



Chronic Rhinosinusitis with Nasal Polyps

Eileen Wang, MD, MPH
Associate Professor
Division of Allergy and Immunology

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Definitions and Types

- Chronic: ≥ 12 weeks
- Rhinitis: inflammation of nasal mucosa
- Sinusitis: inflammation of sinuses
- Nasal polyps: benign bilateral growths in the nasal cavity and sinuses
- 2 phenotypes of chronic rhinosinusitis (CRS)
 - Chronic rhinosinusitis **with** nasal polyps (CRSwNP)
 - Chronic rhinosinusitis **without** nasal polyps (CRSsNP)

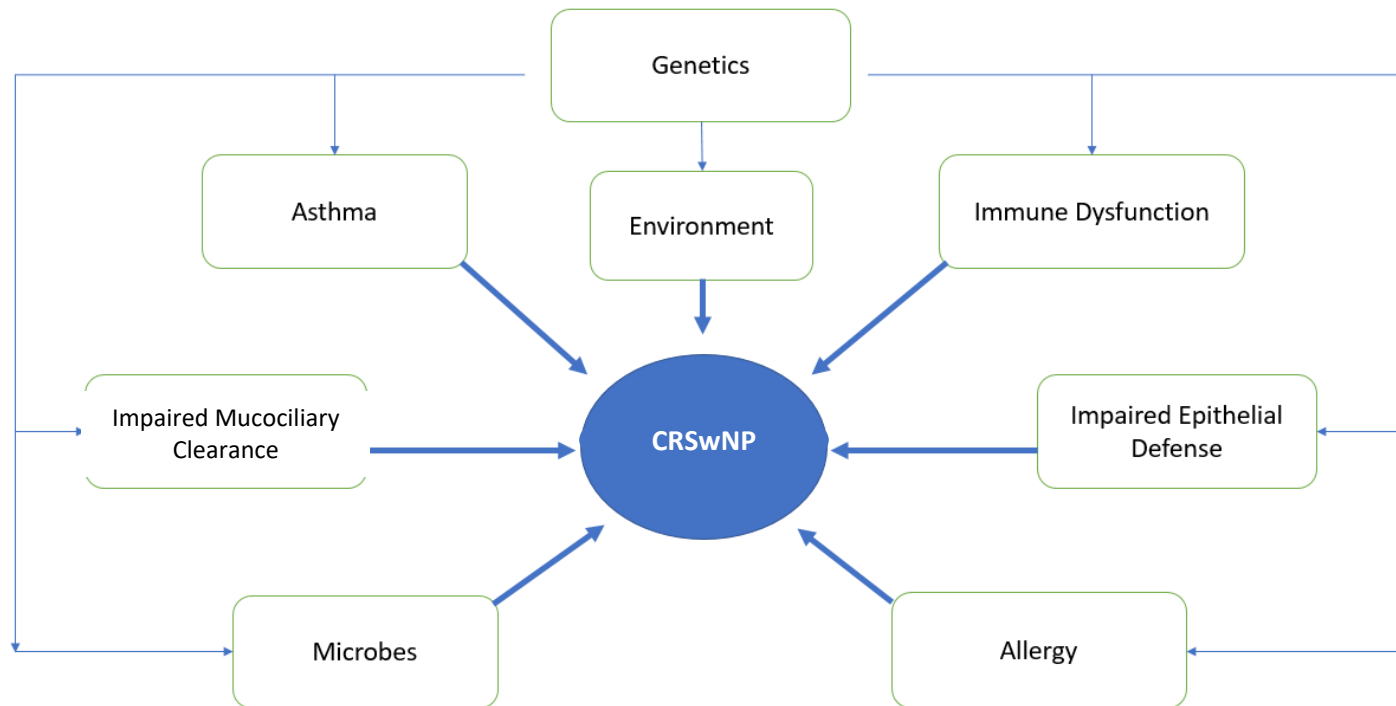
Management of the patient with rhinosinusitis. In: Krouse JH, et al. *Managing the Allergic Patient*, Elsevier; 2008;103-129.

Epidemiology

- Prevalence of chronic rhinosinusitis \approx 11% to 12% based on US and European studies
 - Few studies examine the incidence and prevalence of CRSwNP specifically
 - European study with a prevalence of CRSwNP \approx 4% in the general population
- Male to female = 2:1
 - Disease is often more severe in women
- Incidence increases with age with a peak \approx 50 years

Hastan D, et al. *Allergy*. 2011;66(9):1216-1223; Blackwell DL, et al. *Vital Health Stat*. 2014:1-161; Lange B, et al. *Clin Otolaryngol*. 2013;38(6):474-480; Hulse KE, et al. *Clin Exp Allergy*. 2014;45:328-346; Stevens WW, et al. *J Allergy Clin Immunol Pract*. 2016;4:565-572; Chen S, et al. *Curr Med Res Opin*. 2020;36(11):1897-1911.

Risk Factors



Adapted from Hsu J, et al. *J Allergy Clin Immunol.* 2013;131(4):977-993; Chen S, et al. *Curr Med Res Opin.* 2020;36(11):1897-1911.

Economic Burden

- Direct costs ≈\$10 to \$13 billion/year in the United States
 - Driven by:
 - Outpatient visits
 - Prescription medical therapy
 - Endoscopic sinus surgery
- Indirect costs linked to CRS-related losses in work productivity >\$20 billion/year

Rudmik L. *Curr Asthma Allergy Rep.* 2017;17(4):20.

Quality of Life Impact

Health state	Health utility score
Perfect health	1
US norms	0.81
COPD (mod)	0.73
Parkinson disease (1st year)	0.67
CAD requiring PCI	0.67
CRS	0.65
Asthma (mod)	0.64
ESRD with HD	0.64
HIV	0.52
Death	0



CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; HD, hemodialysis; MOD, moderate; PCI, percutaneous coronary intervention.

Adapted from DeConde AS, Soler ZM. *Am J Rhinol Allergy*. 2016;30(2):134-139.

