

Severity Assessment, Patient Selection, and Comparison of Treatment Options for CRSwNP: Are We Ready to Set Our Sights on a Standard?

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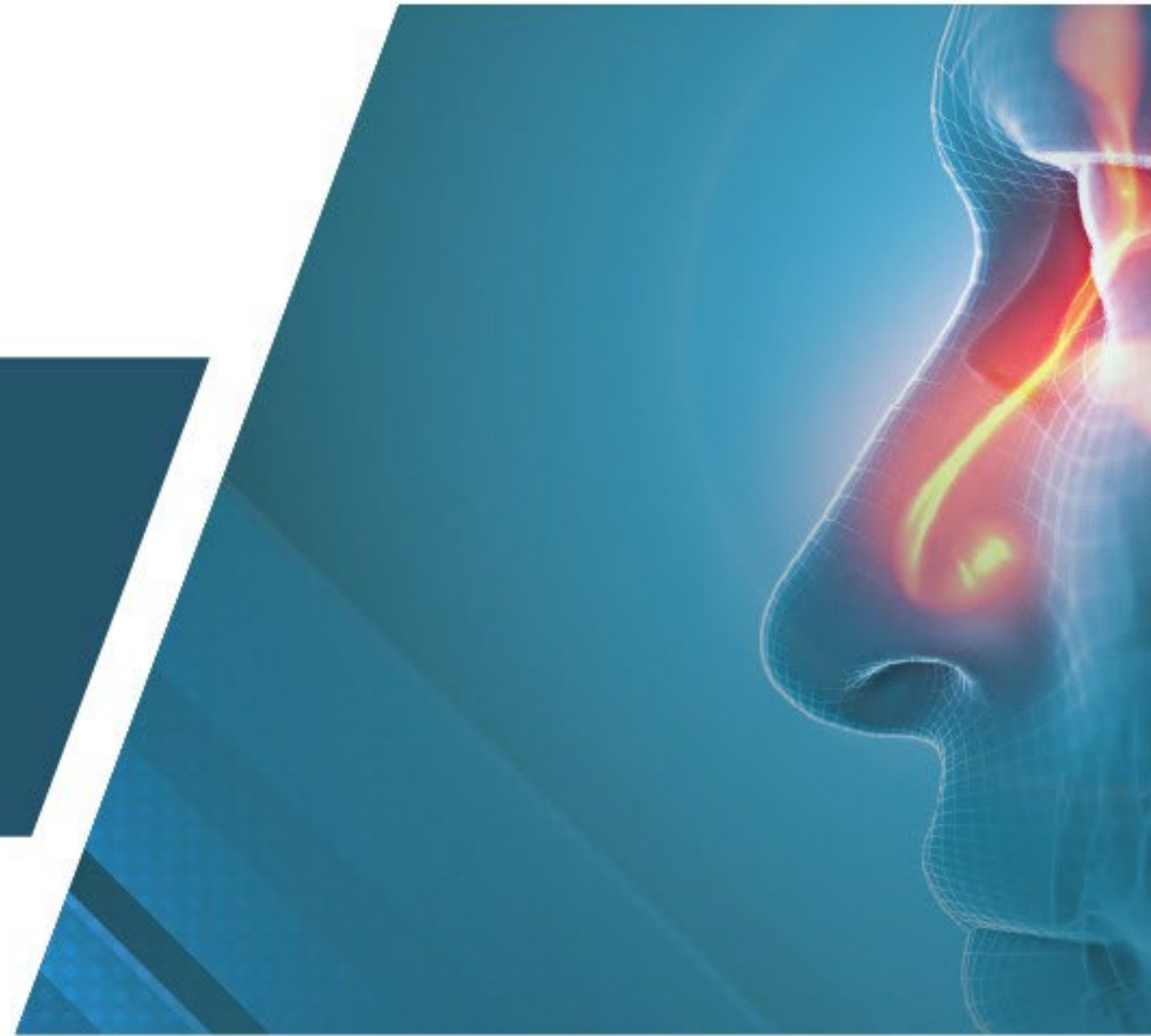
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Consulting: GI Reviewers, LLC. Independent reader for CRS biologics studies

Learning Objectives

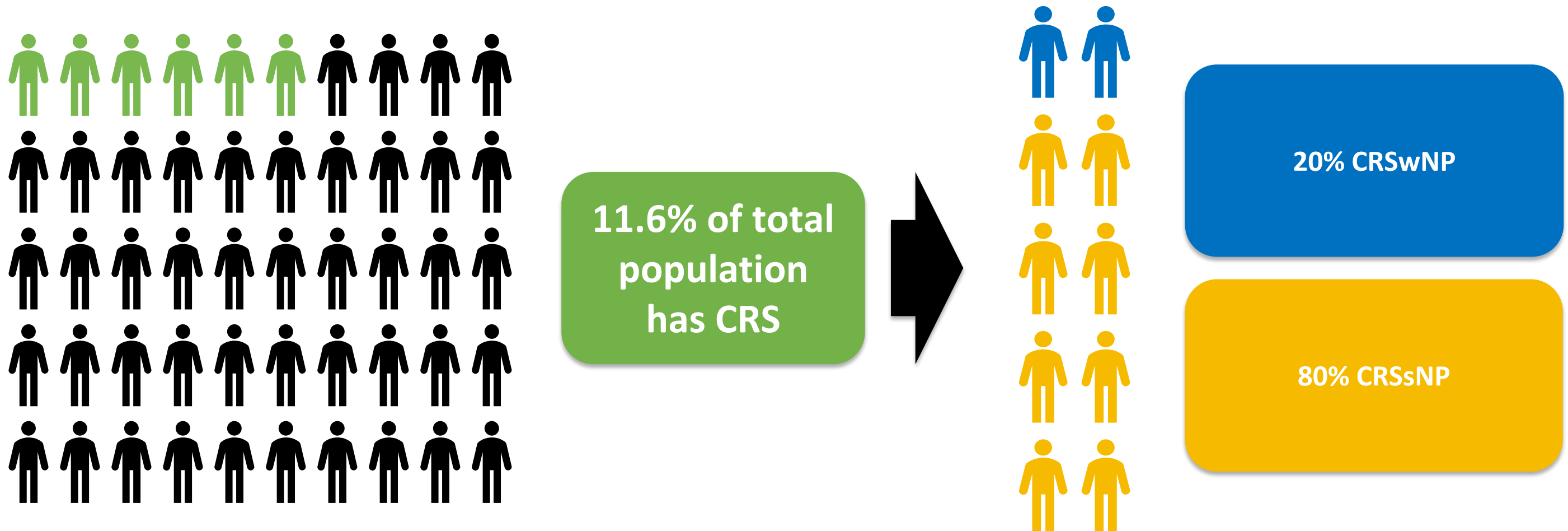
- Apply evidence-based guidance to assess the severity and QOL impact of CRSwNP
- Evaluate clinical trial data on the efficacy and safety of biologics and surgical options for patients with CRSwNP
- Incorporate current guidelines and expert recommendations into the positioning of biologic therapy, sinus surgery, and OCS for the treatment of patients with CRSwNP

