Eosinophilic disorder as comorbidities in Asthma

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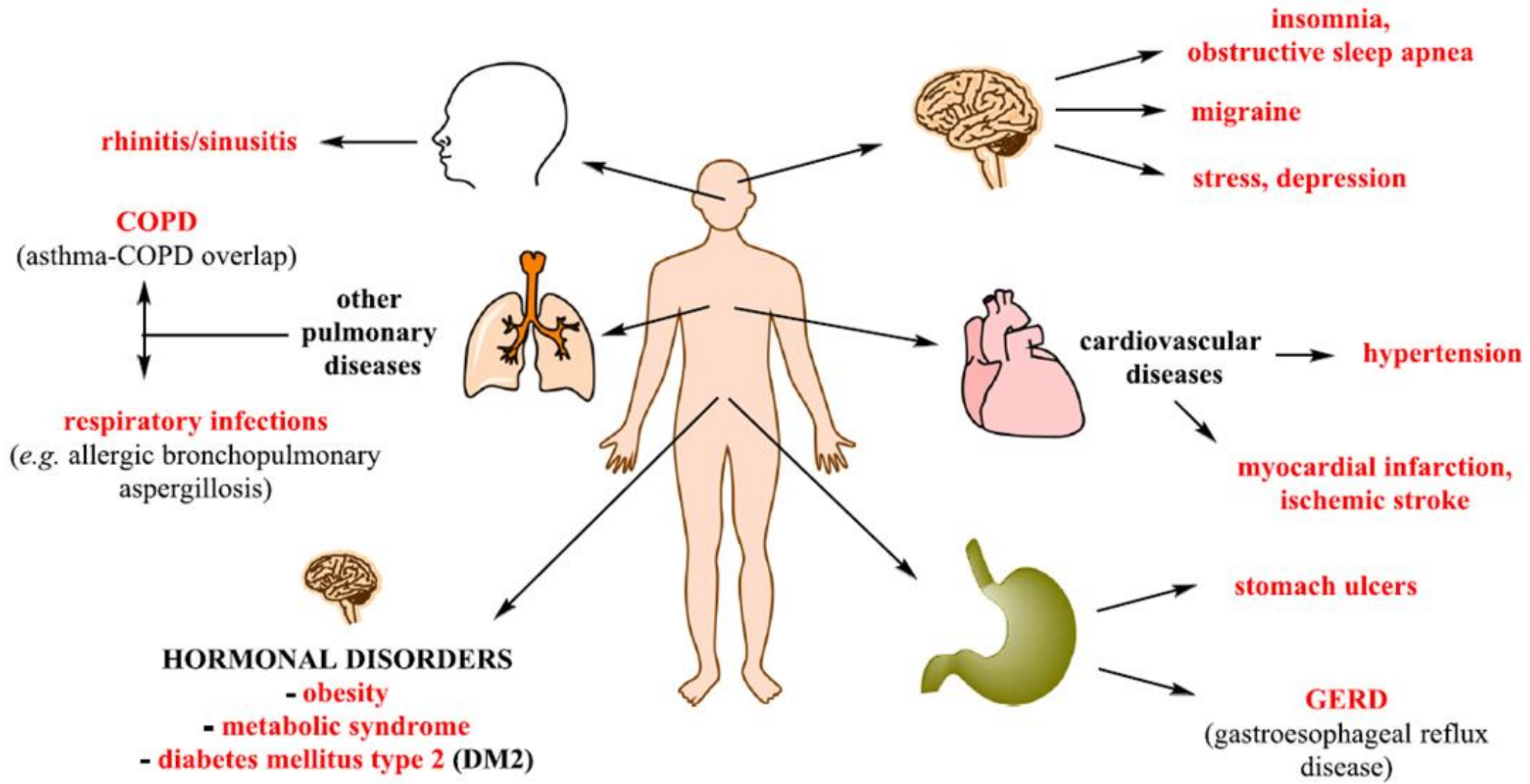
Contents

Asthma and comorbidities



Allergy Asthma Clin Immunol (2021) 17:95

Asthma and comorbidities

Respiratory tract/Pulmonary comorbidities		Extrapulmonary comorbidities
Upper respiratory tract	Lower respiratory tract	
VCD/ILO	Dysfunctional breathing	Obesity
OSA	COPD	CVD
Allergic rhinitis	Bronchiectasis	GERD
CRS ± Nasal polyp		Diabetes mellitus
		Anxiety/Depression

Pol Arch Intern Med. 2022; 132: 16250. doi:10.20452/pamw.16250

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Pol Arch Intern Med. 2022; 132: 16250. doi:10.20452/pamw.16250

PART D. MANAGING ASTHMA WITH MULTIMORBIDITY AND IN SPECIFIC POPULATIONS

KEY POINTS

- Multimorbidity is common in patients with chronic diseases such as asthma. It is important to identify and manage multimorbidity, as it contributes to impaired quality of life, increased healthcare utilization, and adverse effects of medications. In addition, comorbidities such as rhinosinusitis, obesity and gastro-esophageal reflux disease may contribute to respiratory symptoms and some contribute to poor asthma control.
- For patients with dyspnea or wheezing on exertion:
  - Distinguish between exercise-induced bronchoconstriction (EIB) and symptoms that result from obesity or a lack of fitness or are the result of alternative conditions such as inducible laryngeal obstruction.
  - Provide advice about preventing and managing EIB.
- All adolescents and adults with asthma should receive ICS-containing controller medication to reduce their risk of severe exacerbations. It should be taken every day or, as an alternative in mild asthma, by as-needed ICS-formoterol for symptom relief.
- Refer patients with difficult-to-treat or severe asthma to a specialist or severe asthma service, after addressing common problems such as incorrect diagnosis, incorrect inhaler technique, ongoing environmental exposures, and poor adherence (see Section 3E, p.104).

Original Article

Nonrespiratory Diseases in Adults Without and With Asthma by Age at Asthma Diagnosis

Jasmin Honkamäki, MD[a], Pinja Ilmarinen, PhD[a,b], Hanna Hisinger-Mölkänen, MD[c], Leena E. Tuomisto, MD, PhD[b], Heidi Andersén, MD[d], Heini Huhtala, MSc[e], Anssi Sovijärvi, MD, PhD[f], Ari Lindqvist, MD, PhD[g], Helena Backman, PhD[h], Bright I. Nwaru, PhD[i], Eva Rönmark, PhD[h], Lauri Lehtimäki, MD, PhD[a,j], Paula Pallasaho, MD, PhD[k], Päivi Piirilä, MD, PhD[f], and Hannu Kankaanranta, MD, PhD[a,b,i] *Tampere, Seinäjoki, Helsinki, and Espoo, Finland; and Stockholm, Umeå, and Gothenburg, Sweden*

Respiratory tract/Pulmonary comorbidities		Extrapulmonary comorbidities
Upper respiratory tract	Lower respiratory tract	
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J Allergy Clin Immunol Pract 2023;11:555-63

Variable	Without asthma (N = 7051)		Physician-diagnosed asthma (N = 879)		P
	Median	Q_1-Q_3	Median	Q_1-Q_3	
Age (y)	50	35-61	47	32-61	**.01**
	N	%	N	%	
Hypertension	1333	18.9	195	22.2	**.02**
Severe cardiovascular disease	344	4.9	50	5.7	.30
Coronary artery disease	165	2.3	18	2.0	.59
Arrhythmia	419	5.9	72	8.2	**.01**
Heart failure	87	1.2	13	1.5	.54
Stroke or TIA	140	2.0	27	3.1	**.03**
Diabetes	404	5.7	63	7.2	.09
Depression	733	10.4	133	15.1	**<.001**
Anxiety or panic disorder	427	6.1	81	9.2	**<.001**
GERD	399	5.7	103	11.7	**<.001**
Chronic kidney failure	51	0.7	7	0.8	.81
Sleep apnea	247	3.5	56	6.4	**<.001**
Osteoporosis	122	1.7	41	4.7	**<.001**
Painful condition	460	6.5	102	11.6	**<.001**
COPD	97	1.4	81	9.2	**<.001**
Obesity*	1152	16.6	302	23.2	**<.001**
No. of nonrespiratory diseases ≥1*	3260	47.0	508	58.7	**<.001**
No. of nonrespiratory diseases ≥2*	1558	22.5	288	33.3	**<.001**
No. of nonrespiratory diseases ≥3*	721	10.4	162	18.7	**<.001**

J Allergy Clin Immunol Pract 2023;11:555-63

Variable	Early-diagnosed asthma (0-11 y)		Intermediate-diagnosed asthma (12-39 y)		Late-diagnosed asthma (40-69 y)	
	OR (95 % CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Hypertension	1.37 (0.84-2.23)	.20	1.12 (0.80-1.58)	.51	1.30 (0.96-1.75)	.09
Severe cardiovascular disease	1.02 (0.43-2.41)	.97	0.91 (0.48-1.71)	.76	1.28 (0.83-1.98)	.26
Arrhythmia	1.27 (0.67-2.39)	.47	1.09 (0.68-1.76)	.72	1.64 (1.11-2.41)	**.01**
Stroke or TIA	1.81 (0.64-5.12)	.27	1.74 (0.85-3.55)	.13	1.43 (0.78-2.64)	.25
Diabetes	0.73 (0.31-1.70)	.46	1.05 (0.63-1.75)	.85	1.41 (0.94-2.11)	.10
Depression	1.00 (0.66-1.53)	.98	1.45 (1.08-1.95)	**.015**	1.74 (1.20-2.52)	**.003**
Anxiety or panic disorder	1.01 (0.59-1.71)	.98	1.85 (1.31-2.61)	**<.001**	1.32 (0.78-2.21)	.30
GERD	1.95 (1.18-3.24)	**.009**	2.14 (1.48-3.08)	**<.001**	2.80 (1.94-4.03)	**<.001**
Sleep apnea	1.10 (0.50-2.43)	.82	2.06 (1.23-3.43)	**.006**	1.99 (1.23-3.20)	**.005**
Osteoporosis	0.58 (0.078-4.24)	.59	2.97 (1.69-5.22)	**<.001**	2.41 (1.41-4.16)	**.001**
Painful condition	1.23 (0.67-2.27)	.50	1.64 (1.12-2.39)	**.011**	2.05 (1.44-2.92)	**<.001**