Pathogenesis of Nasal Polyps

Abnormal barrier; increased microbial burden



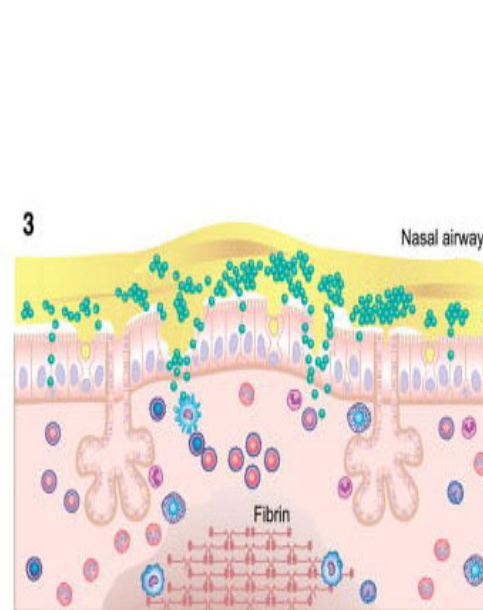
Recruitment and expansion of inflammatory cells, tissue swelling, inflammation



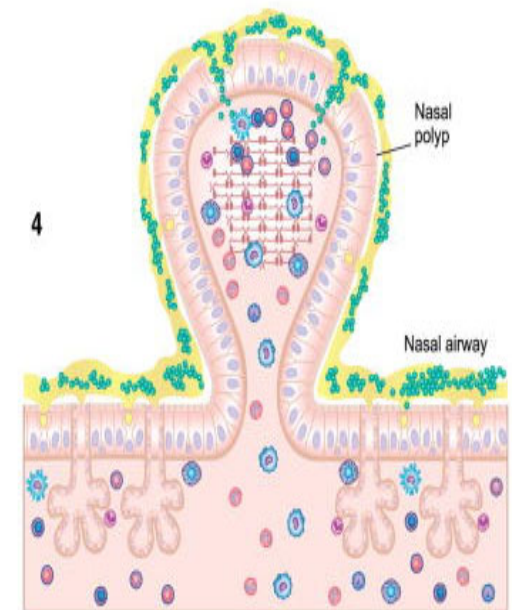
Cross-linked fibrin deposition



Tissue remodeling with loss of submucosal glands in polyp and profound inflammatory cell expansion



Recruitment and expansion of inflammatory cells, tissue swelling, inflammation, and deposition of crosslinked fibrin



Tissue remodeling with loss of submucosal glands in polyp and profound inflammatory cell expansion

Stevens WW, et al. *J Allergy Clin Immunol Pract.* 2016;4(4):565-572.

Inflammatory Subtypes or Endotype

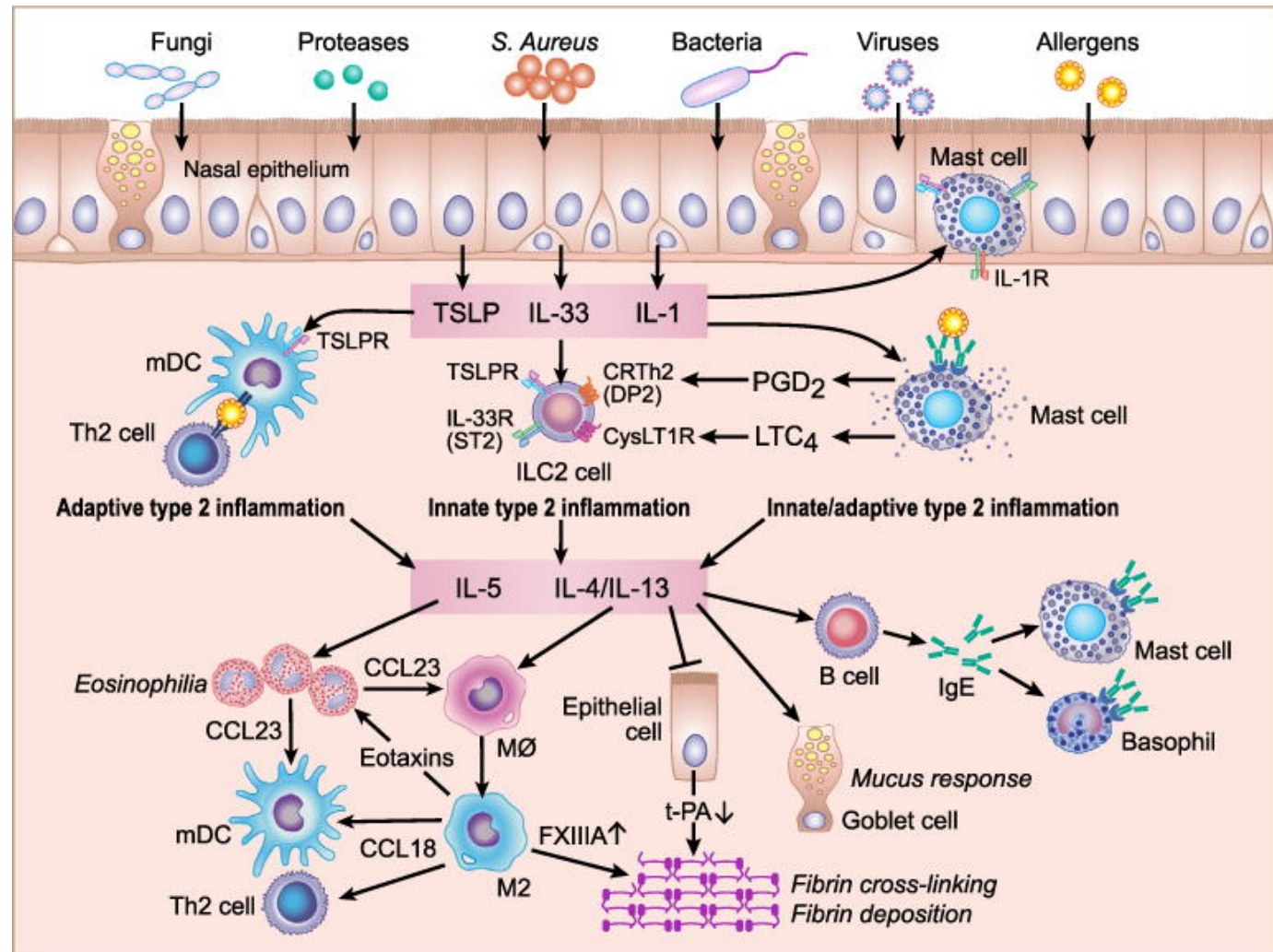
Endotype	Cytokines	Cells
Type 1 (T1)	IFN γ , IL-12	NK cells, CD8+ T cells, Th1, ILC1
Type 2 (T2)	IL-4, IL-5, IL-13	Eosinophils, basophils, Th2, ILC2
Type 3 (T3)	IL-17, IL-8	Neutrophils, Th17, ILC3
Untypeable		

NK, natural killer.

Stevens WW, et al. *J Allergy Clin Immunol Pract.* 2016;4(4):565-572; Kato A, et al. *Allergy.* 2022;77(3):812-826; Staudacher AG, et al. *Ann Allergy Asthma Immunol.* 2020; 124; 318-325.