The Disease Burden of CRSwNP



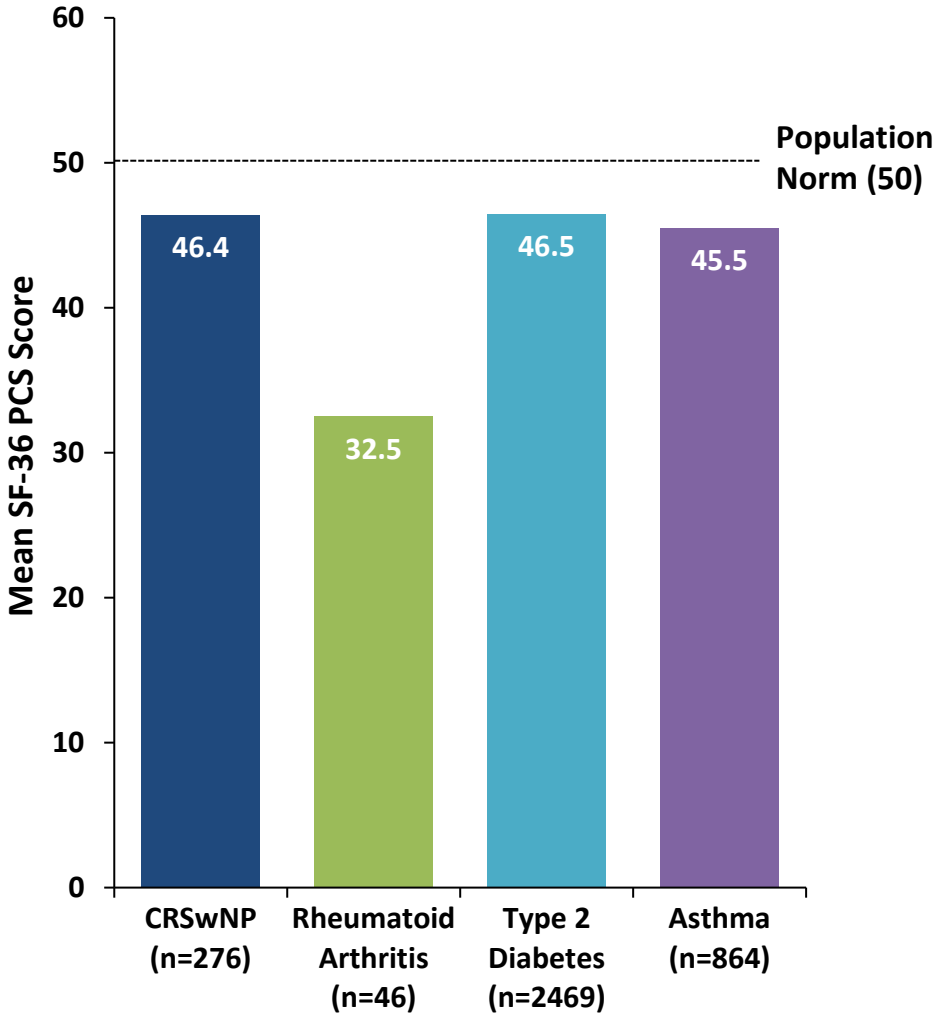
Prevalence of CRS, CRSwNP, & CRSsNP

CDC: 28.9 million American adults have CRS¹

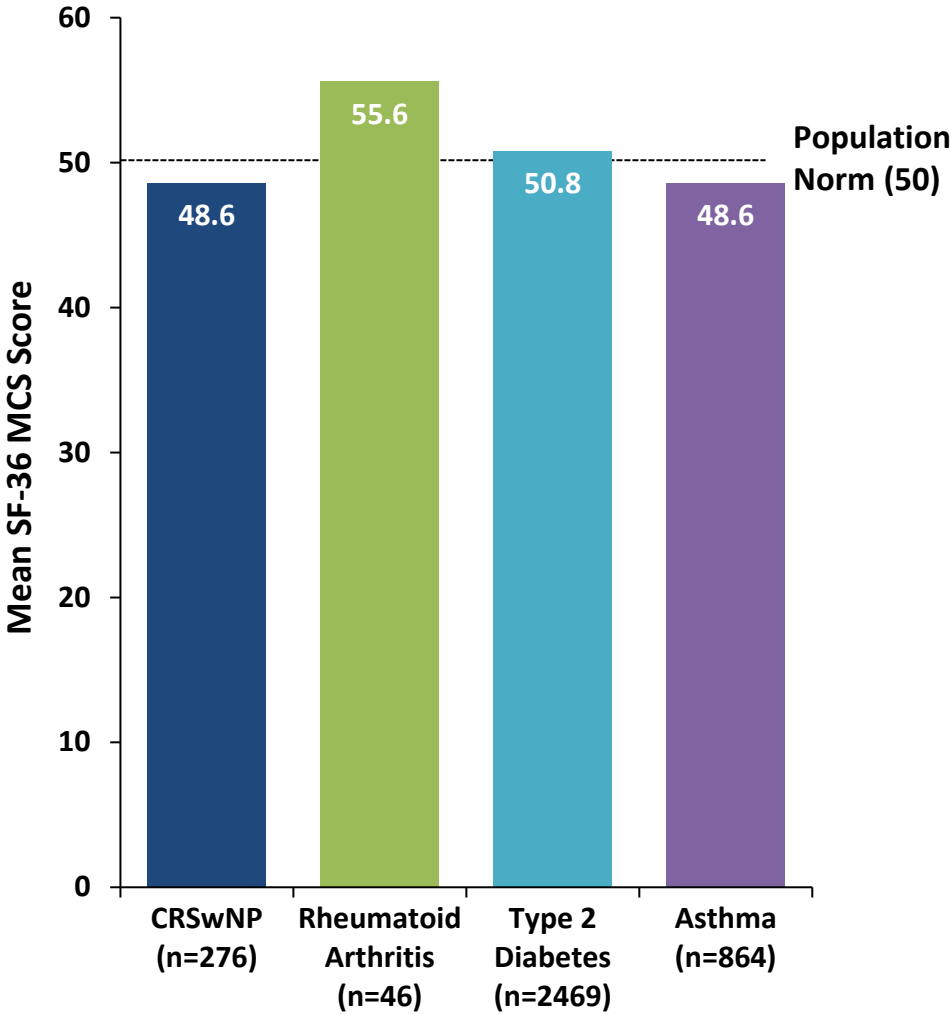


The Burden of CRSwNP

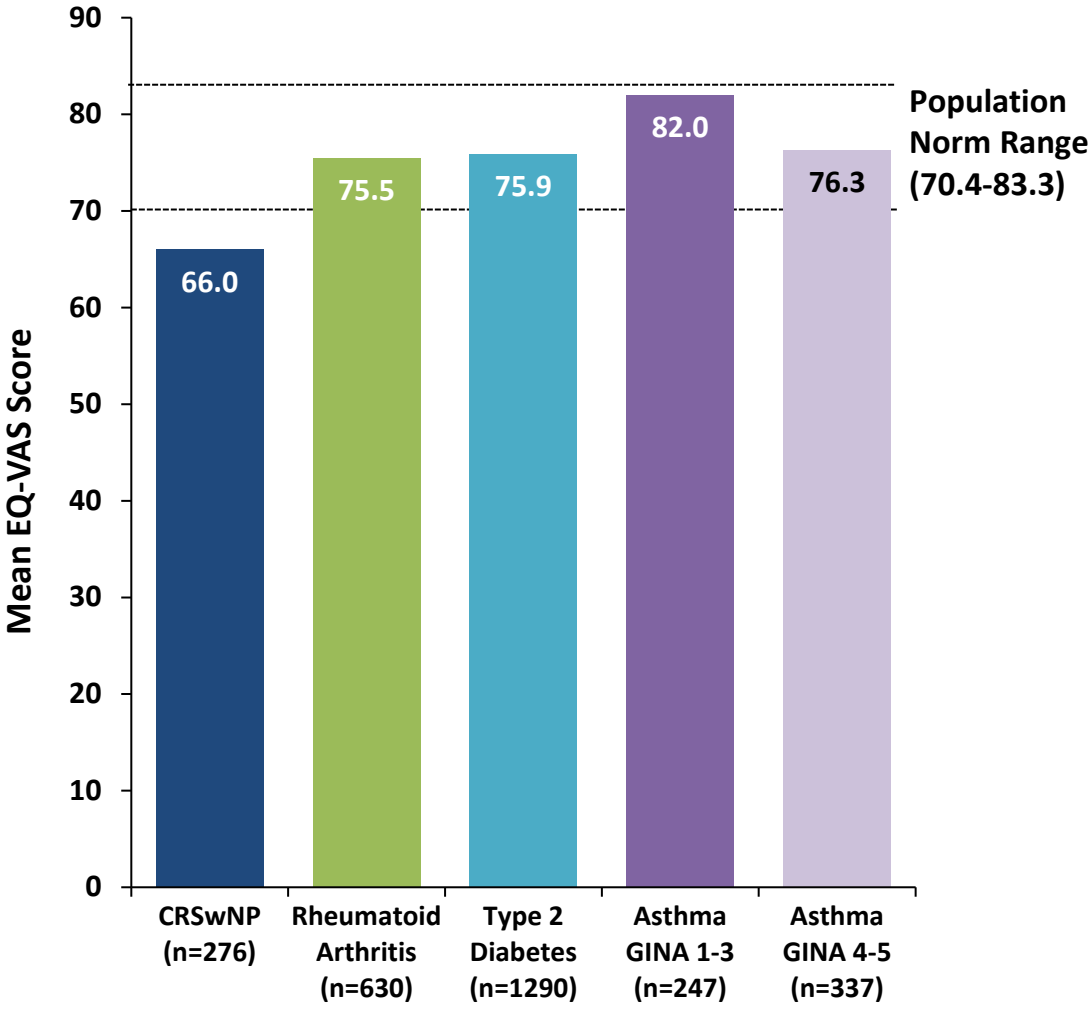
SF-36 PCS Scores



SF-36 MCS Scores

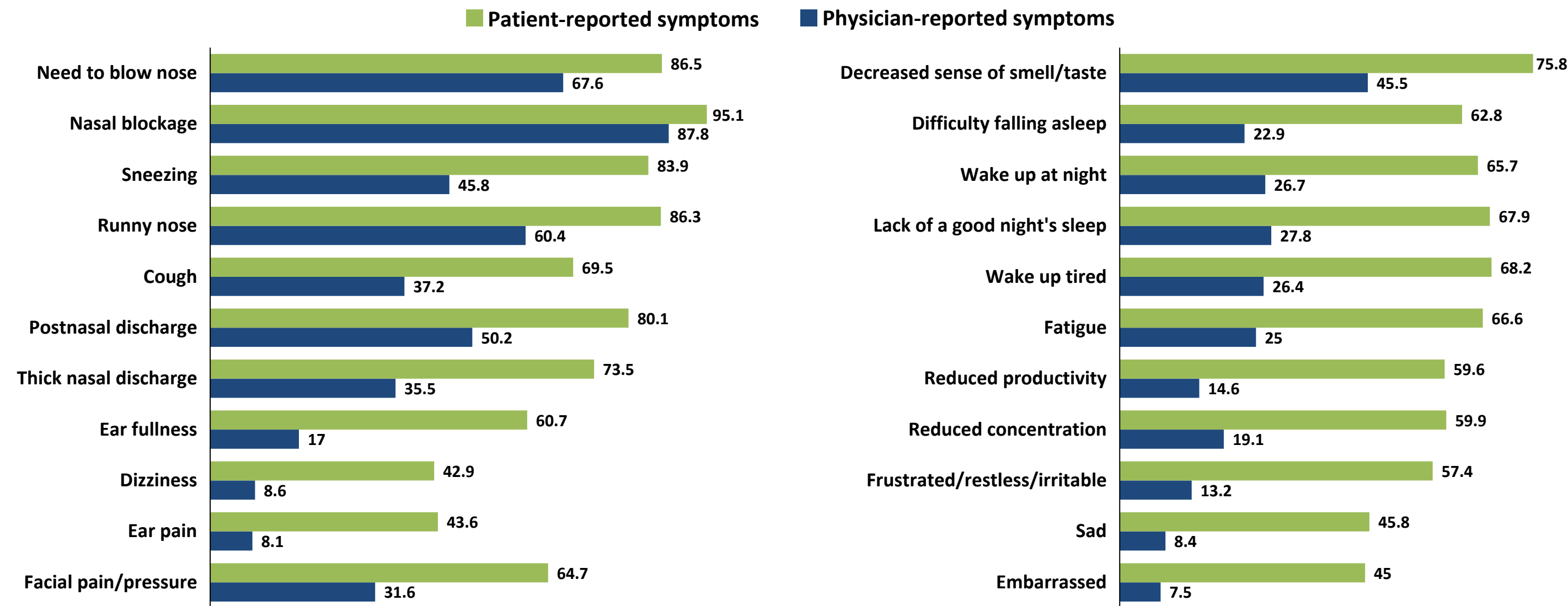


EQ-VAS Scores



EQ-VAS, EuroQoL-5 Dimension Visual Analog Scale; GINA, Global Initiative for Asthma; MCS, mental component summary; PCS, physical component summary; SF-36, 36-item Short Form Questionnaire.
Maspero JF, et al. *J Asthma Allergy*. 2023;16:323-332.

