopy at 12 months post-ESS	Patients with polypoid changes in the middle turbinate were significantly more likely to have recurrence of NPs within 12 months vs patients without these changes (p=0.03)	III	17	Fair
Kim et al. 2019 [46] South Korea	134	Retrospective	LMS, global osteitis score	Complete disease control according to EPOS 2012 criteria	In multivariate analysis, higher pre-operative LMS was associated with worse disease control (p=0.045)	III	17	Fair
Meng 2019 [112] China	272	Prospective, observational	E/M ratio using LMS, LKS	Recurrence of NPs on endoscopy (± symptoms) within 3 years of FESS	E/M ratio was a significant predictor of recurrence (AUROC 0.947), and more accurate than LKS (AUROC 0.762) and LMS (AUROC 0.542). E/M ratio threshold of 2.55 had sensitivity of 95.8% and specificity of 91.1% for predicting recurrence	III	18	Fair
Nakamaru 2020 [51] Japan	69	Retrospective	Endoscopic polyp score	Recurrent CRSwNP during 9–114 (median 62) months	After adjustment for confounders, pre-operative polyp score was a significant predictor of recurrence (OR 1.90; 95% CI 1.18–3.06; p=0.008)	III	16	Fair
Wu 2020 [53] Taiwan	107	Prospective cohort	LMS	Revision surgery for 5 years post-ESS	After adjustment for confounders, pre-operative LMS was an independent risk factor for revision surgery (OR 1.29; 95% CI 1.075–1.536; p=0.06). A LMS >13.5 had sensitivity of 93.75% and specificity of 64.71% for predicting need for revision	III	18	Fair
Beswick 2021 [107] USA	165	Prospective, observational	E/M ratio using LMS	Post-operative SNOT-22 score, BSIT	Elevated pre-operative E/M ratio was correlated with BSIT improvement, but not with SNOT-22 improvement or polyp recurrence	III	16	Fair

Table 2 *continued*. Anatomical features on CT imaging or endoscopy that were investigated for an association with surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
De Corso 2021 [54] Italy	80	Prospective, observational	LMS	Disease control (LKS ≥2 and SNOT-22 score ≥20) at 12 months post-ESS	On univariate analysis, pre-operative LMS >12 was associated with poor disease control at 12 months (RR 4.28; 95% CI 1.67–10.97; p<0.01)	III	16	Fair
Gan 2021 [55] China	77	Prospective, observational	LMS	Endoscopic recurrence of NP during 1-year post-ESS	Patients with recurrent NP had a significantly higher mean pre-operative bilateral LMS than patients who did not develop recurrence (p=0.0001)	III	16	Fair
Kim 2021 [109] South Korea	129	Prospective, observational, incorporated machine learning	LMS	Recurrent symptoms within 1 year	Having a LMS >19 was significantly predictive of recurrence (p=0.018)	III	16	Fair
Bai 2022 [59] USA	94	Prospective, observational, incorporated machine learning	Modified LMS	Recurrent NPs on endoscopy within 2–5 years after ESS	Modified LMS was predictive of polyp recurrence (p<0.05)	III	15	Fair
Ji 2026 [94] China	152	Retrospective	Pre-operative LMS and LKS	Recurrence during 6–36 months after ESS	Higher LMS independently predicted recurrence (OR 1.38 per 1-point increase; 95% CI 1.16–1.65; p=0.002). LKS was associated with recurrence in univariate analysis but not after adjustment (OR 1.21; 95% CI 0.98–1.49; p=0.072).	III	16	Fair
Kirtsreesakul 2026 [91] Thailand	437	Retrospective	Pre-operative modified Lund–Kennedy and Lund–Mackay scores	Time to recurrence after ESS	Both modified Lund–Kennedy and Lund–Mackay scores were retained as predictors in the LASSO-penalised Cox model.	III	18	Fair
Zhong 2026 [93] China	603	Retrospective	Preoperative Lund–Mackay and Lund–Kennedy scores	Time to postoperative recurrence	A higher Lund–Mackay score was independently associated with recurrence (HR 1.055 per 1-point increase; 95% CI 1.009–1.102; p=0.018). The Lund–Kennedy score did not differ between recurrent and nonrecurrent patients and was not independently associated with recurrence.	III	17	Fair
Zhang 2026 [96] China	178	Retrospective	Preoperative Lund–Mackay CT score	Recurrence within 24 months	Higher preoperative Lund–Mackay score was independently associated with recurrence (OR 1.928; 95% CI 1.475–2.522).	III	17	Fair
Zhang 2026 [97] China								
				In a mixed population of patients with CRSwNP/CRSsNP				
Sil 2007 [115] UK	109	Post hoc analysis of prospective cohort study	LMS, endoscopic polyp score	Consecutive courses of systemic rescue medication over a 2 month period	CT score strongly predicted a poor outcome (p<0.0001; AUROC 0.835), as did grade of polyposis (p=0.017; AUROC 0.702)	III	15	Fair
Toros 2007 [116] Turkey	86	Prospective observational cohort	LKS, LMS	Symptomatic improvement at 1, 6 and 12 months post-ESS on VAS of 0–10	Pre-operative total CT score and pre-operative endoscopy score was each significantly correlated with post-operative symptom score at 1 (p≤0.005), 6 (p≤0.001) and 12 months (p≤0.001) post-ESS	IV	13	Poor
Psaltis 2008 [68] Australia	40	Prospective, observational	LMS	Presence of any ongoing symptoms or any mucosal abnormality for 8 months post-ESS	Patients who had ongoing post-operative symptoms or ongoing mucosal inflammation had significantly higher pre-operative CT scores than patients with a good symptomatic or mucosal outcomes (p=0.004 for both parameters)	III	17	Fair

Table 2 *continued*. Anatomical features on CT imaging or endoscopy that were investigated for an association with surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Bhandarkar 2011 [8] USA	190	Prospective, observational cohort	Osteitis on CT	LKS, QoL using RSDI and CSS, olfactory function using SIT	After adjustment for confounders (including polyposis), QoL was significantly more likely to improve in patients without vs with osteitis (OR 3.85; p=0.011)	III	19	Fair
Okushi 2012 [113] Japan	138	Prospective, observational	Total REC scorea	Improvement in paranasal sinus opacification on CT	Total REC score was significantly associated with a poor rate of improvement at ≥6 months after primary ESS	III	17	Fair
Tsuzuki 2019 [80] Japan	281	Retrospective	LMS	Endoscopic score at 12–24 (mean 16.4) months post-ESS	After adjustment for confounders, LMS was a significant predictor of poor endoscopic scores (p=0.0004)	III	19	Fair

Table 2 *legend*. a Post-operative assessment. AUROC, area under the receiver operating characteristic curve; BSIT, Brief Smell Identification Test; BTT, butanol threshold test; CI, confidence interval; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; CSS, Chronic Sinusitis Survey; CSSIT, cross-cultural smell identification test; CT, computed tomography; E/M, ethmoid-to-maxillary; EPOS, European Position Paper on Rhinosinusitis and Nasal Polyps; ESS, endoscopic sinus surgery; ETOC, European Test of Olfactory Capabilities; FESS, functional endoscopic sinus surgery; NP(s), nasal polyp(s); LKS, Lund-Kenndy Score; LMS, Lund-Mackay score; OCS, olfactory cleft score based on opacification (0=no opacification; 1= ≤25%, 2=25–50%, 3=50–75% and 4=>75% opacification); OR, odds ratio; QoL, quality of life; REC, residual ethmoid cell (calculated from 3 sections each in the left and right ethmoid sinus [6 sections] each graded from 0 to 3 based on presence of lamina, thickness of any lamina present and presence of complete or incomplete air cells); RSDI, Rhinosinusitis Disability Index; RR, risk ratio; SIT, Smell Identification Test; SNOT-22, 22-item SinoNasal Outcome Test; VAS, Visual Analogue Scale; vs, versus

other studies linked higher pre-operative endoscopic scores to worse long-term outcomes (>5 years), including recurrent CRSwNP and severe symptoms for a variable number of years after surgery [51,114]. These findings were consistent in mixed studies involving both CRSwNP and CRSsNP patients [115,116]. Finally, the endoscopic presence of eosinophilic mucin was associated with poor post-operative outcomes in some studies [25,49]. Our results demonstrate that the association between LKS and post-operative outcomes is moderately well supported whereas the association with eosinophilic mucin is only weakly supported.

Nasal polyp tissue biomarkers

Many studies have examined the effects of tissue, cellular or serum markers on outcomes in patients with CRSwNP (Table 3) [21,31,36 38,40,42,43,46,47,51,52,54,55,58,59,90,91,93-95,97,108,109,112,118-140] with fewer studies conducted in mixed populations [66,76,77,84,141-148].

Tissue eosinophils

Multiple studies that have investigated the relationship between tissue eosinophil counts in resected surgical specimens and post-operative outcomes have consistently reported that high levels of tissue eosinophils were associated with worse outcomes, including an increased rate of endoscopic and/or symptomatic recurrence [38,42,51,55,108,112,125,130,131,133,135,138,149,150], disease control using the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) 2012 criteria [46,100], need for revision ESS [21,47,151], olfactory function at 3 or 6 months post-ESS [139] and QoL at 12 months post-ESS using the RSDI instrument [37] (Table 3). These studies showed that post-operative outcomes were predicted by eosinophil counts [21,51,55,108,112,119,120,123,125,133,135,139] and by eosinophils as a percentage of total cells [21,112,123,125,135,151]. Similar

Table 3. Inflammatory cells in tissue (histopathological features, biopsy, scraping) or blood, investigated as predictive markers of surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
In patients with CRSwNP-only								
Adnane 2015 [37] Morocco	58	Prospective, observational	Mucosal eosinophil density, squamous metaplasia, glandular hypertrophy	QoL using RSDI at 12 months post-ESS	After adjustment for confounders, high mucosal eosinophilia was a significant predictor of QoL improvement (p=0.001)	III	18	Fair
Gelardi 2009 [31] Italy	161	Prospective, observational	Nasal cytology	Need for repeat ESS within 10 years	The presence of eosinophils >20% and mast cells >10% (of total cells) moderately increased the risk for repeat ESS (OR 1.60; p=0.28), but risk was highest in patients with this cytology profile + asthma + aspirin sensitivity (OR 4.50; p=0.04)	IV	12	poor
Tosun 2010 [123] Turkey	42	Retrospective	Mucosal eosinophil density	NP recurrence in 30–90 (mean 53) months post-ESS	The rate of recurrence was 81.8% in patients with ≥4 eosinophils/1000 µm2 vs 25.0% in patients with ≤3 eosinophils/1000 µm2 (p=0.0001)	III	17	fair
Brescia 2015 [38] Italy	179	Prospective observational	Eosinophilia (≥10 eosinophils/HPF), serum eosinophil count and percent, serum basophil count and percent, serum ECP levels	Endoscopic evidence of grade ≥1 polyposis during median of 36 months after ESS	After adjustment for confounders, tissue eosinophilia was a significant predictor of recurrence (RR 3.68; 95% CI 0.19–11.38; p=0.025) and serum basophil percentage showed a trend for being predictive of recurrence (p=0.079). A panel of 3 variables (age <65 years, serum basophil percentage and eosinophilic pathology) had AUROC of 0.702, sensitivity 41.7%, specificity 88.4%, PPV 35.7% and NPV 90.7%	III	19	Fair
Nakamaru 2020 [51] Japan	69	Retrospective	Tissue eosinophil count	Recurrent CRSwNP during 9–114 (median 62) months	After adjustment for confounders, intraoperative tissue eosinophil count was a marginally significant predictor of recurrence (OR 1.00; 95% CI 1.00–1.01; p=0.024)	III	16	Fair
Grgić 2015 [108] Croatia	30	Prospective, observational	Eosinophils/HPF, IgE, IL-5 and VEGF levels in nasal tissue	Endoscopic evidence of grade ≥1 polyposis at 6 months post-ESS	The rate of recurrence was 41% in patients with >20 eosinophils/HPF vs 12% in patients with ≤20 eosinophils/HPF levels (p<0.05). On multiple linear regression analysis, pre-operative tissue levels of IgE, IL-5 and VEGF were not significantly predictive of subjective score after 12 months	IV	14	Poor
Lou 2015 [125] China	387	Retrospective	Tissue eosinophil count and percent, FeNO	Endoscopic evidence of diseased mucosa + bothersome symptoms for ≥1 month and need for maximal medical therapy	On multivariate analysis, significant predictors of recurrence were tissue eosinophil count and percent (AUROC 0.969; p<0.001) and FeNO (AUROC 0.812; p<0.001), but tissue eosinophilia was a significantly better predictor than FeNO (p<0.001). Eosinophils ≥27% had sensitivity of 96.7%, specificity of 92.5%, PPV 94.1% and NPV of 95.8%. Eosinophils ≥55 cells/HPF had sensitivity of 84.7%, specificity of 97.1%, PPV of 97.4% and NPV or 86.2%	III	20	Good
Bassiouni 2016 [21] Australia	20 + 20 controls	Retrospective case-control study	Inflammatory cell infiltration	Need for revision surgery	Tissue from patients who needed later revision surgery had significantly higher numbers of eosinophils/field (p<0.001), total cells/field (p<0.001), percentage of eosinophils (p<0.001), percentage of lymphocytes (p<0.001) and ELR compared with tissue from patients who did not subsequently need revision surgery	IV	18	Fair
Nikakhlagh 2015 [40] Iran	93	Prospective, observational	Histopathological subtype (Hellquist classification)	Recurrence based on symptoms and endoscopy	The allergic subtype was a significant predictor of recurrence (p=0.0006) compared with other subtypes; chronic inflammatory and seromucinous subtypes were not associated with increased rate of recurrence	III	17	Fair
Telmesani 2010 [12] Saudi Arabia	82	Prospective, observational	Mucosal changes (Milbrath grade), bony changes (Biedlingmaier grade)	Recurrence within 1 year	The presence of osteitis was a significant predictor of recurrence after first or second/third ESS (p<0.0005)	III	15	Fair
Brescia 2016 [42] Italy	143	Prospective, observational	Eosinophilia (>10 eosinophils per field)	Recurrent polyposis of grade ≥1 on endoscopy during a median of 24 months post-ESS	Eosinophilic histology was the only independent predictor of recurrence in multivariate analysis (p=0.033)	III	20	Good

Table 3 *continued*. Inflammatory cells in tissue (histopathological features, biopsy, scraping) or blood, investigated as predictive markers of surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Brescia 2017 [43] Italy	280	Retrospective	Serum eosinophil count and percent, serum basophil count and percent	Endoscopic evidence of grade ≥1 polyposis during median of 30 months after ESS	Patients with recurrence had significantly higher eosinophil and basophil counts and percentages vs patients without recurrence. Thresholds predictive of recurrence were eosinophil count ≥0.24 cells x 109/L (OR 2.57; 95% CI 1.33–5.06; p=0.003), eosinophils ≥3.7% (OR 2.19; 95% CI 1.15–4.24; p=0.0112), basophil count ≥0.03 cells x 109/L (OR 2.19; 95% CI 1.15–4.24; p=0.0115) and basophils ≥0.5% (OR 2.24; 95% CI 1.17–4.38; p=0.011)	III	16	Fair
Brescia 2021 [119] Italy	51	Retrospective	Serum eosinophil count and percent, serum basophil count and percent	Endoscopic evidence of grade ≥1 polyposis during 5 years after ESS	Among patients with eosinophilic CRSwNP, those who had recurrence had significantly higher eosinophil and basophil counts and percentages pre-operatively and during follow-up vs without recurrence (p<0.05 for all parameters)	III	15	Fair
Brescia 2016 [120] Italy	240	Prospective observational	Serum eosinophil and basophil count, ELR, BLR, NLR	Endoscopic evidence of grade ≥1 polyposis during median of 36 months after ESS	Compared with patients without recurrence, those with recurrence had significantly higher pre-operative eosinophil levels (p=0.0041), basophil levels p=0.0056), NLR (p=0.03), ELR (p=0.0001) and BLR (p=0.0002). Cut-offs for prognostic purposes were NLR 1.76, ELR 0.14 and BLR of 0.02	III	18	Fair
Lou 2016 [126] China	366	Retrospective with cluster analysis	Tissue inflammatory pattern	Endoscopic evidence of diseased mucosa + bothersome symptoms for ≥1 month and need for maximal medical therapy	Recurrence rates were highest (98.5%) in the cluster of patients with an eosinophil-predominant pattern, second in those with mixed inflammatory pattern (75.0%) and third in patients with a neutrophil-predominant pattern (46.4%), but were low in patients with patterns predominant in plasma cells (6.9%) or lymphocytes (6.4%)	III	20	Good
Guo 2018 [123] Canada	102	Prospective, observational	Serum eosinophil count and percent; serum basophil count and percentage	≥2 episodes of endoscopic polyp recurrence (grade ≥1) during 12–15 months post-ESS	Baseline eosinophil counts and percent were significantly higher in patients with multiple vs no recurrences (p=0.007 and 0.055, respectively). Eosinophil count ≥0.25 x 109 cells/L was associated with increased risk (OR 3.63; sensitivity 81.8%, specificity 44.6%), as was eosinophil percentage ≥2.6% (OR 5.12; sensitivity 90.9%, specificity 33.8%)	III	17	Fair
Kim 2019 [46] South Korea	134	Retrospective	Tissue eosinophilia, tissue neutrophilia (cells/HPF)	Complete disease control according to EPOS 2012 criteria	In multivariate analysis, tissue eosinophilia and tissue neutrophilia were significantly associated with improved disease control (p=0.032 and p=0.005, respectively)	III	17	Fair
Kim 2019 [47] South Korea	375	Retrospective, cluster analysis	Age, asthma, eosinophilia, blood eosinophil levels, E/M ratio, LMS	Revision surgery within 4 years	Revision-free rates were lower in 3 clusters characterised by (1) asthma + eosinophilic NPs (66.7%; p=0.013), (2) no asthma + eosinophilic NPs + higher E/M ratio (66.7%; p=0.017) or (3) no asthma + non-eosinophilic NPs + age <35 years (70.9%; p=0.001) compared with cluster characterised by no asthma + non-eosinophilic NPs + age ≥ 35 years (98.0%)	III	19	Fair
Meng 2019 [112] China	272	Prospective, observational	Tissue eosinophil percentage and total eosinophil count, blood eosinophilia count and percentage	Recurrence of NPs on endoscopy (± symptoms) within 3 years of FESS	Tissue eosinophil percentage was a significant predictor of recurrence (AUROC 0.916), and more accurate than total eosinophil count (AUROC 0.801). A tissue eosinophil percentage threshold of 26% had sensitivity of 78.0% and specificity of 96.4% for predicting recurrence	III	19	Fair
Wang 2021 [52] China	346	Prospective cohort	Blood eosinophil percentage	Presence of CRS symptoms and/or NPs, and management with intranasal CS and ≤2 short courses of antibiotics or systemic CS within 24 months of ESS	After adjustment for confounders, blood eosinophil percentage was associated with a significantly increased risk of recurrence (OR 1.57; 95% CI 1.31–1.77; p<0.001)	III	18	Fair
De Corso 2021 [54] Italy	80	Prospective, observational	Eosinophils >20% of total cells, neutrophils >50% of total cells or both on nasal cytology, serum eosinophil count and percent, serum basophil count and percent	Disease control (LKS ≥2 and SNOT-22 score ≥20) at 12 months post-ESS	On univariate analysis, the risk of poor disease control at 12 months was increased in patients with nasal eosinophilia (RR 8.42; 95% CI 2.72–15.12; p<0.01), nasal neutrophilia (RR 3.10; 95% CI 1.24–7.71; p<0.05) and mixed pattern (RR 25.11; 95% CI 19.41–30.01; p<0.01), and in those with blood eosinophilia (RR 4.34; 95% CI 1.48–12.05; p<0.01)	III	16	Fair

Table 3 *continued*. Inflammatory cells in tissue (histopathological features, biopsy, scraping) or blood, investigated as predictive markers of surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Gan 2021 [55] China	77	Prospective, observational	Peripheral blood eosinophil and neutrophil count, tissue eosinophil and neutrophil count, tissue levels of IL-5, -8, -17A, -17E, -18 and -27, IFN-γ	Endoscopic recurrence of NP during 1-year post-ESS	Compared with patients who did not have recurrent NP, those with recurrence had significantly higher peripheral blood neutrophil counts (p=0.026), tissue eosinophil count (p<0.0001), tissue neutrophil count (p<0.0001), tissue levels of IFN-γ (p=0.001), IL-17A (p<0.0001), IL-17E (p<0.0001) and IL-18 (p<0.0001)	III	16	Fair
Kim 2021 [109] South Korea	129	Prospective, observational, incorporated machine learning	Subepithelial neutrophil count	Recurrent symptoms within 1 year	Having >45 HNE-positive neutrophils in the subepithelial area was significantly predictive of recurrence (p=0.013)	III	16	Fair
Belsky 2021 [118] USA	23	Retrospective	Mast cell burden in polyp tissue	Endoscopic evidence of polypoid oedema or need for oral/injected CS treatment in 6 months post-ESS	The risk of polypoid oedema was significantly higher in patients with high mast cell levels in epithelium (HR 1.28; 95%CI 1.05–1.57; p=0.02) or stroma (HR 1.10; 95% CI 1.01–1.20; p=0.02), but percentage of cells expressing TIM3 was not significantly associated with outcomes	IV	14	Poor
Wu 2021 [138] Taiwan	108	Prospective, observational	CLC in nasal secretions, inflammatory cells in polyp tissue	Endoscopic evidence of recurrence + symptoms lasting ≥1 week despite intranasal CS during 12–33 months post-ESS	In binary logistic regression analysis, the risk of recurrence was association with CLC protein levels in nasal secretions (OR 1.04; 95% CI 1.01–1.07; p=0.006) and percent eosinophils in polyp tissue (OR 1.06; 95% CI 1.02–1.10; p=0.002). A CLC cut-off of 34.243 ng/mL had AUROC of 0.801, sensitivity 92.6%, specificity 87.5%, PPV 92.6%, NPV 87.5%. Eosinophil cut-off of 26.125% had AUROC of 0.816, sensitivity 94.1%, specificity 87.5%, PPV 91.3%, NPV 87.2%	III	15	Fair
Ji 2026 [94] China	152	Retrospective	Peripheral blood eosinophils >5%	Recurrence during 6–36 months after ESS	Blood eosinophils >5% independently predicted recurrence (OR 3.62; 95% CI 1.78–7.38; p<0.001).	III	16	Fair
Canakci 2025 [90] Turkey	102	Retrospective	Blood eosinophils, EMR, total IgE, NLR, PLR, SII and SIRI	Endoscopic evidence of CRSwNP recurrence within 3 years after ESS	Total IgE and PLR were significantly higher in recurrent than non-recurrent patients (p=0.036). Eosinophils, EMR, SII and SIRI were higher in recurrent patients than healthy controls, but these comparisons do not establish their ability to discriminate recurrence from non-recurrence. None of the blood biomarkers was reported as an independent predictor in multivariable analysis.	III	16	Fair
Zhang 2025 [95] China	102	Prospective	Peripheral blood eosinophil and neutrophil counts and percentages, combined with clinical and patient-reported variables	EPOS-defined suboptimal disease control after FESS	Peripheral blood eosinophil and neutrophil counts were selected by LASSO as the principal objective clinical variables for predicting suboptimal disease control. Their combination with individual preoperative CRS-PRO items produced the best-performing model.	III	18	Fair
Kirtsreesakul 2026 [91] Thailand	437	Retrospective	Pre-operative blood eosinophil count	Time to recurrence after ESS	Blood eosinophil count was retained in the multivariable LASSO-penalised Cox model for postoperative recurrence.	III	18	Fair
Zhong 2026 [93] China	603	Retrospective	Peripheral blood eosinophil count and percentage; tissue eosinophil count and percentage	Time to postoperative recurrence	Recurrent patients had higher blood and tissue eosinophil levels than nonrecurrent patients. In multivariable Cox analysis, tissue eosinophil percentage remained independently associated with recurrence (HR 1.008 per 1% increase; 95% CI 1.002–1.013; p=0.009). Tissue eosinophil count, blood eosinophil count and blood eosinophil percentage were not independently associated with recurrence. Patients with allergic rhinitis had markedly greater tissue, but not peripheral blood, eosinophilia.	III	17	Fair