Type 2 Inflammation

- Most cases of CRSwNP in the United States are driven by type 2 inflammation
 - IL-4, IL-5, IL-13
 - Eosinophilia



Kato A. *Allergol Int.* 2015;64(2):121-130

Biomarkers for T2-Driven CRSwNP

Eosinophils

- **Circulating eosinophilia**
- Eosinophils in sinonasal tissue
- Eosinophil granule proteins in sinonasal tissue
- IL-5 in nasal polyp tissue

Immunoglobulin (Ig) E levels

- **Serum total IgE levels**
- Total and specific IgE levels in nasal polyp tissue
- **Specific IgE levels against *Staphylococcus aureus* enterotoxins**

Staudacher AG, et al. *Ann Allergy Asthma Immunol.* 2020;124(4):318-325.

Diagnosis: Signs and Symptoms

Subjective

Nasal blockage/obstruction
and/or

Nasal discharge

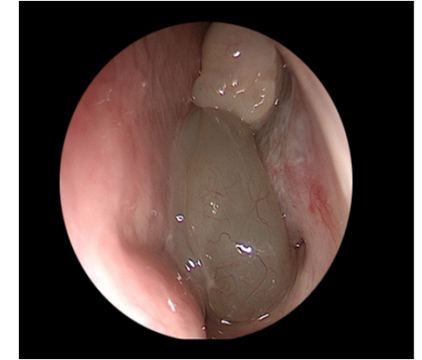
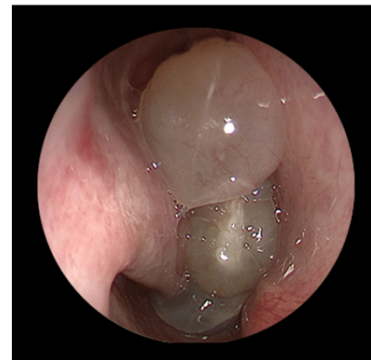
+/- Facial pain/pressure

+/- Reduction/loss of smell

Duration ≥ 12 weeks

Objective

Verify presence of polyps with imaging or endoscopy



Symptoms do not reliably distinguish between CRSwNP and CRSsNP.

Bachert C, et al. *World Allergy Organ J.* 2014;7(1):25; Image source: Ryan MW. UTSouthwestern Medical Center.
utswmed.org/medblog/nasal-polyps-advanced-sinus-surgery/

Disease Measurement Tools

Patient-Reported Quality of Life (QOL) Tools

22-item Sinonasal
Outcome Test
(SNOT-22)

Endoscopic Tools

Nasal Polyp Score
(NPS)

Radiographic Tools

Lund Mackay (LM)

Orlandi RR, et al. *Int Forum Allergy Rhinol.* 2021;11(3):213-739.

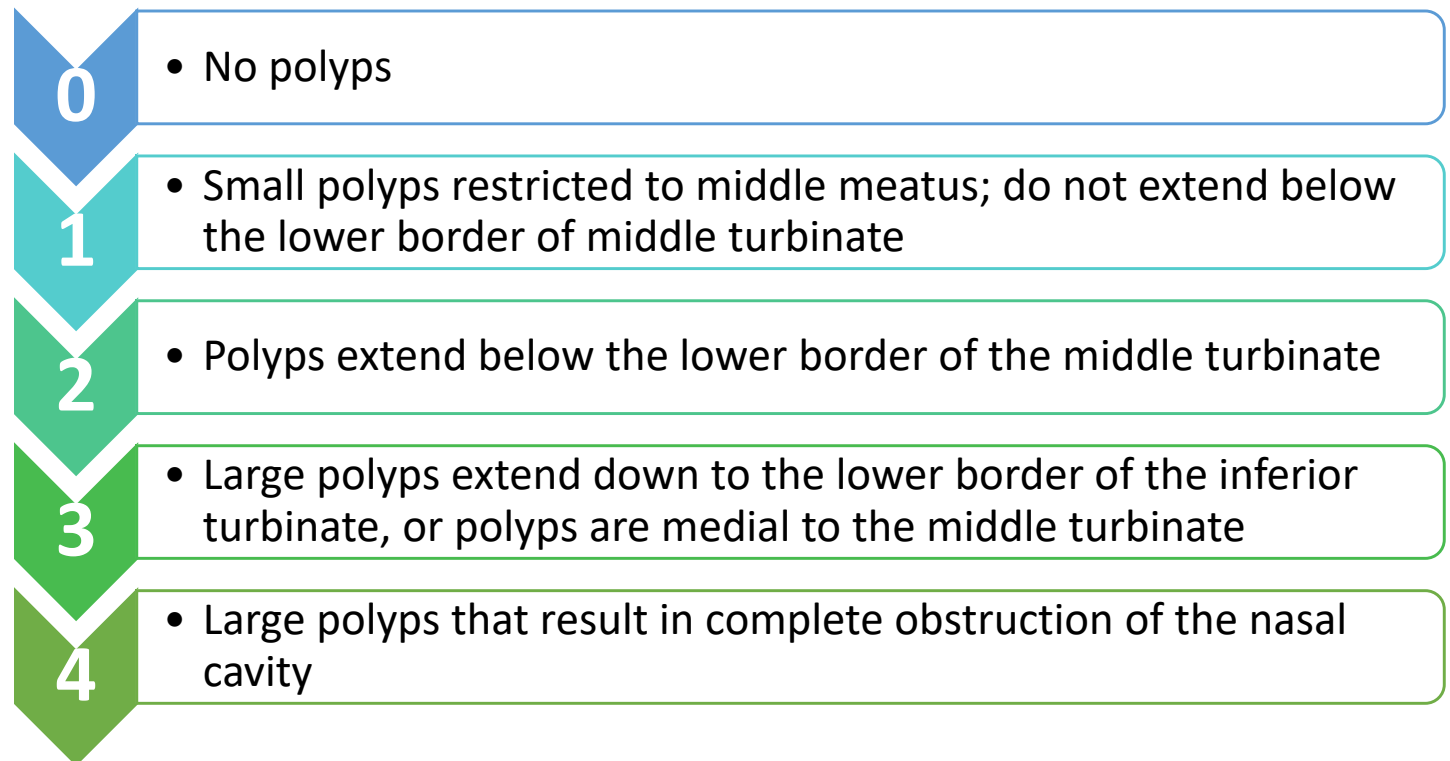
Patient-Reported QOL Tools: Sinonasal Outcome Test (SNOT-22)

Need to blow nose	Dizziness	Fatigue
Nasal blockage	Ear pain	Reduced productivity
Sneezing	Facial pain/pressure	Reduced concentration
Runny nose	Decreased sense of smell/taste	Frustrated/restless/irritable
Cough	Difficulty falling asleep	Sad
Postnasal drainage	Wake up at night	Embarrassed
Thick nasal discharge	Lack of good night's sleep	
Ear fullness	Wake up tired	

- Each problem scored from “no problem” to “as bad as it can be”
- Score range 0-110
- **Suggested stratification:**
 - Mild 8-20
 - Moderate >20-50
 - Severe >50

Nasal Polyp Score (NPS)

- Assessed endoscopically
- Scale ranges from 0 (no polyp) to 4 (large polyps) for each side
- Total score 0-8



Côté DWJ, Wright ED. Objective Outcomes in endoscopic sinus surgery. In: Iancu C, ed. *Advances in Endoscopic Surgery*. IntechOpen; 2011.