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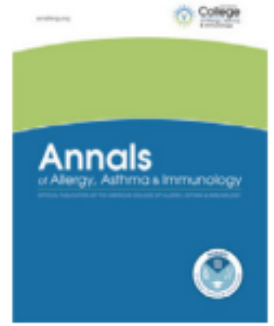
Contents lists available at ScienceDirect

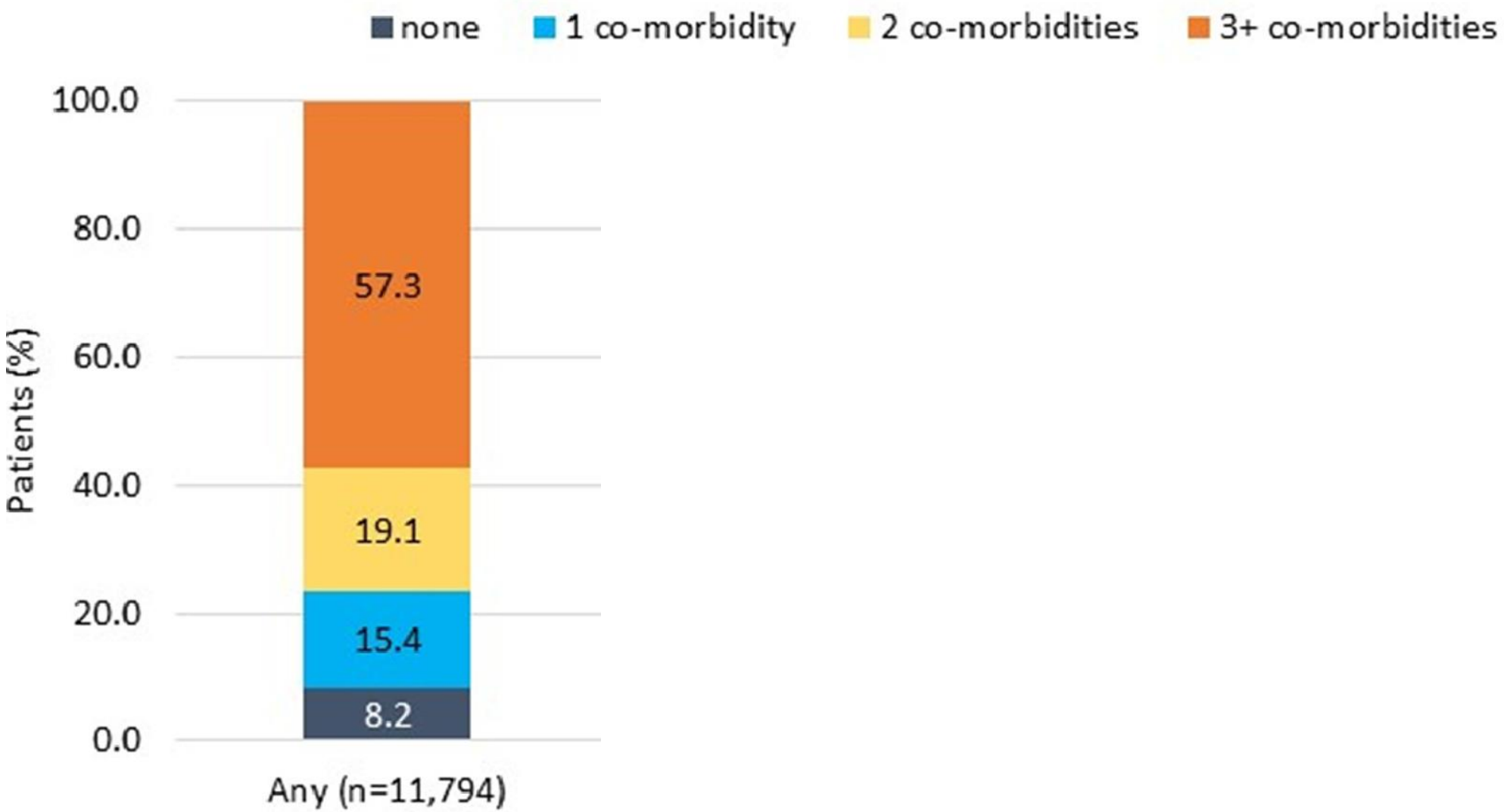


Original Article

Analysis of comorbidities and multimorbidity in adult patients in the International Severe Asthma Registry

Ghislaine Scelo PhD, Carlos A Torres-Duque MD, Jorge Maspero PhD, Trung N. Tran MD, PhD, Ruth Murray PhD, Neil Martin MD, PhD, Andrew N. Menzies-Gow PhD, FRCP, Mark Hew PhD, FRACP, Matthew J. Peters PhD, Peter G. Gibson MBBS, FRACP, George C. Christoff MD, MPH, PhD, Todor A Popov MD, PhD, Andréanne Côté MD, MSc, FRCPC, Celine Bergeron MD, FRCPC, MSc, Delbert Dorscheid MD, PhD, J. Mark FitzGerald MD, FRCPC, Kenneth R. Chapman MD, Louis Philippe Boulet MD FRCPC, Mohit Bhutani MD, FRCPC, FCCP, Mohsen Sadatsafavi MD, PhD, Libardo Jiménez-Maldonado MD, Mauricio Duran-Silva MD, Bellanid Rodriguez BSc, Carlos Andres Celis-Preciado MD, MSc, Diana Jimena Cano-Rosales MD, Ivan Solarte MD, MHPE, Maria Jose Fernandez-Sanchez MD, MSc, Patricia Parada-Tovar BSc, Anna von Bülow MD, PhD, Anne Sofie Bjerrum MD, PhD, Charlotte S. Ulrik MD, DMSc, Karin Dahl Assing MD, Linda Makowska Rasmussen MD, PhD, Susanne Hansen PhD, Alan Altraja MD, PhD, Arnaud Bourdin MD, PhD, Camille Taille MD, PhD, Jeremy Charriot MD, PhD, Nicolas Roche MD, PhD, Andriana I. Papaioannou MD, PhD, Konstantinos Kostikas MD, PhD, Nikolaos G. Papadopoulos MD, PhD, FRCP, Sundeep Salvi MD, PhD, Deirdre Long RGN, RANP, MSc, Patrick D. Mitchell MD MRCPI, Richard Costello MB, MD, FRCPI, Concetta Sirena PhD, Cristina Cardini MD, Enrico Heffler MD, PhD, Francesca Puggioni MD, Giorgio Walter Canonica MD, Giuseppe Guida MD, PhD, Takashi Iwanaga MD, PhD, Mona Al-Ahmad MBBCh FRCPC, Désirée Larenas Linnemann MD, FAAAAI, Dist.Intl.FACAAI, Ulises García MD, Piotr Kuna MD, PhD, João A. Fonseca MD, PhD, Riyad Al-Lehebi MD, FRCPC, Mariko Koh Siyue MBBS, MRCP (UK), FCCP, **Chin Kook Rhee MD, PhD**, Borja G. Cosio MD, PhD, Luis Perez de Llano MD, PhD, Diahn-Warng Perng (Steve) MD, PhD, Erick Wan-Chun Huang MD, PhD, Hao-Chien Wang MD, PhD, Ming-Ju Tsai M.D, PhD, Bassam Mahboub MD, Laila Ibraheem Jaber Salameh PhD, David Jackson MRCP PhD, John Busby PhD, Liam G. Heaney MD, Paul Pfeffer MRCP(UK), PhD, Amanda Grippen Goddard DO, Eileen Wang MD, MPH, Flavia Hoyte MD, Michael E. Wechsler MD, Nicholas Chapman DO, Rohit Katial MD, Victoria Carter BSc, Lakmini Bulathsinhala MPH, Neva Eleangovan BSc, Con Ariti MSc, Juntao Lyu PhD, David Price FRCGP and Celeste Porsbjerg MD, PhD

Ann Allergy Asthma Immunol. 2023 Aug 26;S1081-1206(23)00630-0.



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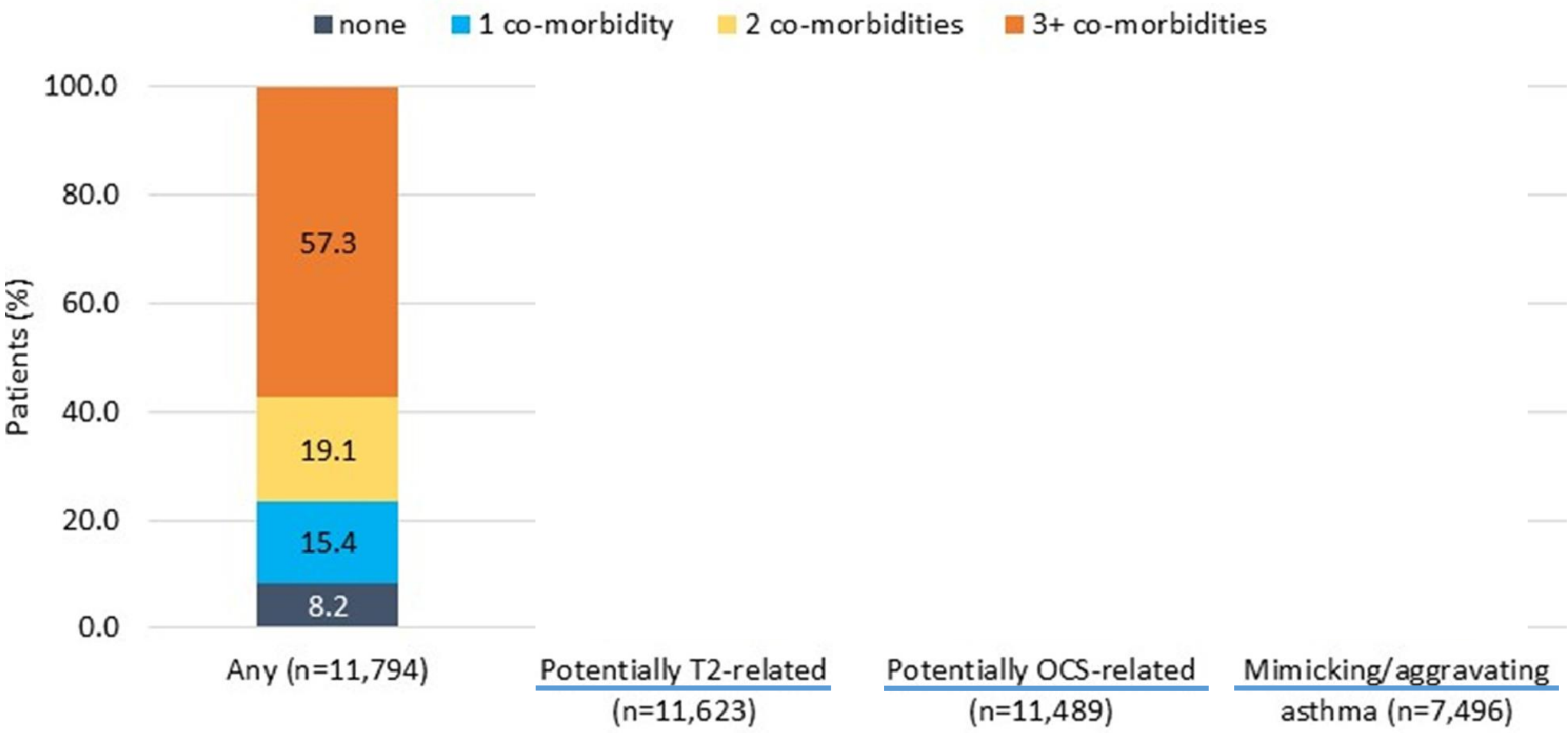