Table 3 *continued*. Inflammatory cells in tissue (histopathological features, biopsy, scraping) or blood, investigated as predictive markers of surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Dharia 2026 [98] USA	325	Retrospective	Absolute eosinophil count	Patient-reported timing and associated symptoms of CRSwNP recurrence after ESS, as well difference of current disease burden based on prior recurrence timing	There were no significant differences between the fast recurrence and slow recurrence groups in terms of current peripheral blood eosinophil count at registry enrollment	III	18	Fair
In a mixed population of patients with CRSwNP/CRSsNP								
Matsuwaki 2008 [66] Japan	56	Prospective, cohort	Mucus or mucosal eosinophilia, presence of ≥120 eosinophils/HPF, positive fungal culture or stain, peripheral eosinophilia (≥520 cells/μL), total IgE	Recurrence of symptoms or need for revision surgery within 5 years of ESS	After adjustment for confounders, mucus or mucosal eosinophilia significantly predicted increased risk of recurrence (OR 3.17; p=0.001), as did peripheral eosinophilia (OR 1.81; p=0.045)	III	17	Fair
Soler 2010 [145] USA	102	Prospective, observational	Tissue eosinophilia (≥10 cells/HPF)	QoL using RSDI, CSS and SF-36 at 4–37 (average 16.5) months post-ESS	Patients with mucosal eosinophilia had less improvement in QoL than patients without eosinophilia, which was significant for RSDI total (p=0.044), RSDI function (p=0.018), CS medication (p=0.013), SF-36 general health (p=0,008), SF-36 physical role (p=0.036) and SF-36 vitality (p=0.034) domains	III	17	Fair
Nakayama 2011 [144] Japan	173	Prospective, observational	Tissue eosinophil count or eosinophilia (≥70 cells/HPF)	Endoscopic evidence of NPs within a mean of 17.5 months post-ESS	Mucosal eosinophilia was a significant predictor of recurrence (HR 3.47; 95% CI 1.65–7.29; p=0.001) and recurrence-free survival was significantly better in patients without vs with eosinophilia (p≤0.008), irrespective of whether or not they had CRSwNP or CRSsNP	III	16	Fair
Vlaminck 2014 [147] Belgium	221	Prospective, observational	Tissue eosinophilia (>5 cells/HPF), eosinophilic mucin containing CLC or presence of fungal hyphae	Endoscopic evidence of recurrence + ≥3 bothersome symptoms lasting ≥1 month and need for systemic treatment in 3 years post-ESS	In patients with CRSwNP, the presence of eosinophils was associated with increased rate of recurrence vs non-eosinophilic CRSwNP (48.0% vs 9.5%) and was highest in the eosinophilic subgroup with eosinophilic mucin (51.3%) or eosinophilic mucin + fungal hyphae (72.2%) and lowest in patients without these features (32.0%). In patients with CRSsNP, recurrence rates were similar in those with and without eosinophilia	III	15	Fair
Boztepe 2016 [141] Turkey	260 + 75 controls	Retrospective, case-control	PLR and NLR in peripheral blood	Recurrence of symptoms within 21–30 (average 35) months of ESS	Pre-operative PLR and NLR were significantly higher in patients with CRS vs healthy controls (p<0.001) and were significantly higher in CRSwNP patients with recurrence vs no recurrence (p<0.001). NLR was a significant predictor of recurrence in the ROC analysis (threshold 3.13) and had AUROC of 0.693, 48.5% sensitivity, 84.9% specificity, 41.0% PPV and 88.4% NPV	IV	14	Poor
Honma 2016 [142] Japan	78	Prospective, cohort	Blood eosinophil count and percent, mucosal eosinophil count	NP recurrence in 1–5 years post-ESS	Blood eosinophil counts and mucosal eosinophil counts were significantly higher in patients who subsequently experienced recurrence vs those who did not (p<0.05). Patients who developed recurrence had a significant decrease in blood eosinophil count after ESS (p<0.05) whereas the decrease was not statistically significant in patients who did not have a recurrence	IV	14	Poor
Younis 2017 [148] USA	113	Prospective, observational	Mucosal eosinophilia (>5% of all leukocytes in 5 visual fields or >5 cells/HPF)	SNOT-22 score at 1-year post-ESS	Mucosal eosinophilia had a significant negative impact on extent of SNOT-22 improvement	III	18	Fair
Liao 2018 [77] China	246	Prospective, observational	28 clinical variables and 39 cellular and molecular variables	Difficult to treat CRS (symptoms despite intranasal CS and ≤2 short courses of antibiotics and systemic CS) within 12 months of ESS	Three clusters of Chinese patients were identified with poor outcomes at 12 months after ESS: (1) eosinophilic CRSwNP with severe pre-operative symptoms; (2) CRS with neutrophilic inflammation; and (3) CRSwNP with long disease duration, high rate of prior ESS and moderate neutrophilic inflammation			

Table 3 *continued*. Inflammatory cells in tissue (histopathological features, biopsy, scraping) or blood, investigated as predictive markers of surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Tajudeen 2019 [146] USA	Relevant biomarkers differed between clusters	III	19	Fair				
Guo 2021 [84] China	101	Retrospective	Mucosal histopathology	Cumulative prednisone use and LKS at 1, 3 and 6 months post-ESS	Post-operative prednisone requirements over 6 months post-ESS were significantly higher in patients with moderate vs mild inflammation (p=0.032), ≥5 eosinophils/HPF (p=0.013) and presence of eosinophil aggregates (p=0.001). The presence of eosinophil aggregates was significantly associated with post-operative prednisone use and LKS at 1, 3 and 6 months	III	15	Fair
Lee 2021 [143] South Korea	189	Prospective, observational	Biological markers (39) in nasal secretions or peripheral blood samples	Uncontrolled CRS (presence of ≥3 symptoms + need for antibiotics or systemic CS within previous 3 months)	Elevated levels of MIP-1β and CCL17 in nasal secretions were significant predictors of uncontrolled CRS within 12 months of ESS	III	19	Fair
	44	Prospective, observational	Tissue remodelling markers (stromal oedema, basement membrane thickening, stromal fibrosis, subepithelial glad proliferation)	LKS ≥4 at 12 months post-ESS	On regression analysis, only subepithelial gland proliferation was predictive of a LKS ≥4 (OR 8.25; 95% CI 1.13–60.32; p=0.038)	III	17	Fair

Table 3 *legend*. [a] This study also included a comparison of CRSwNP patients with CRSsNP (n=40) and healthy controls (n=40), but the analysis of relationship to recurrence was limited to patients with CRSwNP, so these data are tabulated here. AFS, allergic fungal sinusitis; AUROC, area under receiver operating characteristic curve; BAFF, B-cell activating factor; BLR, basophil-to-lymphocyte ratio; CCL, confidence interval; CLC, Charcot-Leyden Crystals; CRS, chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; CRTH2, chemoattractant receptor-homologous molecule expressed on Th2 cells; CS, corticosteroids; CSS, Chronic Sinusitis Survey; CT, computed tomography; ds-DNA, double-strand DNA; E/M, ethmoid-to-maxillary; ECP, eosinophil cationic protein; ELR, eosinophil-to-lymphocyte ratio; EMCRS, eosinophilic mucin chronic rhinosinusitis; EPOS, European Position Paper on Rhinosinusitis and Nasal Polyps; ERM, eosinophilic-rich mucin; ESS, endoscopic sinus surgery; FESS, functional endoscopic sinus surgery; FeNO, fraction of exhaled nitric oxide; GAPDH, glyceraldehyde 3-phosphate dehydrogenase; HNE, hydroxynonenal; HPF, high powered field; HR, hazard ratio; IFN, interferon; Ig, immunoglobulin; IL, interleukin; LKS, Lund-Kennedy score; MIP, macrophage inflammatory protein; mRNA, messenger RNA; NLR, neutrophil-to-lymphocyte ratio; NP(s), nasal polyp(s); NPV, negative predictive value; OR, odds ratio; PBMC, peripheral blood mononuclear cells; PLR, platelet-to-lymphocyte ratio; PPV, positive predictive value; QoL, quality of life; ROC, receiver operating characteristic; RR, relative risk; RSDI, Rhinosinusitis Disability Index; SE, Staphylococcus aureus endotoxins; SNOT-22, 22-item SinoNasal Outcome Test; T&T, Toyota & Takagi; TNF, tumour necrosis factor; VEGF, vascular endothelial growth factor; vs, versus.

results were seen in mixed studies, with pre-operative eosinophil count or percentage associated with an increased risk of worse outcomes, including endoscopic or symptomatic recurrence [66,144,146,147], post-operative corticosteroid requirements [146], need for revision ESS [66] and poorer subjective parameters, including QoL and SNOT-22 scores (Table 3) [76,145].

However, the definition of the threshold eosinophil count varied considerably among studies, and included >4 cells per 1,000 μm^2 [133], 5 cells/high powered field (HPF) [76,146,147], 10 cells/HPF [38,42,145], 20 cells/HPF [108], 70 cells/HPF [144] or 120 cells/HPF [66]. Lou and colleagues used ROC analysis to define a cut-off of 55 cells/HPF for patients with CRSwNP with 87.4% sensitivity and 97.1% specificity for predicting endoscopic recurrence, with or without symptoms, in the 2 years following ESS (126). The AUROC values for tissue eosinophil count as a predictor of recurrence (Table 4) ranged from 0.7354 (fair accuracy) to 0.969 (excellent accuracy) [112,121,125,135].

Lymphocytes, neutrophils and mast cells

Other cell types investigated for their relationship with outcomes in patients with CRSwNP were lymphocytes [21], neutrophils [46,109] and mast cells [118,122] (Table 3). One study found that patients who needed revision surgery had a higher lymphocyte percentage in resected tissue compared with those who did not require subsequent ESS [21]. Studies from Korea reported on the relationship between neutrophils and outcomes. The first noted that the number of neutrophils per HPF was a significant independent predictor of disease control in multivariate analysis [46], and the second demonstrated that having >45 hydroxynonenal-positive neutrophils in subepithelial tissue was significantly predictive of recurrence [109]. Two small and low-quality studies reported a relationship between mast cell levels in resected tissue and outcomes, with one showing that higher levels correlated with worse endoscopic findings at 90 days after ESS [122] and the other reporting a significantly increased risk of endoscopic oedema at 6 months post-ESS in patients with high epithelial mast cell levels [118]. Although associations were reported between post-operative ESS outcomes and tissue neutrophils and mast cells, these findings stemmed from low- to moderate-quality studies.

Other studies [47,76,77,126] have attempted to use cluster analyses to identify inflammatory cell patterns that might be associated with ESS outcomes (Table 3). Lou and colleagues classified patients into five clusters depending on the percentage of specific cell types in resected tissue [126]. Patients with a marked eosinophilic pattern (>75% tissue eosinophils) had the highest rate of recurrence (98.5%) followed by those with a mixed inflammatory pattern (tissue eosinophils around 40%) with recurrences of 75.0%, whereas recurrence rates were less than 7% in patients with plasma cell- or lymphocyte-predominant patterns [126]. However, strategies based on patterns or classification systems based on clustering analyses have not been incorporated into routine clinical practice and thus have a limited clinical role.

Tissue cytokines

Several studies have investigated the role of cytokines and other molecules measured in the tissue as potential predictive factors of post-operative outcomes. The relationship between tissue biomarker levels and outcomes was examined in 12 studies of CRSwNP [36,55,59,90,108,124,128,130,134,137-139] and in two studies of mixed populations [77,147] (Table 3). The following molecular biomarkers were investigated: interleukins (ILs), total IgE, eosinophilic cationic protein (ECP), interferon-gamma (IFN-γ), eotaxin-1 and chemoattractant receptor-homologous molecule expressed on T_H2 cells (CRTH2; Table 5).

The evidence regarding these tissue molecules is weak and, in some cases, conflicting. Since the quality of the publications was fair or poor, these molecular tissue biomarkers were not considered applicable for use as predictive factors. Here, we present a summary of the findings.

Interleukins

The most common tissue cytokines investigated were from the IL family [36,55,59,108,124,128,134,139,140,152], with IL-5 being most commonly examined [36,59,108,128,134,139,140,153]. All these studies reported a significant relationship between tissue IL-5 levels and poor outcomes, including endoscopic recurrence [59,128,134,140], need for revision surgery [36,140] and impaired olfactory function [139] with only one exception [108]. The authors of this last paper indeed found no significant independent relationship between symptom scores tissue levels of total IgE, IL-5 or vascular endothelial growth factor (VEGF) [108].

Other relevant ILs associated with worse outcomes were IL-1 (outcome was recurrent CRSwNP at 18 months post-ESS) [124], IL-17A (outcomes were endoscopic score at 6 months post-ESS [124] and endoscopic recurrence of CRSwNP at 1 year post-ESS [55]), and IL-17E and IL-18 (both associated with endoscopic recurrence of NPs at 1 year post-ESS) [55].

Immunoglobulins

As described above, Grgić and colleagues found no significant independent relationship between tissue levels of total IgE and symptom scores 12 months after ESS [108]. However, Van Zele and colleagues found significantly higher levels of IgE specific to *Staphylococcus aureus* endotoxins at the primary surgery in patients later needing revision surgery than in those not needing a second surgery [36]. In a prospective study, Bai and colleagues found that high tissue levels of anti-double strand DNA IgG were significantly predictive of endoscopic recurrence of NPs within 2 to 5 years of ESS [59].

Eosinophilic cationic protein

The studies by Van Zele and colleagues and Bai and colleagues described above also reported a significant relationship between tissue levels of ECP and ESS outcomes (need for revision ESS [36] or endoscopic recurrence [59]).

Interferon-gamma

The relationship between IFN-γ and outcomes has been reported in three studies with contradictory results. The case control study by Van Zele and colleagues reported that patients with tissue samples positive for IFN-γ had a significantly better outcome (lower risk of revision ESS) than patients with IFN-γ–negative samples [36]. In contrast, Gan and colleagues reported no significant difference in the rate of endoscopic recurrence 1 year after ESS in patients who tested positive versus negative for IFN-γ. However, they did note that the mean IFN-γ level was significantly lower in patients who experienced recurrence than in those who did not (p=0.001) [55]. Other researchers found that IFN-γ was not a significant independent predictor of outcomes

Table 4. Accuracy, sensitivity and specificity of biomarkers predictive of outcome in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	Predictive factor	Outcome	AUROC	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Tissue parameters								
Lou 2015 [125] China	Eosinophil count	Endoscopic recurrence (± symptoms) over 24 months	0.969	55/HPF	87.4	97.1	–	–
	Eosinophil percentage		0.969	27%	96.7	92.5	–	–
Meng 2019 [112] China	Eosinophil count	Endoscopic recurrence (± symptoms) over 24 months	0.916	–	–	–	–	–
	Eosinophil percentage		0.801	–	–	–	–	–
Qi 2020 [130] China	Eosinophil percentage	Endoscopic + symptomatic recurrence	0.928	30	92.0%	84.6	–	–
Deng 2022 [151] China	Eosinophil percentage	Repeat surgery	0.741	25.6%	70.8	80.6	–	–
	SERPINB10 level		0.773	2.34	79.1	91.7	–	–
	Eosinophil percentage + SERPINB10 level		0.917	as above	95.8	83.3	–	–
Chen 2022 [121] China	CRTH2 expression	Endoscopic recurrence in 1 year	0.911	5	87.5	85.7	–	–
	Eosinophil count		0.735	–	–	–	–	–
Wang 2022 [135] China	Eosinophil count	Endoscopic + symptomatic recurrence	0.792	–	–	–	–	–
	Eosinophil percentage		0.875	–	–	–	–	–
Wu 2022 [138] Taiwan	Eosinophil percentage	Endoscopic + symptomatic recurrence	0.916	26.125	94.1	87.5	91.3	87.2
Gong 2023 [160] China	HO-1 level	Symptomatic recurrence	0.800	–	–	–	–	–
Biomarkers non-sinonasal surface								
Qi 2020 [130] China	CLC mRNA level (log2 normalised to GAPDH)	Endoscopic + symptomatic recurrence	0.932	–6.419	92.0	88.5	–	–
Wu 2021 [138] Taiwan	CLC protein level		0.933	34.2 ng/mL	92.6	87.5	92.6	87.5
Zhang 2022 [139] China	IL-5 level	No olfactory improvement	0.743	–	95.5	52.6	–	–
	Periostin level		0.648	–	95.5	42.1	–	–
Blood parameters								
Boztepe 2016 [141] Turkey	NLR	Symptomatic recurrence	0.693	3.13	48.5	84.9	41.0	88.4
	PLR		0.631	208.7	39.4	88.9	–	–
Brescia 2016 [120] Italy	NLR	Endoscopic recurrence	0.600	1.7	58.3	55.2	24.6	84.1
	ELR		0.678	0.1	66.7	63.0	31.1	88.3
	BLR		0.662	0.02	66.7	89.6	61.5	91.5
Ninomiya 2018 [129] Japan	Serum periostin levels	Endoscopic recurrence	0.595	115.5 ng/mL	60.7	61.9	–	–
Meng 2019 [112] China	Eosinophil count	Endoscopic recurrence (± symptoms) over 24 months	0.540	–	–	–	–	–
	Eosinophil percentage		0.578	–	–	–	–	–
Lu 2020 [127] China	Serum ECP level	Endoscopic recurrence despite rescue therapy	0.729	21.8 µg/L	77.8	73.5	–	–
Chen 2022 [121] China	Eosinophil count	Endoscopic recurrence in 1 year	0.783	–	–	–	–	–
Wang 2022 [135] China	Eosinophil percentage	Endoscopic and symptomatic recurrence	0.694	–	–	–	–	–
	Serum BAFF level		0.842	–	–	–	–	–
Wang 2022 [136] China	Eotaxin	Recurrence	0.753	43.6	66.7	80.6	–	–
	G-CSF		0.665	134.0	50.0	86.1	–	–
	IL-17A		0.703	9.8	41.7	97.2	–	–
	IL-6		0.666	1.0	44.0	86.1	–	–
	MCP-1		0.642	47.6	41.7	83.3	–	–
	RANTES		0.764	6426.0	63.9	83.1	–	–

Table 4 *legend*. Shading indicates accuracy of predictor based on the area under the receiver operating characteristic (AUROC) curve, where AUROC of 0.5 to 0.6 is considered as failure (orange), 0.6 to 0.7 is considered poor accuracy (light grey), 0.7 to 0.8 fair (blue), 0.8 to 0.9 good (yellow) and ≥0.9 excellent (green). AUROC, area under receiver operating characteristic curve; BAFF, B-cell activating factor; BLR, basophil-to-lymphocyte ratio; CLC, Charcot-Leyden Crystals; CRTH2, chemoattractant receptor-homologous molecule expressed on Th2 cells; ECP, eosinophil cationic protein; ELR, eosinophil-to-lymphocyte ratio; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; G-CSF, granulocyte colony stimulating factor; HO-1, haemoxygenase-1; HPF, high powered field; IL, interleukin; MCP, monocyte chemotactic protein;; mRNA, messenger RNA; NLR, neutrophil-to-lymphocyte ratio; NPV, negative predictive value; PLR, platelet-to-lymphocyte ratio; PPV, positive predictive value; RANTES, Regulated upon Activation, Normal T Cell Expressed and Presumably Secreted; SERPINB10, serine protease inhibitor B10.

based on multivariable regression analysis [128].

Eotaxin-1

Nakayama and colleagues found no significant relationship between tissue levels of eotaxin-1 (also known as C-C motif chemokine [CCL]11) and recurrent disease at 2 or more years after ESS, in a multivariable analysis that adjusted for confounders [128].

Chemoattractant receptor-homologous molecule expressed on T_H2 cells

One study examined the expression of CRTH2 in tissue samples [121], and found that patients who subsequently developed recurrence had significantly higher levels of CRTH2 mRNA and CRTH2-expressing cells compared with those who did not have recurrence, and when compared with healthy controls (p=0.006). They also found that CRTH2 had an AUROC of 0.917, and was a more accurate predictor of recurrence within 12 months of ESS than tissue eosinophil level (AUROC 0.7354), asthma (AUROC 0.6115) or blood eosinophil count (AUROC 0.7083) [121].