Lund MacKay Score

- Most used radiographic staging system for CRS
- Scoring 6 bilateral areas of sinus opacification from 0-2 (no mucosal thickening, partial opacification, total opacification)
 - Maxillary
 - Anterior ethmoids
 - Posterior ethmoids
 - Sphenoid
 - Frontal
 - Ostiomeatal complex
- Total: 0-24
- Using a score ≥ 4 in the setting of related sinonasal symptoms has sensitivity >85% and a positive predictive value of >80% for the diagnosis of CRS

Lund VJ, MacKay S. *Rhinology*. 1993;31(4):183-184; Bhattachacharyya N. *Curr Allergy Asthma Rep*. 2010;10(3):171-174.

Key Comorbidities to Consider

Asthma

- Recommended screening in patients with CRSwNP

Allergic rhinitis

- Inhalant allergy may be a disease-modifying factor in CRSwNP

Aspirin/NSAID hypersensitivity →
aspirin and/or NSAID-exacerbated
respiratory disease (AERD or NERD)

- Important clinical phenotype

Cystic fibrosis (CF)

- ≈90% of patients with CF have comorbid CRSwNP

NSAID, nonsteroidal anti-inflammatory drug.

Chen S, et al. *Curr Med Res Opin.* 2020;36(11):1897-1911; Bachert C, et al. *J Asthma Allergy.* 2021;14:127-134; Orlandi RR, et al. *Int Forum Allergy Rhinol,* 2021;11(3):213-739.

Key Points

- CRS has significant impacts on QOL and high direct and indirect costs
- There are multiple endotypes of CRSwNP
- In the United States, the majority are driven by type 2 inflammation, characterized by T2 cytokines (IL-4, IL-5, IL-13) and peripheral eosinophilia
- Understanding key comorbid conditions can help reduce morbidity and guide management



Treatment Landscape

Patient Counseling: Treatment Expectations

*This is a chronic inflammatory condition.
There is no cure.*



- **Goals of treatment:**
 - Improve symptoms and QOL
 - Control inflammation and associated comorbidities
 - Increase medical efficacy
 - Confirm pathology

Treatment Options

Normal saline
irrigation

Topical
corticosteroids

Oral
corticosteroids

Antibiotics

Surgical
intervention

Steroid-eluting
stents

Biologic agents

Nasal Saline Irrigation

Decreases irritants and allergens in the nose and sinuses

Clears mucosa for better medication delivery

2021 Consensus Statement: use in CRS

- Improves symptoms, QOL, and endoscopic findings
- High volume (>60 cc) is more beneficial
- Duration >8 weeks
- A preponderance of benefit > harm
- Recommended (grade B)

Orlandi RR, et al. *Int Forum Allergy Rhinol.* 2021;11(3):213-739.



Topical Intranasal Corticosteroid Therapy

Intranasal delivery: intranasal steroid spray (standard delivery)

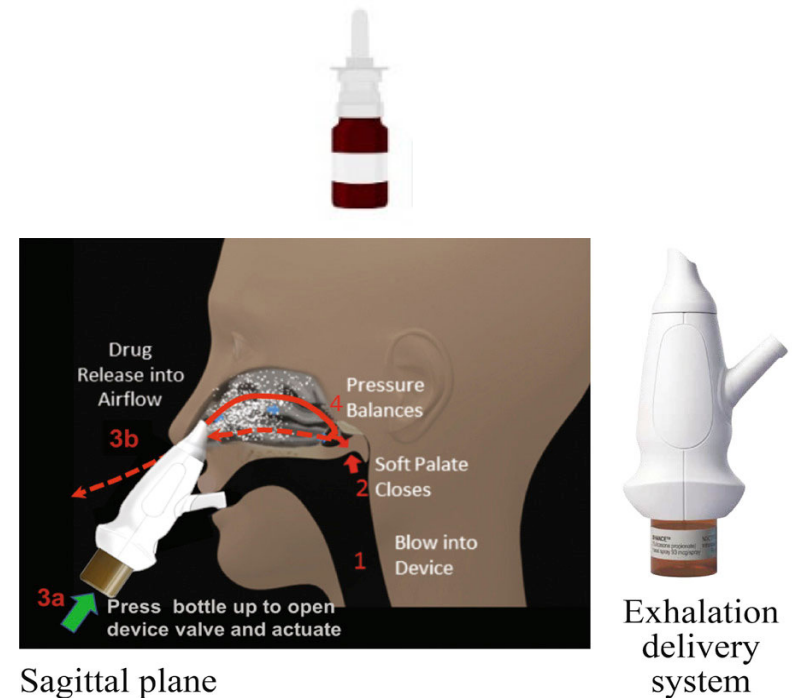
- Improves symptoms, QOL, endoscopy scores, polyp size
- Strongly recommended based on benefits > harms (grade A)

Intranasal delivery: atomizer/nebulizer/exhalation device

- Some benefit over standard delivery and placebo
- Recommended/options if other methods fail (grade A)

Orlandi RR, et al. *Int Forum Allergy Rhinol.* 2021;11(3):213-739.

Leopold DA, et al. *J Allergy Clin Immunol.* 2019;143(1):126-134.



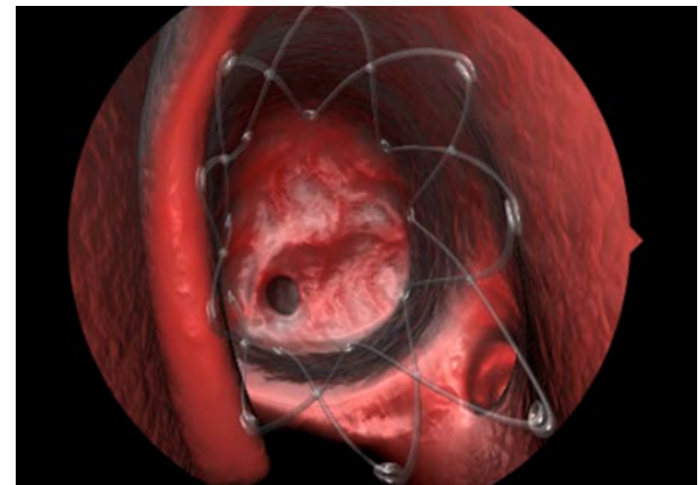
Topical Intranasal Corticosteroid Therapy

Intranasal delivery: steroid added to nasal saline irrigation

- Improves symptoms, QOL, endoscopy scores in postoperative patients
- Strong recommendation if not controlled with standard delivery, particularly following sinus surgery (grade A evidence)

Corticosteroid-eluting stent

- Reduces ethmoid obstruction, polyp grade, revision surgery rates
- Option after prior ethmoid surgery (grade A)



Orlandi RR, et al. *Int Forum Allergy Rhinol.* 2021;11(3):213-739.