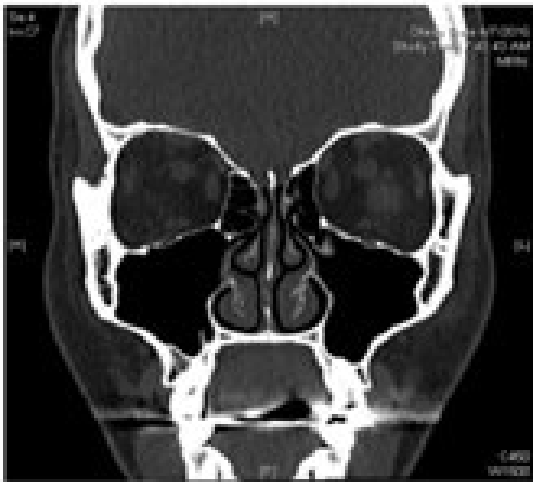
Discrepancies Between Patient and Provider Perceptions of Disease Burden



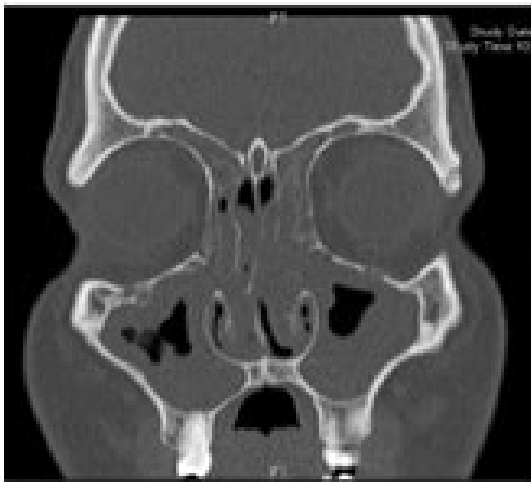
Discrepancies between patients and physicians highlight a need for strategies to improve the assessment of CRSwNP severity and its associated burden.

Symptoms and Burden of CRSwNP

Control



Severe CRSwNP



Symptoms

- Nasal obstruction and/or congestion*
- Nasal secretions, postnasal drip*
- Loss/reduced sense of smell*
- Facial pressure or pain*
- Difficulty breathing
- Upper teeth pain
- Headache
- Snoring

Psychosocial Impact

- Poor-quality sleep
- Increased daytime fatigue
- Inability to focus
- Lost workplace productivity
- Depression
- Embarrassment
- Loss of confidence
- Anxiety

*Cardinal symptoms of CRSwNP.
Bachert C, et al. *J Asthma Allergy*. 2021;14:127-134; ACAAI. Chronic rhinosinusitis with nasal polyps. Available at: <https://acaai.org/allergies/allergic-conditions/chronic-rhinosinusitis-with-nasal-polyps/>



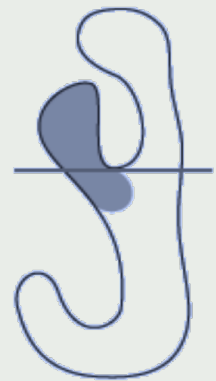
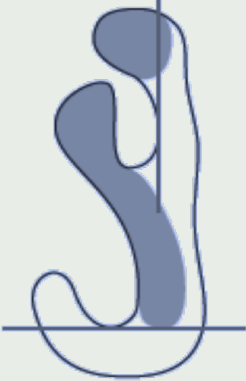

Assessment of Disease Severity and QOL Impact



Evaluating CRSwNP Severity and Health Impact: Which Tools to Use?

Type of Assessment	Tool	Information provided
Clinician-reported	<ul style="list-style-type: none">• Nasal Polyp Score (NPS)• Lund Kennedy Endoscopic Score (LK)• Lund-MacKay CT Score (LMK-CT)	<ul style="list-style-type: none">• Size & extent of nasal polyps• Staging based on polyps, discharge, edema, scarring, crusting• Staging based on sinus opacification
Patient-reported (Specific to nasal symptoms)	<ul style="list-style-type: none">• Sinonasal Outcome Test (SNOT-22)• Nasal Congestion Score (NCS)• University of Pennsylvania Smell Identification Test (UPSIT)	<ul style="list-style-type: none">• Symptom burden on QOL• Symptom severity• Olfactory function
	<ul style="list-style-type: none">• Chronic Sinusitis Survey (CSS)• Rhinosinusitis Disability Index (RSDI)• Nasal Polyposis Quality of Life (NPQ)	<ul style="list-style-type: none">• CRS-related symptoms & medication use• Physical, functional, & emotional impact• HRQOL impairment (specific to CRSwNP)
Patient-reported (Overall well-being)	<ul style="list-style-type: none">• 36-Item Short Form Survey (SF-36)• EuroQol-5D (EQ-5D)	<ul style="list-style-type: none">• QOL• QOL

Nasal Polyp Score (NPS)

Score	0	1	2	3	4
Polyp size/ location					
Anatomical description	No polyps	Small polyps in the middle meatus not reaching below the inferior border of the middle turbinate	Polyps reaching below the lower border of the middle turbinate	Large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate	Large polyps causing complete obstruction of the inferior nasal cavity

- Polyps are evaluated on each side through nasal endoscopy* each visit and graded based on polyp size, resulting in scores of 0 to 4
- Sum of the left and right nostril scores is the NPS
- Severe CRSwNP is defined by NPS ≥5

*Large nasal polyps may also be assessed by routine anterior rhinoscopy.
Gelardi M, et al. *Acta Otorhinolaryngol Ital.* 2022;42(1):75-81; Sanofi US. Measures of disease severity in CRSwNP. Adapted from Ferguson BJ, et al. *Nasal Polyposis.* 2010:103-110

Sinonasal Outcome Test (SNOT-22)

SNOT-22

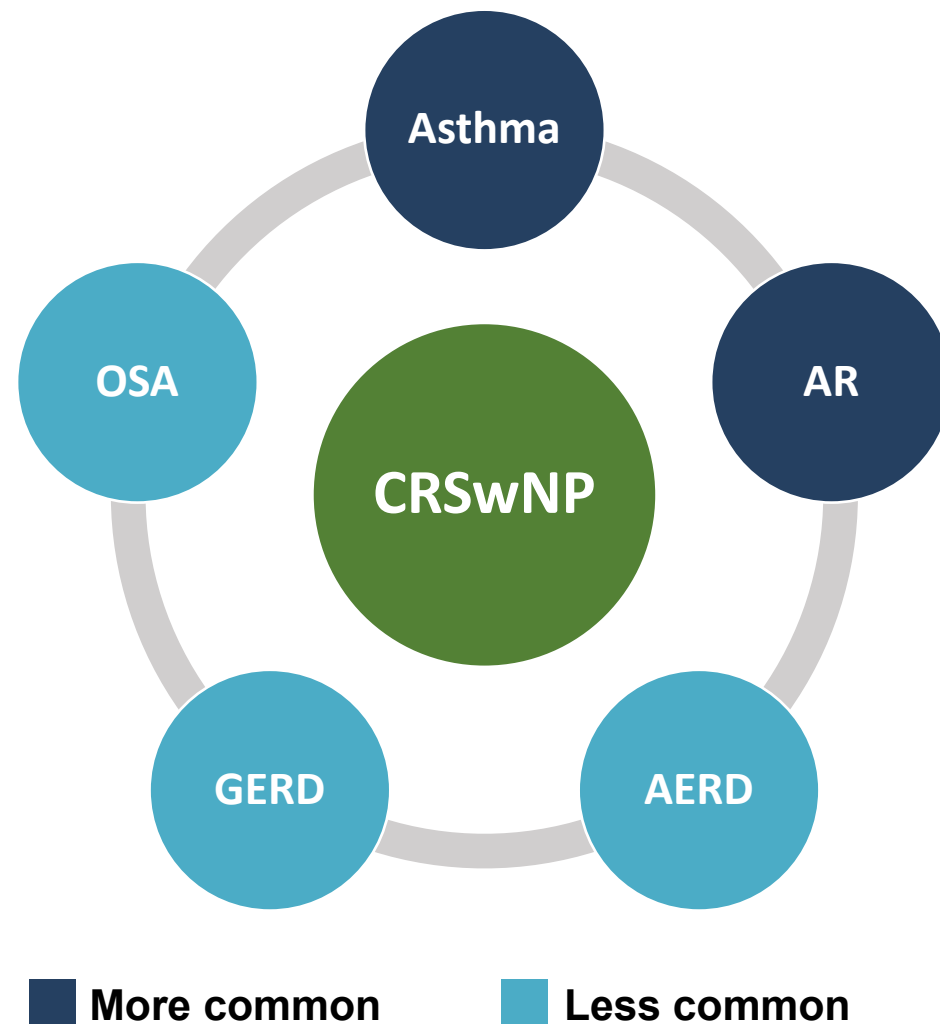
- 22-items disease-specific, validated, PRO measure
- Key diagnostic symptoms included in the EPOS definition for CRS, as well as other items of importance to patients with CRS
- Values ≥ 50 identify severe disease
- Suitable tool for practice in terms of ease of use
- Increasingly used to measure the disease-specific QOL in clinical practice

Symptoms *most* important to patients

- Nasal blockage/congestion
- Sense of smell/taste
- Thick nasal discharge
- Need to blow nose
- Postnasal discharge

Evaluating CRSwNP Severity and Health Impact: The Importance of Considering Comorbidities