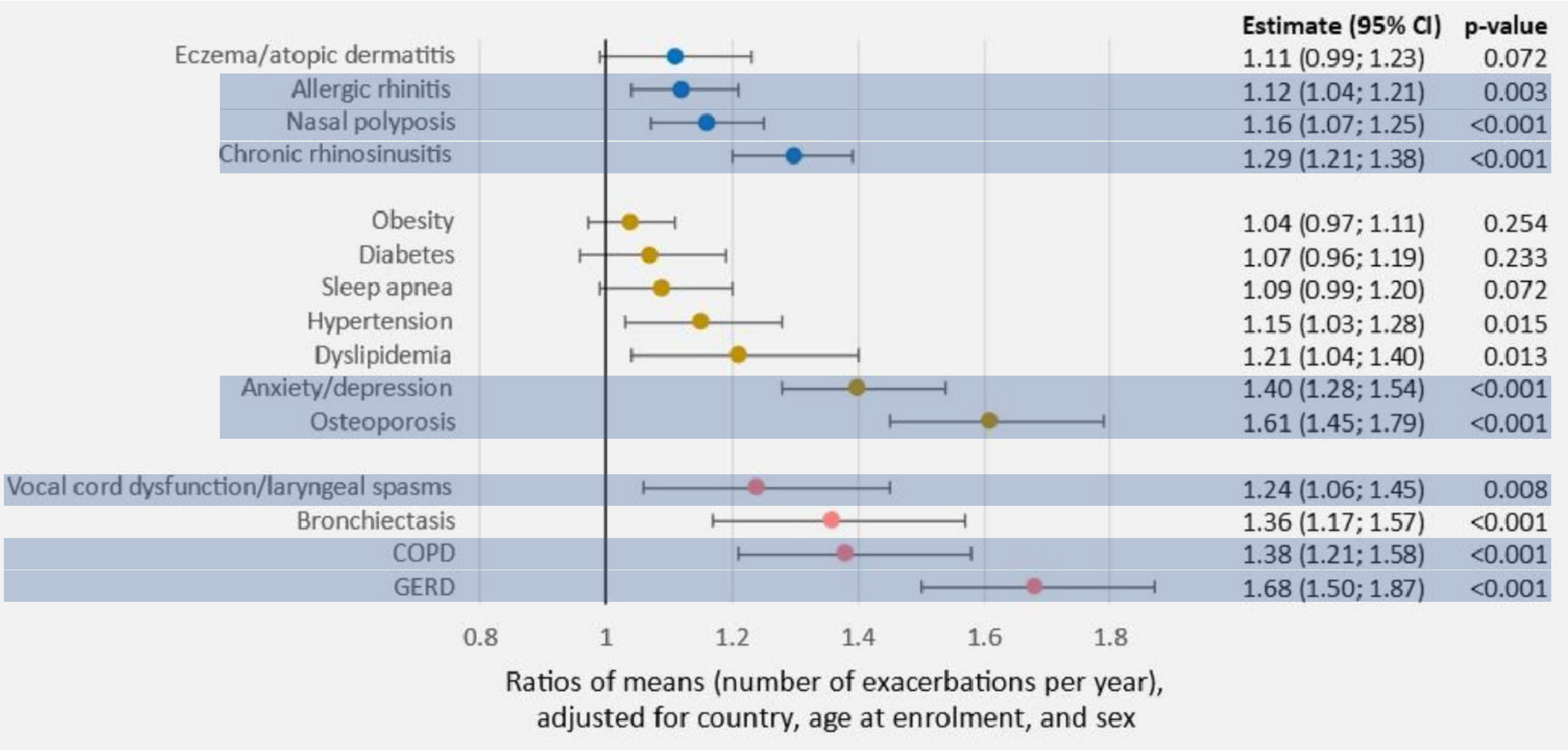
Ann Allergy Asthma Immunol. 2023 Aug 26;S1081-1206(23)00630-0.

Eczema/atopic dermatitis
Allergic rhinitis
Nasal polyposis
Chronic rhinosinusitis

Obesity
Diabetes
Sleep apnea
Hypertension
Dyslipidemia
Anxiety/depression
Osteoporosis

Vocal cord dysfunction/laryngeal spasms
Bronchiectasis
COPD
GERD

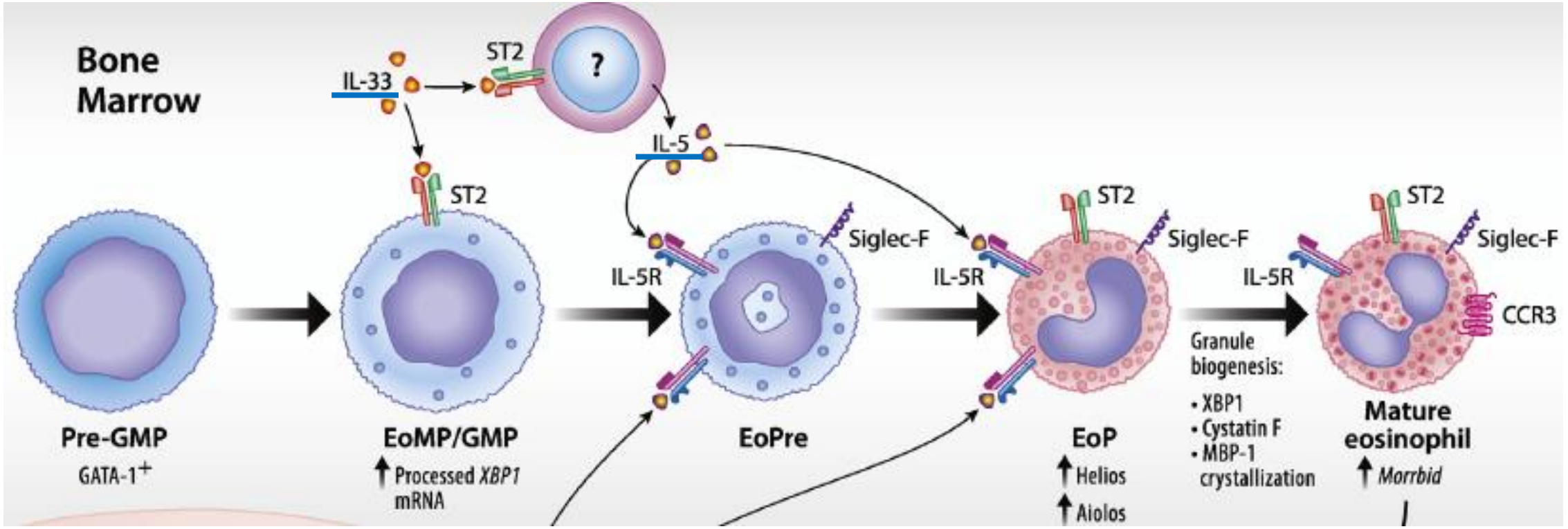
Ann Allergy Asthma Immunol. 2023 Aug 26;S1081-1206(23)00630-0.



Ann Allergy Asthma Immunol. 2023 Aug 26;S1081-1206(23)00630-0.

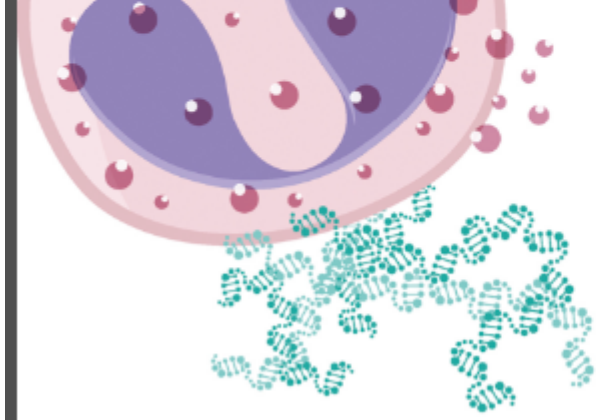
Contents

Eosinophil



J Allergy Clin Immunol 2018;141:505-17

Roles of eosinophil granule proteins and extracellular traps



	Helminth toxicity	Antibacterial	Antiviral	Immune system	Epithelial activation and remodeling factor expression
EPX	✓	—	—	—	✓
MBP	✓	✓	—	Neutrophil, mast cell and basophil activation	✓
ECP	✓	✓	✓	—	—
EDN	—	—	✓	Dendritic cell recruitment and activation	—
CLC/gal-10	—	—	—	Th2 activation	—
EET	—	✓	—	—	—

Mayo Clin Proc. 2021 Oct;96(10):2694-2707. doi: 10.1016/j.mayocp.2021.04.025.