Antibiotics

Short-term nonmacrolide oral antibiotics: recommended against (grade B)

- Potential reduction in polyp size without a change in symptoms
- Should generally not be prescribed except in acute exacerbation

Macrolide antibiotics are an option (grade B)

- May improve symptoms, imaging, and endoscopy findings, but the results are mixed
- Lead to more sustained benefits in patients with neutrophil-dominant polyps or who are unresponsive to corticosteroids
- Adverse effects may include gastrointestinal, ototoxicity, cardiotoxicity, hepatotoxicity, drug-drug interactions

Topical antibiotics should not be routinely used (grade A-)

- Results of systematic reviews and randomized clinical trials have failed to show the benefit

Orlandi RR, et al. *Int Forum Allergy Rhinol*. 2021;11(3):213-739.

Systemic Corticosteroids

Strong evidence for use during flares and for short-term use (grade A)

- Short-term benefit likely 8-12 weeks
- Beneficial perioperatively: decreased blood loss, operative time

Longer-term use carries a risk of harm and is not well supported in the literature

Given the many adverse effects of systemic corticosteroids, efforts should be made to minimize overall exposure to systemic steroids by:

- Topical steroid preparations instead of systemic corticosteroids
- Corticosteroid-sparing medications such as biologic agents
- Surgical intervention when appropriate

Orlandi RR, et al. *Int Forum Allergy Rhinol*. 2021;11(3):213-739.

Systemic Corticosteroid Adverse Effects

Organ system	
Ophthalmologic	Cataracts, glaucoma
Cardiovascular	Hypertension
Gastrointestinal	Gastritis, peptic ulcer disease
Immune	Increased susceptibility to infections
Hematologic	Leukocytosis
Neuropsychiatric	Insomnia, mania, psychosis, dysphoria, depression, euphoria
Musculoskeletal	Osteopenia/osteoporosis, avascular necrosis, myopathy
Dermatologic	Acne, hirsutism, striae, skin thinning, purpura
Endocrinologic	Diabetes/hyperglycemia, adrenal insufficiency, weight gain, cushingoid appearance, fluid retention

Hox V, et al. *Clin Transl Allergy*. 2020;10;1; McEvoy CE, Niewoehner DE. *Chest*. 1997;111(3):732-743.

Other Treatment Options

Antileukotriene agents: option (grade A)

- Montelukast or zafirlukast (leukotriene receptor antagonist)
- Zileuton (5-lipoxygenase inhibitor)

Aspirin desensitization in AERD patients: recommended (grade A)

- Reduced polyp recurrence, surgical revisions, and improved QOL
- Adverse effects include gastrointestinal bleeding, clotting dysfunction
- Consider after surgical removal of nasal polyps
- Joint Task Force 2023: conditional recommendation, moderate certainty evidence
 - Balance benefits and harms

Orlandi RR, et al. *Int Forum Allergy Rhinol.* 2021;11(3):213-739.

Rank MA, et al. *J Allergy Clin Immunol.* 2023;151(2):386-398.

Surgery

Appropriateness Criteria for Surgery in CRSwNP

- Surgery can be appropriately offered when:
 - CT evidence of disease (LM score ≥ 1) **AND** SNOT-22 ≥ 20
 - Following treatment with intranasal corticosteroid of ≥ 8 weeks **AND** a short course of systemic corticosteroid (1-3 weeks duration)

Orlandi RR, et al. *Int Forum Allergy Rhinol.* 2021;11(3):213-739; Rudmik L, et al. *Int Forum Allergy Rhinol.* 2016;6(6):557-567.

Improvement Following Surgery

Rhinosinusitis Disability Index Scores

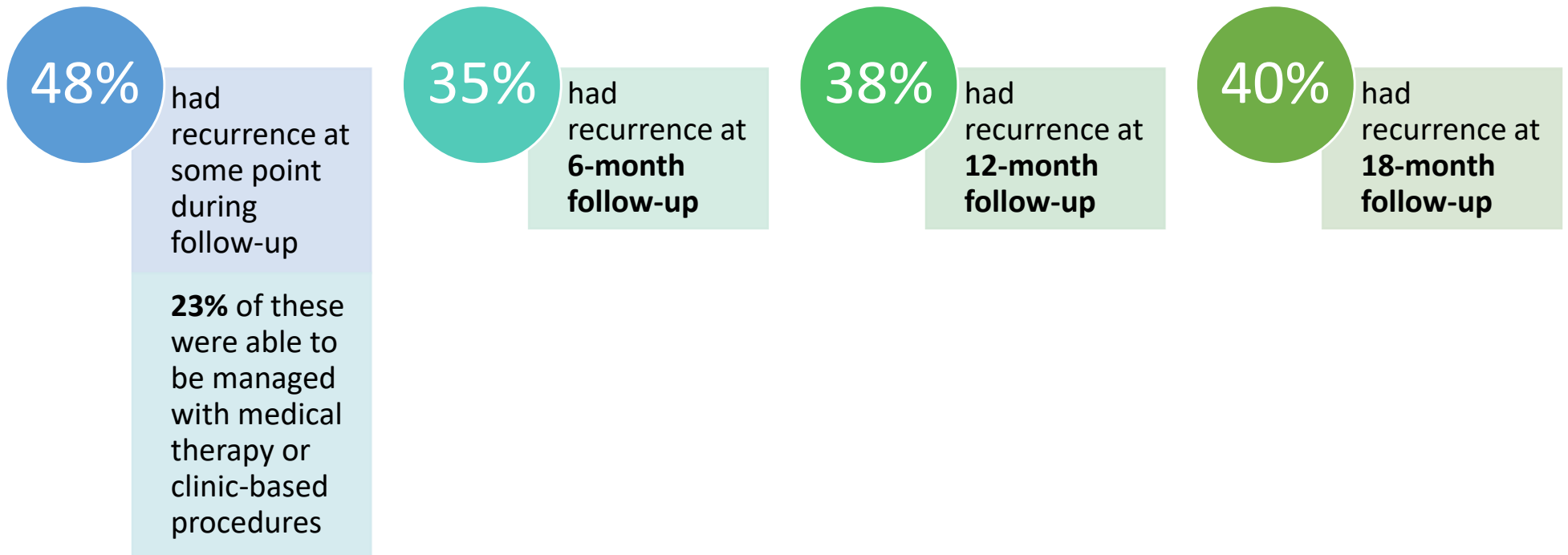
- Observational cohort study of 59 adults
- 38% response rate for long-term follow-up (mean follow-up 10.9 years)
- Minimal clinically important difference value of 8.7
- 17% required additional sinus surgery
- 80% of patients requiring revision sinus surgery had CRSwNP and half had AERD

	Preoperative	6-month postoperative	12-month postoperative	18-month postoperative	Long-term follow-up
CRSwNP	44.7	23.1	27.0	25.6	24.9
CRSsNP	47.9	27.3	14.8	20.2	14.3
Total cohort	46.2	24.8	21.1	23.2	19.9

Adapted from Smith TL, et al. *Int Forum Allergy Rhinol.* 2019;9(8):831-841.