Comorbidities of CRSwNP



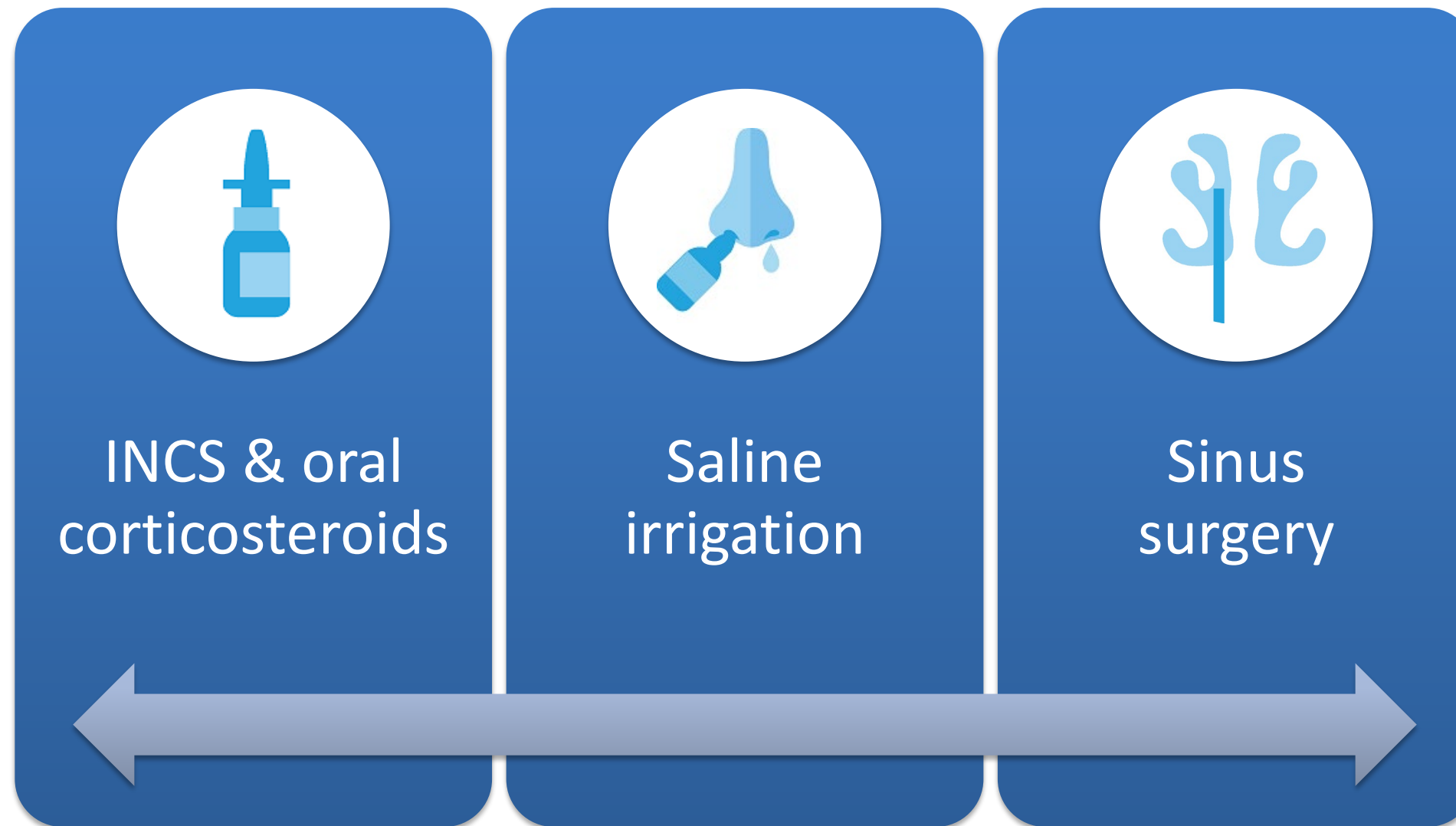
CRSwNP in the presence of comorbidities:

- Is associated with *more severe disease*
- Imposes a *heavier symptom burden*
- Is more *difficult to treat*

The Treatment Landscape for CRSwNP



Traditional Interventions for CRSwNP



INCS, intranasal corticosteroids.

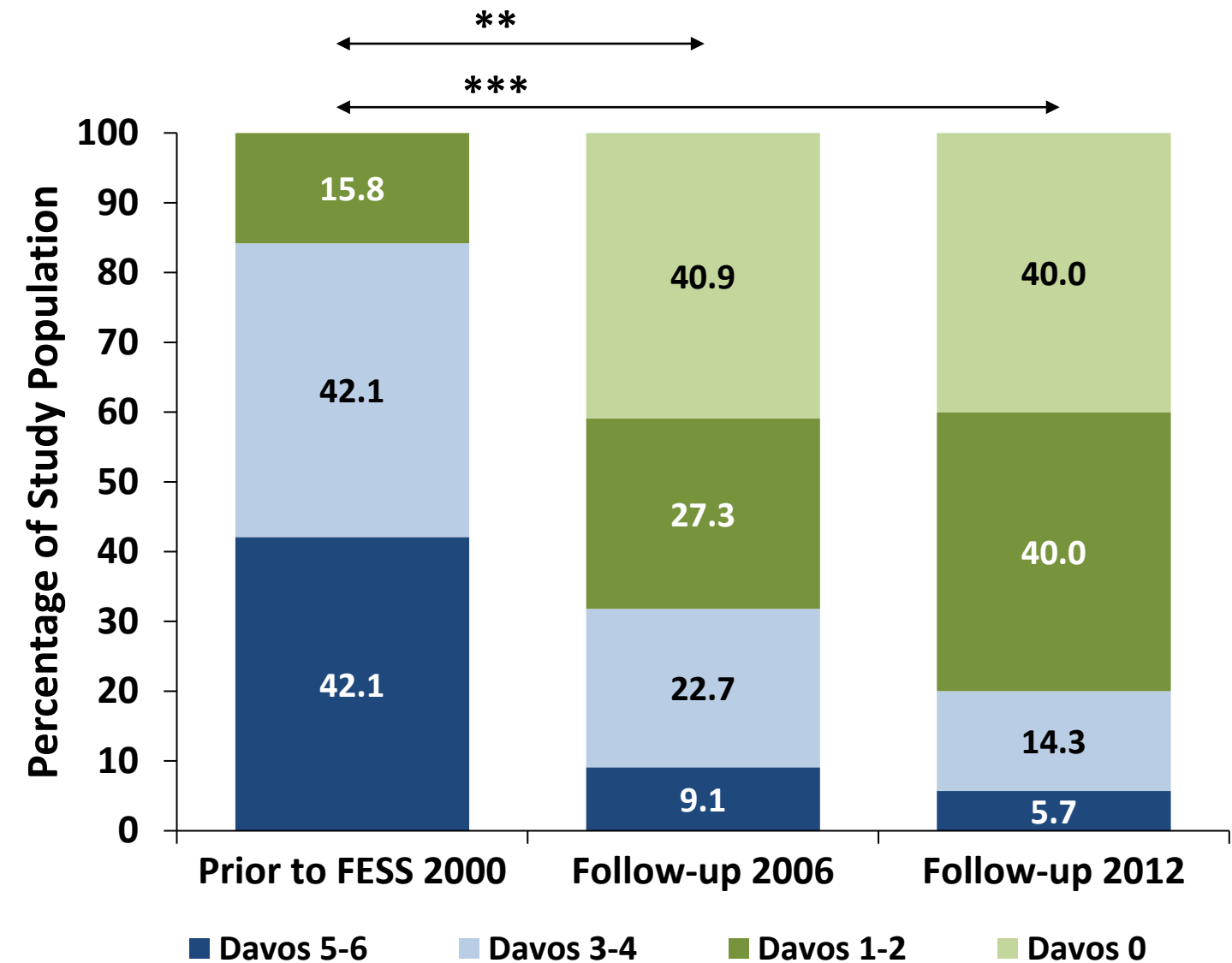
Blaiss MS. *Allergy Asthma Proc.* 2020;41(6):413-419.

Strengths and Weaknesses of OCS and FESS

	Benefits	Shortcomings
Oral Corticosteroids (OCS)	<ul style="list-style-type: none"> • Improvement of QOL • High efficacy with major symptom relief 	<ul style="list-style-type: none"> • Rapid recurrence • Dependence on OCS • Risk of significant side effects (eg, development of osteoporosis, diabetes, and psychosis)
Functional Endoscopic Sinus Surgery (FESS)	<ul style="list-style-type: none"> • Improvement of QOL • High efficacy with major symptom relief • Overall well-tolerated ambulatory surgery • Immediate benefits • Allows for better access for topical therapy • Anatomic defects that cause nasal obstruction such as septal deviations can be corrected at the same time 	<ul style="list-style-type: none"> • High recurrence rate of polyps • Need for general anesthesia • Need for follow-up debridements and assessment of healing overall several months • Orbital and skull base complications (rare)

Outcomes Following Endoscopic Sinus Surgery

- 12-year postsurgical follow-up (graph):
 - 78.9% rate of disease recurrence
 - 36.8% need for revision surgery
- Repeated surgeries increases risk for surgical complications, diminishing success rates, and permanent scarring
 - Complication rates: 1.8% – 14.3% (epistaxis most common)
- No significant difference in inflammatory markers* before and after ESS



*IL-5, IL-5R α , TGF- β 1, MPO, IL-18, ECP, total IgE and specific IgE antibodies against *S aureus* enterotoxins (SAE-IgE); ** $P < .01$; *** $P < .001$.

ECP, eosinophilic cationic protein; Ig, immunoglobulin; IL, interleukin; MPO, myeloperoxidase; TGF, transforming growth factor.

Calus L, et al. *Clin Trans Allergy*. 2019;9(1):30.

Approved Biologics for CRSwNP

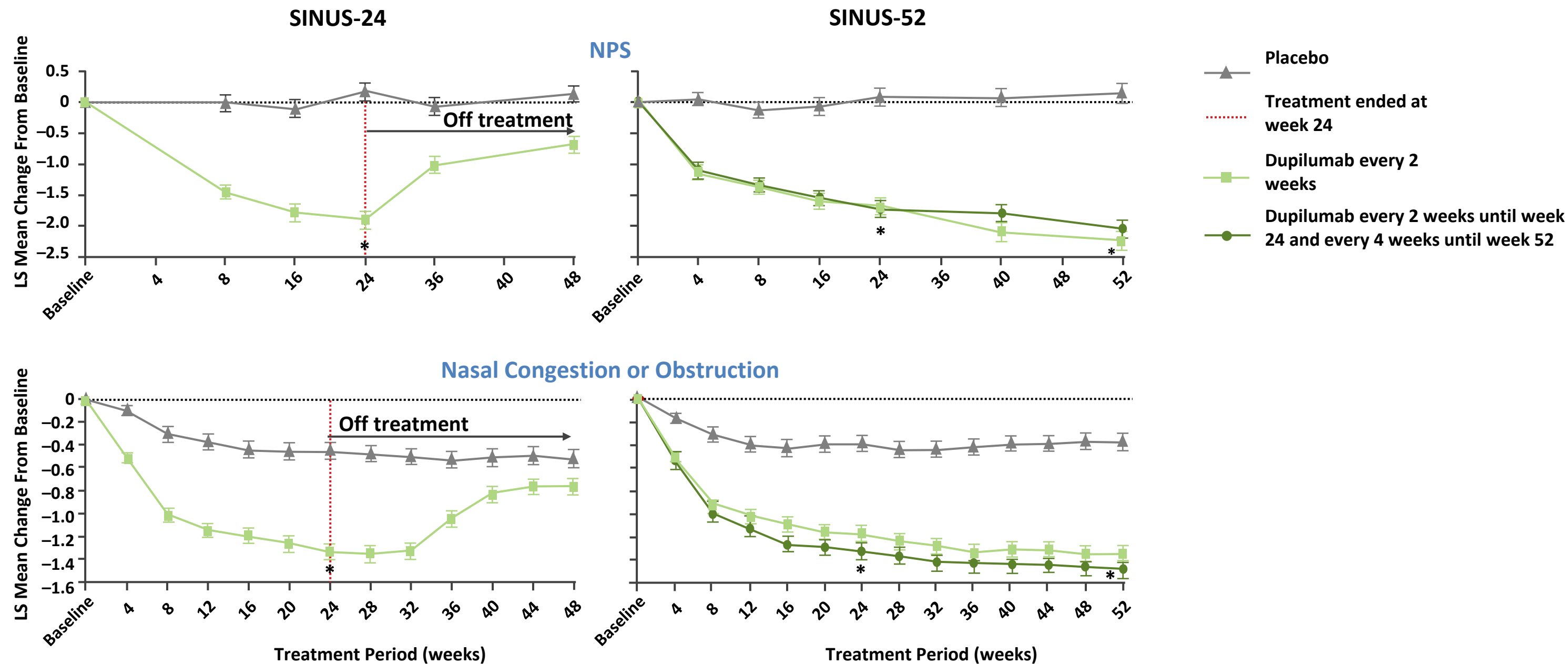
Biologic	Therapeutic Target	Approval	CRSwNP Indication(s)	Dosing
Dupilumab	IL-4 IL-13	June 2019	Add-on maintenance for adults with uncontrolled CRSwNP	300 mg Q2W
Omalizumab	IgE	December 2020	Add-on maintenance for adults with inadequate response to INCS for CRSwNP	75–600 mg Q2W–Q4W*
Mepolizumab	IL-5	July 2021	Add-on maintenance for adults with inadequate response to INCS for CRSwNP	100 mg Q4W