Sino-nasal mucosa surface biomarkers (nasal scraping and nasal secretion)

Several studies investigated the relationship between outcomes and markers in sinonasal surface samples (including nasal scraping and collection of nasal secretions) both in patients with CRSwNP alone [31,54,130,138,139] and in mixed populations (Table 3) [66,84]. In these studies, eosinophil levels in nasal scrapings or discharge were associated with worse ESS outcomes; furthermore, weak evidence was observed for an association between the presence of Charcot-Leyden crystals (CLCs) and cytokines (such as IL-5 or periostin) in mucus and poor ESS outcomes [121,137].

Two studies in patients with CRSwNP [31,54] and one in patients with CRS with or without NPs [66] investigated association between eosinophil levels in nasal scrapings or discharge and worse outcome. In the first study in patients with CRSwNP, nasal cytology showing eosinophil counts >20% of total cells were associated with a more than 8-fold increase in the risk of poor disease control at 12 months post-ESS [54]. In this study, neutrophil counts >50% increased the risk of poor disease control by 3-fold, but the presence of both high eosinophil and high neutrophil percentages was associated with a 25-fold increase in the risk [54]. In the second study in patients with CRSwNP, eosinophil counts >20% were associated with a non-significant increase in the risk of repeat ESS within 10 years (OR 1.60; p=0.28). However, when combined with clinical factors such as asthma and/or N-ERD, the association became statistically significant (OR 4.50; p=0.04) [31]. In the mixed population study, the presence of eosinophils in mucus or in mucosal tissue samples significantly increased the risk of recurrent CRS in the 5 years after ESS [66].

Vlaminck and colleagues noted that endoscopic presence of eosinophilic mucin was predictive of CRSwNP recurrence (Table 3) [58]. The combination of eosinophilic mucin and tissue eosinophilia was more predictive of recurrence than eosinophilia alone in patients with CRS with or without NPs [147]. In this study, recurrence rates were even higher in patients with eosinophilic mucin, tissue eosinophilia and fungal hyphae [147].

CLCs are thin hexagonal crystals that form when galectin-10 is released from lysed eosinophils [154]. Two studies in patients with CRSwNP reported that CLCs in nasal secretions were predictive of endoscopic and symptomatic recurrence [130,138]. Although CLC levels were measured differently in the two studies, either as mRNA [130] or as protein [138], the accuracy was remarkably consistent, with AUROC values of 0.932 and 0.933, respectively; the sensitivity (~92%) and specificity (~88%) were also similar in both studies (Table 4).

Other biomarkers, especially cytokines, were also investigated – specifically in secretions. Some authors demonstrated that higher IL-5 levels in nasal secretions were significantly correlated with a higher number of repeated surgeries [155]. Other studies demonstrated that IL-5 levels in nasal secretions were a significant independent predictor of poor olfactory function at 3–6 months after ESS in patients with CRSwNP, but the accuracy was only fair, based on the AUROC of 0.743 (Table 4) [139].

The accuracy of a model incorporating IL-5 with eotaxin 3 and periostin levels in nasal secretions, tissue eosinophil counts, SNOT-22 scores, CT modified olfactory zone scores, sinus scores and endoscopic scores had good accuracy (AUROC 0.824; sensitivity 80.0%; specificity 63.3%) [139]. A study in a mixed population reported that elevated levels of macrophage inflammatory protein (MIP)-1α and CCL17 were significant predictors of poor disease control after ESS [84].

Table 5. Biomarkers in tissue or blood, or histopathological features on biopsy samples that were investigated as predictive markers of surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Voegels 2005 [134] Brazil	39	Prospective, observational	Mucosal cytokines	Recurrent NP for 18 months post-ESS	Pre-operative IL-1 and IL-5 levels were significantly higher in patients with vs without recurrence (p<0.001)	IV	12	Poor
Calus 2019 [140] Belgium	47	Prospective	IL-5 and other biomarkers	Endoscopic score 6- and 12-years post-ESS	Significantly better symptom score and total nasal endoscopic polyp score compared with before surgery (p<0.001); patients with detectable IL-5 in tissue have an increased risk for the need of revision surgery over time	III	22	Good
Van Zele 2014 [36] Belgium	36	Case control	Mucosal cytokine profile	Need for revision surgery	Compared with patients undergoing primary ESS, those undergoing revision surgery had significantly higher levels of IgE to SE (p<0.0001), ECP (p=0.002) and IL-5 (p=0.017). The risk of revision was significantly lower in patients with samples positive for IFN-γ (OR 0.047; 95% CI 0.0079–0.29)	IV	15	Fair
Nakayama 2016 [128] Japan	36	Retrospective	Tissue levels of CCL11, IL-5 and IFN-γ	Recurrent CRSwNP >2 years post-ESS	After adjustment for confounders, tissue IL-5 mRNA level was a significant predictor of severe mucosal oedema (p=0.03)	III	16	Fair
Corredera 2018 [122] USA	24	Prospective, observational	TIM3-expressing mast cells in NPs	SNOT-22 and LKS at 90 days post-ESS	TIM3+ mast cells were seen in both epithelial and stromal layers, but were more prevalent in the epithelium (p=0.001). With increasing mast cell percentage, there was a correlative worsening in endoscopic severity based on comparing pre- and post-operative LKS (p=0.029). In the subgroup of patients with asthma, increased percent of TIM3+ mast cells correlated with worse post-operative LKS (p=0.001). Pre-operative oral CS did not affect mast cell numbers or their influence on worse post-operative endoscopic disease severity (p=0.020)	IV	14	Poor
Ninomiya 2018 [129] Japan	369	Prospective, observational	Serum periostin levels	Endoscopic confirmation of NP recurrence with symptoms of CRS or purulent discharge for ≥28 days post-ESS	Serum periostin level ≥115.5 ng/mL was predictive of recurrence (p=0.0072); AUROC was 0.595, sensitivity 60.7%, specificity 61.9%	IV	14	Poor
Wei 2018 [215] China	78	Prospective, observational	Tissue cytokine levels	Recurrent NP for 8 years post-ESS	Four clusters identified based on the predominant inflammatory cytokine profile: (1) IL-6, IL-8, MPO, IL1β and TGF-β1; (2) IgE, ECP, IL-5 and IgE specific for SE; (3) IL-17, and (4) TNF-α and IFN-γ. Recurrence was highest in cluster 1 (72.7%), followed by cluster 2 (15.4%) and cluster 3 (7.7%) and lowest in cluster 4 (5.3%)	III	16	Fair
Qi 2020 [130] China	51 + 20 controls	Retrospective	CLC mRNA level in nasal cytology	Endoscopic evidence of NP + ≥1 symptom lasting ≥1 week despite intranasal CS	After adjustment for confounders, CLC mRNA level was a significant predictor of recurrence (OR 2.880; 95% CI 1.214–6.832; p=0.016). A CLC mRNA cut-off of –6.419 (normalised to GAPDH mRNA and log2 transformed) had an AUROC of 0.932, sensitivity of 92.0% and specificity of 88.5%. Tissue eosinophil percentage was also predictive (OR 1.07; 95% CI 1.015–1.13; p=0.011) with AUROC of 0.928, and 30% cut-off having sensitivity of 92.0% and specificity of 84.6%	III	18	Fair
Huang 2020 [124] China	21 + 12 controls	Prospective, observational	IL-17A expression in nasal tissue	LKS at 6 months post-ESS	Pre-operative IL-17A expression was negatively correlated with the reduction in LKS at 6 months post-ESS rs= –0.58 (p=0.006)	III	16	Fair
Lu 2020 [127] China	58	Prospective, observational	Serum ECP level	Endoscopic evidence of NPs and mucopus for ≥2 months despite rescue therapy	On multivariate regression analysis, serum ECP level ≥21.8 µg/L was a significant predictor of recurrence (OR 54.80; 95% CI 2.30–1327.30; p=0.014), with sensitivity of 77.8%, specificity of 73.5%, NPV of 35.0% and PPV of 94.7% The 1-year recurrence rate was 5.3% in patients with ECP <21.8 and 35.0% in those with ECP ≥21.8 µg/L (HR 7.6; 95% CI 1.6–36.8; p=0.011)	III	16	Fair
Rosati 2020 [131] Italy	44	Prospective, observational	Tissue eosinophilia (>20% of total cells), IL-5 reactivity in polyp tissue	Endoscopic or CT evidence of recurrent polyposis + symptoms in 8–10 years after surgery	The proportion of patients with pre-ESS eosinophilia was significantly higher in patients with vs without recurrent polyposis (77.8% vs 26.9%; p<0.05), as was the proportion of patients with high IL-5 reactivity prior surgery (88.9% vs 30.8%; p<0.05)	IV	13	Poor

Table 5 *continued*. Biomarkers in tissue or blood, or histopathological features on biopsy samples that were investigated as predictive markers of surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Pre-operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Bai 2022 [59] USA	94	Prospective, observational, incorporated machine learning	ECP, anti-dsDNA IgG and 18 inflammatory mediators in polyp tissue	Recurrent NPs on endoscopy within 2–5 years after ESS	Log (ECP), log (anti-dsDNA IgG) and log (IL-5) were predictive of polyp recurrence ($p<0.05$ for each)	III	15	Fair
Chen 2022 [121] China	41 + 17 controls	Prospective, case-control	CRTH2 expression in nasal tissue	Recurrent NPs on endoscopy within 12 months post-ESS	CRSwNP patients with recurrence had significantly higher levels of CRTH2 mRNA vs without recurrence ($p=0.04$) and vs controls ($p=0.006$) and more CRTH2-expressing cells ($p=0.03$ and $p<0.001$, respectively). Using a threshold of >5 CRTH2-expressing cells, CRTH2 expression was an accurate predictor of recurrence (AUROC 0.917, sensitivity 87.5%, specificity 85.7%), with greater accuracy than tissue eosinophil number (AUROC 0.7354), asthma (AUROC 0.6115) and blood eosinophil number (AUROC 0.7083)	III	17	Fair
Wang 2022 [135] China	120 + 60 controls	Prospective, observational	Blood and tissue eosinophil percent, tissue eosinophil count (cells/HPF), serum BAFF level	Endoscopic evidence of recurrence + symptoms lasting ≥1 week despite intranasal CS for 36 months post-ESS	After adjustment for potential confounders, the following were significant predictors of recurrence: blood eosinophil percent (OR 2.16; 95% CI 1.19–4.2936; $p=0.006$), tissue eosinophil count (OR 2.67; 95% CI 1.312–5.798; $p=0.025$), tissue eosinophil percent (OR 3.57; 95% CI 1.926–7.04; $p<0.001$) and serum BAFF level (OR 3.31; 95% CI 1.47–6.85; $p<0.001$). Based on AUROC, serum BAFF level (0.842; $p<0.001$) and tissue eosinophil percent (0.875; $p<0.001$) were more accurate predictors than tissue eosinophil count (AUROC 0.792; $p<0.001$) or blood eosinophil percent (0.964; $p=0.002$)	III	16	Fair
Wang 2022 [136] China	72 (primary cohort) + 120 (validation cohort)	Prospective, case control	Serum levels of 30 cytokines	Primary vs revision surgery	Serum levels of eotaxin, IL-17A and RANTES were significantly higher in patients undergoing recurrent vs primary ESS in both cohorts ($p<0.05$). Accuracy was greater with eotaxin levels (AUROC 0.729 [$p<0.001$], sensitivity 65.0%, specificity 70.0%) or RANTES levels (AUROC 0.776 [$p<0.001$], sensitivity 66.7%, specificity 75.0%) than with IL-17A levels (AUROC 0.617 [$p=0.027$], sensitivity 81.7%, specificity 41.7%)	III	16	Fair
Zhang 2022 [139] China	85	Prospective cohort	Mucus cytokine levels and tissue eosinophil count	Olfactory function using T&T at 3–6 months post-ESS	In multivariate regression analysis, IL-5 level in nasal mucus was a significant predictor of poor olfactory function (OR 1.88; 95% CI 1.08–3.27; $p<0.05$). The AUROC was 0.743 ($p<0.001$), sensitivity 95.5% and specificity 52.6%. A predictive model that included levels of IL-5, eotaxin-3, periostin, tissue eosinophil count, SNOT-22 score, modified olfactory zone score on CT, LMS and LKS had AUROC of 0.824, sensitivity 80.0%, and specificity of 63.3%	III	18	Fair
Deng 2022 [151] China	60	Case-control (primary surgery vs repeat surgery patients)	SERPINB10 expression in nasal tissue	Repeat surgery	Tissue SERPINB10 mRNA and protein levels and immunoreactivity, were significantly higher in patients undergoing repeat vs primary ESS (all $p\leq0.005$). Tissue SERPINB10 level was associated with a significantly increased risk of recurrent surgery (OR 1.98; 95% CI 1.15–3.43; $p=0.014$); levels ≥2.34 had AUROC 0.773 ($p<0.001$), sensitivity of 79.1% and specificity of 91.7%, and showed greater accuracy than a tissue eosinophil percentage ≥25.6% (AUROC 0.741 [$p=0.002$], sensitivity 70.8%, specificity 80.6%). The combination of both SERPINB10 level and tissue eosinophil percent had AUROC of 0.917 ($p=0.001$), sensitivity of 95.8% and specificity of 83.3%	III	16	Fair
Zhang 2026 [97] China	312	Retrospective	Preoperative serum levels of inflammatory markers (eotaxin-1, periostin, IL-5, total IgE)	Recurrence after ESS	LASSO and multivariate analyses identified as independent predictors serum eotaxin-1 level (OR = 1.02 per pg/mL), and serum periostin level (OR = 1.04 per ng/mL).	III	18	Fair

Table 5 *legend*. AUROC, area under receiver operating characteristic curve; BAFF, B-cell activating factor; BLR, basophil-to-lymphocyte ratio; CCL, C-C motif chemokine; CI, confidence interval; CLC, Charcot-Leyden Crystals; CRS, chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; CRTH2, chemoattractant receptor-homologous molecule expressed on T_H2 cells; CS, corticosteroids; CSS, Chronic Sinusitis Survey; CT, computed tomography; ds-DNA, double-strand DNA; E/M, ethmoid-to-maxillary; ECP, eosinophil cationic protein; ELR, eosinophil-to-lymphocyte ratio; EMCRS, eosinophilic mucin chronic rhinosinusitis; EPOS, European Position Paper on Rhinosinusitis and Nasal Polyps; ERM, eosinophilic-rich mucin; ESS, endoscopic sinus surgery; FESS, functional endoscopic sinus surgery; FeNO, fraction of exhaled nitric oxide; GAPDH, glyceraldehyde 3-phosphate dehydrogenase; HPF, high powered field; HR, hazard ratio; IFN, interferon; Ig, immunoglobulin; IL, interleukin; LKS, Lund-Kennedy score; MPO, myeloperoxidase; mRNA, messenger RNA; NLR, neutrophil-to-lymphocyte ratio; NP(s), nasal polyp(s); NPV, negative predictive value; OR, odds ratio; PBMC, peripheral blood mononuclear cells; PPV, positive predictive value; QoL, quality of life; RANTES, Regulated upon Activation, Normal T Cell Expressed and Presumably Secreted; ROC, receiver operating characteristic; RR, relative risk; RSDI, Rhinosinusitis Disability Index; SE, *Staphylococcus aureus* endotoxins; SERPINB10, serine protease inhibitor B10; SF-36, 36-item Short Form health survey; SNOT-22, 22-item SinoNasal Outcome Test; T&T, Toyota & Takagi; TGF, transforming growth factor; TIM3, transmembrane immunoglobulin and mucin domain protein 3; TNF, tumour necrosis factor; VEGF, vascular endothelial growth factor; vs, versus.

Biomarkers in peripheral blood samples

Twenty-three studies investigated biomarkers in pre-operative peripheral blood samples, with 20 evaluating patients with CRSwNP alone [38,43,47,52,54,55,90,91,93-95,97,112,119,120,123,127,129,135,136] and three including mixed populations (Table 3) [84,141,142]. We summarised in Table 4 the most interesting results especially when authors included ROC analyses reporting AUROC, specificity and sensitivity.

White blood cells including blood eosinophilia

Among the different white blood cell types, blood eosinophil count was among the most frequently evaluated parameters, although with contradictory results; half of the studies supported an association [43,120], while the others did not [30,39, 102, 142] (Table 3).

Brescia and colleagues reported significantly higher pre-operative levels of eosinophils and basophils in patients who developed recurrence than in those who did not [43,120], and defined predictive thresholds for a range of serum parameters (Table 4). Guo and colleagues also reported serum eosinophil counts and percentages to be predictive for the risk of recurrence after ESS [123]. The predictive threshold of eosinophil count for revision ESS was remarkably similar in the studies by Brescia and colleagues and Guo and colleagues (240 and 250 x 10^9 cells/μL, respectively; Table 6) [43,123]. On the other hand, other studies did not demonstrate a relationship between peripheral cell counts or percentages and outcomes [30,39,102,142]. In this study serum eosinophil count showed poor accuracy for predicting recurrence as reported in Table 4.

In summary, eosinophils are the most commonly studied white blood cells in relation to predictive outcomes of ESS. As described above, the evidence is contradictory, with AUROC values (between 0.5 and 0.7) suggesting poor predictive performance (Table 4). For this reason, peripheral blood eosinophil counts themselves may not be a reliable predictive factor of poorer post-operative outcomes and further studies are needed. A key challenge with laboratory test results and tissue cell counts is their high intra-individual variability, influenced by several factors such as smoking, medications (corticosteroids, biologics), infections and seasonal changes.

Real-life studies in patients with CRSwNP demonstrated that combining laboratory markers with clinical history may enhance the accuracy of predicting the risk of uncontrolled CRSwNP following surgery [156,157]. Nevertheless, further studies are required for a more reliable predictive model.

Finally, rather than examining the levels of individual cell types, the ratios of different white blood cell types to each other were investigated for predictability of recurrence of NPs. Authors demonstrated that ratios were significantly predictive of endoscopic and symptomatic recurrence (Table 3) [120]. Nevertheless, these ratios demonstrated limited clinical utility, with AUROC values (between 0.6 and 0.7) suggesting poor predictive performance (Table 4).

Other molecular biomarkers in the peripheral blood

Peripheral blood biomarkers with potential predictive value of post-ESS outcomes that were investigated included periostin [129], eotaxin and ECP [127,136], serum IL levels (IL-5, IL-17) [136,139], monocyte chemotactic protein (MCP), MIP, Regulated upon Activation, Normal T cell Expressed and presumably Secreted (RANTES), CCL17, granulocyte colony stimulating factor (G-CSF), B-cell-activating factor [84,135,136], cathepsin D, serine protease inhibitor B10 (SERPINB10), epithelial membrane antigen, complement component 3 (C3), CD86 and receptor for advanced glycation end products [151,158,159], tissue gamma-delta (γδ)T-cells and haemoxygenase-1 (HO-1) [160,161], expression of Toll-like receptor (TLR)2, TLR9 and MIP-1α [162,163] (Table 5).

Although many of these biomarkers were found to be significantly predictive of ESS outcomes, the accuracy for prediction of recurrence varied. For some biomarkers, such as periostin, IL-6, G-CSF and MCP-1, predictive accuracy was low (AUROC <0.7). Others demonstrated fair accuracy – eotaxin (AUROC 0.753), ECP

Table 6. Thresholds for serum blood cell levels that predict the re-appearance of endoscopic nasal polyps over the years after ESS in patients with chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps

	Threshold	OR for recurrence (95% CI)	P-value
Patients with CRSwNP			
Eosinophil count (43) [a]	240 cells/μL	2.57 (1.33–5.06)	0.003
Eosinophil count (123) [b]	250 cells/μL	3.63	–
Eosinophil percent (43) [a]	3.7%	2.19 (1.15–4.24)	0.0112
Eosinophil percent (123) [b]	2.6%	5.12	–
Basophil count (43) [a]	30 cells/μL	2.19 (1.15–4.24)	0.0115
Basophil percent (43) [a]	0.5%	2.24 (1.17–4.38)	0.011
ELR (120) [c]	0.14	–	–
BLR (120) [c]	0.02	–	–
NLR (120) [c]	1.76	–	–
Patients with CRSwNP or CRSsNP			
NLR (141) [d]	3.13	1.57 (1.14–2.18)	0.006

[a] Recurrence defined as endoscopic evidence of grade ≥1 polyposis during a median of 30 months after ESS. [b] Recurrence defined as ≥2 episodes of endoscopic polyp recurrence grade ≥1 during 12–15 months after ESS. [c] Recurrence defined as endoscopic evidence of grade ≥1 polyposis during a median of 36 months after ESS. [d] Recurrence defined as recurrence of symptoms within 21–30 (average 25) months of ESS.
BLR, basophil-to-lymphocyte ratio; CI, confidence interval; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; ELR, eosinophil-to-lymphocyte ratio; ESS, endoscopic sinus surgery; NLR, neutrophil-to-lymphocyte ratio; OR, odds ratio.

(AUROC 0.729), IL-17A (AUROC 0.703), IL-5 (AUROC 0.743) and RANTES (AUROC 0.764)] – while only BAFF showed good predictive performance (AUROC 0.842; Table 4).
At present, local biomarkers (tissue biopsy or epithelial surface biomarkers) appear to be more reliable in predicting the surgical success of ESS in comparison with systemic/peripheral blood markers. Consequently, they seem to offer broader clinical applicability.

Novel or emerging experimental biomarkers

Some novel emerging experimental biomarkers measured peri-operatively in tissue and/or blood, were associated with an increased risk of poor disease control following ESS [151,158,159]. We summarize the studies reporting these factors including cathepsin D activity [159], SERPINB10 mRNA and protein levels [151], stromal expression of epithelial membrane antigen (EMA) and CD86 [158] and receptor for advanced glycation end products (RAGE) [164] (Table 7).
Other interesting results were obtained studying the tissue γδT-cells and HO-1 that were linked to worse outcomes and increased recurrence risk [161]. HO-1 also showed good accuracy (AUROC 0.80) [152,160].
Elevated C3 in serum was associated with recurrence in two studies [162,163]. Additionally, low expression of TLR2, TLR9 and amyloid A, and high MIP-1α in tissue predicted endoscopic recurrence [162,163]. Despite these promising preliminary results, clinical applicability remains limited.