International Journal of Chronic Obstructive Pulmonary Disease Dovepress
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ORIGINAL RESEARCH

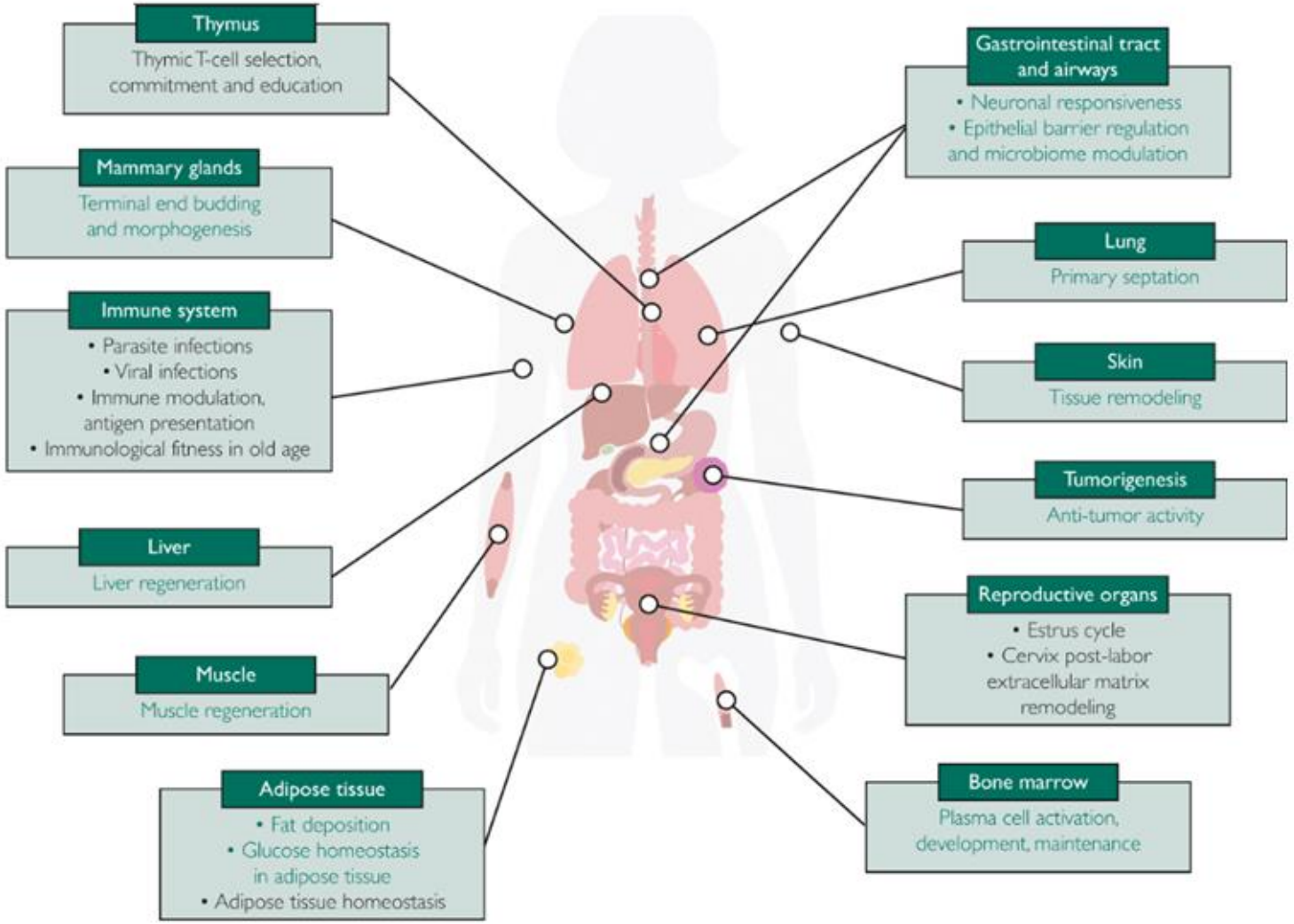
Incidence and Prognostic Factors of Respiratory Viral Infections in Severe Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Table 5 Factors Associated with Viral Detection in Severe Chronic Obstructive Pulmonary Disease Exacerbation Based on Multivariable Logistic Regression Analysis

	Univariable		**Multivariable Model[a]**	
	OR (95% CI)	***P* value**	**OR (95% CI)**	***P* value**
Age >70	0.89 (0.47–1.7)	0.732	0.878 (0.43–1.80)	0.723
Female, sex	1.22 (0.63–2.36)	0.564	1.40 (0.68–2.87)	0.357
Nasopharyngeal symptoms	2.09 (1.13–3.87)	0.019	1.98 (1.03–3.78)	0.040
Use of ICS	1.70 (1.04–2.80)	0.036	1.69 (1.01–2.84)	0.047
Eosinophil<100/uL	1.84 (1.12–3.04)	0.018	1.74 (1.03–2.92)	0.038
CRP>0.5 mg/dL	2.86 (1.302–6.27)	0.009	2.76 (1.24–6.15)	0.013
ANC>4.8, $\times 10^9$/L	1.90 (0.997–3.622)	0.051	1.41 (0.71–2.80)	0.332

Jang et al. IJCOPD 2021

Physiologic processes of eosinophils



Mayo Clin Proc. 2021 Oct;96(10):2694-2707. doi: 10.1016/j.mayocp.2021.04.025.

TABLE 1 Definition of Hypereosinophilia (HE) and of the Hypereosinophilic Syndrome (HES)

Name/term	Abbreviation	Definition and criteria
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Allergy. 2023;78:47–59.

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Hypereosinophilic syndrome	HES	a) criteria for blood HE fulfilled and: b) organ damage and/or dysfunction attributable to tissue HE[b] and: c) exclusion of other disorders or condition as major reason for organ damage

Allergy. 2023;78:47–59.

Classification of eosinophil disorders

Nasosinus

- Eosinophilic rhinosinusitis
- Nasal polyposis

Eye

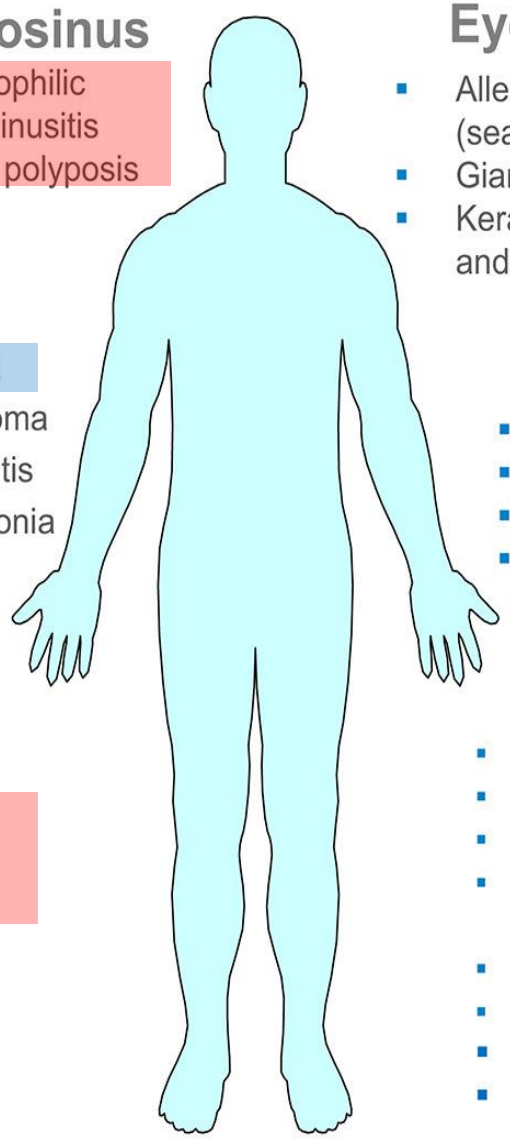
- Allergic conjunctivitis (seasonal and perennial)
- Giant papillary conjunctivitis
- Keratoconjunctivitis (atopic and vernal)

Skin

- Atopic dermatitis
- Urticarial dermatitis
- Chronic contact dermatitis
- Pemphigoid
- Ectoparasites
- Eosinophilic folliculitis
- Eosinophilic cellulitis (Wells syndrome
- Eosinophilic dermatosis of hematologic malignancy
- T-cell lymphoma
- Eosinophilic ulcer of the oral mucosa

Lung

- Eosinophilic asthma
- Eosinophilic granuloma
- Eosinophilic bronchitis
- Eosinophilic pneumonia
- Simple pulmonary eosinophilia
- Eosinophil pleuritis
- Occupational lung syndromes
- Allergic bronchopulmonary aspergillosis
- Tropical pulmonary eosinophilia



Systemic

- Eosinophilic granulomatosis with polyangiitis (EGPA)
- Eosinophilic leukemia
- IgG4-related disease
- Eosinophilia myalgia syndrome
- Episodic angioedema with eosinophilia (Gleich syndrome)
- Acute transplant graft rejections
- Drug reactions
- Hematologic malignancy
- Inborn errors of immunity with eosinophilia

Connective Tissue

- Eosinophilic myositis
- Eosinophilic synovitis
- Eosinophilic arthritis
- Eosinophilic fasciitis

GI Tract

- Eosinophilic esophagitis
- Eosinophilic gastritis
- Eosinophilic enteritis
- Eosinophil gastrointestinal disorder (EGID)
- Eosinophilic cholecystitis
- Eosinophilic colitis
- Eosinophilic pancreatitis
- Eosinophilic hepatitis