*Dosing depends on serum total IgE level and body weight.

Q2W, every 2 weeks; Q4W, every 4 weeks.

Bachert C, et al. *Lancet*. 2019;394:1638-1650; Geveart P, et al. *J Allergy Clin Immunol*. 2020;146:595-605; Han JK, et al. *Lancet Respir Med*. 2021;9:1141-1153; Hopkins C, et al. *Eur Respir J*. 2020;56:4616.

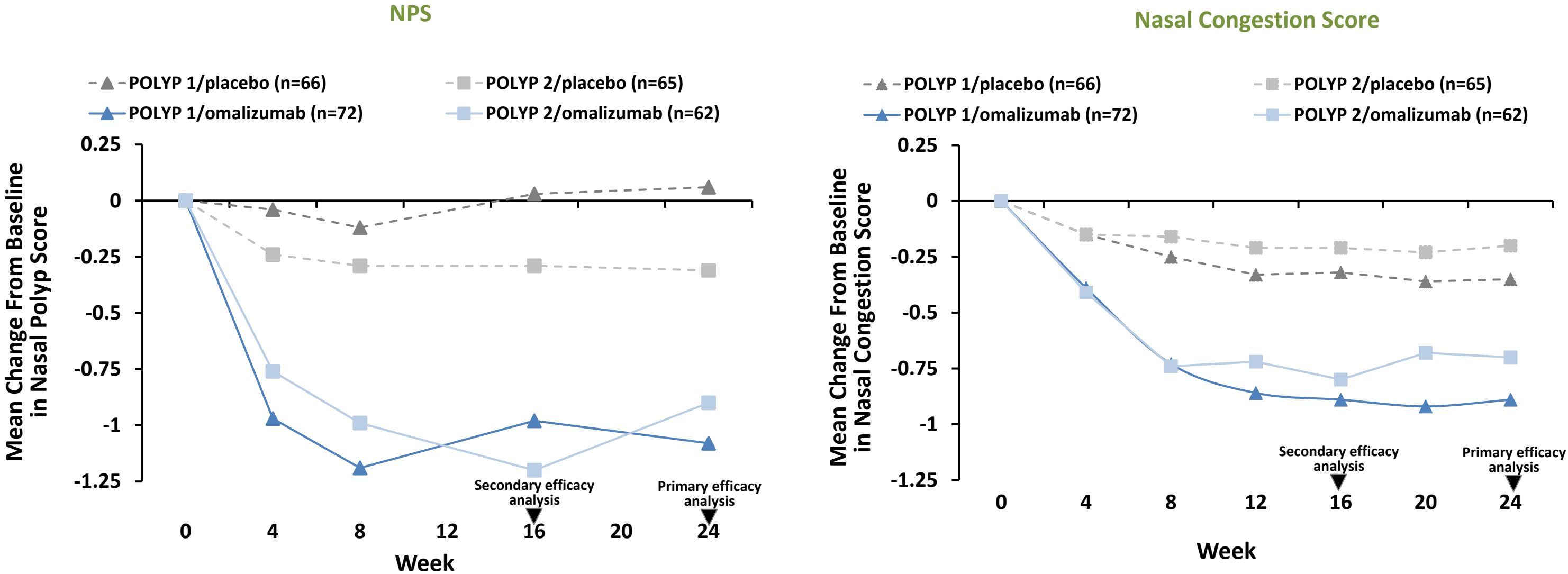
Clinical Trial Efficacy of Dupilumab in CRSwNP: NPS and Nasal Congestion or Obstruction



LS, least squares.
Bachert C, et al. *Lancet*. 2019;394:1638-1650.