Microbiological factors

There were 12 studies investigating the impact of microbiological factors on outcomes (Table 8), with five studies involving patients with CRSwNP alone [55,96,111,165,166] and seven in mixed cohorts [68,167-172]. The studies evaluated the impact of the nasal microbiome on outcomes after ESS, focusing on bacterial profiles and biofilm presence. Post-ESS outcomes were worse in patients with a lower titre of *Corynebacterium* and *Actinobacteria* and higher *S. aureus* levels [55]. Biofilm presence was linked to worse post-operative symptoms and endoscopy scores. *S. aureus* and *Pseudomonas aeruginosa* colonisation correlated with higher rates of repeat ESS [172]. Conversely, intracellular *S. aureus* did not predict clinical outcomes post-ESS [169].
The association between microbial factors and ESS outcomes remains preliminary, with the quality of most studies being fair, thus their clinical applicability is still uncertain. Conversely, studies on microbiome, biofilm and bacterial colonisation have yielded interesting results.

Sinus microbiome

Five studies investigated the impact of the nasal or sinus microbiome on outcomes; four in patients with CRSwNP [55,111,166] and one in a mixed cohort [170]. The retrospective study by Lee and colleagues compared outcomes at 6 months after ESS in patients with CRSwNP and found that pre-operative secretions from the middle meatus contained either no bacteria (a negative culture), normal bacteria or non-normal bacteria [111]. Among

Table 7. Experimental or novel biomarkers investigated for their relationship to surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N	Type of study	Operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
In patients with CRSwNP-only								
Pawlowska-Goral 2013 [159] Poland	24	Case-control (primary ESS vs repeat surgery patients)	Cathepsin D activity in resected NPs	Repeat surgery	Mean cathepsin D activity was significantly higher in patients undergoing repeat surgery than in patients undergoing primary ESS ($p \leq 0.05$)	IV	11	Poor
Batzakakis 2014 [158] Greece	42	Case-control (primary ESS vs repeat surgery patients)	Mucin-1, EMA, CD86, CD54 (ICAM-1), c-myc oncogene in resected nasal cells and NP stromal cells	Repeat surgery	Patients in the repeat surgery group had significantly higher expression of EMA ($p<0.001$) and CD86 ($p=0.021$) in stromal cells. In logistic regression, stromal EMA was significantly associated with repeat surgery (OR 1.09; 95% CI 1.02–1.17; $p<0.001$)	IV	15	Fair
Dzaman 2015 [164] Poland	25 + 26 controls	Case-control (repeat surgery patients vs healthy controls)	HMGB1 and RAGE expression in sinonasal mucosa	Repeat surgery	There was no difference in HMGB1 expression between patients and controls. Patients undergoing repeat ESS had significantly higher RAGE expression compared with healthy controls ($p<0.0000001$). RAGE expression significantly correlated with higher LMS ($p<0.00001$), NP size ($p<0.00013$) and number of prior sinus surgeries ($p=0.04$)	IV	14	Poor
Lee 2017 [161] China	36 [a]	Retrospective, observationala	γδT-cells in NP tissue	Repeat surgery for 12 months post-ESS	15/27 patients (55.6%) with samples positive for γδT-cells developed recurrence compared with 1/8 patients (12.5%) who were negative for γδT-cells ($p=0.02$). Pre-operative γδT-cell expression was associated with higher tissue eosinophil count, worse nasal obstruction severity and higher LKS (all pre-operative)	IV	13	Poor
Wang 2020 [163] China	97 + 30 controls	Retrospective case-control	Serum complement C3 level	NP of grade ≥1 on endoscopy for 15 months post-ESS	Pre-operative and post-operative C3 levels were significantly higher in patients who later developed recurrence vs those who did not ($p=0.01$); at the time of recurrence, C3 levels were comparable with the original pre-operative level (mean 109.6 vs 112.2 mg/dL, respectively)	IV	16	Fair
Deng 2022 [151] China	60 [b]	Case-control (primary ESS vs repeat surgery patients)	SERPINB10 expression in nasal tissue	Repeat surgery	Tissue SERPINB10 mRNA and protein levels, and immunoreactivity, were significantly higher in patients undergoing repeat vs primary ESS (all $p \leq 0.005$). Tissue SERPINB10 level was associated with a significantly increased risk of recurrent surgery (OR 1.98; 95% CI 1.15–3.43; $p=0.014$); levels ≥2.34 had AUROC 0.773 ($p<0.001$), sensitivity of 79.1% and specificity of 91.7%, and showed greater accuracy than a tissue eosinophil percentage ≥25.6% (AUROC 0.741 [$p=0.002$], sensitivity 70.8%, specificity 80.6%). The combination of both SERPINB10 level and tissue eosinophil percent had AUROC of 0.917 ($p=0.001$), sensitivity of 95.8% and specificity of 83.3%	IV	16	Fair
Gong 2023 [160] China	32 [c]	Prospective, observationalc	HO-1 expression in maxillary sinus NPs	CRS-related nasal congestion and discharge lasting >1 week and developing 12 months after ESS	HO-1-positive cell counts were negatively correlated with pre-operative SNOT-22 score ($p=0.012$). HO-1 cell count was a significant predictor of recurrence (OR 0.71; 95% CI 0.53–0.94; $p=0.016$), with AUROC of 0.80 ($p=0.004$)	IV	12	Poor

Table 7 *continued*. Experimental or novel biomarkers investigated for their relationship to surgical outcomes in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N	Type of study	Operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Tănase 2025 [174] Romania	30	Prospective, single-centre pilot cohort	Ki-67 expression in nasal-polyp tissue, measured as the mean number of immunohistochemically positive cells in five randomly selected HPFs	Endoscopically confirmed nasal-polyp recurrence at 6 months after ESS; SNOT-22 score	Recurrence occurred in 9/30 patients. Mean Ki-67 expression was higher in patients with recurrence than in those without recurrence (74.3 ± 11.1 vs 53.1 ± 11.6 positive cells/HPF; p=0.003). Ki-67 expression was positively correlated with SNOT-22 scores (r=0.42; p=0.02). No multivariable analysis, prognostic cut-off or AUROC was reported.	III	14	Poor
In a mixed population of patients with CRSwNP/CRSsNP								
Lane 2006 [162] USA	30 + 10 controls	Prospective, observational	Markers of innate immunity (TLR1–10, GAPDH, β-actin, HPRT, MIP-1α, RANTES, GMCSF, TNF-α, complement factor B, complement factor P, C3, 18s mRNA)	Recurrence or persistent of NPs on endoscopy in 6–9 months post-ESS	Significantly lower expression of TLR2 (p=0.003), TLR9 (p=0.002) and serum amyloid A (p=0.04), and higher expression of MIP-1α (p<0.05) was seen in tissue from patients who later developed recurrent/persistent CRS vs those who did not develop recurrence	IV	11	Poor

Table 7 *legend*. [a] This study also included a comparison of CRSwNP patients with CRSsNP patients (n=25) and healthy controls (n=27) which were evaluated in a retrospective case-control analysis; the analysis of relationship to recurrence was evaluated in a prospective observational analysis limited to patients with CRSwNP, so these data are tabulated here. [b] This study also included a comparison of CRSwNP patients with CRSsNP patients (n=40) and healthy controls (n=40), but the analysis of relationship to recurrence was limited to patients with CRSwNP, so these data are tabulated here. [c] This study also included a comparison of CRSwNP patients with CRSsNP patients (n=31) and healthy controls (n=14), which were evaluated in a case-control analysis; the analysis of relationship to recurrence was evaluated in a prospective observational analysis limited to patients with CRSwNP, so these data are tabulated here.

AUROC, area under the receiver operating characteristic curve; C3, complement component 3; CI, confidence interval; CRS, chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; EMA, epithelial membrane antigen; ESS, endoscopic sinus surgery; γδ, gamma-delta; GAPDH, glyceraldehydr-3-phosphate dehydrogenase; GMCSF, granulocyte-macrophage colony stimulating factor; HMGB1, high mobility group box 1; HO-1, haemoxygenase-1; HPRT, hypoxanthine phosphoribosyltransferase; ICAM-1, intercellular adhesion molecule 1; LKS, Lund-Kennedy score; LMS, Lund-Mackay score; MIP-1α, macrophage inflammatory protein 1α; mRNA, messenger RNA; NP(s), nasal polyp(s); OR, odds ratio; RAGE, receptor for advanced glycation end products; RANTES, Regulated upon Activation, Normal T Cell Expressed and Presumably Secreted; SERPINB10, serine protease inhibitor B10; SNOT-22, 22-item SinoNasal Outcome Test; TLR, Toll-like receptor; TNF, tumour necrosis factor; vs, versus.

patients with normal or non-normal bacterial flora, there was no difference in the incidence of a poor versus good outcome (presence of pathological secretions and/or polypoid mucosa on endoscopy) within 6 months of ESS, but in patients with a negative culture, only 2/16 patients (12.5%) had a poor surgical outcome while 14/16 (87.5%) had a good outcome [111].

Two studies investigated the bacterial profile of nasal secretions from the middle meatus in patients with CRSwNP and its relationship to endoscopic recurrence [55,166]. In both studies, a lower relative abundance of species from the *Corynebacterium* genus was associated with a significantly higher rate of poor outcomes [55,166]. Lower relative abundance of *Anaerococcus* and *Tepidimonas* spp. were also associated with poor 6-month outcomes in one study, such as poor endoscopic improvement (<50%) and the need for revision surgery, antibiotics or SCS [166]. In the other study, lower abundance of *Actinobacteria* spp. and higher levels of *Staphylococcus* spp. were associated with poor 1-year outcomes [55]. Similar results were seen in a separate study

Table 8. Microbiological factors predictive of outcomes after ESS in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
In patients with CRSwNP-only								
Jelavic 2012 [165] Bosnia and Herzegovina	40	Prospective, observational	Sinonasal colonisation with *Helicobacter pylori*	Endoscopic and symptom scores at 1-year post-ESS	Individual and total symptom scores at 1-year post-ESS were not significantly different between patients with vs without H. pylori colonisation, but endoscopic improvement at 1 year was significantly better in the group with vs without H. pylori colonisation (p=0.017)	III	18	Fair
Lee 2014 [111] South Korea	71	Retrospective	Presence of normal bacterial flora, non-normal bacteria or no bacteria in secretions in middle meatus	Presence of pathological secretions and/or polypoid mucosa on endoscopy at 6 months post-ESS	Among 16 patients with a negative culture, 14 (87.5%) had a good surgical outcome, whereas the percentage of patients with a good vs poor outcome was similar in patients with normal flora (46.2% vs 53.8%) or in those with a positive culture of non-normal bacteria (54.8% vs 45.2%)	III	17	Fair
Kim 2020 [166] South Korea	31 + 6 controls	Prospective, observational	Microbiome of nasal secretions in the middle meatus	Endoscopic improvement of <50%, need for revision surgery, antibiotic or systemic CS within 6 months of ESS	Patients who had a suboptimal outcome showed significantly lower relative abundance of Corynebacterium (p=0.049), Anaerococcus (p=0.033) and Tepidimonas genera (p=0.197) compared with patients who had an optimal outcome and healthy controls	III	15	Fair
Gan 2021 [55] China	77	Prospective, observational	Microbiome of nasal secretions in the middle meatus	Endoscopic recurrence of NP during 1-year post-ESS	Patients with recurrent NPs had lower levels of Actinobacteria phyla (p=0.011) and Corynebacterium genera (p=0.0012) and higher levels of Staphylococcus genera (p=0.017) compared with patients who did not have recurrence, but the differences were no longer significant after correction for multiple testing	III	16	Fair
Zhang 2026 [96] China	178	Retrospective	Preoperative nasal-secretion cultures classified as pathogen-negative, bacterial-positive or fungal-positive; bacterial isolates included mainly *Corynebacterium, Staphylococcus* and *Haemophilus influenzae*; fungal isolates included mainly *Candida albicans* and *Aspergillus*	Nasal-symptom VAS, Lund–Kennedy endoscopic score and Lund–Mackay CT score at 12 weeks after ESS; CRSwNP recurrence within 24 months	Early postoperative VAS, Lund–Kennedy and Lund–Mackay scores were progressively worse from the pathogen-negative to bacterial-positive and fungal-positive groups, with significant differences between groups. Microbial culture category was not identified as an independent predictor of recurrence. Corynebacterium colonization showed a non-significant trend toward lower recurrence risk (p=0.065).	III	17	Fair
In a mixed population of patients with CRSwNP/CRSsNP								
Psaltis 2008 [68] Australia	40	Prospective, observational	Presence of biofilm in middle meatus or ethmoid cavity, positive fungal stain or culture	Presence of any ongoing symptoms or any mucosal abnormality for 8 months post-ESS	Overall, patients with biofilms were more likely to have ongoing post-operative symptoms (OR 7.43; 95% CI 1.78–31.10; p=0.01) or ongoing mucosal inflammation (OR 7.00; 95% CI 1.74–28.18; p=0.01), as were patients with fungus (symptoms: OR 5.92; 95% CI 1.27–27.72; p=0.0305; mucosal inflammation: OR 6.37; 95% CI 1.16–34.95; p=0.034)	III	17	Fair
Hochstim 2010 [168] USA	24	Prospective, observational	Biofilm present in the ethmoid sinus	Persistent mucosal inflammation	15/24 patients had biofilm present, and it was extensive (>50% of total mucosal surface) in 7patients. Eight biofilm-positive patients had persistent inflammation compared with 0 biofilm-negative patients (p=0.009)	IV	10	Poor
Singhal 2011 [171] Australia	39	Prospective, observational	Biofilm present in the sinonasal tissue (any biofilm, monobacterial or polybacterial biofilm)	Symptom severity (VAS, SNOT-20, GARS) and endoscopic grade over 12 months after ESS	Compared with patients with single-species biofilms, those with polybacterial biofilms required significantly more follow-up visits (p=0.04), had significantly poorer endoscopy scores (p=0.001). Patients with S. aureus biofilms (when S. aureus was the only or one of several bacteria) had worse symptom VAS and GARS scores compared with other biofilm subgroups	III	18	Fair

Table 8 *continued*. Microbiological factors predictive of outcomes after ESS in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Operative factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Tsou 2013 [172] Taiwan	87 + 80 controls	Prospective, observational	Presence of *Pseudomonas aeruginosa* and SPLUNC1 expression levels in nasal secretions during ESS	Repeat surgery within 6 months	19/42 (45.2%) of patients positive for P. aeruginosa required repeat surgery compared with 3/45 (6.7%) patients who were negative for P. aeruginosa (p<0.001). Non-CRS controls and CRS patients who were negative for P. aeruginosa had significantly higher levels of SPLUNC1 compared with CRS patients who were positive for P. aeruginosa (p<0.001)	IV	13	Poor
Ramakrishnan 2015 [170] USA	56 + 26 controls	Cross-sectional and prospective, observational	Microbiome of secretions from the ethmoid or neighbouring sinus	Optimal outcome (>50% reduction in endoscopy score, no need for antibiotics or systemic CS or no revision surgery needed in 6 months post-ESS	Compared with patients with suboptimal outcomes, those with an optimal outcome had significantly increased abundance of isolates from the Actinobacteria phylum (p=0.016), including Corynebacterium genera (p=0.027). The richness (p=0.049), evenness (p=0.004) and complexity (p=0.005) of baseline microbiota were significantly higher in patients with optimal vs suboptimal outcomes	III	15	Fair
Ou 2016 [169] Australia	40 + 8 controls	Prospective, observational	ICSA in nasal epithelial cells	Infections, symptom severity VAS, SNOT-20 score and LKS for up to 12 months after ESS	There was no difference between ICSA-positive and ICSA-negative patients in symptom severity, endoscopic score, number of additional outpatient consultations, swabs taken for suspected infections, S. aureus-positive swabs or number of antibiotic prescriptions over the 12 months post-ESS	IV	14	Poor
Carey 2017 [167] USA	46	Prospective, observational	Denatonium-stimulated bactericidal activity of cells against *P. aeruginosa* cultured from sinonasal epithelial cells removed during ESS	SNOT-22 scores at 3, 6 and 12 months post-ESS	In patients with CRSwNP, SNOT-22 scores were higher at 3, 6 and 12 months after ESS (significant only at 6 months; p=0.012) in those whose cells were more responsive to denatonium stimulation. No such effect was seen in patients with CRSsNP	III	15	Fair

Table 8 *legend*. CI, confidence interval; CRS, chronic rhinosinusitis; CRSsNP, without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; CS, corticosteroids; ESS, endoscopic sinus surgery; GARS, global assessment of rhinosinusitis symptom severity; ICSA, intracellular Staphylococcus aureus; LKS, Lund-Kennedy score; NP(s), nasal polyp(s); OR, odds ratio; SNOT-20 or -22, 20- or 22-item SinoNasal Outcome Test; SPLUNC1, short palate, lung and nasal epithelium clone 1 protein; VAS, Visual Analogue Scale; vs, versus.

in a mixed population of patients with CRS, which found that a low abundance of bacteria from the *Actinobacteria phylum* or *Corynebacterium* genus in secretions of the ethmoid or neighbouring sinuses were associated with poorer endoscopic or clinical outcomes in the 6 months after ESS [170].

Biofilms

Three studies examined the relationship between the presence of biofilm (a complex, organised community of bacteria/fungi that anchor to surfaces of tissues [173]) in sinonasal tissue and outcomes following ESS, in mixed cohorts [68,168,171]. In all three studies, patients with biofilm present had worse outcomes in terms of post-operative symptoms [68], ongoing mucosal inflammation [68,168], endoscopy scores [171] and the need for follow-up visits [171]. One study noted that post-operative symptom scores were worse in patients who had *S. aureus* present as the only or as one of several bacteria (*S. aureus*, *Haemophilus influenzae*, *P. aeruginosa*, fungi) in the biofilm [171].

Colonisation by other bacteria

One study in patients with CRSwNP showed that those with sinonasal *Helicobacter pylori* colonisation had significantly better improvement in endoscopic scores and slower polyp regrowth at 1 year after ESS compared with patients who did not have *H. pylori* colonisation [165]. However, *H. pylori* was not prognostic for symptomatic improvement.

On the other hand, the presence of *P. aeruginosa* in nasal secretions at the time of ESS was associated with a higher rate of repeat ESS within 6 months in patients with either CRSwNP or CRSsNP [172]. The extent to which *P. aeruginosa* contributes to post-surgical outcomes may be partially mediated by the patient's innate immune system and the ability of their sinonasal cells to protect themselves against such infections. Compared with *P. aeruginosa* positive patients, those who were negative for *P. aeruginosa* had significantly higher levels of the short palate, lung and nasal epithelium clone 1 (SPLUNC1), a protein that protects mucosal surfaces against infection [172]. A separate study showed that patients whose sinonasal cells showed bactericidal effects against *P. aeruginosa* had better SNOT-22 scores at

Table 9. Surgical or peri-operative treatment factors and post-operative treatment factors in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
In patients with CRSwNP-only								
McMains 2006 [181] USA	15	Prospective, cohort	Post-operative aspirin desensitisation for patients with Samter's triad	SNOT-22, CT score, endoscopy score, revision surgery within 24 months	Among the patients with Samter's triad, 0/5 who had aspirin desensitisation required revision surgery vs 8/10 patients who did not undergo aspirin desensitisation (p=0.003)	IV	15	Fair
Wright 2007 [189] Canada	26	Prospective, randomised, double-blind	Oral prednisone 30 mg/day for 5 days before and 9 days after ESS	Operative difficulty, symptom VAS, LKS, POSE score	During ESS, patients in the placebo group had more inflamed mucosa and more difficult ESS vs patients in the prednisone group. Total endoscopy scores were significantly lower in the prednisone vs placebo group (p=0.02) and LKS, POSE, and symptoms severity tended to be higher (worse) in the placebo vs prednisone group at all timepoints, albeit not statistically significant	II	23	Good
Kang 2008 [179] South Korea	32	Prospective, open-label comparison	Post-operative topical CS (daily low-dose vs weekly high-dose)	Recurrent NPs on endoscopy within 1 year of revision ESS	The incidence of post-operative NPs was significantly lower in the group receiving weekly high-dose topical CS (7.1%) than in the group receiving daily low-dose CS (44.4%; p=0.04)	II	17	Fair
Vuralkan 2011 [187] Turkey	50	Prospective, randomised, open-label comparison	Post-operative intranasal mometasone vs oral montelukast	Recurrent polyposis, SNOT-22 score LMS, tissue eosinophil count at 6 months post-ESS	12/25 patients (48%) receiving montelukast vs 5/25 (20% receiving mometasone developed nasal polyp recurrence. Montelukast was associated with a significant improvement in sense of smell vs mometasone (p<0.05), but there were no significant differences between groups in other outcomes assessed	II	14	Poor
Vento 2012 [186] Finland	60	Prospective, randomised, double-blind comparison	Intranasal triamcinolone acetate vs placebo	Polyp size, symptoms, rhinomanometric parameters, olfactory function at 9 months post-ESS	Triamcinolone significantly reduced polyp size vs placebo at 3 months in patients who did not have aspirin intolerance (p=0.007), but difference was no significant at 6 or 9 months, and there no difference in patients with aspirin intolerance. There was no difference between triamcinolone and placebo in changes in symptoms, nasal resistance, nasal volume or sense of smell	II	20	Good
Bassiouni 2013 [34] Australia	299 (338 surgeries)	Retrospective cohort	Type of ESS (standard or Draf 3 drillout)	Recurrent NPs on CT (LKS ≥3)	Draf 3 surgery was associated with a lower rate of recurrence (p=0.060)	III	18	Fair
Kim 2013 [180] South Korea	30	Prospective, comparative	Maxillary sinus saline irrigation with pressure device 9 times in first 2 months post-ESS	Endoscopic score; presence of poor outcome (NPs or extensive granulation tissue on endoscopy or uncontrolled purulent discharge) at 3 months post-ESS	1/15 patients having maxillary sinus irrigation had a poor outcome (recurrent NPs) at 3 months compared with 7/15 in the standard treatment group (p=0.035; recurrent NPs: n=1; extensive granulation tissue: n=1; uncontrolled purulent discharge: n=2; extensive granulation tissue + uncontrolled purulent discharge: n=3); total endoscopic scores at 3 months were significantly worse in the group receiving standard care vs maxillary sinus irrigation (p=0.01)	III	16	Fair
Saafan 2013 [182] Egypt	200	Randomised, prospective comparison	Microdebrider vs conventional instruments	Symptoms on VAS, endoscopic score, saccharin clearance test, operative time, surgical conditions, healing, debridement, complications, polyp recurrence	Microdebridement was associated with improved olfaction on VAS (p<0.001), shorter operative time (83 vs 94 minutes; p<0.05), better surgical conditions/dryness of the operative field (p<0.001) and a lower rate of post-operative synechiae (p<0.001) compared with conventional ESS, but all other post-operative changes were similar in the two groups	II	20	Good
Chen 2016 [177] China	42	Prospective comparison with a historical control group	Extensive ESS vs FESS	Symptoms on VAS (0 to 10), respiratory function and asthma control at 1-year post-ESS	In patients with CRSwNP and asthma, extensive ESS was associated with significantly better olfactory function (p=0.015) and endoscopy E-score (p<0.001) at 1-year post-ESS; there was no difference between groups in 1-year respiratory function or ACT	III	17	Fair
Van Gerven 2018 [185] Spain	72	Randomised, open-label comparison	Intranasal CS vs intranasal CS + montelukast	Symptom VAS, polyp size, LMS, olfactory function using BAST-24 at 12 months post-ESS	There was no difference in any outcome in patients who received montelukast + intranasal CS vs those who received intranasal CS alone	II	18	Fair