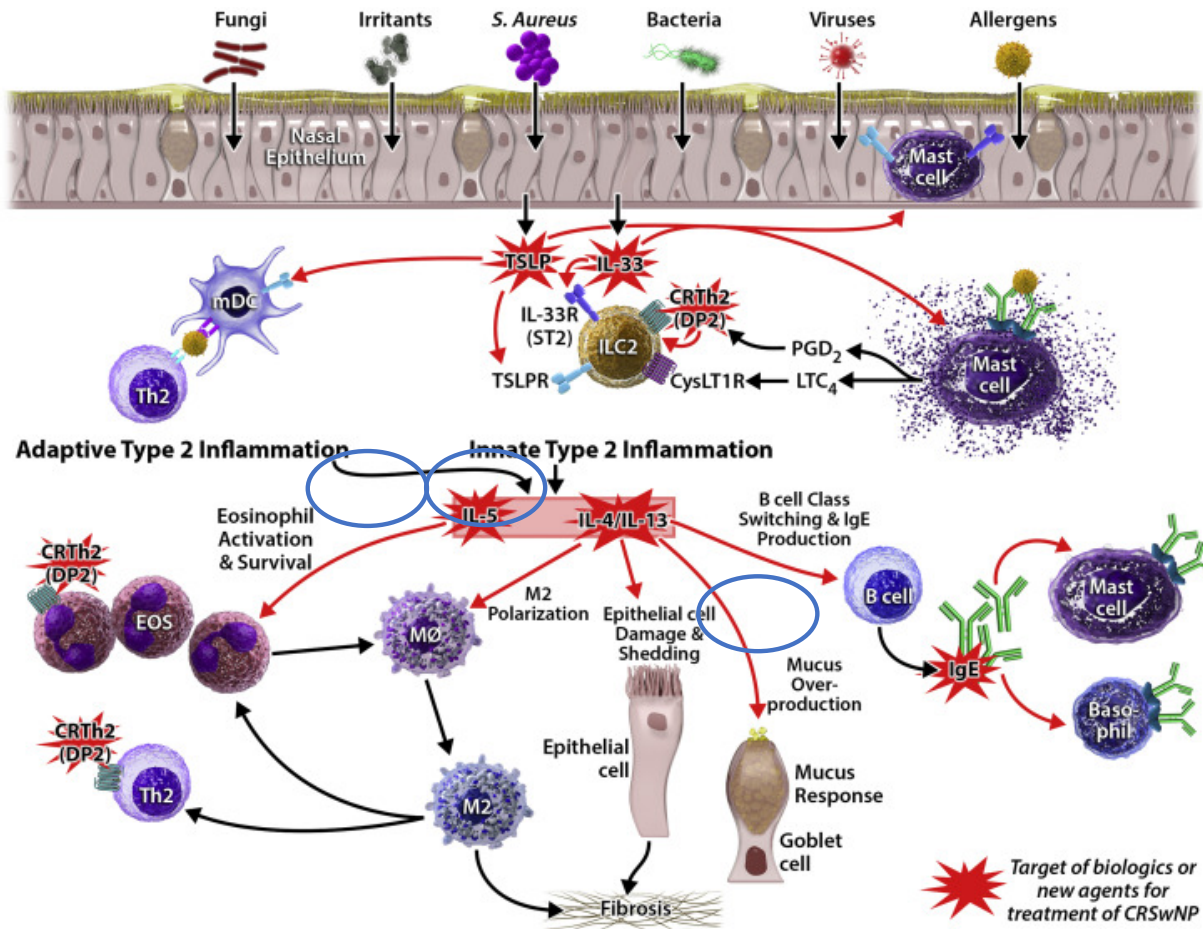
Recurrence After Surgery

- Prospective observational study of 363 adults with CRSwNP who underwent endoscopic sinus surgery
 - Followed for 18 months



DeConde AS, et al. *Laryngoscope*. 2017;127(3):550-555.

Biologics Target Disease Pathophysiology



Laidlaw TM, et al. *Ann AAI*. 2020;124(4):326-332.

- Approved Biologics
 - Dupilumab
 - Omalizumab
 - Mepolizumab
- Emerging Biologics
 - Tezepelumab
 - Benralizumab
 - Depemokimab

Dupilumab

- **SINUS-24** and **SINUS-52** studies, total N = 276 and 448
- Two phase 3 trials: **24- and 52-week**, randomized, double-blind, parallel group study
- Dupilumab SQ versus placebo (added to mometasone furoate), every 2 wks for 24 and 52 wks, respectively
- Major inclusion criteria:
 - Poorly controlled despite surgery and/or nasal steroids
- Two co-primary endpoints were met:
 - Difference in least squares means of change from baseline for total endoscopic nasal polyps score: -2.06 (95% CI: -2.43, -1.69) AND -1.80 (95% CI: -2.10, -1.51)
 - Difference in least squares means of change from baseline at week 24 in nasal congestion/obstruction symptom severity score: -0.89 (95% CI: -1.07, -0.71) AND -0.87 (95% CI: -1.03, -0.71)
- The key secondary endpoints were met:
 - Reduced need for systemic corticosteroids or surgery
 - Improvements in smell and chronic rhinosinusitis symptoms

Bachert C, et al. Lancet 2019; 394:1638–50.

Bachert C, et al. JACI 2020; 145(3):725–39.