Clinical Trial Efficacy of Omalizumab in CRSwNP: NPS and Nasal Congestion Score

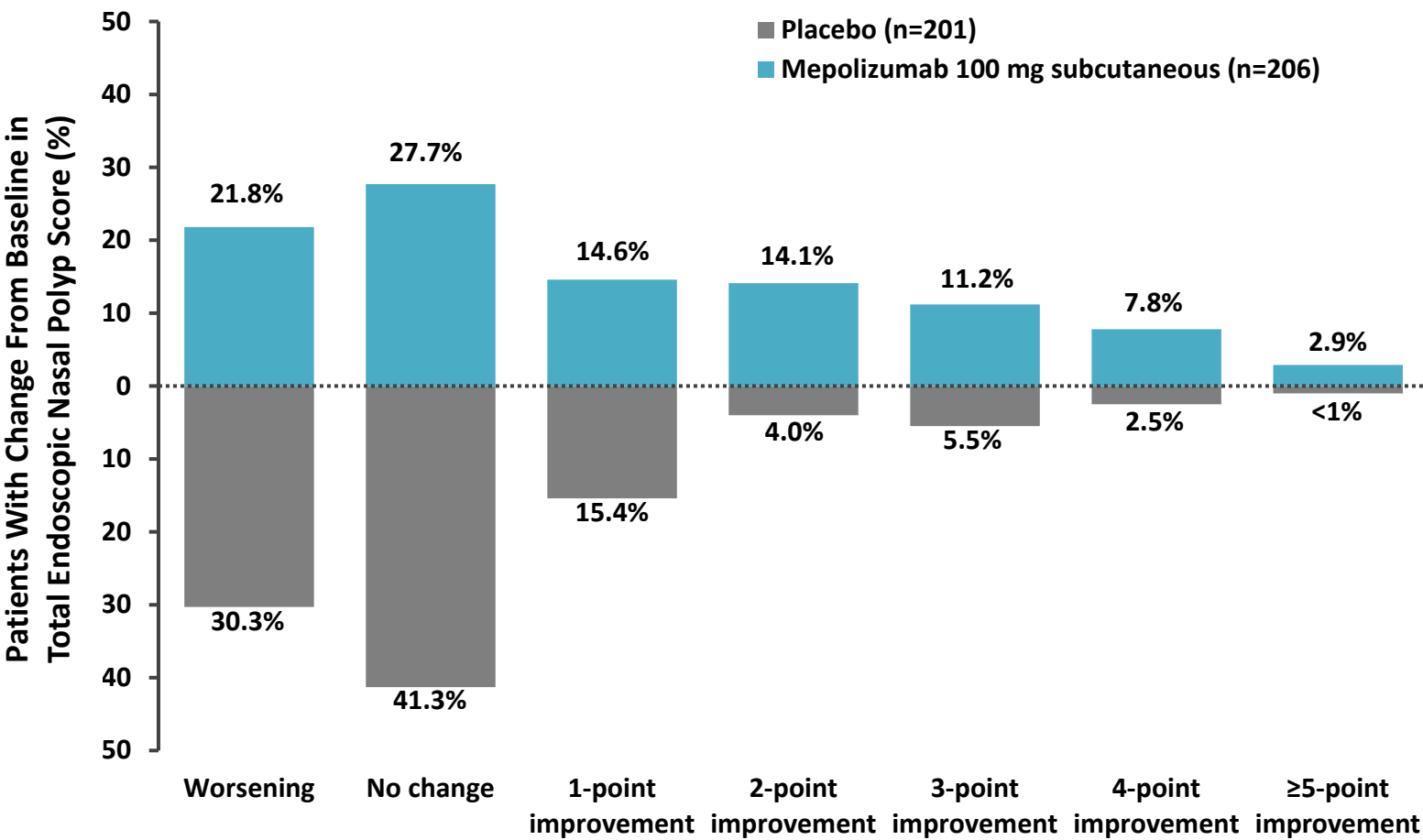
POLYP 1 & POLYP 2



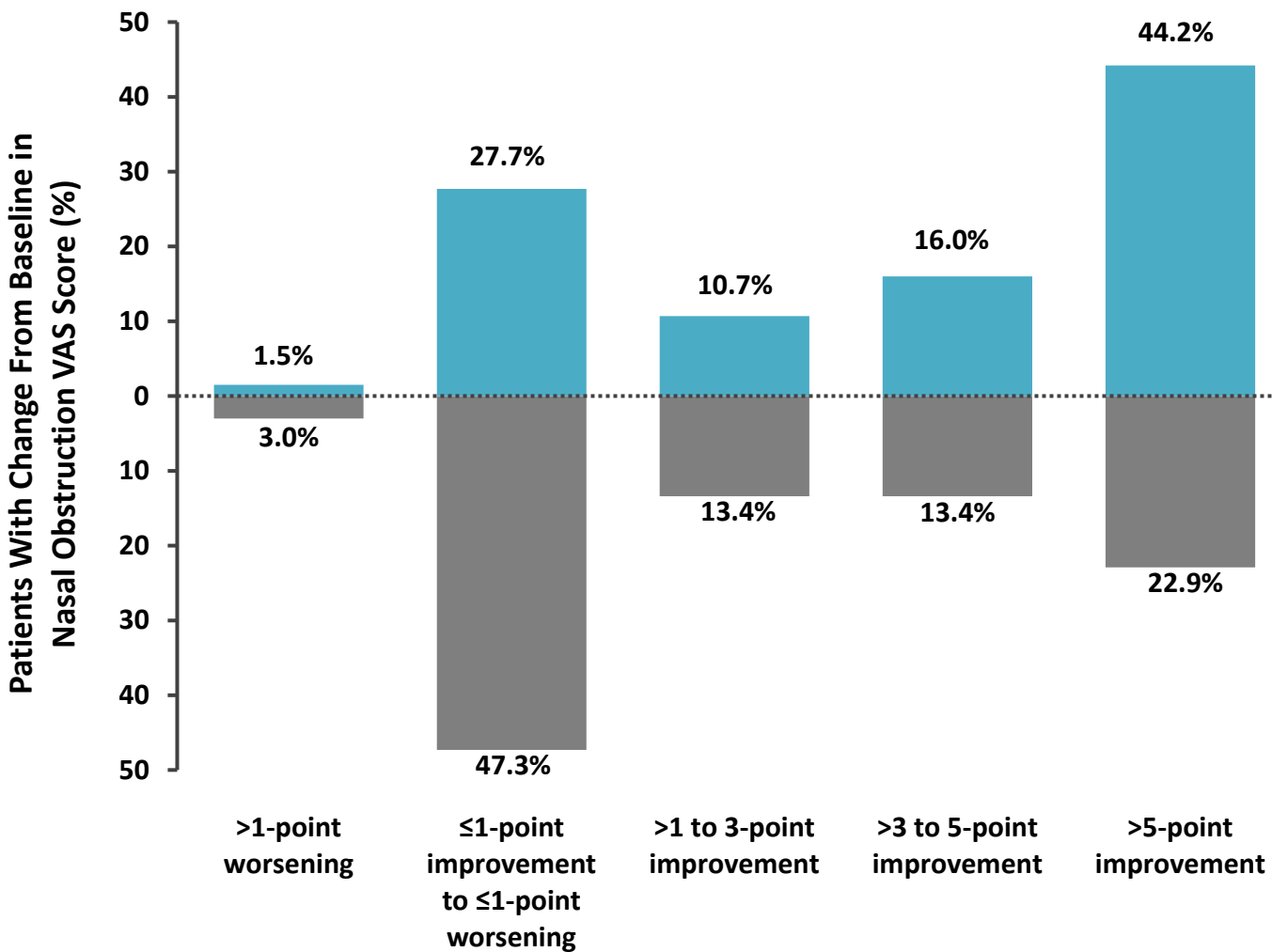
Clinical Trial Efficacy of Mepolizumab in CRSwNP: NPS and Nasal Obstruction VAS Score

SYNAPSE

NPS



Nasal Obstruction VAS

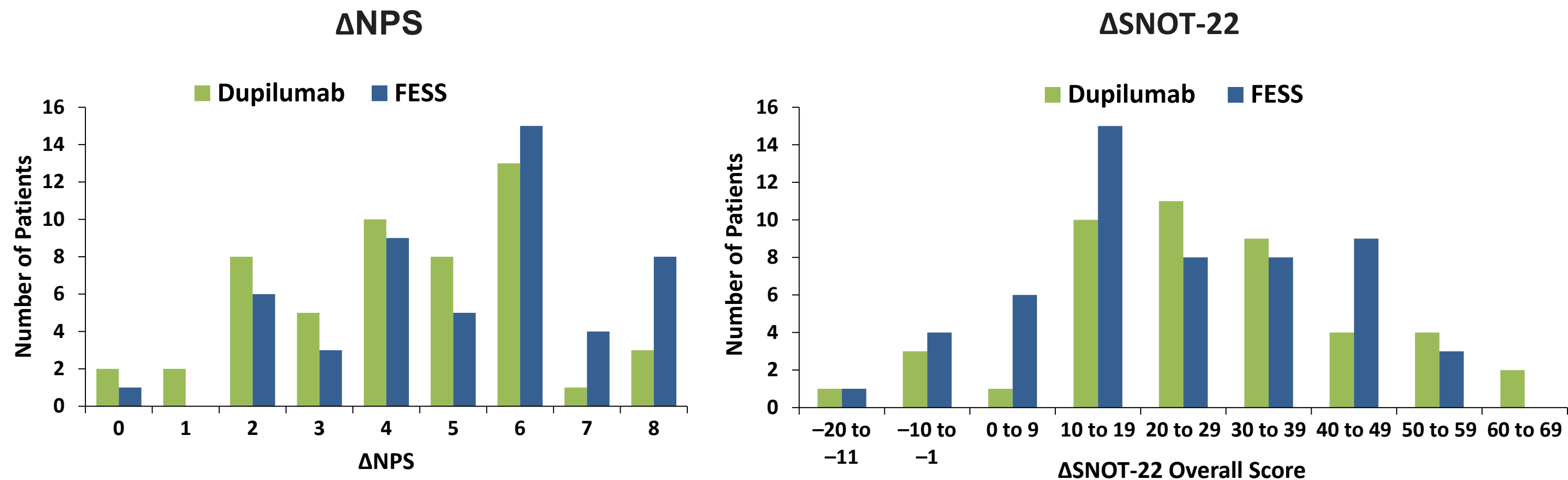


Biologics for CRSwNP in Clinical Trials: Additional Efficacy Outcomes and Safety

Biologic	LMK-CT	SNOT-22	Subsequent Need for Surgery	AEs
Dupilumab	-7.44 [†] -5.13 ^{††}	—	↓ HR=0.243 (0.169 to 0.351)*	More frequent vs PBO
Omalizumab	—	-24.7 vs -8.6 [‡] -21.6 vs -6.6 ^{‡‡}	↓ 22.6% [‡] 27.8% ^{‡‡}	Similar between groups
Mepolizumab	—	—	↓ HR=0.43 (0.25 to 0.76)**	15% vs 9% with PBO

[†]SINUS-24; ^{††}SINUS-51; [‡]POLYP 1; ^{‡‡}POLYP 2; **P* <.0001; ***P* =.0032.
 AE, adverse event; HR, hazard ratio; PBO, placebo.
 Bachert C, et al. *Lancet*. 2019;394:1638-1650; Geveart P, et al. *J Allergy Clin Immunol*. 2020;146:595-605; Han JK, et al. *Lancet Respir Med*. 2021;9:1141-1153; Hopkins C, et al. *Eur Respir J*. 2020;56:4616.

Dupilumab Treatment vs FESS for CRSwNP: Retrospective Matched Cohort Study



In this retrospective matched cohort study, both therapies reduced symptoms in patients with CRSwNP. Dupilumab was associated with improved olfaction and decreased cough, postnasal drainage, and thick nasal drainage vs FESS, while FESS was associated with a greater reduction in polyp burden.

FESS, functional endoscopic sinus surgery.
Dharmarajan H, et al. *Int Forum Allergy Rhinol.* 2022;12(8):986-995.

Dupilumab Treatment vs FESS for CRSwNP: Comparison of Prospective ESS Cohort vs Phase 3 Biologic Trial Data

NPS distribution at 24 Weeks						
Patients n (%)						
Intervention	NPS=0	NPS=1	NPS=2	NPS=3	NPS=4	NPS ≥5
ESS (n=79)	48 (61)	7 (9)	14 (18)	←	10 (13)	→
Dupi-24 (n=143)	←		66 (46)	→	27 (19)	50 (35)
Oma-1&2 (n=128)	←		42 (31)	→	30 (25)	56 (44)

More patients had lower NPS scores with ESS vs both dupilumab and omalizumab at 24 weeks (*P* <.001 for both comparisons)

NPS distribution at 52 Weeks						
Patients n (%)						
Intervention	NPS=0	NPS=1	NPS=2	NPS=3	NPS=4	NPS ≥5
ESS (n=20)	9 (45)	4 (20)	6 (30)	←	1 (5)	→
Dupi-52 (n=295)	←		136 (46)	→	47 (16)	112 (38)
Mepo (n=206)	6 (2.9)	16 (7.8)	23 (11.2)	29 (14.1)	30 (14.6)	104 (50)

More patients had lower NPS scores with ESS vs both dupilumab and mepolizumab at 52 weeks (*P* <.001 for both comparisons)

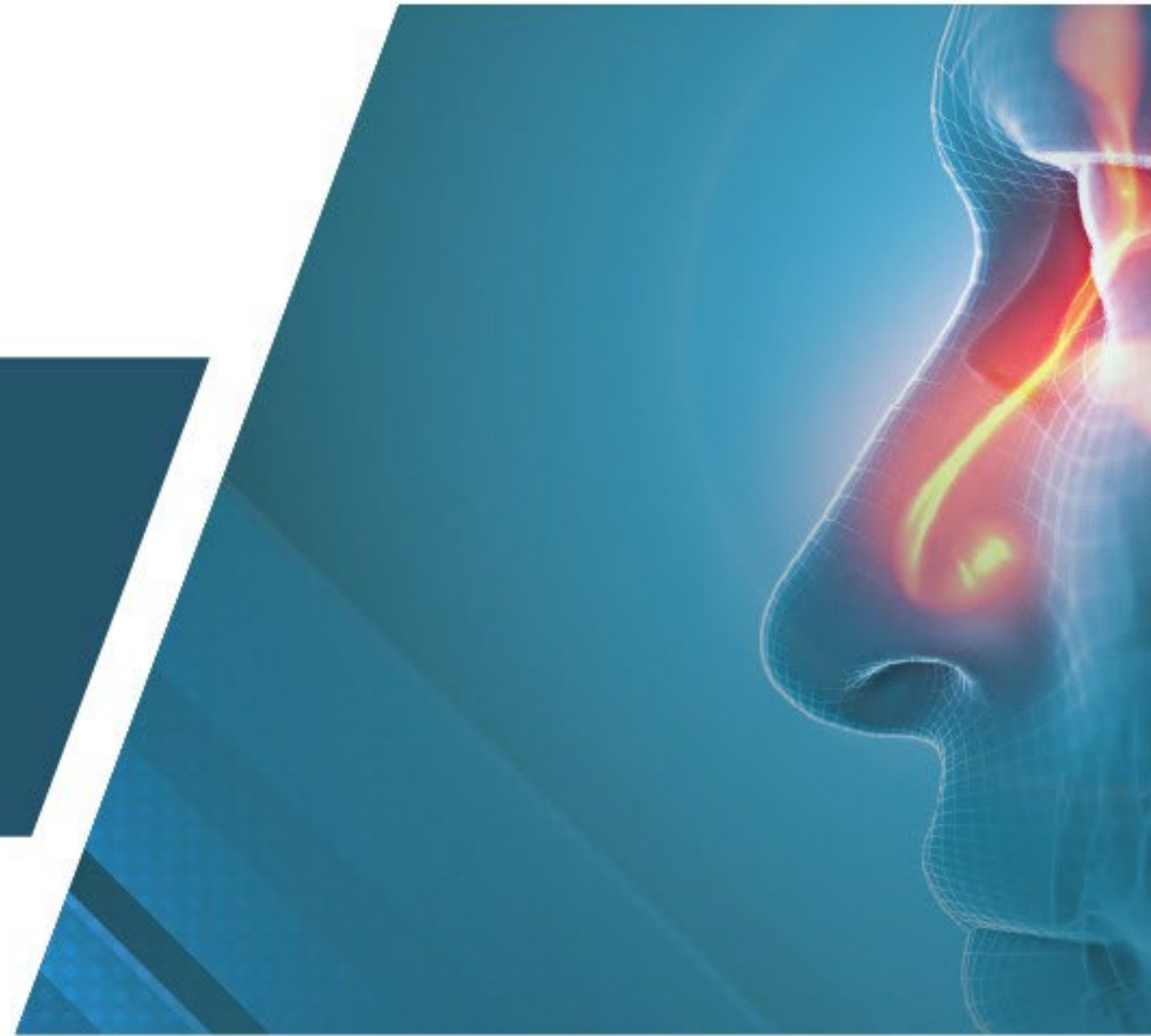
Note: Gold shading represents where a minority of patients scored in each group.
 Dupi-24, dupilumab LIBERTY NP SINUS-24; Dupi-52, dupilumab LIBERTY NP SINUS-52; Mepo, mepolizumab-SYNAPSE; OMA-1&2, omalizumab POLYP-1&2.
 Miglani A, et al. *Int Forum Allergy Rhinol.* 2023;13(2):116-128.