Table 9 *continued*. Surgical or peri-operative treatment factors and post-operative treatment factors in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
Stryjewska-Makuch 2019 [184] Poland	33	Randomised, open-label comparison	Mometasone nasal spray (S) vs montelukast (P) vs mometasone nasal spray + montelukast (S+P)	SNOT-22, symptom VAS, LKS at 12 months post-ESS	In patients with N-ERD, all treatments were associated with significant improvements in VAS, SNOT-22 and LKS at 12 months post-ESS vs pre-ESS, but the improvement in the LKS was significantly better in the combination therapy group vs S (p=0.015) or vs P (p=0.03)	II	17	Fair
Bogdanov 2020 [175] Germany/ Ukraine/ UK/ Switzerland	52	Randomised, open-label comparison	Use of oral prednisolone 1-4 weeks pre-ESS	Olfactory function using "Sniffin' Sticks"	Pre-operative CS improved olfactory function compared with ESS without pre-operative CS	II	16	Fair
Chauhan 2020 [176] India	120	Prospective randomised comparison	Microdebrider vs conventional instruments	Symptoms on VAS at 3 or 6 months post-FESS	No patients in the microdebrider group developed synechiae vs 25% in the conventional FESS group; symptom severity at 3 and 6 months post-FESS was significantly lower in the microdebrider vs conventional FESS group at 3 (p=0.033) and 6 months (p=0.023)	II	14	Poor
Loftus 2020 [50] USA	536	Retrospective	CS compliance, timing of surgery, type/extent of surgery	Revision surgery ≥6 months after ESS (mean 52.9 months of follow-up)	After adjustment for confounders, ESS before 2009 was associated with an increased risk of revision (OR 2.42; 95% CI 1.26–4.65; p=0.008)	III	20	Good
San Nicoló 2020 [183] Germany	61	Retrospective comparison	SOC alone vs SOC + AD vs SOC + montelukast	Polyp grade on endoscopy, SNOT-22 score, QoL at 6–72 (mean 35) months post-ESS	In patients with N-ERD, AD or montelukast resulted in better polyp grade vs SOC alone and montelukast was associated with significantly greater reductions in cough, ear fullness, ear pain and total SNOT-22 scores compared with AD at >12 months post-ESS	III	17	Fair
Wang 2020 [188] China	104	Randomised, double-blind comparison	Intranasal buffered hypertonic vs physiological saline derived from seawater	SNOT-22 score, symptom VAS, LKS, saccharine clearance time at 2, 8, 16 and 24 weeks post-ESS	There were no significant between-group differences at 2, 16 or 24 weeks post-ESS. At 8 weeks post-ESS, LKS and saccharine clearance times were significantly better in the group using buffered hypertonic vs physiological saline (p=0.01), driven mainly by improvements in patients with non-eosinophilic CRSwNP	II	21	Good
Gomes 2022 [178] Italy	168	Retrospective comparison	Reboot surgery vs ESS	Polyp recurrence, olfactory function in 2 years post-surgery	There was a significantly higher rate of recurrence during 2 years of follow-up in the ESS vs Reboot surgery group (p<0.05). Both types of surgery significantly improved olfactory function over the first 12 months; these improvements were maintained in the Reboot surgery group but worsened in the ESS group and were significantly different at 18 (p=0.007) and 24 months (p=0.001)	III	16	Fair
Ji 2026 [94] China	152	Retrospective	Adherence to postoperative INCS	Recurrence during 6–36 months after ESS	Irregular postoperative INCS use independently predicted recurrence (OR 2.43; 95% CI 1.16–5.11; p=0.019). Regular use was defined as daily treatment during ≥80% of follow-up.	III	16	Fair
Workman 2024 [195] USA	100	Retrospective	Surgical extent evaluated with CoSI	Symptom severity on SNOT-22 at 24 months	SNOT-22 scores improved up to 24 months. Preoperative CoSI scores in revision surgery patients were 49.4 ± 26.0, improving to 91.0 ± 8.1 postoperatively. SNOT-22 scores for primary ESS patients and patients with a preoperative CoSI score of less than 70 improved by 26.4 and 28.1 points, respectively, in contrast to patients with a preoperative CoSI of 70 or greater	III	17	Fair
Yu 2025 [196] USA	70	Retrospective	Prior surgical extent evaluated with CoSI	Impact of CoSI on SNOT-22 and ACT improvements after surgery in CRSwNP with asthma	The CoSI <70 group had a greater average SNOT-22 improvement than the CoSI 70 or greater group from baseline to 2 years postoperatively (30.8 ± 20.5 vs. 20.4 ± 14.9, p = 0.042). In uncontrolled asthma, the average ACT improvement was significantly greater for the CoSI <70 group than the CoSI 70 or greater group (3.9 ± 2.2 vs. 0.88 ± 1.4, p = 0.029)	III	16	Fair

Table 9 *continued*. Surgical or peri-operative treatment factors and post-operative treatment factors in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

Reference	N of patients	Type of study	Factors analysed	Outcomes assessed	Relevant results	Level of evidence	Downs and Black scores	Quality of evidence
In patients with CRSwNP-only								
Bugten 2008 [190] Norway	111	Prospective, randomised comparison	Post-operative saline irrigation vs NAP of the middle meatus or nasal cavity debridement on post-operative days 6 and 12	Symptom severity on VAS 56 weeks post-ESS, acute rhinosinusitis episodes in post-operative weeks 12–56	Compared with saline irrigation, nasal debridement was associated with significantly better improvement in nasal congestion and sneezing in the overall cohort and in patients with CRSwNP; no intervention was better than saline irrigation for preventing acute rhinosinusitis or need for antibiotics	II	16	Fair
Murthy 2013 [70] UK	81	Prospective, observational	Surgical technique	Symptom severity on VAS at 12 months post-ESS	Patients who underwent polypectomy had the greatest improvement in post-operative symptoms ($p<0.001$)	III	16	Fair
Yelverton 2016 [193] Colombia	50	Retrospective	Post-operative montelukast (within-patient comparison of periods of compliance vs noncompliance)	Revision surgery, SNOT-20, LKS for 3–122 (mean 46.5) months post-ESS	13/50 patients (26%) needed revision surgery after stopping montelukast. SNOT-20 scores ($p<0.001$) and LKS ($p=0.002$) were significantly lower during compliance with montelukast vs during lapses; similar trends were seen in most patient subgroups (eosinophilic CRSwNP, Samter's triad, asthma and allergic fungal sinusitis) but did not reach statistical significance in smaller groups (Samter's triad and allergic fungal sinusitis)	III	18	Fair
Galletti 2018 [191] Italy	96	Retrospective comparison	ESS with vs without CAN	LMS, disease recurrence, nasal resistance on rhinomanometry, SNOT-22 score, RhinoQoL, symptom severity on VAS at 1-year post-ESS	Compared with standard ESS, ESS with CAN was associated with significantly lower LMS ($p=0.009$), lower rate of disease recurrence (35% vs 60%; $p=0.014$), less nasal resistance ($p=0.007$), greater reduction in symptoms ($p=0.008$) and greater reductions in symptom frequency ($p=0.004$), bothersomeness ($p=0.004$), and impact ($p=0.002$) at 1-year post-ESS	III	16	Fair
Nanda 2018 [192] India	40	Prospective, randomised, comparison	Daily PPI + SOC vs SOC alone	Signs and symptoms of CRS, patient comfort/relief (Likert scale) at 3 months post-ESS	Patients receiving a PPI had better improvement in symptoms of nasal obstruction, nasal discharge and postnasal drip, and in signs of mucopurulent discharge and mucosal oedema compared with the SOC alone At 3 months, 80% of patients in the PPI group were comfortable or very comfortable compared with 60% in the SOC alone group (OR ~2.6; statistically significant)	II	14	Poor
Li 2020 [197] a China	123	Prospective, randomised comparison	Intranasal dexamethasone twice daily for 6 months vs standard post-operative care	LKS, SNOT-20 score, olfactory function, cure (symptom free, endoscopic healing without oedema or mucinous secretion) at 3, 6 and 12 months post-ESS	Patients who used dexamethasone for 6 months post-operatively had significantly higher cure rates at 12 months (95.2% vs 90.2%; $p<0.05$), as well as significantly better LKS (2.23 vs 7.45; $p<0.05$), SNOT-20 scores (2.10 vs 9.38; $p<0.05$), and olfactory function (normosmia: 93.6% vs 73.8%; $p<0.05$)	II	19	Fair
Huang 2019 [194] China	30	Prospective, randomised comparison	Intranasal budesonide dissolved in normal saline vs normal saline	LKS, and VAS, SNOT-20, SF-36, SAS, and SDS scores	At 3 months, significant improvement in: scores of polyposis, mucosal oedema, secretions and total score of LKS; VAS scores of nasal blockage, hyposmia and rhinorrhoea; and SNOT-22 results in both groups. Scores of polyposis, mucosal oedema, secretions and scarring and total LKS were significantly better in the experimental group than in control group No significant differences were observed in SF-36, SAS or SDS scores before or 3 months after ESS within or between the two groups.	III	23	Good

Table 9 *legend*. [a] This study included only patients with CRSsNP [184]. ACT, Asthma Control Test; AD, aspirin desensitisation; BAST, Barcelona Smell Test; CAN, computer-assisted navigation; CI, confidence interval; CRS, chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; CS, corticosteroid; CSS, Chronic Sinusitis Survey; CT, computed tomography; ESS, endoscopic sinus surgery; FESS, functional endoscopic sinus surgery; LKS, Lund-Kennedy score; LMS, Lund-Mackay score; NAP, nonabsorbable packing; N-ERD, non-steroidal anti-inflammatory drug-exacerbated respiratory disease; NP(s), nasal polyps(s); OR, odds ratio; POSE, Peri-operative Sinus Endoscopy; PPI, proton pump inhibitor; QoL, quality of life; RhinoQoL, Rhinosinusitis Quality of Life Survey; SAS, Self-Rating Anxiety Scale; SDS, Self-Rating Depression Scale; SF-36, Short-Form 36-Item Questionnaire; SNOT-20 or -22, 20- or 22-item SinoNasal Outcome Test; SOC, standard of care; VAS, Visual Analogue Scale; vs, versus.

6 months after ESS than those whose cells did not show such bactericidal activity, but this was noted only in the CRSwNP subgroup [167]. In contrast, the presence of intracellular S. aureus in nasal epithelial cells was not predictive of symptom severity, endoscopy scores, number of outpatient consultations or antibiotic prescriptions in the 12 months after ESS among patients with CRSwNP/CRSsNP [169].

Surgical factors

Twenty-seven studies examined the effect of surgical techniques or peri-operative treatment on outcomes (Table 9), with 20 studies exclusively in patients with CRSwNP [34,50,94,175-189,195-196], six studies in mixed cohorts [70,190-194] and in one study in a CRSsNP only cohort [197]. Interestingly ESS performed before 2009 was a significant independent predictor of the need for revision ESS [50], implying that surgical techniques may have improved over time. Over the years, increasing emphasis has been placed on the importance of a complete primary surgery and on essential elements required for safe and effective ESS. Authors compared QOL and disease severity outcomes after functional ESS (FESS) based on the completeness of surgical intervention, demonstrating a significant mean improvement on SNOT-22 total scores with complete surgery over targeted approaches [198]. Given the relevance of these aspects in interpreting surgical outcomes, specific assessment tools for ESS have also been described [199,200].

Other studies further examined the impact of extended surgery on outcomes [34,177,178,201], reporting that more extensive surgery was associated with better outcomes.

Jian et al. [202], in a prospective series of 72 patients with CRSwNP undergoing FESS, observed that middle turbinate management (partial or complete resection) was associated with a higher probability of improved olfactory function at 6 months post-operatively.

One retrospective study in 299 patients showed that the Draf 3 procedure was associated with a lower rate of recurrent CRSwNP on CT compared with standard ESS [34]. Another retrospective study of 168 patients found that those undergoing reboot ESS (complete removal of inflamed mucosa from all affected sinuses) had significantly lower rates of CRSwNP recurrence and maintained olfactory function for longer compared with those undergoing standard ESS [178]. A prospective study in 42 patients with CRSwNP and comorbid asthma found that extensive ESS resulted in better olfactory function and endoscopic scores at 1-year post-ESS but had no impact on asthma control or respiratory function [177]. Accordingly, researchers demonstrated that expanded types of FESS significantly improved QOL and reduced revision surgery rates compared with a group of patients that underwent a less extended surgery. Multivariate analysis showed that patients with prior surgeries and higher baseline SNOT-22 scores appeared to benefit more from more extensive surgery [203].

Recently more evidence further emphasizes the relevance of previous surgical extent as a determinant of outcomes after revision ESS [195,196]. The extent of previous surgery may influence postoperative outcomes, as persistent disease after limited prior ESS may reflect residual disease that could benefit from further surgical treatment rather than a true failure of surgery. These studies [195,196] have shown that a lower extent of previous ESS is associated with greater improvement following revision surgery, supporting the concept that surgical completeness represents an important predictor of postoperative benefit. Therefore, the extent and quality of previous surgery should be considered when evaluating outcomes after revision ESS and when selecting patients who may derive greater benefit from further surgical intervention.

In contrast to the findings of a protective effect of extensive surgery, a nationwide population-based study found that a more extensive initial procedure was associated with higher revision rates in CRSwNP patients [14]. Notably, total ethmoidectomy at index surgery was associated with improved revision-free survival; however, this benefit was not observed in patients with N-ERD [204]. In line with these observations, Zhang and colleagues conducted a 5-year randomized prospective study to evaluate the long-term outcomes of extended surgical approaches in patients with recurrent CRSwNP [205]. Radical ESS and radical ESS + Draf 3 were associated with a lower rate of revision surgery and a longer time to recurrence compared with FESS. The addition of Draf 3 to radical ESS did not result in better clinical outcomes than radical ESS alone. Nevertheless, by 5 years, all groups exhibited similarly high recurrence rates.

The effects of surgical technique as a possible predictive factor for poor ESS outcomes was also investigated in a mixed population reported by Galletti and colleagues [17]. In this study, the

use of computer-assisted navigation (CAN) was associated with significantly better outcomes (symptom frequency and severity, endoscopic appearance and nasal resistance on rhinomanometry) at 1-year post-ESS compared with ESS without CAN (191). Other studies in patients with CRSwNP showed that use of a micro-debrider was associated with better olfactory function [182] and lower symptom severity scores [176] compared with ESS using only non-powered instruments.

A limitation of this review is that surgical factors, although considered in the analysis, represent complex domains that deserve further dedicated investigation. Their impact on outcomes after revision ESS is likely influenced by multiple interacting variables, including surgical extent, technical aspects of the procedure, and postoperative management strategies, which are difficult to fully capture within a review primarily focused on pre-operative predictors. Future studies specifically addressing these factors, ideally through standardized definitions and prospective designs, will be important to further refine outcome prediction and optimize patient selection.

It cannot be excluded that, in the coming years, the use of biologics may significantly reduce the need for extended surgery, given their efficacy and the high rates of remission achievable with such treatments [206]. Nevertheless, it should be considered that access to biologics remains limited in certain countries, where extended surgical approaches continue to play an important role, particularly in patients at higher risk of recurrence.

Peri- and post-operative treatment as factors influencing ESS outcomes

In the post-operative period, patients may be prescribed saline irrigation, antihistamines, haemostatic agents, intranasal corticosteroid-containing (mometasone, budesonide, hydrocortisone, triamcinolone, dexamethasone) ointments/sprays, each of which may affect post-ESS outcomes differently. The authors acknowledge the clinical relevance of this topic and recognise that it warrants a more exhaustive and dedicated analysis. However, as with surgical factors, it falls beyond the primary scope of this review. Nonetheless, a concise summary of the available evidence is provided.

Saline irrigation

Irrigation of the nasal sinuses with saline solution is a standard part of ESS post-operative care. Of the studies investigating the influence of saline irrigation on post-ESS outcomes (Table 9), two explored different types of saline irrigation in patients with CRSwNP [180,188]. The first study compared standard post-operative care plus low-pressure high-volume saline irrigation of the maxillary sinus, using a low pressure-type device twice a week in the first week, weekly in the next two weeks, and then twice in the following month versus standard post-operative care alone [180]. At 3 months post-ESS, patients who had used the low-pressure high-volume device had significantly better endoscopic scores and a lower rate of recurrent disease on endoscopy compared with the standard post-operative care-alone group [180]. The second study was a high-quality, randomised, double-blind comparison of isotonic seawater and buffered hypertonic seawater [188]. There were no significant between-group differences in endoscopic or symptom scores at 2, 16 or 24 weeks post-ESS. However, at 8 weeks post-ESS, LKS and saccharine clearance times were significantly better in the group that used buffered hypertonic seawater versus physiological seawater (p=0.01), driven mainly by improvements in patients with non-eosinophilic CRSwNP [188].

Corticosteroids

Six studies examined the effect of peri-operative local and SCS on outcomes, four in patients with CRSwNP [175,179,186,189], one in patients with CRSsNP [197] and one in a mixed population [194] (Table 9). The use of various intranasal (local) and oral (systemic) dosage forms of corticosteroids pre-, peri- and post-operatively was analysed.

Data from the literature suggest that INCS are among the most prognostically relevant medicines, as both their use and adherence to use in the post-operative period play a critical role in determining surgical outcomes [175,179,186,188,195,196,207]. Local corticosteroids markedly improved the overall symptoms (standardised mean difference −0.49; p<0.00001) and the proportion of responders (risk ratio 0.59; p<0.00001) post-ESS compared with placebo; in addition, NP size decreased and NP recurrence was prevented [208]. To aid local drug administration, Wang and colleagues tested the application of a 3D-printed track-guided precise drug delivery device for the sinuses after ESS versus glucocorticoids formulated as a nasal spray [209]. The sinus drug delivery device was more precise and thus superior to nasal sprays in controlling the recurrence of CRS [210].

Budesonide nasal irrigation improved LKS in patients with CRS after ESS in the following domains: scores of nasal polyps, mucosal oedema, secretions and total LKS [194]. Three months after ESS, visual analogue scale (VAS) scores of nasal blockage, hyposmia and rhinorrhoea, as well as SNOT-22 results also improved significantly [194]. When budesonide nasal irrigation was compared with fluticasone spray in patients with CRSwNP after ESS, those treated with budesonide had greater improvement in SNOT-22 and LKS in comparison with fluticasone at 6 months [210].

Kang and colleagues compared two topical corticosteroid strategies after ESS: one in which patients administered low-dose triamcinolone nasal spray twice a day for 2 months, and one in which gauze soaked in high-dose triamcinolone was applied (under endoscopic guidance) to the site of NP removal once a week for 8 weeks [179]. At 1 year after surgery, the incidence of recurrent CRSwNP was significantly lower in the group that had received high-dose topical corticosteroids than in the group

using twice daily intranasal sprays (7.1% vs 44.4%) [179]. In a prospective, randomised trial, mometasone furoate-impregnated biodegradable nasal dressings that were used during the healing process drastically improved endoscopic appearance post-operatively in patients with CRSwNP [211]. Interestingly, significant improvements were documented at all the post-operative visits in patients who had received dressings soaked with 8 mL of mometasone furoate in comparison with those who had received dressings soaked with 4 mL of the solution [211].

In a separate randomised, double-blind, placebo-controlled study, patients with CRSwNP who used intranasal triamcinolone post-operatively had significantly smaller NPs at 3 months compared with patients in the placebo group, but only in the subgroup of patients with aspirin intolerance, and there was no significant difference between the INCS and placebo groups in other parameters or at other timepoints [186]. In contrast, Li and colleagues reported a significantly higher cure rate, better endoscopy scores, SNOT-20 scores and olfactory function in a mixed population who received intranasal dexamethasone twice daily for 6 months in addition to standard post-operative care, compared with patients who received standard care alone [197].

SCS were assessed in two randomised studies in patients with CRSwNP [175,189]. In the first study, patients received prednisone perioperatively (5 days before ESS and for 9 days thereafter) [189]. Patients in the corticosteroid group had significantly better post-operative total endoscopy scores compared with the placebo group, and there was a trend towards greater improvement in symptom severity, but this was not statistically significant [189]. In the second study, the authors specifically analysed pre-operative SCS in a prospective study of 52 patients with CRSwNP (31 underwent ESS without pre-operative corticosteroids and 21 received open-label prednisolone for 1–4 weeks before ESS) [175]. The authors concluded that corticosteroids improved olfaction in CRSwNP comparable to surgery. In addition, they observed that changes in relation to corticosteroids predicted olfactory outcomes post-operatively. Regarding olfactory dynamics, results demonstrated that olfactory function increased 1 month after surgery and decreased 3 months post-operatively [175].

It should be emphasized that studies investigating the pre-operative use of SCS provide limited data on their potential adverse effects. The authors of this review consider such information to be of particular clinical relevance, as the potential benefits derived from pre- or post-operative administration of SCS should always be carefully weighed against the short- and long-term risks. In particular, the long-term adverse effects of SCS tend to be underestimated in the current literature and clinical practice, despite their potentially significant impact.