Do Not Distribute

Do Not Distribute

Approved Biologics

Drug	Target	Approval in US	Age (years)	Dosing and Frequency for CRSwNP		Route	Phase 3 Clinical Trial Results		
							Nasal Polyp Burden	Nasal Congestion	Reduced Need for Surgery
Dupilumab	IL-4Rα (blocks IL-4 and IL-13)	2017 A.D. 2018: Asthma 2019: CRSwNP (add on) 2022: EoE 2022: Prurigo Nodularis	A.D.≥0.5; Asthma≥6; CRSwNP≥18; EoE≥12	300 mg	Q2W	s.q. prefilled auto-injector or syringe	✓	✓	✓
Omalizumab	IgE	2003 Asthma 2016 CSU 2020: CRSwNP (add on)	Asthma≥6; CSU≥12; CRSwNP≥18	75-600 mg (based upon weight, IgE level)	Q2W Q4W	s.q. prefilled syringe	✓	✓	Not done
Mepolizumab	IL-5	2015 Asthma 2019 EGPA 2020 HES 2021: CRSwNP (add on)	Asthma≥6; EGPA≥18; HES≥12 CRSwNP≥18	100 mg	Q4W	s.q. prefilled auto-injector or syringe	✓	✓	✓

Omalizumab

- **POLYP1** and **POLYP2** studies, N = 138 and 127
- Two phase 3 trials: **24-week**, randomized, double-blind, parallel group study
- Omalizumab versus placebo (added to standard of care), every 2-4 wks for 24 wks
- Major inclusion criteria:
 - Inadequate response to standard of care therapy
- Two co-primary endpoints were met:
 - Difference in least squares means of change from baseline for total endoscopic nasal polyps score: -1.14 (95% CI: -1.59, -0.69) AND 0.59 (95% CI: -1.05, -0.12)
 - Difference in least squares means of change from baseline for daily nasal congestion score: -0.55 (95% CI: -0.84, -0.25) AND -0.5 (95% CI: -0.80, -0.19)
- The key secondary endpoints was met:
 - Sino-nasal Outcome Test-22 (SNOT-22) for health-related quality of life
 - University of Pennsylvania Smell Identification Test (UPSIT) for sense of smell
 - Posterior and anterior rhinorrhea scores for post-nasal drip and runny nose, respectively

Gevaert P, et al. JACI 2020; 146(3):595-605.

Bachert C, et al. JACI 2020; 145(3):725-39.

Do Not Distribute

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Mepolizumab	IL-5	2015 Asthma 2019 EGPA 2020 HES 2021: CRSwNP (add on)	Asthma \geq 6; EGPA \geq 18; HES \geq 12 CRSwNP\geq18	100 mg	Q4W	s.q. prefilled auto-injector or syringe	✓	✓	✓

Mepolizumab

- **SYNAPSE** Phase 3 trial: **52-week**, randomized, double-blind, parallel group study (N>400)
- Mepolizumab 100mg SQ versus placebo (added to standard of care), every 4 wks for 52 wks
- Major inclusion criteria:
 - Severe bilateral nasal polyps (average nasal obstruction VAS symptom score > 5 and an endoscopic score of at least 5 out of a maximum score of 8, minimum score of 2 in each nasal cavity)
 - At least one prior surgery for nasal polyps in the previous 10 years
 - Recurrent nasal polyps despite treatment with SOC and in current need of nasal polyp surgery
- Two co-primary endpoints were met:
 - Median change for total endoscopic nasal polyps score: -0.73 (95% CI: -1.11, -0.34)
 - Median change for nasal obstruction visual analogue scale score: -3.14 (95% CI: -4.09, -2.18)
- The key secondary endpoint was met:
 - Time to first actual nasal surgery up to week 52 – mepolizumab showed a reduction of 57% (p=0.003) versus placebo (hazard ratio [95% CI]: 0.43 [0.25, 0.76]).

Bachert C, et al. JACI 2020; 145(3):725–39.

Hopkins C, et al. ERJ 2020; 56(64):4616.

<https://www.gsk.com/en-gb/media/press-releases/nucala-mepolizumab-is-the-first-anti-il5-biologic-to-report-positive-phase-3-results-in-patients-with-nasal-polyps>.

Accessed 3/20/2020.

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Mepolizumab	IL-5	2015 Asthma 2019 EGPA 2020 HES 2021: CRSwNP (add on)	Asthma \geq 6; EGPA \geq 18; HES \geq 12 CRSwNP\geq18	100 mg	Q4W	s.q. prefilled auto-injector or syringe	✓	✓	✓

Updates Since Original Trials

Dupilumab

- Additional evidence for improvement in sense of smell, as early as day 3
- Transient eosinophilia with dupilumab did not affect efficacy and rarely associated with clinical symptoms

Omalizumab

- Open-label extension study demonstrating improvement was sustained with treatment at 52 weeks

Mepolizumab

- Post hoc analysis of SYNAPSE revealed mepolizumab reduced risk of further sinus surgery irrespective of baseline blood eosinophil counts and time since last surgery

- Joint Task Force 2023: biologics received conditional recommendation based on moderate certainty of evidence
 - Consider other options or use together with biologics such as INCS, surgery. For AERD, aspirin therapy after desensitization.

Mullol J, et al. *J Allergy Clin Immunol Pract.* 2022;10(4):1086-1095.e5; Cantone E, et al. *J Pers Med.* 2022;12(8):1215; Wechsler ME, et al. *J Allergy Clin Immunol Pract.* 2022;10(10):2695-2709; Gevaert P, et al. *J Allergy Clin Immunol.* 2022;149(3):957-965.e3; Fokkens WJ et al. *Allergy.* 2023;78(3):812-821.; Rank MA, et al. *J Allergy Clin Immunol.* 2023;151(2):386-398.

Comparisons

EVEREST (NCT04998604): phase 4 RCT, dupilumab vs omalizumab, N=422

- First head-to-head trial comparing 2 biologics in patients with CRSwNP and comorbid asthma
- Sponsor Sanofi
- Primary objective: evaluate efficacy of dupilumab compared to omalizumab in reducing polyp size and improving sense of smell

Meta-analyses:

- **Cai S, et al:** 7 RCTs involving 1913 patients, 4 biologics (benralizumab, dupilumab, mepolizumab, omalizumab)
 - Dupilumab better effects in decreasing NPS and nasal congestion severity
 - Benralizumab least effective in reducing nasal congestion severity and SNOT-22
 - No significant differences between effects of the other biologics
- **Oykhman P, et al:** 29 RCTs involving 3461 patients
 - Moderate to high certainty: dupilumab ranks among most beneficial for 7 of 7 outcomes, omalizumab 2 of 7, mepolizumab 1 of 7 and aspirin therapy after desensitization 1 of 7

De Prado Gomez L, et al. *Am J Rhinol Allergy*. 2022;36(6):788-795; Cai S, et al. *J Allergy Clin Immunol Pract*. 2022;10(7):1876-1886.e7; Oykhman P, et al. *J Allergy Clin Immunol*. 2022;149(4):1286-1295; <https://clinicaltrials.gov/study/NCT04998604>

Emerging Biologic Treatments

Benralizumab (anti-IL-5R α)