JTFPP Guidelines for the Medical Management of CRSwNP: Comparative Effects of Biologics and ASA-D

	Patient-Important Outcomes						Surrogate Outcomes	
	HRQOL SNOT-22 (0-110) [‡]	Symptoms VAS (0-10 cm)	Smell UPSIT (0-40) [†]	Rescue OCS	Rescue Polyp Surgery	Adverse Events	Nasal Polyp Size (0-8)	CT Score LMK (0-24)
Standard care*	50.11	6.84	14.04	31.96%	21.05%	73.78%	5.94	18.35
Dupilumab	-19.91 (-22.50, -17.32)	-3.25 (-4.31, -2.18)	10.96 (9.75, 12.17)	-21.73 (-24.61, -18.22) RR 0.32 (0.23, 0.43)	-16.35 (-18.13, -13.48) RR 0.22 (0.14, 0.36)	0.13 (-8.12, 9.88) RR 1.00 (0.88, 1.13)	-2.04 (-2.73, -1.35)	-7.51 (-10.13, -4.89)
Omalizumab	-16.09 (-19.88, -12.30)	-2.09 (-3.15, -1.03)	3.75 (2.14, 5.35)	-12.46 (-23.65, 12.78) RR 0.61 (0.26, 1.40)	-7.40 (-11.04, -2.43) RR 0.65 (0.48, 0.88)	-2.60 (-15.58, 13.28) RR 0.96 (0.79, 1.18)	-1.09 (-1.70, -0.49)	-2.66 (-5.70, 0.37)
Mepolizumab	-12.89 (-16.58, -9.19)	-1.82 (-3.13, -0.50)	6.13 (4.07, 8.19)	-10.23 (-15.98, -2.88) RR 0.68 (0.50, 0.91)	-12.33 (-15.56, -7.22) RR 0.41 (0.26, 0.66)	-3.07 (-13.44, 9.07) RR 0.96 (0.82, 1.12)	-1.06 (-1.79, -0.34)	
ASA Desensitization	-10.61 (-14.51, -6.71)	-2.74 (-3.92, -1.57)	2.72 (-1.17, 6.61)		-16.00 (-19.79, 0.21) RR 0.24 (0.06, 1.01)	209.21 (8.30, 901.87) RR 3.84 (1.11, 13.22)	-0.95 (-2.44, 0.55)	-0.31 (-3.50, 2.88)
Classification of intervention (colour) ²⁴							Certainty (shading) ^{24,29}	
Most beneficial			Intermediate beneficial		Least beneficial/not clearly different from placebo	No data (blank)	High/moderate (solid)	
Most harmful			Intermediate harmful				Low/very low (shaded)	

ASA, acetylsalicylic acid; CT, computed tomography; HRQOL, health-related quality of life; JTFPP, Joint Task Force on Practice Parameters; RR, relative risk.
 Rank MA, et al. *J Allergy Clin Immonol.* 2023;151(2):386-398; Oykhman P, et al. *J Allergy Clin Immonol.* 2022;149(4):1286-1295

Recommendations for Treatment Approach



Defining the Goals of CRSwNP Treatment

- Disease control has emerged as a key concept in CRS management
- Impressions of disease control can differ between physicians and patients; good control should be defined by improvements in physician- and patient-reported outcomes

Patient-reported outcomes:

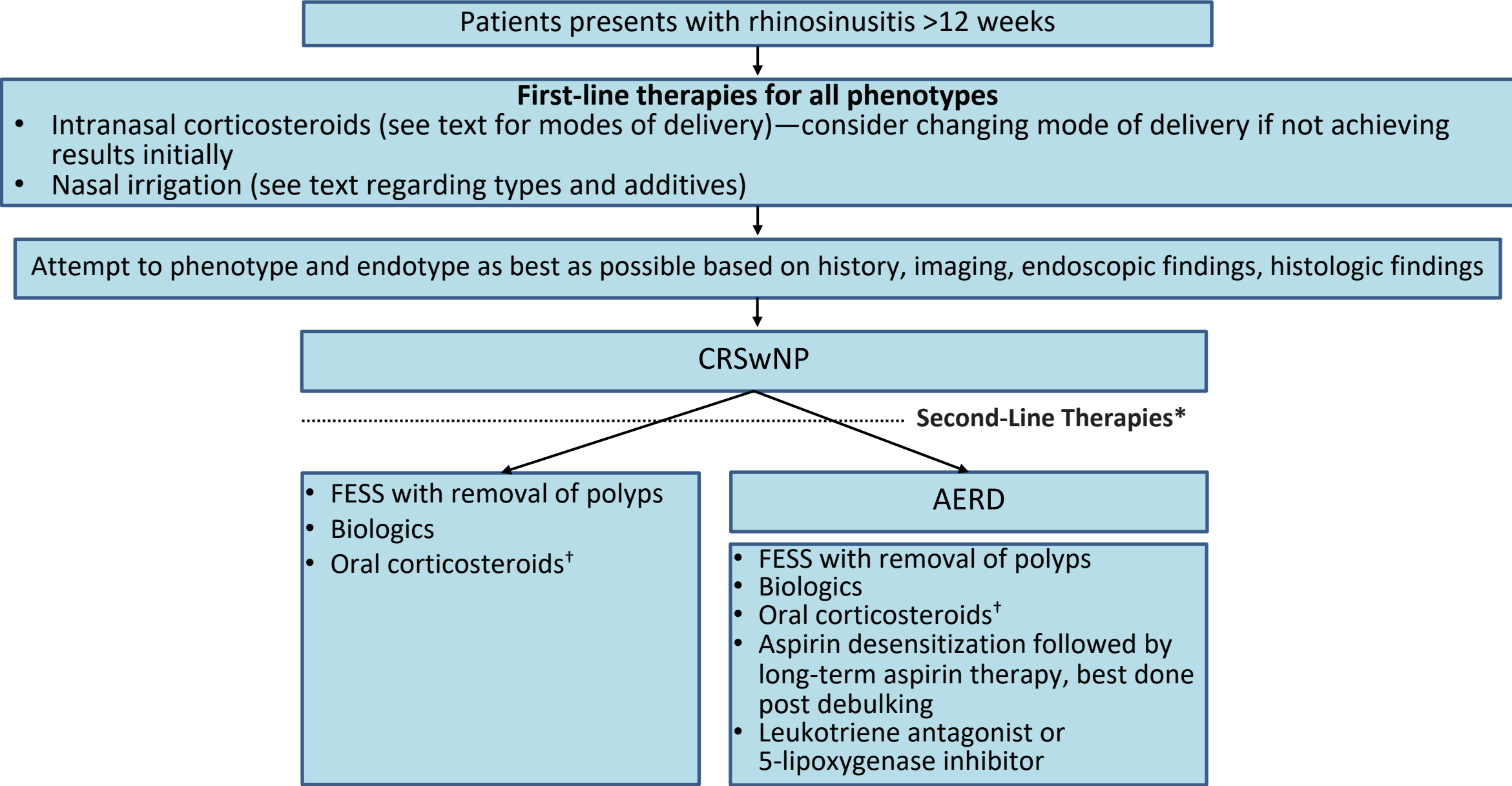
- SNOT-22
- Smell loss
- Congestion scores
- Benefits on comorbidities (asthma, allergy, middle ear problems)

Physician-reported outcomes:

- NPS
- CT scan scores
- Smell tests

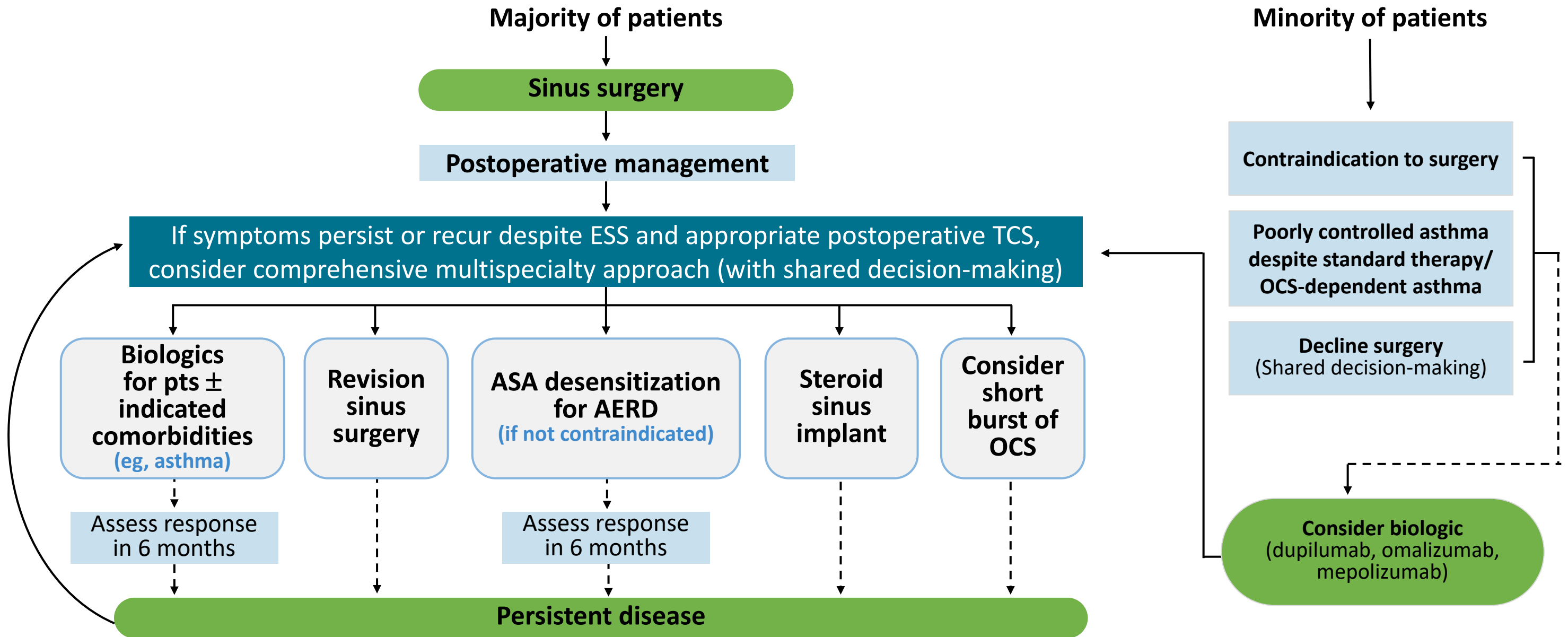
- Additional challenges to assessment of CRS control:
 - Lack of consensus on most effective grading of nasal polyps and most appropriate smell test
 - Loss of smell and nasal blockage seem to be the most bothersome symptoms, but importance varies by patient

ACAAI Yardstick for the Medical Management of CRS



*Not in order of recommendation or preference; [†]Oral steroids should be limited in use and not as chronic therapy.

Multidisciplinary Management Algorithm for CRSwNP (Escalation for Refractory Disease)



Indications for Biologic Therapy in CRSwNP

EUFOREA/EPOS 2023 Update

Indication for Biological Treatment in CRSwNP
Presence of bilateral polyps in patient who had EDSS**

↓ **THREE** criteria are required

Criteria	Cut-off Points
Evidence of type 2 inflammation	Tissue eos ≥ 10 /hpf, OR blood eos ≥ 150 OR total IgE ≥ 100
Need for systemic corticosteroids or contraindication to systemic steroids	≥ 2 courses per year OR long term (>3 months) low-dose steroids
Significantly impaired quality of life	SNOT-22 ≥ 40
Significant loss of smell	Anosmic on smell test (score depending on test)
Diagnosis of comorbid asthma	In case of asthma: regular need for inhaled corticosteroids

Eos, eosinophil; EPOS, European Position Paper on Rhinosinusitis; EUFOREA, European Forum for Research and Education in Allergy and Airways Disease; hpf, high-power field.
Bachert C, et al. *J Allergy Clin Immunol*. 2021;147:29-36; Fokkens WJ, et al. *Rhinology*. 2023;61(3):194-202.

Selecting a Biologic Therapy

Confirm
diagnosis of
uncontrolled
severe CRSwNP

Check for
comorbidity
(eg, asthma,
allergies) &
consequences

Determine if
type 2
inflammation is
likely

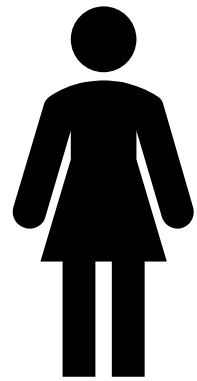
Inform patient
of treatment
options,
perspectives, &
risks

Select surgery
or biologic with
an informed
patient using
shared
decision-
making

Select biologic
drug (note
limitations
applicable for
specific drugs)

Treatment Approach: Case Patient Examples

Patient 1



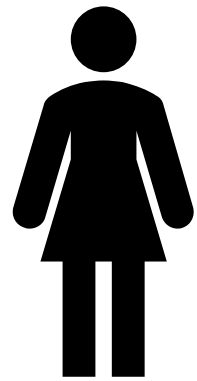
37-year-old woman diagnosed with CRSwNP 5 years ago. Treatment has consisted of INCS and OCS on two occasions in the previous year. NCS=2, NPS=5, SNOT-22=59



Based on the patient's characteristics, she is a good candidate for ESS, which is recommended as first-line intervention for the majority of patients.

Treatment Approach: Case Patient Examples

Patient 2



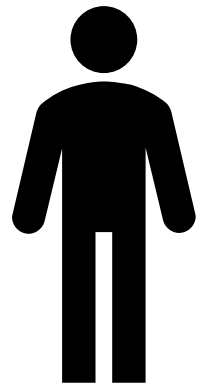
62-year-old woman with a 10-year history of CRSwNP. Underwent ESS 8 years ago. Treatment has consisted of INCS, and OCS on 3 occasions in the previous year. NCS=3, NPS=7, SNOT-22=62



Based on the patient's history of surgery, and polyp recurrence and need for OCS, she would be a good candidate for biologic therapy.

Treatment Approach: Case Patient Examples

Patient 3

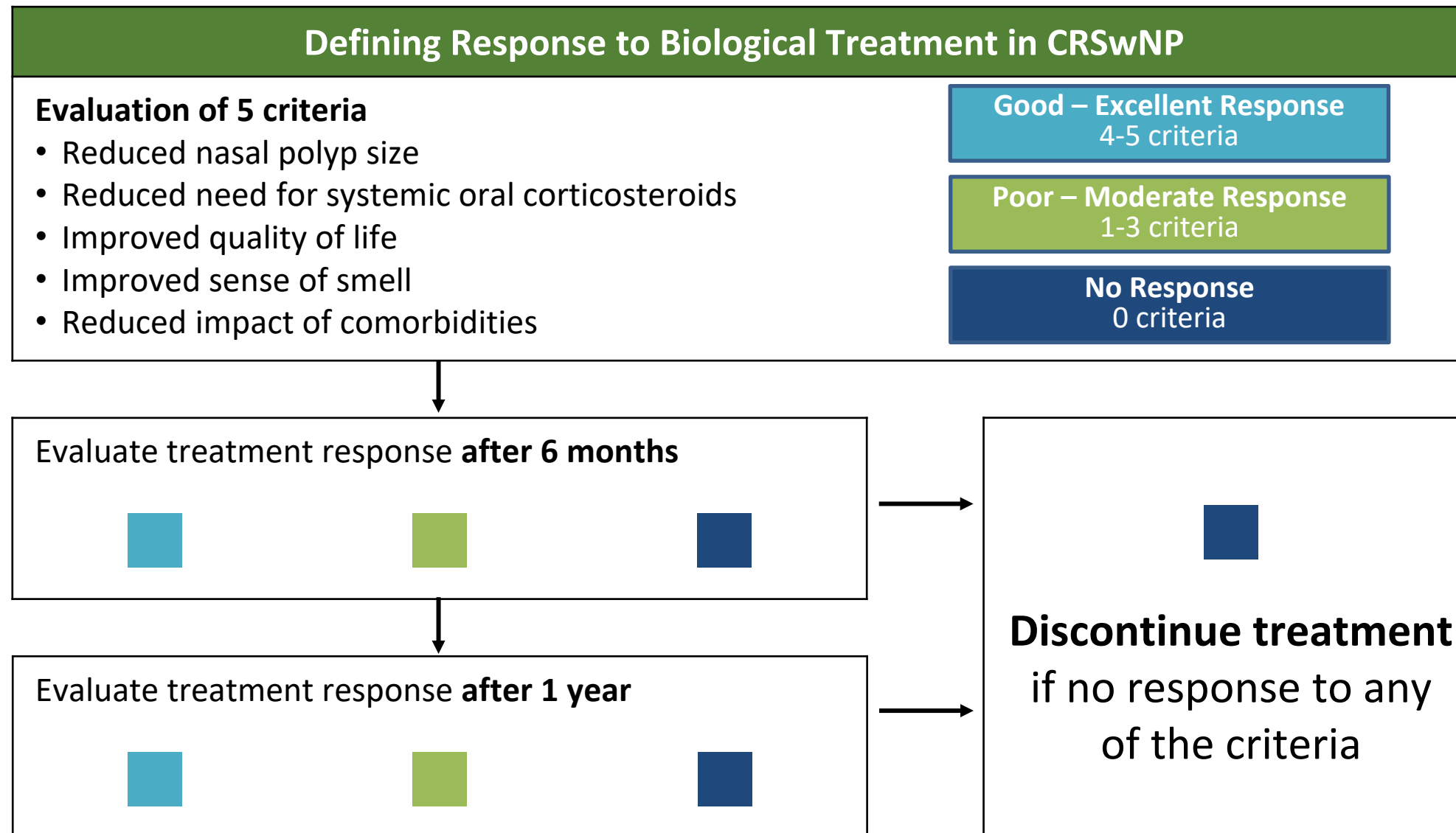


50-year-old man with a 12-year history of CRSwNP, asthma, and AERD. Has undergone ESS twice. Treatment regimen includes INCS and medium-dose ICS/LABA. NCS=3, NPS=7, SNOT-022=71, FEV₁=65%



Given the patient's comorbidities and history of surgery, he would be a good candidate for biologic therapy.

Evaluating the Response to Biologic Treatment (EPOS/EUFOREA 2023 Update)



Interactive Poster Session



Summary

- CRSwNP is a disease with a high symptom burden that results in significant detrimental effects on physical and psychological well-being
- Effective disease management requires thorough patient evaluation to establish disease severity, identify comorbidities, and determine level of disease control, all of which are important for guiding treatment selection
- For patients with severe uncontrolled disease, surgical intervention is recommended, but recurrence is frequent
- Multiple approved biologic therapies have demonstrated good safety and efficacy in moderate-to-severe CRSwNP, offering an alternative to repeat surgeries and the need for systemic steroids (which are associated with significant adverse outcomes with long-term use)

Questions & Answers



Thank You!