To minimise the adverse effects of SCS use, a corticosteroid-eluting spacer was employed immediately after ESS but results have been inconclusive [212]. Conversely, corticosteroid-eluting stents alleviated local inflammation significantly after ESS and also reduced levels of ECP, myeloperoxidase, loss of smell, total VAS and peri-operative sinus endoscopy scores [213].

Leukotriene receptor antagonists

Four studies investigated the use of montelukast, a leukotriene receptor antagonist, on outcomes (Table 9); three were randomised, open-label studies in patients with CRSwNP [184,185,187] and one was a retrospective study in a mixed cohort [193].

Varulkan and colleagues compared intranasal mometasone with oral montelukast in patients with CRSwNP and found that montelukast was associated with significantly better improvement in olfactory function compared with mometasone, but a higher rate of NP recurrence (48% vs 20%) at 6 months post-ESS [187]. However, Van Gerven and colleagues found that adding montelukast to INCS had no impact on outcomes at 12 months post-ESS compared with INCS alone [185]. The other prospective randomised study was conducted in 33 patients with CRSwNP and concomitant N-ERD who were randomised to one of three treatment groups: intranasal mometasone, oral montelukast or the combination of both [184]. Endoscopic and symptom scores were significantly improved at 12 months after ESS in all the groups, but the improvement in LKS was significantly greater in the combination treatment group than in the mometasone- or montelukast-only groups [184].

The retrospective study in the mixed cohort of patients compared intraindividual outcomes during periods of compliance versus noncompliance with montelukast, with each patient acting as their own control [193]. Symptom and endoscopic scores were significantly lower (showing greater improvement) during periods of compliance compared with non-compliance [193].

Other treatments

Two studies investigated the effect of post-operative aspirin treatment after desensitization in patients with N-ERD [181,183]. In the smaller of these studies (n=15), none of the five patients who underwent aspirin desensitization needed revision surgery in the 2 years after ESS compared with 8/10 patients who did not undergo desensitization (p=0.003) [181]. In the larger retrospective study (n=61), the addition of aspirin desensitization or oral montelukast to standard post-operative care was associated with a better NP grade during follow-up (mean 35 months) compared with standard care alone in patients with CRSwNP and N-ERD [183]. However, those who had received montelukast had better symptomatic improvement during follow-up than those who underwent desensitization [183].

Although antihistamines such as cetirizine may be used in the post-operative period, our literature search did not yield any data on outcomes after antihistamine use after ESS. Finally, a small randomised study in a mixed cohort of CRS patients (n=40) found that adding a daily dose of a proton pump inhibitor (PPI) to the standard post-operative regimen of INCS (fluti-

Table 10. Summary on the results of this review including the number of articles specifically addressing the association of the clinical factor and poor outcomes after surgery, level of evidence and the quality of the research in chronic rhinosinusitis with (CRSwNP) or without (CRSsNP) nasal polyps.

	Number of articles analysed	Level of evidence (I–VII)	Downs and Black scores (Mean, min max)	Quality of evidence	Association between risk factor and poor outcomes after surgery*
Clinical factors (demographics, comorbidities, lifestyle, previous treatments)					
Age	40	III	18.9 (16–20)	Fair (37) Good (3)	Association weakly supported
Sex	8	III/IV	17.5 (13–21)	Poor (1) Fair (7)	Association weakly supported
Asthma	33	III/IV	17.1 (11–21)	Poor (2) Fair (31)	Association well supported
Allergy	11	II/III	16.9 (16–20)	Fair (10) Good (1)	Association moderately-well supported
Aspirin intolerance/N-ERD	16	III/IV	16.7 (12–20)	Poor (2) Fair (12) Good (2)	Association well supported
Previous surgery (time from last surgery, involvement of frontal sinus, number of surgeries)	15	III	18.2 (15–20)	Fair (11) Good (4)	Association well supported
Severity and duration of symptoms pre-op including high burden of quality of life (pre-operative SNOT-22 scores)	16	III	16.9 (16–20)	Fair (15), Good (1)	Association well supported
Life-style factors or occupational factors	12	III	18.0 (17–19)	Fair (12)	Association weakly supported
Pre-operative radiological findings					
High LMS	34	III/IV	17.8 (13–20)	Poor (3) Fair (29) Good (2)	Association well supported
High E/M ratio	4	III	18.4 (16–19)	Fair (4)	Association moderately supported
Osteitis	5	III/IV	17.4 (17–19)	Fair (5)	Association moderately supported
Pre-operative endoscopic factors					
High LKS	8	III/IV	16.6 (14–18)	Poor (1) Fair (7)	Association moderately supported
Prescence of ERM	4	II/III/IV	16.4 (14–19)	Poor (1) Fair (3)	Association weakly supported
Biomarkers					
Tissue eosinophils	29	III/IV	16.8 (14–20)	Poor (2) Fair (25) Good (2)	Association well supported
Eosinophils in sinonasal surface	4	III/IV	17.1 (14–19)	Poor (2) Fair (2)	Association weakly supported
Blood eosinophils	9	III/IV	16.1 (13–22)	Poor (2) Fair (7)	Association weakly supported
IL-5	9	III/IV	16.2 (13-22)	Poor (2) Fair (6) Good (1)	Association moderately supported
Microbiological factors					
Biofilms	4	III/IV	15.1 (10–18)	Poor (1) Fair (3)	Association weakly supported
Peri-operative factors					
Surgical technique	27	III	17.2 (16–18)	Fair (27)	Association moderately-well supported
Post-operative use of local/systemic corticosteroids	7	II/III/IV	18.2 (15–23)	Fair (5) Good (2)	Association moderately-well supported
Post-operative use of saline	2	II	19.7 (19–23)	Fair (1) Good (1)	Association weakly supported

* Well supported: further research is very unlikely to change our confidence in the estimate of effect. Moderately-well supported: further research may have an impact on our confidence in the estimate of effect and may change the estimate. Moderately supported: further research is very likely to have an impact on our confidence in the estimate of effect and is likely to change the estimate. Weakly supported: any estimate of effect is very uncertain. E/M, ethmoid-to-maxillary; ERM, eosinophilic-rich mucin; IL, interleukin; LKS, Lund-Kennedy score; LMS, Lund-Mackay score; max, maximum; min, minimum; N-ERD, non-steroidal anti-inflammatory drug-exacerbated respiratory disease; SNOT-22, 22-item SinoNasal Outcome Test.

casone) significantly improved symptoms after ESS compared with INCS alone [192]. The authors suggested that the addition of a PPI may relieve symptoms associated with laryngopharyngeal reflux, which can exacerbate sinonasal symptoms in patients with CRS [192].

Limitations

The most significant limitation in conducting this review was the varied definitions of poor surgical outcomes employed by different researchers. The lack of consensus in guidelines on this issue has understandably contributed to the heterogeneity in defining poor outcomes and the timing of outcome assessments. Historically, some authors have prioritised endoscopic recur-

rence of NPs, while others have focused primarily on symptoms, QoL or olfactory function. This discrepancy also stems from the fact that in the past, the concept of disease control received less emphasis compared with recurrence of NPs. For future research, consistency in adhering to published definitions of disease states from EPOS 2020/European Forum for Research and Education in Allergy and Airway disease (EUFOREA) may be helpful [214]. It should be reported that specifically for the evaluation of quality of life after surgery the current utilized PROMs (i.e SNOT-22) may partially capture lower airway symptoms in patients with asthma, potentially leading to overestimation of sinonasal disease burden. Unfortunately, specific PROMs including the burden on quality of life for upper and lower airways have not been used and this currently represents un unmet need.
Another limitation is that many studies did not consistently perform predictive analyses using ROC curves, nor did they always conduct multivariate analyses to account for confounding factors. It is worthwhile to note that conflicting results might exist due to sample size variations, regional differences and different methodologies. Finally, there is a lack of high-quality literature (most were 'fair' on the Downs and Black scale), with only a few studies scoring in the 'good' category.

Conclusions

Following this systematic review, it is evident that numerous attempts have been made to identify predictive factors of outcomes after ESS in patients with CRSwNP. It is important to emphasise that there is presently no universally accepted predictive system for identifying those at risk for poor surgical outcomes that can yet be applied in clinical practice. The authors have identified the most significant predictive factors for poorer surgical outcomes (especially the outcomes that can be used in routine clinical practice) by synthesising the results of a large number of studies (Table 10). Based on the results of this review, the factors that were shown to be predictive of poor outcomes and well supported by the literature evidence were asthma, N-ERD, previous surgery (time from last surgery, involvement of frontal sinus, number of surgeries), severity and duration of symptoms pre-operatively, high pre-operative LMS and high tissue eosinophil counts. The factors that were moderately-to-well supported by the literature data were allergy, surgical related factors and lack of post-operative use of corticosteroids. The factors that were moderately supported by the literature data were high E/M opacification ratios at CT scan, high endoscopic LKS, osteitis and IL-5 as biomarkers. Finally the factors analysed that were weakly supported by literature as risk factors were age, sex, blood eosinophils, biofilms, eosinophils om the sinonasal surface, eosinophilic mucin and life style factors.
By synthesizing the available evidence, this review provides a clinically oriented framework of the predictors most consistently associated with outcomes after revision ESS. These factors should be considered as complementary tools to support individualized clinical decision-making rather than as standalone determinants of outcome, potentially facilitating preoperative risk stratification and patient counselling.
The data from this review could be instrumental in assisting clinicians identify patients with a high likelihood of poorer surgical outcomes, and as such, contribute to more precise and personalised medical care. This approach would facilitate the selection of the most appropriate therapy tailored to the individual when considering ESS for patients with CRSwNP. A predictive model using a combination of clinical, imaging and biomarker data would be a valuable addition in this scenario. Future research in this area to provide evidence-based recommendations remains an important unmet need in clinical practice.

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Author contributions

The systematic review was conducted within an international expert collaborative group, with defined roles in study conception, literature screening, data extraction, domain-specific interpretation, drafting, and critical revision. Given the breadth of this systematic review, the involvement of a relatively large number of contributors was necessary to ensure comprehensive data evaluation, and domain-specific expertise across different aspects of the study. EDC, CP, WF, PH, CH were involved in the conceptualization of the study. Literature screening and data extraction were performed independently by EDC, CP, LMD, CM with methodological oversight by EDC. Final inclusion decisions were validated by senior authors CP and EDC. The first draft of the manuscript was written by EDC. Subsequent sections were refined collaboratively with topic-specific input from co-authors with recognized expertise in surgery, biomarkers, microbiology, and clinical epidemiology. (CH, ARS, AP, VL, MW, LK, PG, AMC, YC, BAS, OP, JKH, JM, MEC, BNL, SS, IA, DV, STS, MD, AT, LS, AJ, CM, LMD, RML). At the first-round sections of the initial document several sections of the paper were rewritten by authors in light of their respective expertise and experience. Two rounds of integration and revision of the draft were carried out, primarily due to the large volume of information. Initially, the possibility of dividing the work into two separate articles was considered; however, following consultation with the editor and agreement among all authors, it was decided to consolidate the material into a single, comprehensive publication. In one final third round all authors critically revised and approved the final manuscript.

Conflict of interest

E. De Corso has received lecture fees and participates in expert board meetings of GSK, Novartis, Sanofi, AstraZeneca and Regeneron. W.J. Fokkens has received grants for research in rhinology (via the Department of Otorhinolaryngology of the Amsterdam University Medical Centre) from ALK, Allergy Therapeutics PLC, Chordate, Novartis, EU, GSK, MYLAN, Sanofi-Aventis and Zon-MW; and has received consultation and/or speaker fees from Bioinspire, GSK, Novartis and Sanofi/Regeneron. C. Pipolo has received lecture fees and participated in expert board meetings of GSK, Sanofi-Regeneron, Novartis and AstraZeneca. C. Hopkins was on the advisory boards of GSK, Dianosic and Sanofi, and on the speaker's bureaus of Mylan and Olympus. A.R. Sedaghat has participated in advisory boards and clinical trials for Sanofi-Regeneron and GSK. S.E. Lee has received consultation and/or speaker fees from AstraZeneca, Genentech, GSK, Lyra Therapeutics, OptiNose and Sanofi/Regeneron. M.B. 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Availability of data and materials

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References

1. Gliklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otolaryngologic care. Otolaryngol Head Neck Surg 1995; 113: 104-109.
2. Hellings PW, Alobid I, Anselmo-Lima WT, et al. EUFOREA/EPOS2020 statement on the clinical considerations for chronic rhinosinusitis with nasal polyps care. Allergy. 2024 May;79(5):1123-1133.
3. Benjamin MR, Stevens WW, Li N, et al. Clinical characteristics of patients with chronic rhinosinusitis without nasal polyps in an academic setting. J Allergy Clin Immunol Pract 2019; 7: 1010-1016.
4. Bhattacharyya N. Assessing the additional disease burden of polyps in chronic rhinosinusitis. Ann Otol Rhinol Laryngol 2009; 118: 185-189.
5. Fokkens WJ, Lund VJ, Hopkins C, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology 2020; 58: 1-464.
6. Hellings PW, Fokkens WJ, Orlandi R, et al. The EUFOREA pocket guide for chronic rhinosinusitis. Rhinology. 2023 Feb 1;61(1):85-89.
7. Kim AS, Willis AL, Laubitz D, et al. The effect of maxillary sinus antrostomy size on the sinus microbiome. Int Forum Allergy Rhinol 2019; 9: 30-38.
8. Bhandarkar ND, Mace JC, Smith TL. The impact of osteitis on disease severity measures and quality of life outcomes in chronic rhinosinusitis. Int Forum Allergy Rhinol 2011; 1: 372-378.
9. Alanin MC, Hopkins C. Effect of functional endoscopic sinus surgery on outcomes in chronic rhinosinusitis. Curr Allergy Asthma Rep 2020; 20: 27.
10. Lourijsen ES, Reitsma S, Vleming M, et al. Endoscopic sinus surgery with medical therapy versus medical therapy for chronic rhinosinusitis with nasal polyps: a multicentre, randomised, controlled trial. Lancet Respir Med 2022; 10: 337-346.
11. Loftus CA, Soler ZM, Koochakzadeh S, et al. Revision surgery rates in chronic rhinosinusitis with nasal polyps: meta-analysis of risk factors. Int Forum Allergy Rhinol 2020; 10: 199-207.
12. Penttilä E, Sillanpää S, Vento SI, et al. Eosinophilia, asthma, NERD and the use of oral corticosteroids predict uncontrolled chronic rhinosinusitis with nasal polyps after surgery. Asian Pac J Allergy Immunol 2024; 42: 50-60.
13. Virkkula P, Penttilä E, Vento SI, et al. Assessing cut-off points of eosinophils, nasal polyp, and Lund-Mackay scores to predict surgery in nasal polyposis: a real-world study. Allergy Rhinol (Providence) 2020; 11: 2152656720956596.
14. Toppila-Salmi S, Lyly A, Simin J, Aakko J, Olsen HH, Lehtimäki L. Predictors of revision endoscopic sinus surgery in Finnish patients with chronic rhinosinusitis with nasal polyps. Clin Transl Allergy 2025; 15: e70032.
15. Eriksen PRG, Jakobsen KK, Aanæs K, Backer V, von Buchwald C. The potential role of biological treatment of chronic rhinosinusitis with nasal polyps: a nationwide cohort study. Rhinology. 2021 Aug 1;59(4):374-379.
16. Norelli F, Schiappoli M, Senna G, et al. Adherence to intranasal steroids in chronic rhinosinusitis with nasal polyposis prior to and during biologic therapy: a neglected matter. J Clin Med 2024; 13: 1066.
17. Lilja M, Koskinen A, Hammarèn-Malmi S, et al. Radiological score, asthma and NSAID-exacerbated respiratory disease predict relapsing chronic rhinosinusitis. Clin Transl Allergy 2025; 15: e70043.
18. Dietz de Loos DAE, Ronsmans S, Cornet ME, et al. Occupational exposure influences control of disease in patients with chronic rhinosinusitis. Rhinology 2021; 59: 380-386.
19. Fokkens WJ, Mullol J, Kennedy D, et al. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): in-depth sinus surgery analysis. Allergy 2023; 78: 812-821.
20. Pfaar O, Beule AG, Laudien M, Stuck BA. Treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) with monoclonal antibodies (biologics): S2k guideline of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery (DGHNO-KHC), and the German College of General Practitioners and Family Physicians (DEGAM). [Article in German]. HNO 2023; 71: 256-263.
21. Bassiouni A, Ou J, Rajiv S, Cantero D, Vreugde S, Wormald PJ. Subepithelial inflammatory load and basement membrane thickening in refractory chronic rhinosinusitis with nasal polyposis: a histopathological study. Int Forum Allergy Rhinol 2016; 6: 248-255.
22. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. PLoS Med 2021; 18: e1003583.
23. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998; 52: 377-384.
24. OECBM Levels of Evidence Working Group. The Oxford Levels of Evidence 2. Oxford Centre for Evidence-Based Medicine; 2011. Available from: https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebm-levels-of-evidence (accessed: October 17, 2023).
25. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008; 336: 924-926.
26. Sedaghat AR, Campbell RG, Douglas RG, et al. Outcome measures for chronic rhinosinusitis with nasal polyps. Rhinology 2024; 62: 1-37.
27. Lund VJ, Kennedy DW. Staging for rhinosinusitis. Otolaryngol Head Neck Surg 1997; 117: S35-40.
28. Lund VJ, Mackay IS. Staging in rhinosinusitus. Rhinology 1993; 31: 183-184.
29. Nahm FS. Receiver operating characteristic curve: overview and practical use for clinicians. Korean J Anesthesiol 2022; 75: 25-36.
30. Danielides V, Katotomichelakis M, Balatsouras D, et al. Evaluation of prognostic factors for olfaction in nasal polyposis treated by endoscopic sinus surgery. Rhinology 2009; 47: 172-180.
31. Gelardi M, Fiorella R, Fiorella ML, Russo C, Soleti P, Ciprandi G. Nasal-sinus polyposis: clinical-cytological grading and prognostic index of relapse. J Biol Regul Homeost Agents 2009; 23: 181-188.
32. Katotomichelakis M, Gouveris H, Tripsianis G, Simopoulou M, Papathanassiou J, Danielides V. Biometric predictive models for the evaluation of olfactory recovery after endoscopic sinus surgery in patients with nasal polyposis. Am J Rhinol Allergy 2010; 24: 276-280.
33. Mendelsohn D, Jeremic G, Wright ED, Rotenberg BW. Revision rates after endoscopic sinus surgery: a recurrence analysis. Ann Otol Rhinol Laryngol 2011; 120: 162-166.
34. Bassiouni A, Wormald PJ. Role of frontal sinus surgery in nasal polyp recurrence. Laryngoscope 2013; 123: 36-41.
35. Bush CM, Jang DW, Champagne JP, Kountakis SE. Epidemiologic fac-