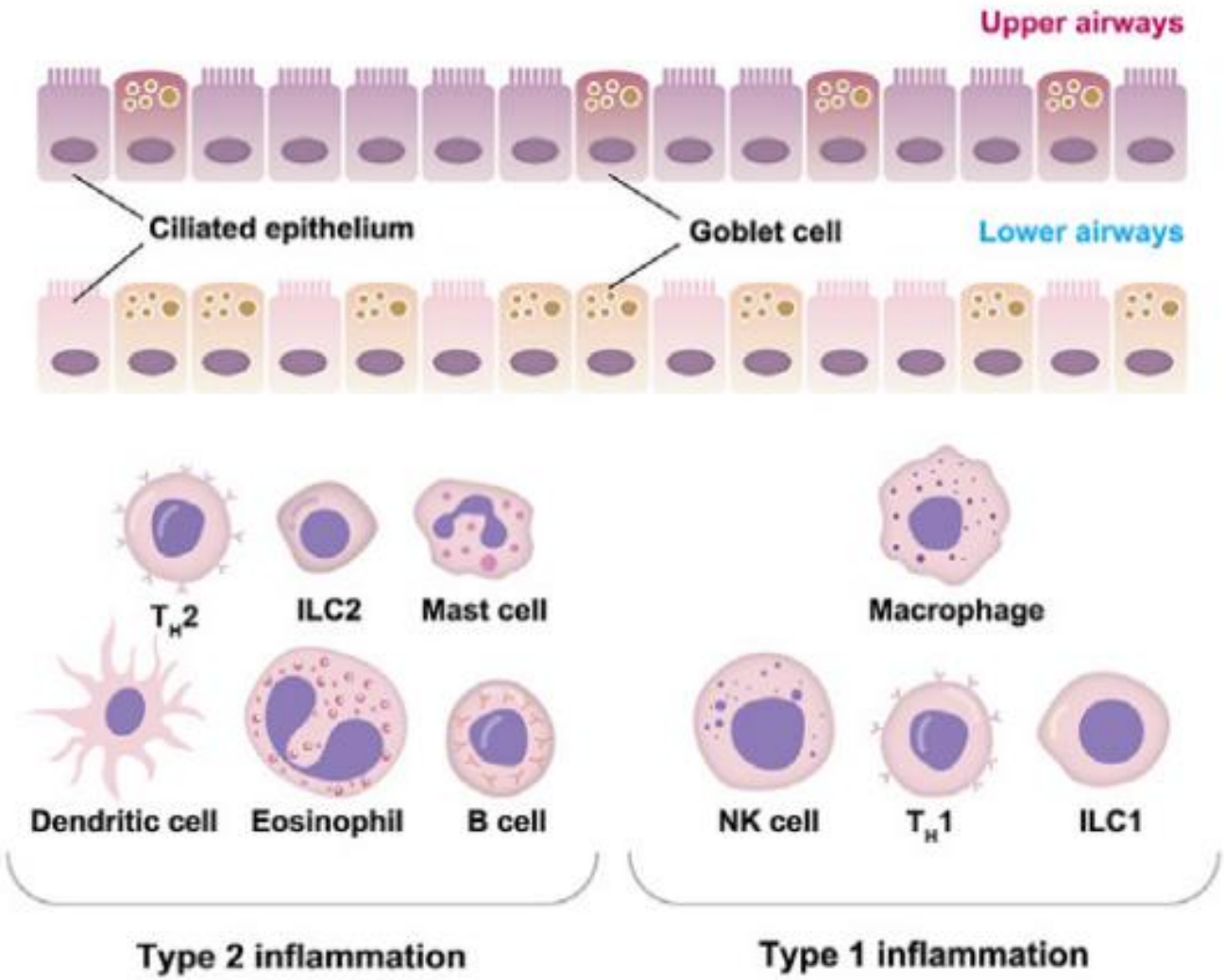
Other

- Eosinophilic ascites
- Eosinophilic myocarditis
- Eosinophilic coronary periarteritis
- Eosinophilic nephritis
- Eosinophilic cystitis
- Eosinophilic prostatitis
- Eosinophilic endometritis and myometritis (uterus)
- Eosinophilic mastitis

Allergy. 2023;78:47–59

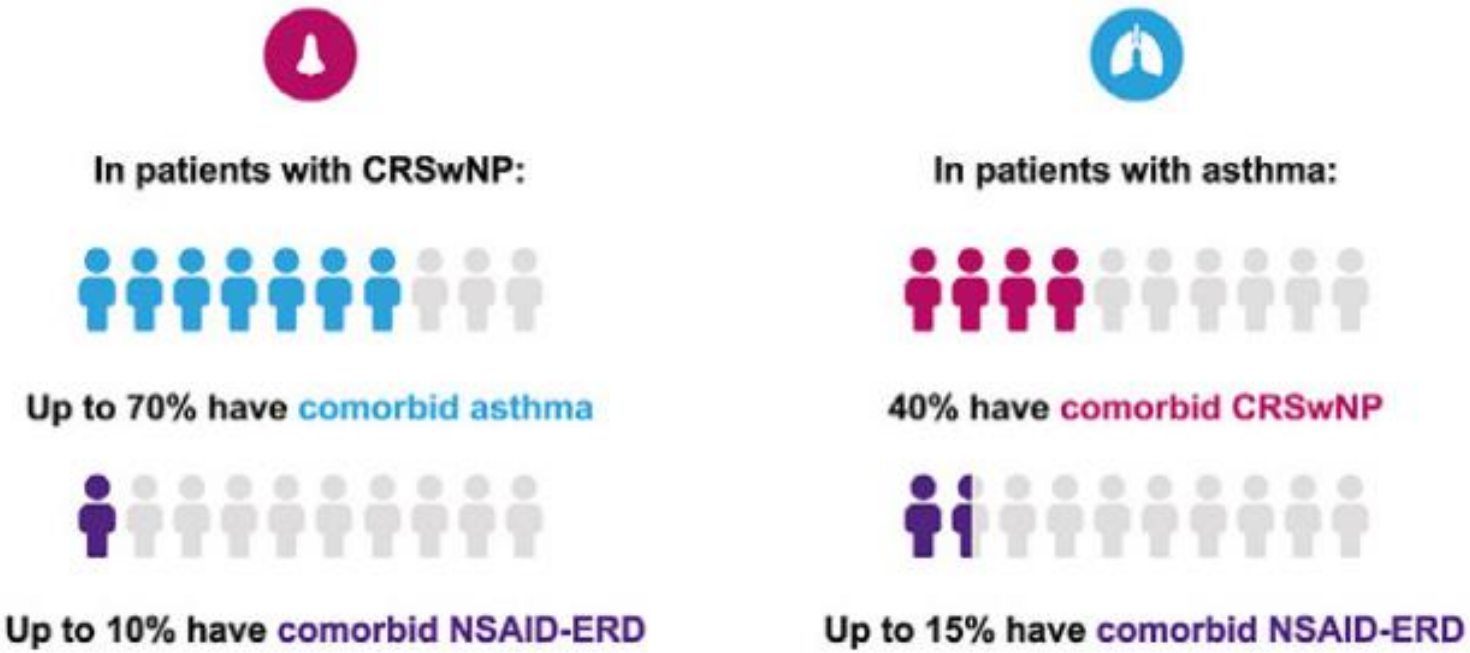
Contents

The upper and lower airways share common cell types and immune interactions



J Allergy Clin Immunol Pract 2023;11:2630-41

Epidemiologic evidence



J Allergy Clin Immunol Pract 2023;11:2630-41

Sinonasal Symptoms

Nasal obstruction/congestion

Nasal discharge (Rinorrhea/PND)