- **OSTRO**: Europe, United States 56-week study, N = 413, met primary endpoints
- **ORCHID**: ongoing, China, Japan, Thailand, Vietnam 56-week study, N ~ 275
- Co-primary endpoints: total nasal polyp score at 56-week endoscopy, mean nasal blockage score (NBS)

Tezepelumab (anti-TSLP)

- **NAVIGATOR** study: significant improvements in SNOT-22 in adolescents and adults with asthma + CRSwNP
- **WAYPOINT**: ongoing phase 3 RCT, N~400, US, Canada, Asia, Europe
 - Co-primary endpoints: total nasal polyp score at 52-week endoscopy; mean nasal congestion score

Depemokimab (long-acting anti-IL5)

- **ANCHOR1, ANCHOR2**: ongoing phase 3 RCTs, US, Asia, South America, Europe
- Co-primary endpoints: total nasal polyp score at 52-week endoscopy; mean nasal obstruction score

Bachert C, et al. JACI. 2022;149(4):1309-1317; Gevaert P, et al. JACI 2016; 118(5):1133-41; <https://clinicaltrials.gov/study/NCT04157335>;
<https://clinicaltrials.gov/study/NCT04851964>; <https://clinicaltrials.gov/study/NCT04718103>; <https://clinicaltrials.gov/study/NCT05281523>;

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Other Possible Future Biologic Therapies

Anti-IL-33

Anti-CRTH2

C-kit inhibitor (imatinib)

Siglec-8 inhibitor

STAT-6 inhibitor

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How to Select Biologic Therapeutics

Factors to consider

- Phenotyping with biomarkers/predictors of response, clinical characteristics, comorbidities
- Shared decision-making and patient preference
- Cost, dosing frequency, methods of administration, adverse effects

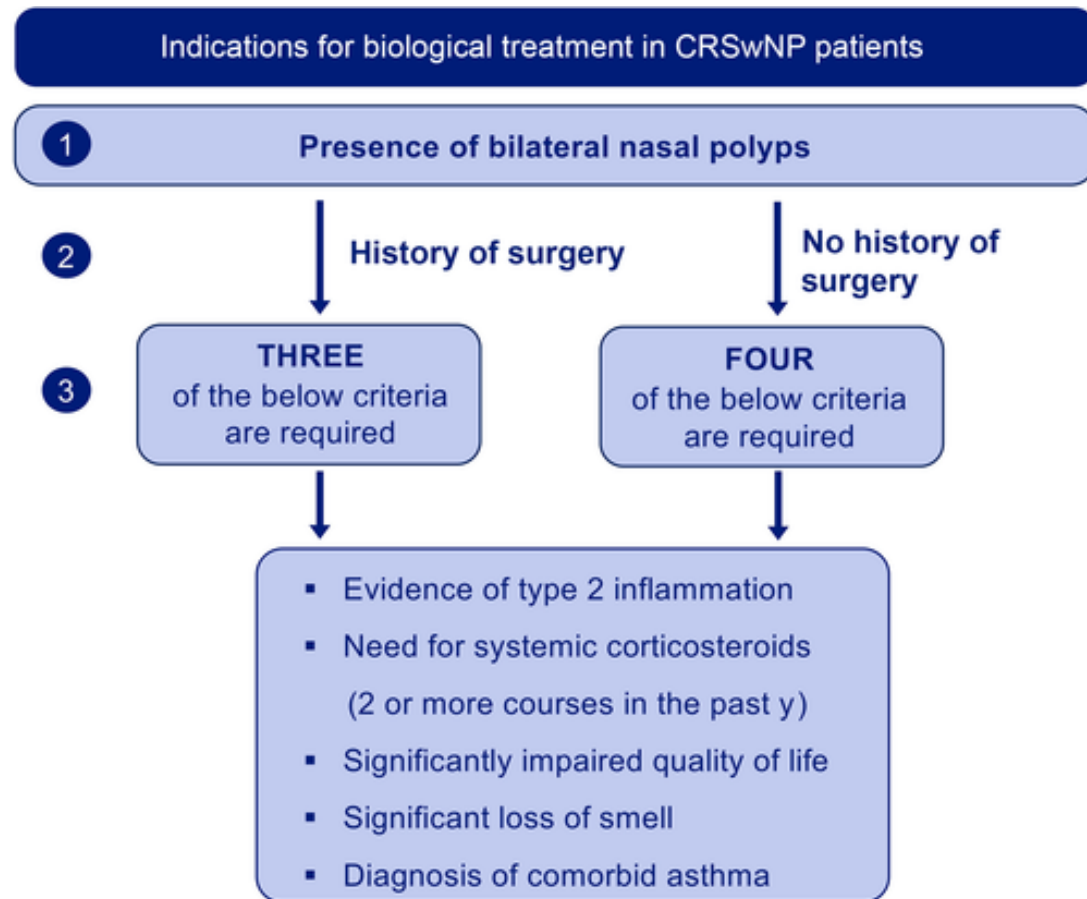
	Dupilumab	Omalizumab	Mepolizumab
Volume of injection	2 mL	Variable	1 mL
Frequency of dosing	Every 2 weeks	Every 2 or 4 weeks	Every 4 weeks
Location for administration	Home	First 3 doses in clinic, then home or clinic	Home or Clinic

Need head-to-head comparisons

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When to Consider Biologics



Conclusion

- CRSwNP has significant burden on QOL, high direct and indirect costs
- Patient education: chronic inflammatory condition without curative treatment
- Goals of treatment to control inflammation and improve QOL
- Treatment options include nasal saline irrigation, topical and systemic corticosteroids, surgical intervention, and biologic therapies
- Biologics, such as dupilumab, omalizumab, and mepolizumab, have been shown to reduce nasal polyp size and improve nasal symptoms in the treatment of CRSwNP

Additional Resources

Organization	Reference
For Patients	
American College of Allergy, Asthma, & Immunology (ACAAI)	acaai.org/allergies/allergic-conditions/chronic-rhinosinusitis-with-nasal-polyps/
American Academy of Allergy, Asthma & Immunology (AAAAI)	www.aaaai.org/tools-for-the-public/conditions-library/allergies/nasal-polyps
American Academy of Otolaryngology-Head and Neck Surgery- ENT Health	www.enthealth.org/conditions/sinusitis/
For Clinicians	
The Joint Task Force on Practice Parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis	Rank MA, et al. <i>J Allergy Clin Immunol.</i> 2023;151(2):386-398.
EUFOREA expert board meeting on uncontrolled severe chronic rhinosinusitis with nasal polyps (CRSwNP) and biologics: definitions and management	Bachert C, et al. <i>J Allergy Clin Immunol.</i> 2020;145(3):725-739.
International consensus statement on allergy and rhinology: rhinosinusitis 2021	Orlandi RR, et al. <i>Int Forum Allergy Rhinol.</i> 2021;11(3):213-739.



Questions?