tors and surgical outcomes in patients with nasal polyposis and asthma. ORL J Otorhinolaryngol Relat Spec 2013; 75: 320-324.
36. Van Zele T, Holtappels G, Gevaert P, Bachert C. Differences in initial immunoprofiles between recurrent and nonrecurrent chronic rhinosinusitis with nasal polyps. Am J Rhinol Allergy 2014; 28: 192-198.
37. Adnane C, Adouly T, Zouak A, Mahtar M. Quality of life outcomes after functional endoscopic sinus surgery for nasal polyposis. Am J Otolaryngol 2015; 36: 47-51.
38. Brescia G, Marioni G, Franchella S, et al. Can a panel of clinical, laboratory, and pathological variables pinpoint patients with sinonasal polyposis at higher risk of recurrence after surgery? Am J Otolaryngol 2015; 36: 554-558.
39. Nguyen DT, Bey A, Arous F, Nguyen-Thi PL, Felix-Ravelo M, Jankowski R. Can surgeons predict the olfactory outcomes after endoscopic surgery for nasal polyposis? Laryngoscope 2015; 125: 1535-1540.
40. Nikakhlagh S, Mohaghegh M, Ranjbari N, Fathizade P, Saki N. Histopathological variants of chronic polypoid rhinosinusitis and clinical outcomes. Biomed Pharmacol J 2015; 8SE: 767-772.
41. Brescia G, Barion U, Pedruzzi B, et al. Sinonasal polyposis in the elderly. Am J Rhinol Allergy 2016; 30: 153-156.
42. Brescia G, Marioni G, Franchella S, et al. A prospective investigation of predictive parameters for post-surgical recurrences in sinonasal polyposis. Eur Arch Otorhinolaryngol 2016; 273: 655-660.
43. Brescia G, Barion U, Zanotti C, Giacomelli L, Martini A, Marioni G. The prognostic role of serum eosinophil and basophil levels in sinonasal polyposis. Int Forum Allergy Rhinol 2017; 7: 261-267.
44. DeConde AS, Mace JC, Levy JM, Rudmik L, Alt JA, Smith TL. Prevalence of polyp recurrence after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. Laryngoscope 2017; 127: 550-555.
45. Khairuddin NK, Salina H, Gendeh BS, Wan Hamizan AK, Lund VJ. Quality of life and recurrence of disease in patients with eosinophilic and non-eosinophilic 1 chronic rhinosinusitis with nasal polyposis. Med J Malaysia 2018; 73: 1-6.
46. Kim JY, Han YE, Seo Y, et al. Revisiting the clinical scoring system for the prognosis of chronic rhinosinusitis with nasal polyps. Yonsei Med J 2019; 60: 578-584.
47. Kim JW, Huh G, Rhee CS, et al. Unsupervised cluster analysis of chronic rhinosinusitis with nasal polyp using routinely available clinical markers and its implication in treatment outcomes. Int Forum Allergy Rhinol 2019; 9: 79-86.
48. Rives P, Espitalier F, Michel G, Blanc X, Fortun C, Malard O. Prospective evaluation of oral corticosteroid as a predictor of postoperative olfactory recovery after functional endoscopic surgery for nasal polyposis. Eur Arch Otorhinolaryngol 2019; 276: 3359-3366.
49. Akiyama K, Samukawa Y, Hoshikawa H. Short-term outcomes of olfaction in patients with eosinophilic chronic rhinosinusitis after endoscopic sinus surgery and an assessment of prognostic factors. Int Forum Allergy Rhinol 2020; 10: 208-216.
50. Loftus CA, Soler ZM, Desiato VM, et al. Factors impacting revision surgery in patients with chronic rhinosinusitis with nasal polyposis. Int Forum Allergy Rhinol 2020; 10: 289-302.
51. Nakamaru Y, Suzuki M, Honma A, et al. Preoperative pulmonary function testing to predict recurrence of chronic rhinosinusitis with nasal polyps. Allergy Rhinol (Providence) 2020; 11: 2152656720946994.
52. Wang X, Meng Y, Lou H, Wang K, Wang C, Zhang L. Blood eosinophil count combined with asthma history could predict chronic rhinosinusitis with nasal polyp recurrence. Acta Otolaryngol 2021; 141: 279-285.
53. Wu CL, Lee TJ, Huang CC, Chang PH, Fu CH. Clinical predictors of revision surgery for chronic rhinosinusitis with nasal polyposis within 5-year follow-up. Am J Otolaryngol 2020; 41: 102654.
54. De Corso E, Settimi S, Tricarico L, et al. Predictors of disease control after endoscopic sinus surgery plus long-term local corticosteroids in CRSwNP. Am J Rhinol Allergy 2021; 35: 77-85.
55. Gan W, Zhang H, Yang F, Liu S, Liu F, Meng J. The influence of nasal microbiome diversity and inflammatory patterns on the prognosis of nasal polyps. Sci Rep 2021; 11: 6364.
56. Hopkins C, Lund V. Does time from previous surgery predict subsequent treatment failure in chronic rhinosinusitis with nasal polyps? Rhinology 2021; 59: 277-283.
57. Kuan EC, Kennedy WP, Patel NN, et al. Preintervention SNOT-22 scores predict outcomes in aspirin exacerbated respiratory disease. Am J Otolaryngol 2021; 42: 103025.
58. Vlaminck S, Acke F, Prokopakis E, et al. Surgery in nasal polyp patients: outcome after a minimum observation of 10 years. Am J Rhinol Allergy 2021; 35: 449-457.
59. Bai J, Huang JH, Price CPE, et al. Prognostic factors for polyp recurrence in chronic rhinosinusitis with nasal polyps. J Allergy Clin Immunol 2022; 150: 352-361.e357.
60. Kim JW, Won TB, Woo H, et al. Age related non-type 2 inflammation and its association with treatment outcome in patients with chronic rhinosinusitis with nasal polyp in Korea. Sci Rep 2022; 12: 1671.
61. Riva G, Tavassoli M, Cravero E, et al. Long-term evaluation of nasal polyposis recurrence: a focus on multiple relapses and nasal cytology. Am J Otolaryngol 2022; 43: 103325.
62. Smith TL, Mendolia-Loffredo S, Loehrl TA, Sparapani R, Laud PW, Nattinger AB. Predictive factors and outcomes in endoscopic sinus surgery for chronic rhinosinusitis. Laryngoscope 2005; 115: 2199-2205.
63. Kim JE, Kountakis SE. The prevalence of Samter's triad in patients undergoing functional endoscopic sinus surgery. Ear Nose Throat J 2007; 86: 396-399.
64. Litvack JR, Griest S, James KE, Smith TL. Endoscopic and quality-of-life outcomes after revision endoscopic sinus surgery. Laryngoscope 2007; 117: 2233-2238.
65. Li Y, Zhang GH, Liu X, Ye J, Zeng ZP. Clinical prognostic factors of chronic rhinosinusitis after endoscopic sinus surgery. ORL J Otorhinolaryngol Relat Spec 2008; 70: 113-117.
66. Matsuwaki Y, Ookushi T, Asaka D, et al. Chronic rhinosinusitis: risk factors for the recurrence of chronic rhinosinusitis based on 5-year follow-up after endoscopic sinus surgery. Int Arch Allergy Immunol 2008; 146 Suppl 1: 77-81.
67. Minovi A, Hummel T, Ural A, Draf W, Bockmuhl U. Predictors of the outcome of nasal surgery in terms of olfactory function. Eur Arch Otorhinolaryngol 2008; 265: 57-61.
68. Psaltis AJ, Weitzel EK, Ha KR, Wormald PJ. The effect of bacterial biofilms on post-sinus surgical outcomes. Am J Rhinol 2008; 22: 1-6.
69. Busaba NY. The impact of a patient's age on the clinical presentation of inflammatory paranasal sinus disease. Am J Otolaryngol 2013; 34: 449-453.
70. Murthy P, Banerjee S. Predictive factors for a good outcome following endoscopic sinus surgery. Indian J Otolaryngol Head Neck Surg 2013; 65: 276-282.
71. Katotomichelakis M, Simopoulos E, Tripsianis G, et al. Predictors of quality of life outcomes in chronic rhinosinusitis after sinus surgery. Eur Arch Otorhinolaryngol 2014; 271: 733-741.
72. Hopkins C, Andrews P, Holy CE. Does time to endoscopic sinus surgery impact outcomes in chronic rhinosinusitis? Retrospective analysis using the UK clinical practice research data. Rhinology 2015; 53: 18-24.
73. Hopkins C, Rimmer J, Lund VJ. Does time to endoscopic sinus surgery impact outcomes in chronic rhinosinusitis? Prospective findings from the National Comparative Audit of Surgery for Nasal Polyposis and Chronic Rhinosinusitis. Rhinology 2015; 53: 10-17.
74. Kim DW, Kim DK, Jo A, et al. Age-related decline of neutrophilic inflammation is associated with better postoperative prognosis in non-eosinophilic nasal polyps. PLoS One 2016; 11: e0148442.
75. Levy JM, Mace JC, Sansoni ER, Soler ZM, Smith TL. Longitudinal improvement and stability of olfactory function in the evaluation of surgical management for chronic rhinosinusitis. Int Forum Allergy Rhinol 2016; 6: 1188-1195.
76. Adnane C, Adouly T, Khallouk A, et al. Using preoperative unsupervised cluster analysis of chronic rhinosinusitis to inform patient decision and endoscopic sinus surgery outcome. Eur Arch Otorhinolaryngol 2017; 274: 879-885.
77. Liao B, Liu JX, Li ZY, et al. Multidimensional endotypes of chronic rhinosinusitis and

their association with treatment outcomes. Allergy 2018; 73: 1459-1469.
78. Miglani A, Divekar RD, Azar A, Rank MA, Lal D. Revision endoscopic sinus surgery rates by chronic rhinosinusitis subtype. Int Forum Allergy Rhinol 2018; 8: 1047-1051.
79. Stein NR, Jafari A, DeConde AS. Revision rates and time to revision following endoscopic sinus surgery: a large database analysis. Laryngoscope 2018; 128: 31-36.
80. Tsuzuki K, Hashimoto K, Okazaki K, Nishikawa H, Sakagami M. Predictors of disease progression after endoscopic sinus surgery in patients with chronic rhinosinusitis. J Laryngol Otol 2019; 133: 678-684.
81. Wang F, Yang Y, Chen H. Vitamin D deficiency are associated with subjective disease severity in Chinese patients with chronic rhinosinusitis with nasal polyps. Am J Otolaryngol 2019; 40: 36-39.
82. Holmes T, Makary C, Unsal AA, Biddinger P, Reyes-Gelves C, Kountakis SE. How does age impact presentation and outcomes in chronic rhinosinusitis? Ann Otol Rhinol Laryngol 2020; 129: 872-877.
83. Al Sharhan SS, Al Bar MH, Assiri SY, et al. Pattern of symptom improvement following endoscopic sinus surgery for chronic rhinosinusitis. BMC Surg 2021; 21: 288.
84. Guo CL, Liao B, Liu JX, Pan L, Liu Z. Predicting difficult-to-treat chronic rhinosinusitis by noninvasive biological markers. Rhinology 2021; 59: 81-90.
85. Huang RJ, Teitelbaum JI, Issa K, et al. Endoscopic sinus surgery in older patients with significant medical comorbidities. Am J Rhinol Allergy 2022; 36: 661-667.
86. Anne J, Sreedharan S, Dosemane D, Shenoy V, Kamath PM, Zubair SM. Predictors of surgical outcomes after functional endoscopic sinus surgery in chronic rhinosinusitis. Indian J Otolaryngol Head Neck Surg 2022; 74: 835-841.
87. Hopkins C, Rudmik L, Lund VJ. The predictive value of the preoperative Sinonasal Outcome Test-22 score in patients undergoing endoscopic sinus surgery for chronic rhinosinusitis. Laryngoscope 2015; 125: 1779-1784.
88. Veloso-Teles R, Cerejeira R. Endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps: clinical outcome and predictive factors of recurrence. Am J Rhinol Allergy 2017; 31: 56-62.
89. Lee JY, Lee SW, Lee JD. Comparison of the surgical outcome between primary and revision endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. Am J Otolaryngol 2008; 29: 379-384.
90. Canakci H, Yazici H, Yayman S, et al. Beyond the CBC: can novel markers predict recurrence in chronic rhinosinusitis with nasal polyposis? Clin Otolaryngol. 2025;50(6):1096–1102.
91. Kirtsreesakul V, Thongsuksai P, Sanghan N, Promsopa C. Prediction model for recurrence after endoscopic sinus surgery in chronic rhinosinusitis with nasal polyps. Am J Rhinol Allergy. 2026;40(2):140–150.
92. Liu Y, Zeng X, Nie Z, et al. Comparison the impacts of asthma and allergic rhinitis on chronic rhinosinusitis with nasal polyps. Laryngoscope. 2025;135(10):3556–3565.
93. Zhong W, Xie S, He H, et al. The association between allergic rhinitis, eosinophilic inflammation, and postoperative recurrence in nasal polyps. Otolaryngol Head Neck Surg. 2026;174(5):1188–1196.
94. Ji J, Yu J, Zhang C, et al. Analysis of risk factors for postoperative recurrence in patients with chronic rhinosinusitis with nasal polyps: a retrospective clinical cohort study. Medicine (Baltimore). 2026;105(1):e46559.
95. Zhang C, Zhang Q, Chen J, et al. Patient-reported outcome measures as predictive tools for disease control in chronic rhinosinusitis with nasal polyps: a prospective study. Clin Transl Allergy. 2025;15(11):e70119.
96. 96. Zhang Y, Liu X, Qiang B, Wang X. Effects of pathogenic bacteria on postoperative nasal function and risk factors for recurrence in chronic rhinosinusitis with nasal polyps after endoscopic sinus surgery. Am J Rhinol Allergy. 2026;40(4):279-289.
97. Zhang J, Li H. Development and Validation of a Nomogram Integrative of Clinical Characteristics and Serum Inflammatory Biomarkers for Predicting Postoperative Recurrence in Patients with Chronic Rhinosinusitis with Nasal Polyps. Int Arch Allergy Immunol. 2026 Feb 6:1-9.
98. Dharia T, Swirnoff J, Laidlaw TM, Buchheit KM. Characteristics associated with rapid chronic rhinosinusitis with nasal polyp recurrence following endoscopic sinus surgery in NSAID-exacerbated respiratory disease. J Allergy Clin Immunol Glob. 2026 Mar 19;5(3):100689.
99. Joustra GE, den Heijer MC, al Yousef RQH, et al. Long-term clinical control in chronic rhinosinusitis: outcomes more than five years after surgery. Eur Arch Otorhinolaryngol. 2025;282:4661–4668.
100. Fokkens WJ, Lund VJ, Mullol J, et al. EPOS 2012: European Position Paper on Rhinosinusitis and Nasal Polyps 2012. A summary for otorhinolaryngologists. Rhinology 2012; 50: 1-12.
101. Ryan MT, Patel K, Fischer JL, et al. Gender differences in outcomes following endoscopic sinus surgery: a systematic review and meta-analysis. Rhinology 2024; 62: 514-525.
102. Ramanathan M, Jr., Tharakan A, Sidhaye VK, Lane AP, Biswal S, London NR, Jr. Disruption of sinonasal epithelial Nrf2 enhances susceptibility to rhinosinusitis in a mouse model. Laryngoscope 2021; 131: 713-719.
103. Velasquez N, Moore JA, Boudreau RM, Mady LJ, Lee SE. Association of air pollutants, airborne occupational exposures, and chronic rhinosinusitis disease severity. Int Forum Allergy Rhinol 2020; 10: 175-182.
104. Hox V, Delrue S, Scheers H, et al. Negative impact of occupational exposure on surgical outcome in patients with rhinosinusitis. Allergy 2012; 67: 560-565.
105. Akhtar S, Ikram M, Azam I, Dahri T. Factors associated with recurrent nasal polyps: a tertiary care experience. J Pak Med Assoc 2010; 60: 102-104.
106. Amali A, Bidar Z, Rahavi-Ezabadi S, Mikaniki N, Sadrehosseini SM. Polypoid change of middle turbinate is associated to an increased risk of polyp recurrence after surgery in patients with chronic rhinosinusitis with nasal polyps. Eur Arch Otorhinolaryngol 2018; 275: 2021-2025.
107. Beswick DM, Smith TL, Mace JC, et al. Ethmoid-to-maxillary opacification ratio: a predictor of postoperative olfaction and outcomes in nasal polyposis? Int Forum Allergy Rhinol 2021; 11: 48-57.
108. Grgić MV, Ćupić H, Kalogjera L, Baudoin T. Surgical treatment for nasal polyposis: predictors of outcome. Eur Arch Otorhinolaryngol 2015; 272: 3735-3743.
109. Kim DK, Lim HS, Eun KM, et al. Subepithelial neutrophil infiltration as a predictor of the surgical outcome of chronic rhinosinusitis with nasal polyps. Rhinology 2021; 59: 173-180.
110. Kim DW, Kim JY, Jeon SY. The status of the olfactory cleft may predict postoperative olfactory function in chronic rhinosinusitis with nasal polyposis. Am J Rhinol Allergy 2011; 25: e90-94.
111. Lee CW, Lee BJ, Yoo SH, Yi JS. Relationship between positive bacterial culture in maxillary sinus and surgical outcomes in chronic rhinosinusitis with nasal polyps. Auris Nasus Larynx 2014; 41: 446-449.
112. Meng Y, Zhang L, Lou H, Wang C. Predictive value of computed tomography in the recurrence of chronic rhinosinusitis with nasal polyps. Int Forum Allergy Rhinol 2019; 9: 1236-1243.
113. Okushi T, Mori E, Nakayama T, et al. Impact of residual ethmoid cells on postoperative course after endoscopic sinus surgery for chronic rhinosinusitis. Auris Nasus Larynx 2012; 39: 484-489.
114. Olivier F, George M, Leuba D, Monnier P, Friedrich JP. Long-term outcomes following functional endoscopic sinus surgery in Samter's triad. J Laryngol Otol 2015; 129: 548-552.
115. Sil A, Mackay I, Rowe-Jones J. Assessment of predictive prognostic factors for functional endoscopic sinus surgery in a 5-year prospective outcome study. Am J Rhinol 2007; 21: 289-296.
116. Toros SZ, Bölükbasi S, Naiboğlu B, et al. Comparative outcomes of endoscopic sinus surgery in patients with chronic sinusitis and nasal polyps. Eur Arch Otorhinolaryngol 2007; 264: 1003-1008.
117. Vandenhende-Szymanski C, Hochet B, Chevalier D, Mortuaire G. Olfactory cleft opacity and CT score are predictive factors of smell recovery after surgery in nasal polyposis. Rhinology 2015; 53: 29-34.
118. Belsky MA, Corredera E, Banerjee H, et al. Association of mast cell burden and TIM-3 expression with recalcitrant chronic rhinosinusitis with nasal polyps. Ann Otol Rhinol

Laryngol 2021; 130: 1069-1077.
119. Brescia G, Contro G, Giacomelli L, Barion U, Frigo AC, Marioni G. Blood eosinophilic and basophilic trends in recurring and non-recurring eosinophilic rhinosinusitis with nasal polyps. Am J Rhinol Allergy 2021; 35: 296-301.
120. Brescia G, Pedruzzi B, Barion U, et al. Are neutrophil-, eosinophil-, and basophil-to-lymphocyte ratios useful markers for pinpointing patients at higher risk of recurrent sinonasal polyps? Am J Otolaryngol 2016; 37: 339-345.
121. Chen W, He S, Xie X, et al. Over-expression of CRTH2 indicates eosinophilic inflammation and poor prognosis in recurrent nasal polyps. Front Immunol 2022; 13: 1046426.
122. Corredera E, Phong BL, Moore JA, Kane LP, Lee SE. TIM-3-expressing mast cells are present in chronic rhinosinusitis with nasal polyps. Otolaryngol Head Neck Surg 2018; 159: 581-586.
123. Guo M, Alasousi F, Okpaleke C, Habib AR, Javer A. Prognosis of chronic rhinosinusitis with nasal polyps using preoperative eosinophil/basophil levels and treatment compliance. Am J Rhinol Allergy 2018; 32: 440-446.
124. Huang JC, Chen XH, Wang ZY, Li X, Chang LH, Zhang GH. Interleukin-17A expression correlated with the prognosis of chronic rhinosinusitis with nasal polyps and the anti-interleukin-17A effect in a murine nasal polyps model. ORL J Otorhinolaryngol Relat Spec 2020; 82: 257-267.
125. Lou H, Meng Y, Piao Y, Wang C, Zhang L, Bachert C. Predictive significance of tissue eosinophilia for nasal polyp recurrence in the Chinese population. Am J Rhinol Allergy 2015; 29: 350-356.
126. Lou H, Meng Y, Piao Y, et al. Cellular phenotyping of chronic rhinosinusitis with nasal polyps. Rhinology 2016; 54: 150-159.
127. Lu PC, Lee TJ, Huang CC, Chang PH, Chen YW, Fu CH. Serum eosinophil cationic protein: a prognostic factor for early postoperative recurrence of nasal polyps. Int Forum Allergy Rhinol 2021; 11: 766-772.
128. Nakayama T, Asaka D, Kanaya H, Kuboki A, Haruna S. Prognostic factors for recurrence after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps. Auris Nasus Larynx 2016; 43: 641-647.
129. Ninomiya T, Noguchi E, Haruna T, et al. Periostin as a novel biomarker for postoperative recurrence of chronic rhinosinitis with nasal polyps. Sci Rep 2018; 8: 11450.
130. Qi S, Yan B, Liu C, Wang C, Zhang L. Predictive significance of Charcot-Leyden crystal mRNA levels in nasal brushing for nasal polyp recurrence. Rhinology 2020; 58: 166-174.
131. Rosati D, Rosato C, Pagliuca G, et al. Predictive markers of long-term recurrence in chronic rhinosinusitis with nasal polyps. Am J Otolaryngol 2020; 41: 102286.
132. Telmesani LM, Al-Shawarby M. Osteitis in chronic rhinosinusitis with nasal polyps: a comparative study between primary and recurrent cases. Eur Arch Otorhinolaryngol 2010; 267: 721-724.
133. Tosun F, Arslan HH, Karslioglu Y, Deveci MS, Durmaz A. Relationship between postoperative recurrence rate and eosinophil density of nasal polyps. Ann Otol Rhinol Laryngol 2010; 119: 455-459.
134. Voegels RL, de Melo Pádua FG. Expression of interleukins in patients with nasal polyposis. Otolaryngol Head Neck Surg 2005; 132: 613-619.
135. Wang G, Li M, Zheng J, et al. Circulating BAFF as novel biomarker in distinguishing chronic rhinosinusitis with nasal polyps endotypes and predicting postoperative recurrence. Int Immunopharmacol 2022; 104: 108515.
136. Wang G, Zheng H, Chen X, et al. Exploration of predictive biomarkers for postoperative recurrence in chronic rhinosinusitis with nasal polyps based on serum multiple-cytokine profiling. Mediators Inflamm 2022; 2022: 1061658.
137. Wei L, Zhang Y, Tan H. Changes of TNF-α, PDGF and HA in nasal secretions and olfactory function of patients with chronic sinusitis before and after endoscopic sinus surgery. Exp Ther Med 2018; 16: 3413-3418.
138. Wu D, Yan B, Wang Y, Zhang L, Wang C. Predictive significance of Charcot-Leyden crystal protein in nasal secretions in recurrent chronic rhinosinusitis with nasal polyps. Int Arch Allergy Immunol 2021; 182: 65-75.
139. Zhang Z, Liu J, Xie L, Cao W, Ma F, Zhang Y. Tissue eosinophils and mucous inflammatory cytokines for the evaluation of olfactory recovery after endoscopic sinus surgery in patients with nasal polyposis. Am J Otolaryngol 2022; 43: 103561.
140. Calus L, Van Bruaene N, Bosteels C, et al. Twelve-year follow-up study after endoscopic sinus surgery in patients with chronic rhinosinusitis with nasal polyposis. Clin Transl Allergy 2019; 9: 30.
141. Boztepe OF, Gün T, Demir M, Gür Ö E, Ozel D, Doğru H. A novel predictive marker for the recurrence of nasal polyposis following endoscopic sinus surgery. Eur Arch Otorhinolaryngol 2016; 273: 1439-1444.
142. Honma A, Takagi D, Nakamaru Y, Homma A, Suzuki M, Fukuda S. Reduction of blood eosinophil counts in eosinophilic chronic rhinosinusitis after surgery. J Laryngol Otol 2016; 130: 1147-1152.
143. Lee HY, Pyo JS, Kim SJ. Distinct patterns of tissue remodeling and their prognostic role in chronic rhinosinusitis. ORL J Otorhinolaryngol Relat Spec 2021; 83: 457-463.
144. Nakayama T, Yoshikawa M, Asaka D, et al. Mucosal eosinophilia and recurrence of nasal polyps - new classification of chronic rhinosinusitis. Rhinology 2011; 49: 392-396.
145. Soler ZM, Sauer D, Mace J, Smith TL. Impact of mucosal eosinophilia and nasal polyposis on quality-of-life outcomes after sinus surgery. Otolaryngol Head Neck Surg 2010; 142: 64-71.
146. Tajudeen BA, Ganti A, Kuhar HN, et al. The presence of eosinophil aggregates correlates with increased postoperative prednisone requirement. Laryngoscope 2019; 129: 794-799.
147. Vlaminck S, Vauterin T, Hellings PW, et al. The importance of local eosinophilia in the surgical outcome of chronic rhinosinusitis: a 3-year prospective observational study. Am J Rhinol Allergy 2014; 28: 260-264.
148. Younis RT, Ahmed J. Predicting revision sinus surgery in allergic fungal and eosinophilic mucin chronic rhinosinusitis. Laryngoscope 2017; 127: 59-63.
149. Kim DH, Han JS, Kim GJ, Basurrah MA, Hwang SH. Clinical predictors of polyps recurring in patients with chronic rhinosinusitis and nasal polyps: a systematic review and meta-analysis. Rhinology 2023; 61: 482-497.
150. Alobid I, Armengot-Carceller M, Pinilla Urraca M, et al. When the nose meets the lab: histopathological analysis in chronic rhinosinusitis with nasal polyps for routine clinical practice. Curr Allergy Asthma Rep 2024; 24: 657-665.
151. Deng Z, Li Z, She Y, Xie B. Increased expression of SERPINB10 associated with postoperative recurrence in chronic rhinosinusitis with nasal polyps. Dis Markers 2022; 2022: 7164318.
152. Renteria AE, Maniakas A, Pelletier A, et al. Utilization of transcriptomic profiling to identify molecular markers predicting successful recovery following endoscopic sinus surgery for chronic rhinosinusitis. Otolaryngol Head Neck Surg 2023; 169: 1662-1673.
153. Lavigne F, Nguyen CT, Cameron L, Hamid Q, Renzi PM. Prognosis and prediction of response to surgery in allergic patients with chronic sinusitis. J Allergy Clin Immunol 2000; 105: 746-751.
154. Ueki S, Miyabe Y, Yamamoto Y, et al. Charcot-Leyden crystals in eosinophilic inflammation: active cytolysis leads to crystal formation. Curr Allergy Asthma Rep 2019; 19: 35.
155. De Corso E, Baroni S, Settimi S, et al. Sinonasal biomarkers defining type 2-high and type 2-low inflammation in chronic rhinosinusitis with nasal polyps. J Pers Medicine 2022; 12: 1251.
156. Penttila E, Sillanpaa S, Vento SI, et al. Eosinophilia, asthma, NERD and the use of oral corticosteroids predict uncontrolled chronic rhinosinusitis with nasal polyps after surgery. Asian Pac J Allergy Immunol 2024; 42: 50-60.
157. Virkkula P, Penttilä E, Vento SI, et al. Assessing Cut-off points of eosinophils, nasal polyp, and Lund-Mackay scores to predict surgery in nasal polyposis: a real-world study. Allergy Rhinol 2020; 11: 2152656720956596.
158. Batzakakis D, Stathas T, Mastronikolis N, Kourousis C, Aletras A, Naxakis S. Adhesion molecules as predictors of nasal polyposis recurrence. Am J Rhinol Allergy 2014; 28: 20-22.