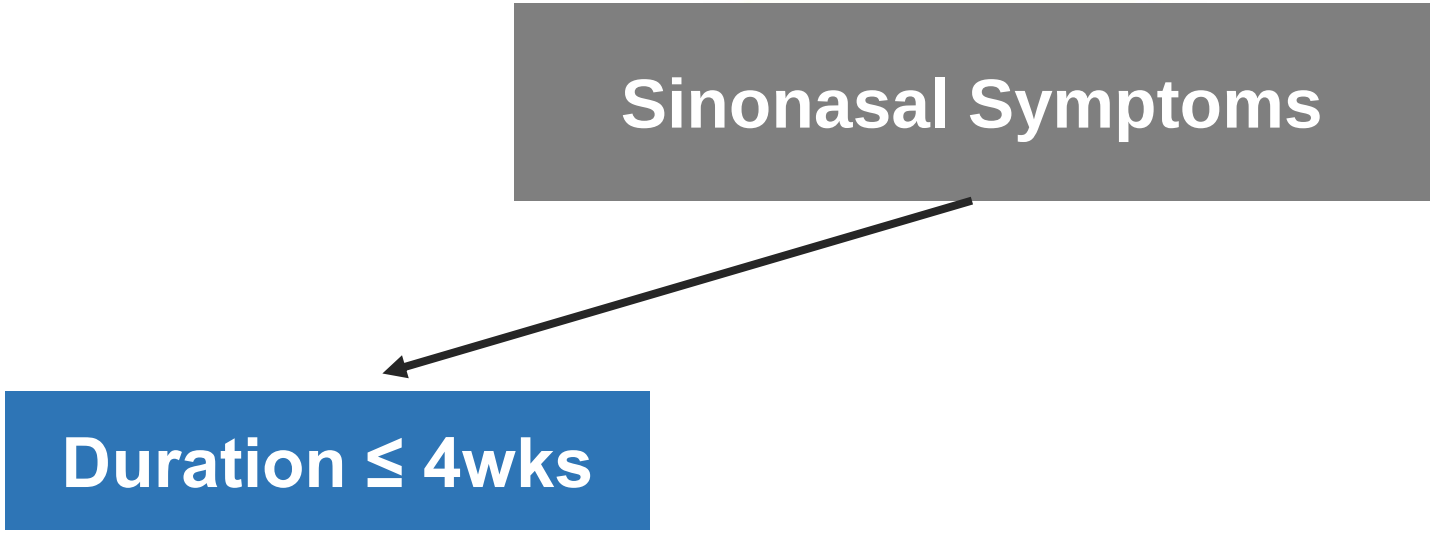
AND

Facial pain or pressure

OR

Reduction/loss of smell

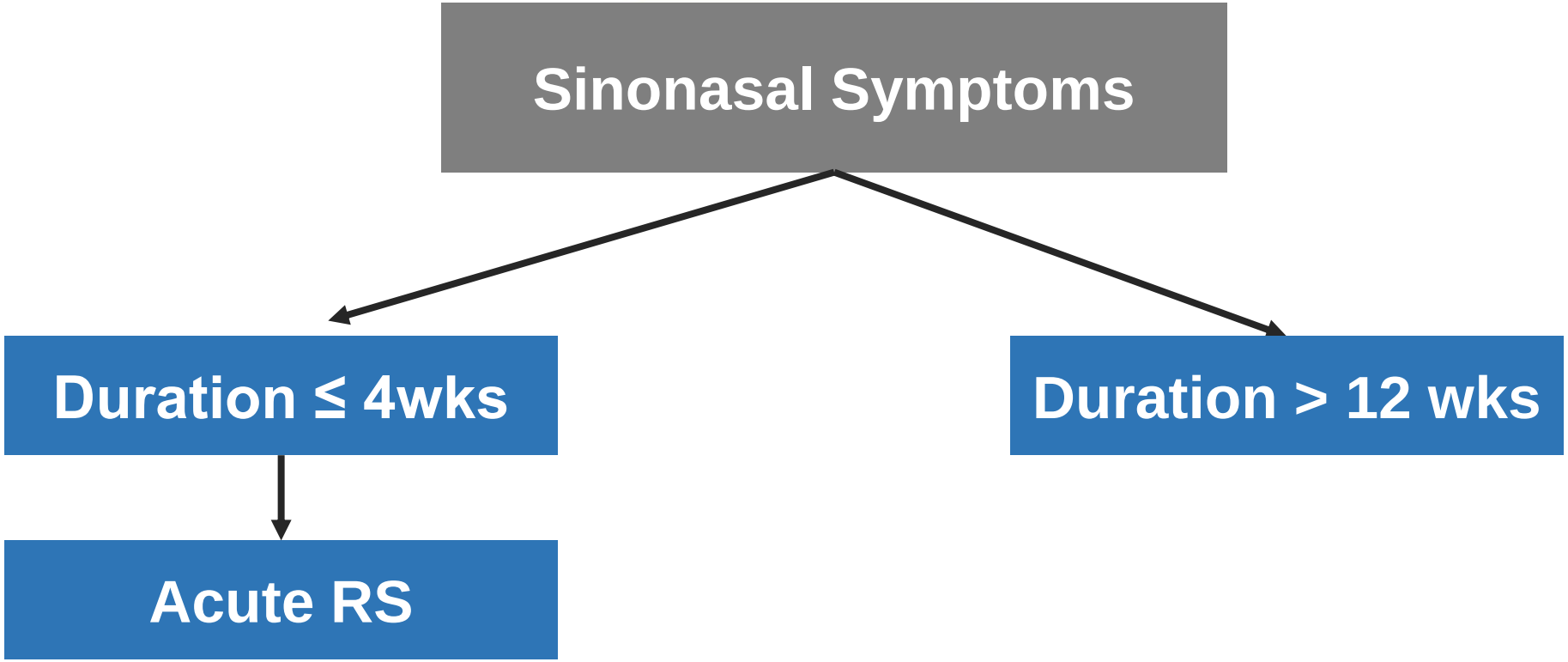
Int Forum Allergy Rhinol.2021;11:213–739



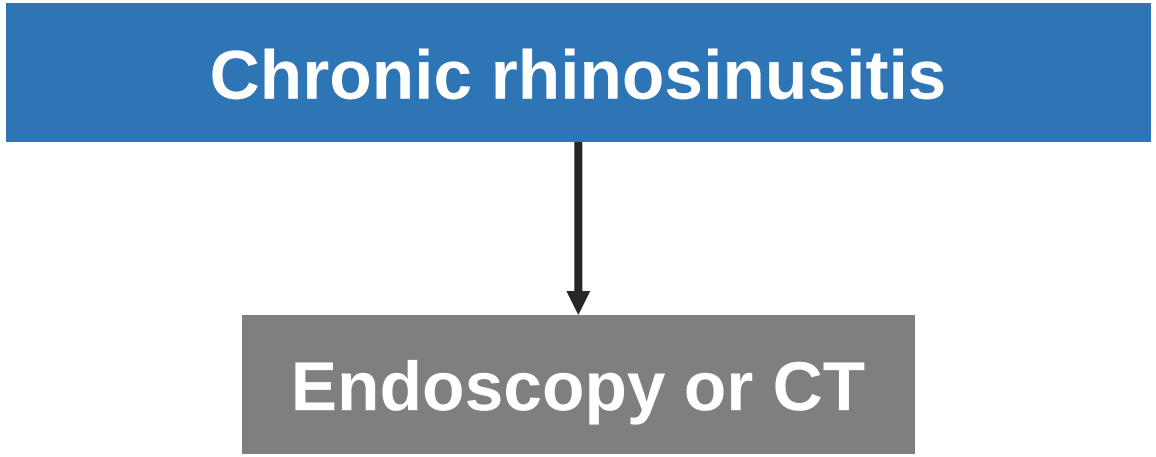
Acute Rhinosinusitis (ARS)

Radiology and endoscopy are not required for diagnosis

Int Forum Allergy Rhinol.2021;11:213–739



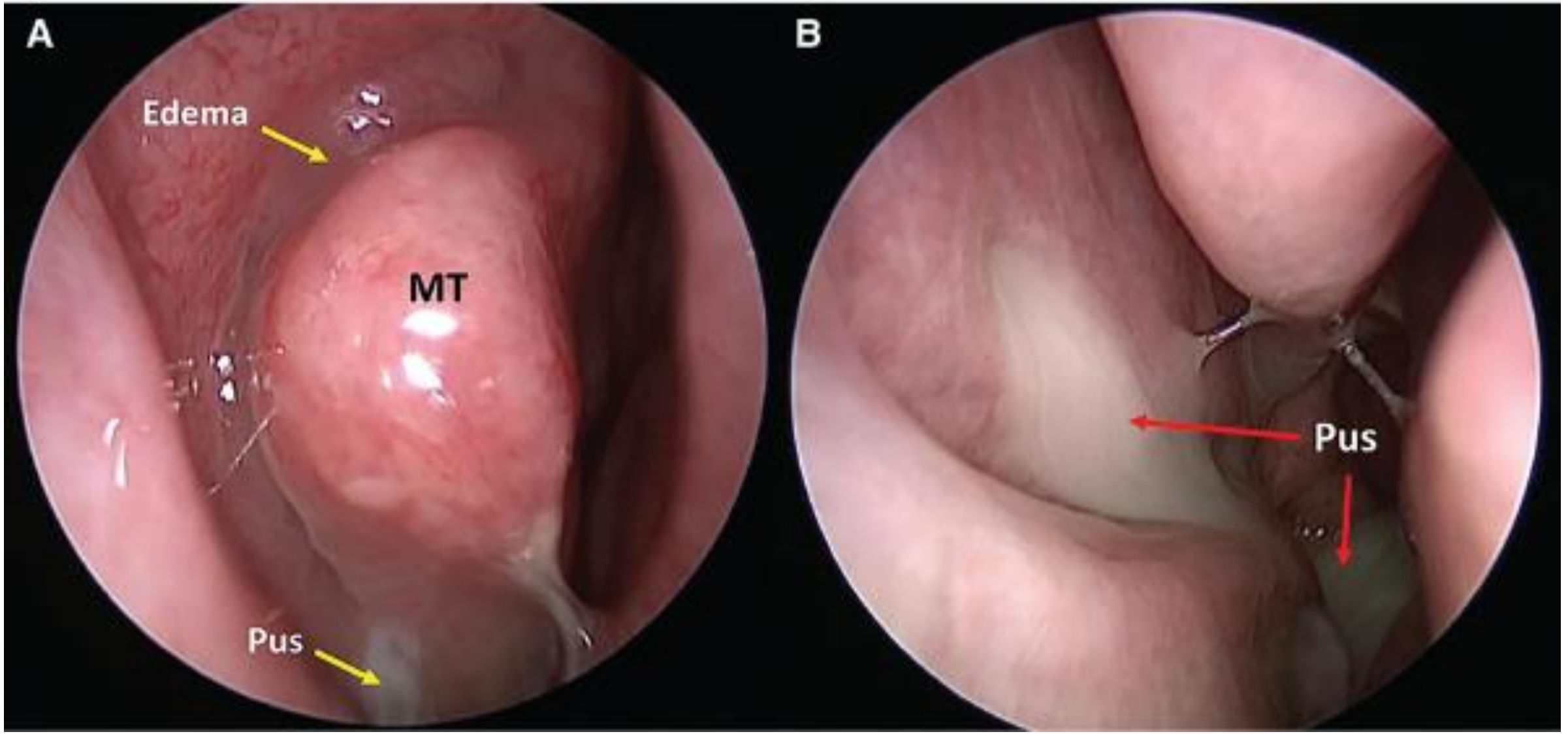
Int Forum Allergy Rhinol.2021;11:213–739



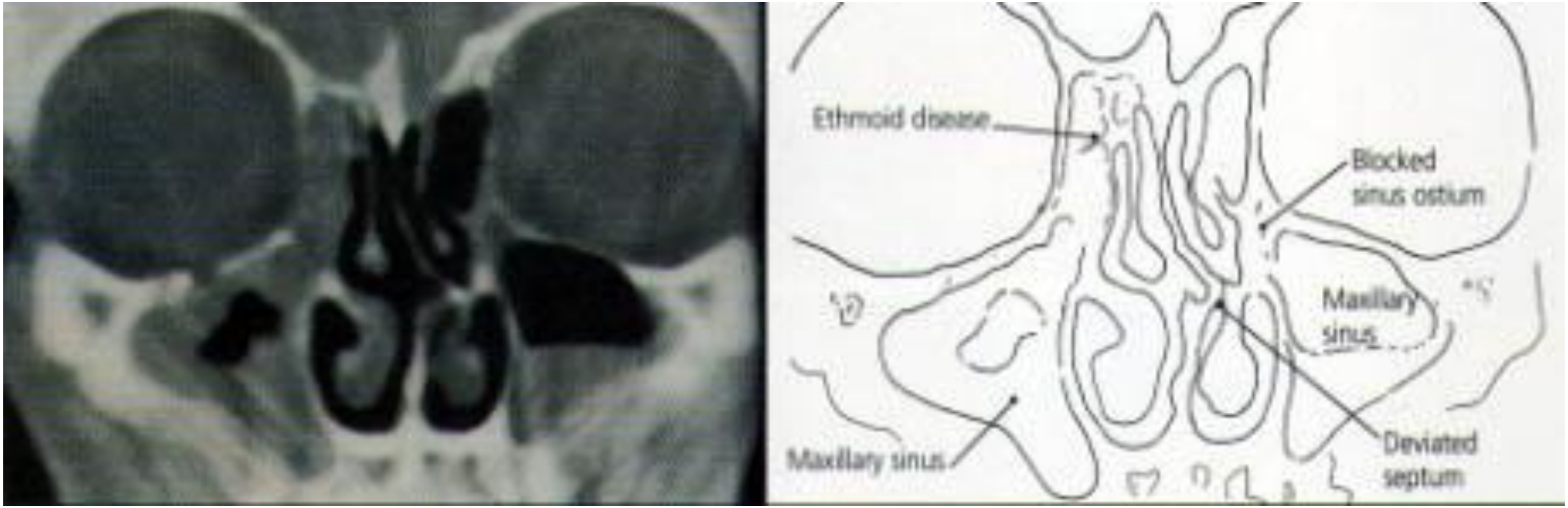
One or more of the following objective findings:

- Evidence of inflammation on nasal endoscopy or computed tomography
- Evidence of purulence coming from paranasal sinuses or ostiomeatal complex