159. Pawłowska-Góral K, Markowski J, Wardas P, Kurzeja E, Witkowska M. Cathepsin D activity in nasal polyps. Clin Biochem 2012; 45: 1251-1253.
160. Gong MJ, Wang YS, Lou M, et al. HO-1: a new marker for predicting postoperative recurrence of CRSwNP. Acta Otolaryngol 2023; 143: 170-175.
161. Lee W, Chang L, Huang Z, et al. A retrospective analysis of γδ t cell expression in chronic rhinosinusitis and its association with recurrence of nasal polyps. ORL J Otorhinolaryngol Relat Spec 2017; 79: 251-263.
162. Lane AP, Truong-Tran QA, Schleimer RP. Altered expression of genes associated with innate immunity and inflammation in recalcitrant rhinosinusitis with polyps. Am J Rhinol 2006; 20: 138-144.
163. Wang F, Yang Y, You Q, Chen H. Prognostic significance of serum complement component 3 in chronic rhinosinusitis with nasal polyps. ORL J Otorhinolaryngol Relat Spec 2020; 82: 67-73.
164. Dzaman K, Szczepanski MJ, Molinska-Glura M, Krzeski A, Zagor M. Expression of the receptor for advanced glycation end products, a target for high mobility group box 1 protein, and its role in chronic recalcitrant rhinosinusitis with nasal polyps. Arch Immunol Ther Exp (Warsz) 2015; 63: 223-230.
165. Jelavic B, Grgić M, Cupić H, Kordić M, Vasilj M, Baudoin T. Prognostic value of Helicobacter pylori sinonasal colonization for efficacy of endoscopic sinus surgery. Eur Arch Otorhinolaryngol 2012; 269: 2197-2202.
166. Kim JH, Kim SH, Lim JY, et al. Association between the sinus microbiota with eosinophilic inflammation and prognosis in chronic rhinosinusitis with nasal polyps. Exp Mol Med 2020; 52: 978-987.
167. Carey RM, Workman AD, Hatten KM, et al. Denatonium-induced sinonasal bacterial killing may play a role in chronic rhinosinusitis outcomes. Int Forum Allergy Rhinol 2017; 7: 699-704.
168. Hochstim CJ, Masood R, Rice DH. Biofilm and persistent inflammation in endoscopic sinus surgery. Otolaryngol Head Neck Surg 2010; 143: 697-698.
169. Ou J, Drilling A, Singhal D, et al. Association of intracellular Staphylococcus aureus with prognosis in chronic rhinosinusitis. Int Forum Allergy Rhinol 2016; 6: 792-799.
170. Ramakrishnan VR, Hauser LJ, Feazel LM, Ir D, Robertson CE, Frank DN. Sinus microbiota varies among chronic rhinosinusitis phenotypes and predicts surgical outcome. J Allergy Clin Immunol 2015; 136: 334-342.e1.
171. Singhal D, Foreman A, Jervis-Bardy J, Wormald PJ. Staphylococcus aureus biofilms: nemesis of endoscopic sinus surgery. Laryngoscope 2011; 121: 1578-1583.
172. Tsou YA, Chen CM, Lin TC, et al. Decreased SPLUNC1 expression is associated with Pseudomonas infection in surgically treated chronic rhinosinusitis patients who may require repeated sinus surgery. Laryngoscope 2013; 123: 845-851.
173. Sanclement JA, Webster P, Thomas J, Ramadan HH. Bacterial biofilms in surgical specimens of patients with chronic rhinosinusitis. Laryngoscope 2005; 115: 578-582.
174. Tănase MI, Cosgarea M, Hendea RM, et al. The role of Ki67 in predicting post-ESS (endoscopic sinus surgery) outcomes in CRSwNP (chronic rhinosinusitis with nasal polyps). Cureus. 2025;17(2):e79748.
175. Bogdanov V, Walliczek-Dworschak U, Whitcroft KL, Landis BN, Hummel T. Response to glucocorticosteroids predicts olfactory outcome after ESS in chronic rhinosinusitis. Laryngoscope 2020; 130: 1616-1621.
176. Chauhan N, Kodinariya J, Jain R, Shah T. A comparative study of microdebrider assisted v/s conventional endoscopic sinus surgery for nasal polyposis. Int J Pharm Res 2020; 12: 333-337.
177. Chen FH, Deng J, Hong HY, et al. Extensive versus functional endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps and asthma: a 1-year study. Am J Rhinol Allergy 2016; 30: 143-148.
178. Gomes SC, Cavaliere C, Masieri S, et al. Reboot surgery for chronic rhinosinusitis with nasal polyposis: recurrence and smell kinetics. Eur Arch Otorhinolaryngol 2022; 279: 5691-5699.
179. Kang IG, Yoon BK, Jung JH, Cha HE, Kim ST. The effect of high-dose topical corticosteroid therapy on prevention of recurrent nasal polyps after revision endoscopic sinus surgery. Am J Rhinol 2008; 22: 497-501.
180. Kim ST, Sung UH, Jung JH, et al. The effect of maxillary sinus irrigation on early prognostic factors after endoscopic sinus surgery: a preliminary study. Am J Rhinol Allergy 2013; 27: e158-161.
181. McMains KC, Kountakis SE. Medical and surgical considerations in patients with Samter's triad. Am J Rhinol 2006; 20: 573-576.
182. Saafan ME, Ragab SM, Albirmawy OA, Elsherif HS. Powered versus conventional endoscopic sinus surgery instruments in management of sinonasal polyposis. Eur Arch Otorhinolaryngol 2013; 270: 149-155.
183. San Nicoló M, Habermann N, Havel M. AERD associated nasal polyposis: efficacy of postoperative antileukotriene therapy in comparison with aspirin desensitization. A retrospective study. Int Arch Allergy Immunol 2020; 181: 790-798.
184. Stryjewska-Makuch G, Humeniuk-Arasiewicz M, Jura-Szołtys E, Glück J. The effect of antileukotrienes on the results of postoperative treatment of paranasal sinuses in patients with non-steroidal anti-inflammatory drug-exacerbated respiratory disease. Int Arch Allergy Immunol 2019; 179: 281-289.
185. Van Gerven L, Langdon C, Cordero A, Cardelús S, Mullol J, Alobid I. Lack of long-term add-on effect by montelukast in postoperative chronic rhinosinusitis patients with nasal polyps. Laryngoscope 2018; 128: 1743-1751.
186. Vento SI, Blomgren K, Hytönen M, Simola M, Malmberg H. Prevention of relapses of nasal polyposis with intranasal triamcinolone acetonide after polyp surgery: a prospective double-blind, placebo-controlled, randomised study with a 9-month follow-up. Clin Otolaryngol 2012; 37: 117-123.
187. Vuralkan E, Saka C, Akin I, et al. Comparison of montelukast and mometasone furoate in the prevention of recurrent nasal polyps. Ther Adv Respir Dis 2012; 6: 5-10.
188. Wang J, Shen L, Huang ZQ, et al. Efficacy of buffered hypertonic seawater in different phenotypes of chronic rhinosinusitis with nasal polyps after endoscopic sinus surgery: a randomized double-blind study. Am J Otolaryngol 2020; 41: 102554.
189. Wright ED, Agrawal S. Impact of perioperative systemic steroids on surgical outcomes in patients with chronic rhinosinusitis with polyposis: evaluation with the novel Perioperative Sinus Endoscopy (POSE) scoring system. Laryngoscope 2007; 117: 1-28.
190. Bugten V, Nordgård S, Steinsvåg S. Long-term effects of postoperative measures after sinus surgery. Eur Arch Otorhinolaryngol 2008; 265: 531-537.
191. Galletti B, Gazia F, Freni F, Sireci F, Galletti F. Endoscopic sinus surgery with and without computer assisted navigation: a retrospective study. Auris Nasus Larynx 2019; 46: 520-525.
192. Nanda MS, Kaur M, Gupta V. Correlation between chronic rhinosinusitis and laryngopharyngeal reflux. Natl J Physiol Pharm Pharmacol 2018; 8: 544-549.
193. Yelverton JC, Holmes TW, Johnson CM, Gelves CR, Kountakis SE. Effectiveness of leukotriene receptor antagonism in the postoperative management of chronic rhinosinusitis. Int Forum Allergy Rhinol 2016; 6: 243-247.
194. Huang ZZ, Chen XZ, Huang JC, et al. Budesonide nasal irrigation improved Lund-Kennedy endoscopic score of chronic rhinosinusitis patients after endoscopic sinus surgery. Eur Arch Otorhinolaryngol 2019; 276: 1397-1403.
195. Workman AD, Kuppusamy K, Lerner DK, et al. Assessing adequacy of surgical extent in CRSwNP: The Completion of Surgery Index. Int Forum Allergy Rhinol. 2025; 15: 9–17.
196. Yu AJ, Phung C, Kuppusamy K, et al. The completeness of surgery index predicts success in CRSwNP with asthma by SNOT-22 and asthma control test. Int Forum Allergy Rhinol. 2026 Feb;16(2):132-137.
197. Li YQ, Sheng LL, Ding Q, Shao HX. Evaluation of endoscopic sinus surgery combined with dexamethasone in the treatment of chronic rhinosinusitis. Indian J Pharm Sci 2020; 82: 124-129.
198. DeConde AS, Suh JD, Mace JC, Alt JA, Smith TL. Outcomes of complete vs targeted approaches to endoscopic sinus surgery. Int Forum Allergy Rhinol 2015; 5: 691-700.
199. Guldager MJ, Wuyts Andersen SA, Melchiors

J, Prokopakis E, Hopkins C, von Buchwald C. Technical skills of endoscopic sinus surgery for performance assessment using the Delphi methodology. Rhinology 2024; 62: 710-715.
200. Reitsma S, Adriaensen G, Cornet ME, van Haastert RM, Raftopulos MH, Fokkens WJ. The Amsterdam Classification of Completeness of Endoscopic Sinus Surgery (ACCESS): a new CT-based scoring system grading the extent of surgery. Rhinology 2020; 58: 538-543.
201. Martin-Jimenez D, Moreno-Luna R, Callejon-Leblic A, et al. Long-term clinical outcomes in patients with chronic rhinosinusitis with nasal polyps associated with expanded types of endoscopic sinus surgery. J Clin Med 2024; 13: 866.
202. Jian F, Lao J, Ge R, Yang Q, Wu S. A prospective cohort study comparing the effects of different middle turbinate treatments on olfactory function recovery in CRSwNP patients after FESS. Rhinology 2025.
203. Martin-Jimenez DI, Moreno-Luna R, Callejon-Leblic A, et al. Improved quality of life in patients with chronic rhinosinusitis with nasal polyps associated with expanded types of endoscopic sinus surgery: A 2-year retrospective study. Int Forum Allergy Rhinol 2024; 14: 1119-1122.
204. Lilja MJ, Koskinen A, Virkkula P, et al. Factors affecting the control of chronic rhinosinusitis with nasal polyps: a comparison in patients with or without NERD. Allergy Rhinol 2021; 12: 21526567211003844.
205. Zhang L, Zhang Y, Gao Y, et al. Long-term outcomes of different endoscopic sinus surgery in recurrent chronic rhinosinusitis with nasal polyps and asthma. Rhinology 2020; 58: 126-135.
206. Fokkens WJ. Revision surgery, biologics, or both? Rhinology 2024; 62: 385.
207. Bertazzoni G, Conti C, Testa G, et al. High volume nasal irrigations with steroids for chronic rhinosinusitis and allergic rhinitis. Eur Arch Otorhinolaryngol 2025; 282: 47-62.
208. Snidvongs K, Kalish L, Sacks R, Sivasubramaniam R, Cope D, Harvey RJ. Sinus surgery and delivery method influence the effectiveness of topical corticosteroids for chronic rhinosinusitis: systematic review and meta-analysis. Am J Rhinol Allergy 2013; 27: 221-233.
209. Wang J, Zhao K, Wang Z, et al. Preliminary application of a 3D-printed track-guided precise drug delivery device for the sinuses after endoscopic sinus surgery. J Biomater Appl 2023; 37: 961-968.
210. Neubauer PD, Schwam ZG, Manes RP. Comparison of intranasal fluticasone spray, budesonide atomizer, and budesonide respules in patients with chronic rhinosinusitis with polyposis after endoscopic sinus surgery. Int Forum Allergy Rhinol 2016; 6: 233-237.
211. Zhao KQ, Yu YQ, Yu HM. Effects of mometasone furoate-impregnated biodegradable nasal dressing on endoscopic appearance in healing process following endoscopic sinus surgery: a randomized, double-blind, placebo-controlled study. Int Forum Allergy Rhinol 2018; 8: 1233-1241.
212. Dautremont JF, Mechor B, Rudmik L. The role of immediate postoperative systemic corticosteroids when utilizing a steroid-eluting spacer following sinus surgery. Otolaryngol Head Neck Surg 2014; 150: 689-695.
213. Zheng L, Chen Z, Jin J, et al. The efficacy of steroid-eluting stents on the local inflammation of chronic rhinosinusitis with nasal polyposis after endoscopic sinus surgery: a multicenter prospective longitudinal study. Eur Arch Otorhinolaryngol 2023; 280: 5417-5431.
214. Fokkens WJ, De Corso E, Backer V, et al. EPOS2020/EUFOREA expert opinion on defining disease states and therapeutic goals in CRSwNP. Rhinology 2024; 62: 287-298.
215. Wei B, Liu F, Zhang J, et al. Multivariate analysis of inflammatory endotypes in recurrent nasal polyposis in a Chinese population. Rhinology 2018; 56: 216-226.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Methods

Methodological quality and risk of bias assessment

The principal methodological strengths were the use of clinically relevant postoperative outcomes, including revision ESS, endoscopic recurrence, validated patient-reported outcome measures, objective olfactory assessment, and radiological or endoscopic scores. Several studies also used prospective designs, relatively large cohorts, and multivariable analyses to adjust for potential confounding.

The main limitations were retrospective or single-centre designs, small sample sizes, heterogeneous patient populations, and considerable variability in the definitions of recurrence, poor disease control, surgical success, and follow-up duration. The extent of surgery and postoperative medical treatment were not consistently standardized or adequately accounted for. Recruitment procedures, losses to follow-up, handling of missing data, and blinding of outcome assessment were also frequently incompletely reported. In several studies, associations were based on univariable analyses or were not adjusted for relevant confounders, such as asthma, N-ERD, previous ESS, baseline disease severity, surgical extent, and postoperative corticosteroid use.

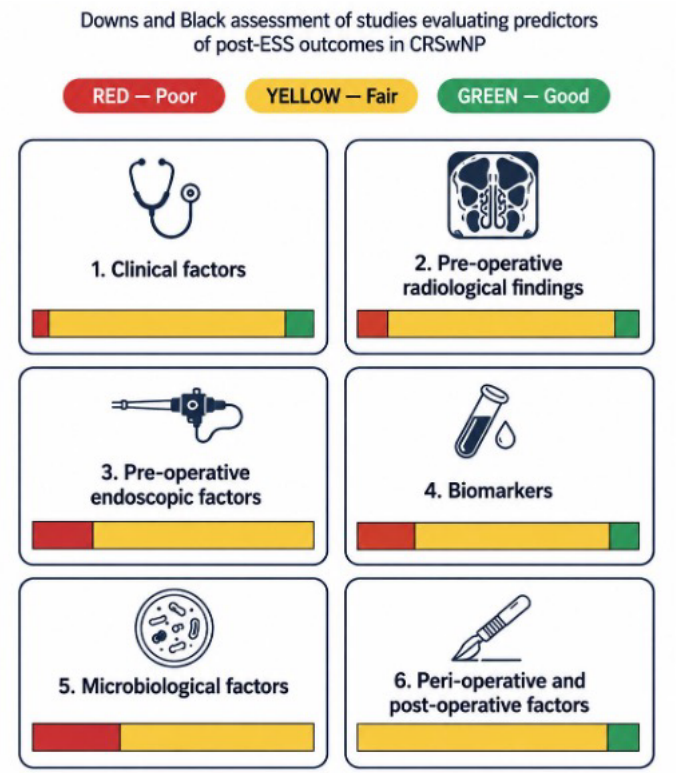
Studies evaluating biomarkers or predictive models were additionally limited by heterogeneous thresholds, data-driven selection of cut-offs, and infrequent internal or external validation, resulting in a potential risk of overfitting and reduced generalizability. Accordingly, greater confidence was assigned to predictors supported by consistent findings across multiple independent cohorts, whereas isolated associations derived from small or methodologically weaker studies were interpreted cautiously.

To facilitate interpretation, we are finally including and overall overview of the methodological quality profile across predictors domains in a Supplementary Figure 1, the methodological quality of the included evidence was predominantly fair according to the Downs and Black checklist, with only a limited number of studies classified as good and some studies classified as poor. No observational study was classified as excellent, partly because the checklist reserves its highest possible scores for randomized controlled trials. Individual scores and quality categories are reported in the corresponding study-characteristics tables, while aggregated scores according to predictor domains are presented in Table 10.

Table S1. PubMed/MEDLINE database search strategy.

Search #	Search query	No. results
#1 – CRSwNP	"Nasal Polyps"[MeSH Terms] OR "CRSwNP" [Title/Abstract] OR "chronic rhinosinusitis with nasal polyp*"[Title/Abstract] OR "CRS with nasal polyp*"[Title/Abstract] OR "nasal polyp*"[Title/Abstract] OR "nasal polyposis"[Title/Abstract]	13,374
#2 – Endoscopic sinus surgery	"Nasal Surgical Procedures"[MeSH Terms] OR "endoscopic sinus surg*"[Title/Abstract] OR "functional endoscopic sinus surg*"[Title/Abstract] OR ESS[Title/Abstract] OR FESS[Title/Abstract] OR "sinus surg*"[Title/Abstract]	33,692
#3 – Predictive and prognostic factors	"Prognosis"[MeSH Terms] OR "Risk Factors"[MeSH Terms] OR predict*[Title/Abstract] OR prognos*[Title/Abstract] OR factor*[Title/Abstract] OR determinant*[Title/Abstract] OR associat*[Title/Abstract] OR comorbid*[Title/Abstract] OR "autoimmune disease*"[Title/Abstract] OR eosinophil*[Title/Abstract] OR allerg*[Title/Abstract] OR smok*[Title/Abstract] OR "eosinophilic inflammation"[Title/Abstract] OR "aspirin intoleran*"[Title/Abstract] OR NSAID-ERD[Title/Abstract] OR N-ERD[Title/Abstract] OR asthma[Title/Abstract] OR "blood eosinophil*"[Title/Abstract] OR "nasal cytology"[Title/Abstract]	13,697,015
#4 – Postoperative outcomes	"Treatment Outcome"[MeSH Terms] OR "Recurrence"[MeSH Terms] OR "Reoperation"[MeSH Terms] OR outcome*[Title/Abstract] OR recurren*[Title/Abstract] OR revision*[Title/Abstract] OR reoperat*[Title/Abstract] OR "poor disease control"[Title/Abstract] OR "disease control"[Title/Abstract] OR efficac*[Title/Abstract] OR scoring[Title/Abstract] OR metric*[Title/Abstract] OR evaluation[Title/Abstract] OR SNOT-22[Title/Abstract] OR "Lund-Kennedy"[Title/Abstract]	7,233,047
#5 – Final search	#1 AND #2 AND #3 AND #4	1,510

Figure S1. Methodological quality profile across predictor domains.



Bars represent the distribution of Downs and Black quality categories reported across predictor entries in Table 10 and do not represent unique studies. CRSwNP, chronic rhinosinusitis with nasal polyps; ESS, endoscopic sinus surgery.