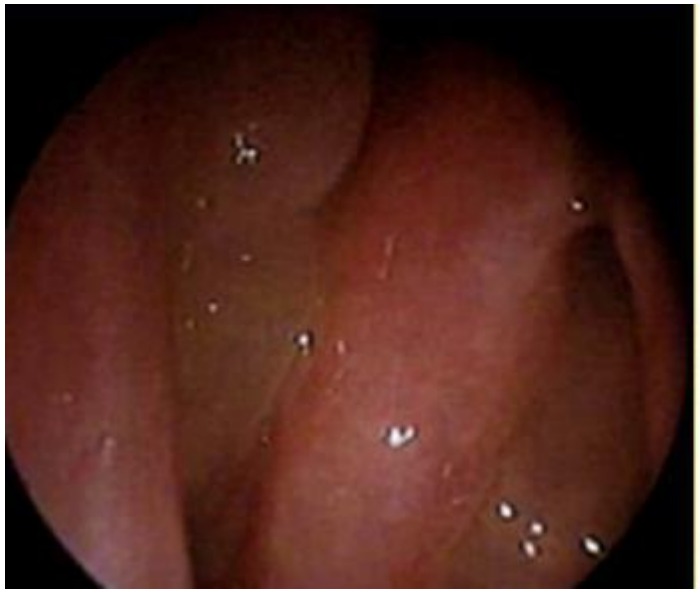
Int Forum Allergy Rhinol.2021;11:213–739

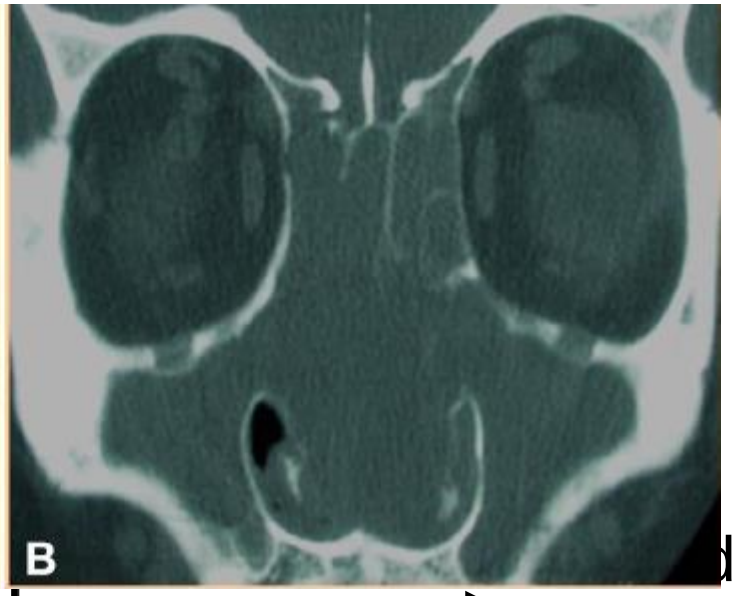


Laryngoscope. 2019;129:1976–1983



https://www.aafp.org/pubs/afp/issues/1998/0901/p707.html





der alternative diagnosis

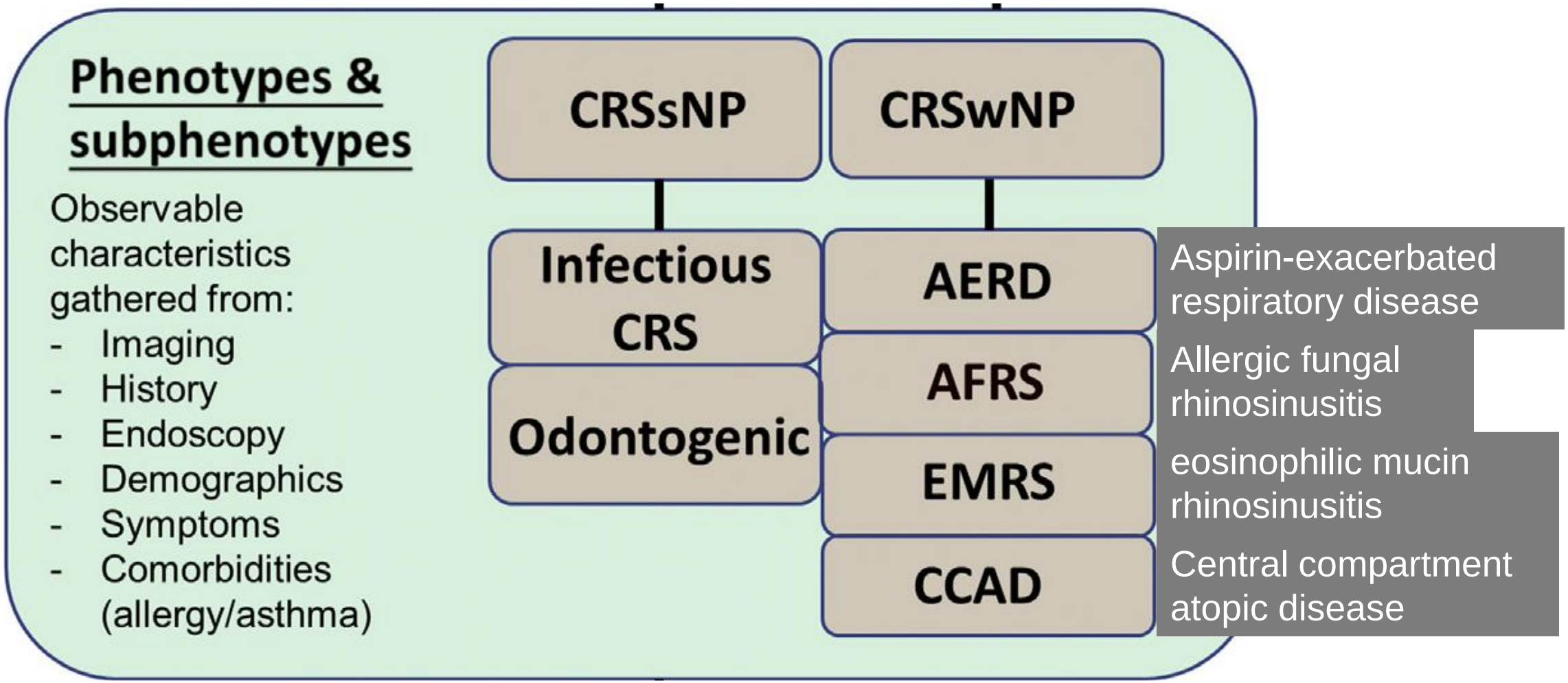
YES

Nasal polyp?

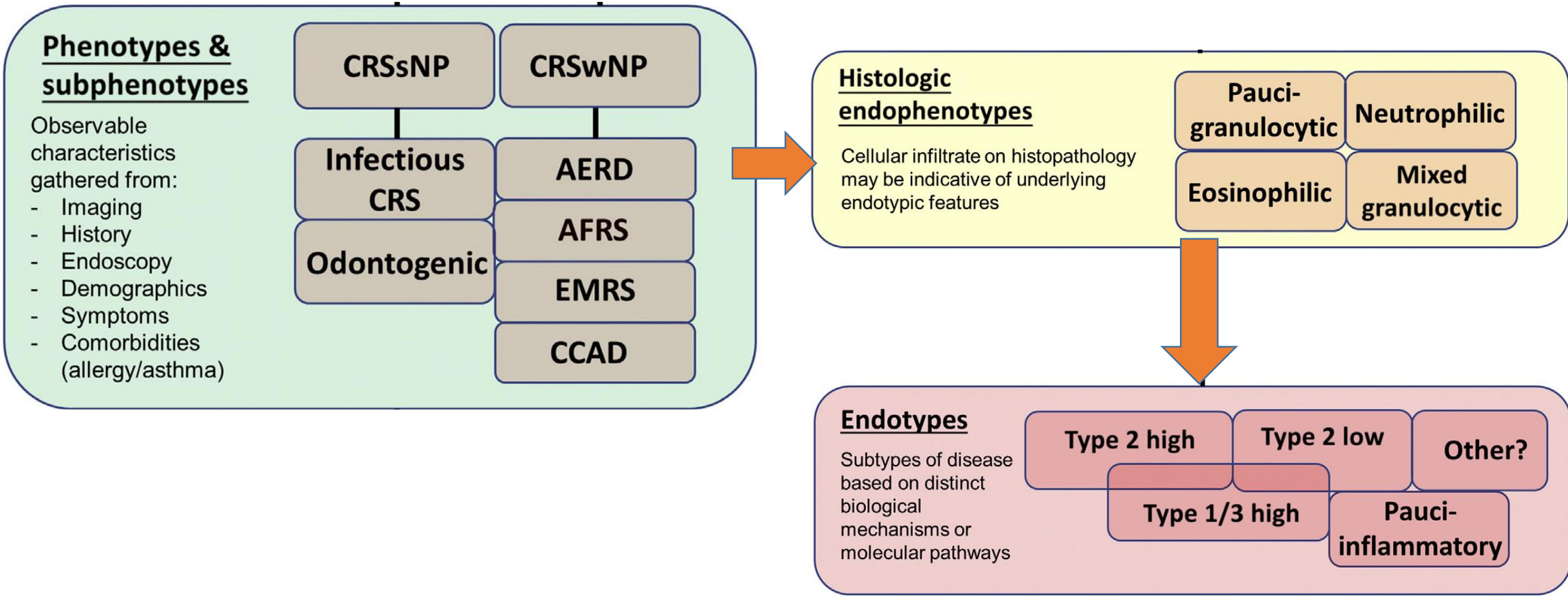
Chronic rhinosinusitis with Nasal polyp

Chronic rhinosinusitis without Nasal polyp

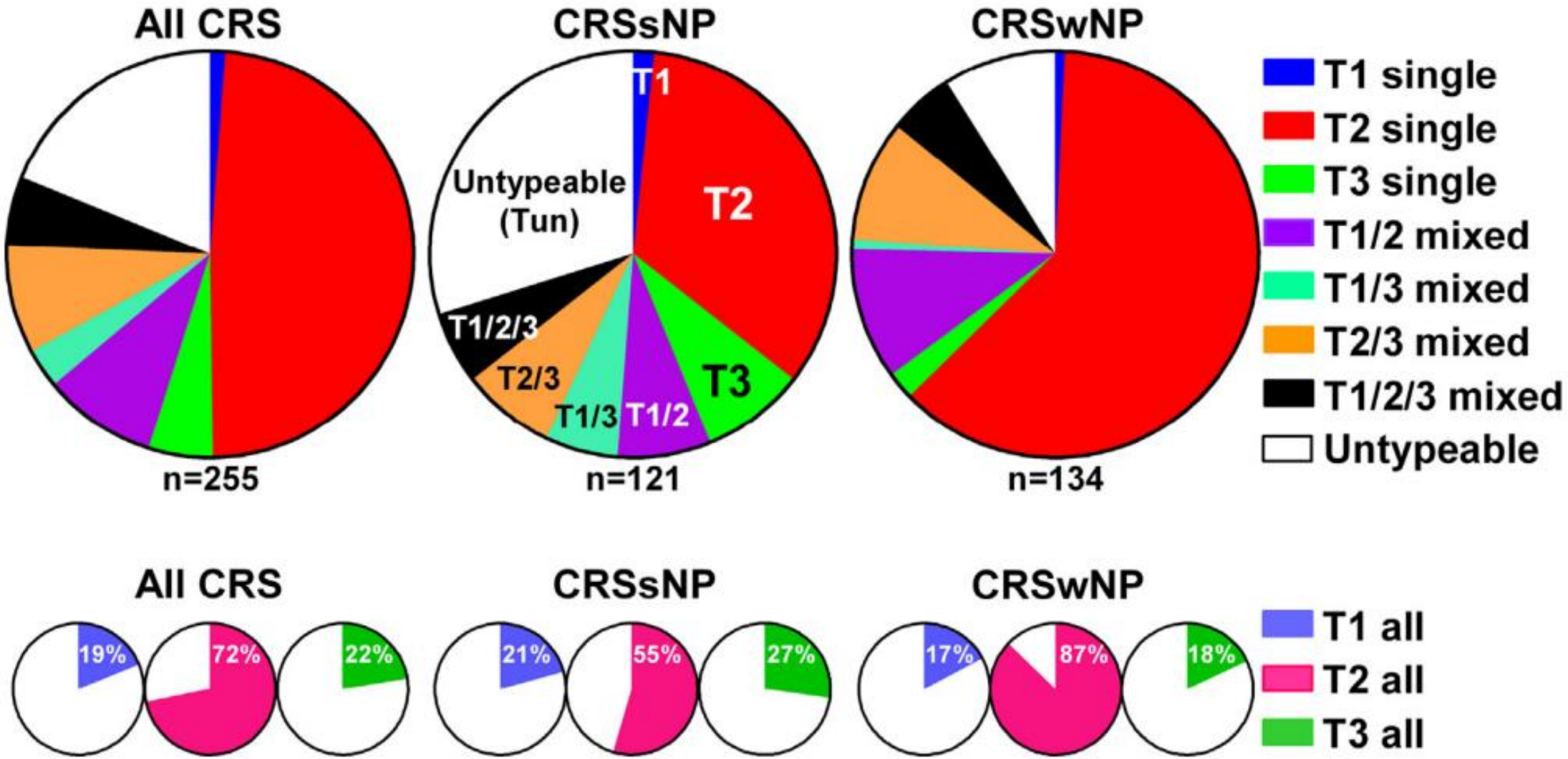
Int Forum Allergy Rhinol.2021;11:213–739



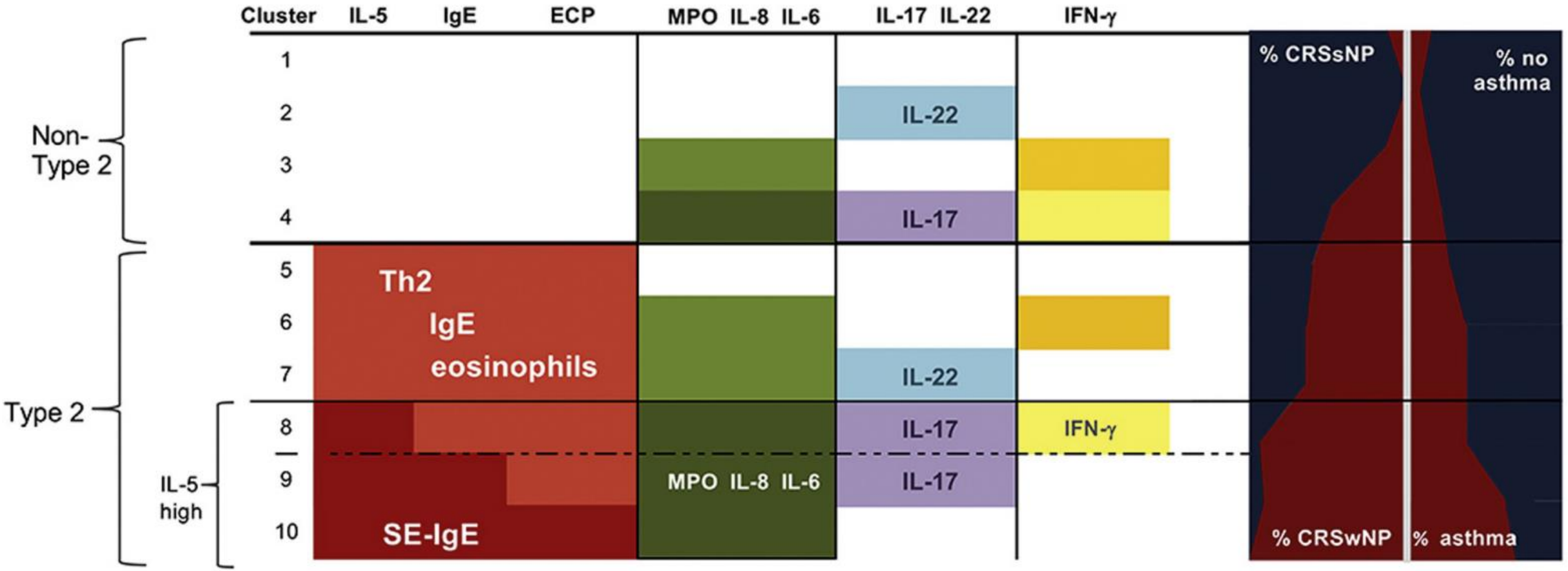
J Allergy Clin Immunol 2022;150:22-32, https://doi.org/10.1016/j.jaci.2022.04.013



J Allergy Clin Immunol 2022;150:22-32, https://doi.org/10.1016/j.jaci.2022.04.013



J Allergy Clin Immunol Pract 2019;7:2812-20



J Allergy Clin Immunol Pract 2022;10:1395-403

Treatment of CRS

CRS without NP

Intra nasal saline irrigation

Intra nasal corticosteroids

Oral antibiotics

Oral steroid

CRS with NP

Intra nasal saline irrigation

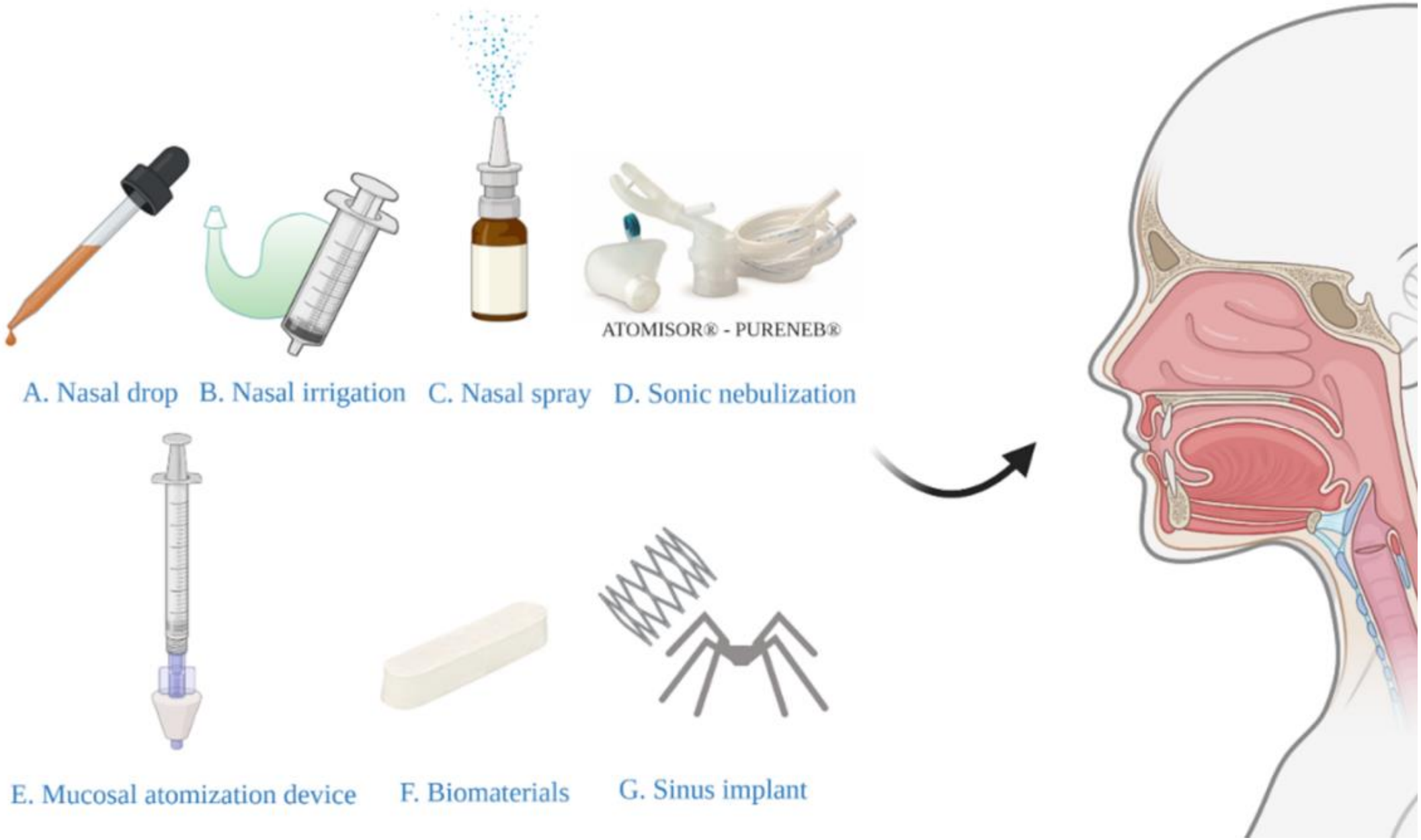
Intra nasal corticosteroids

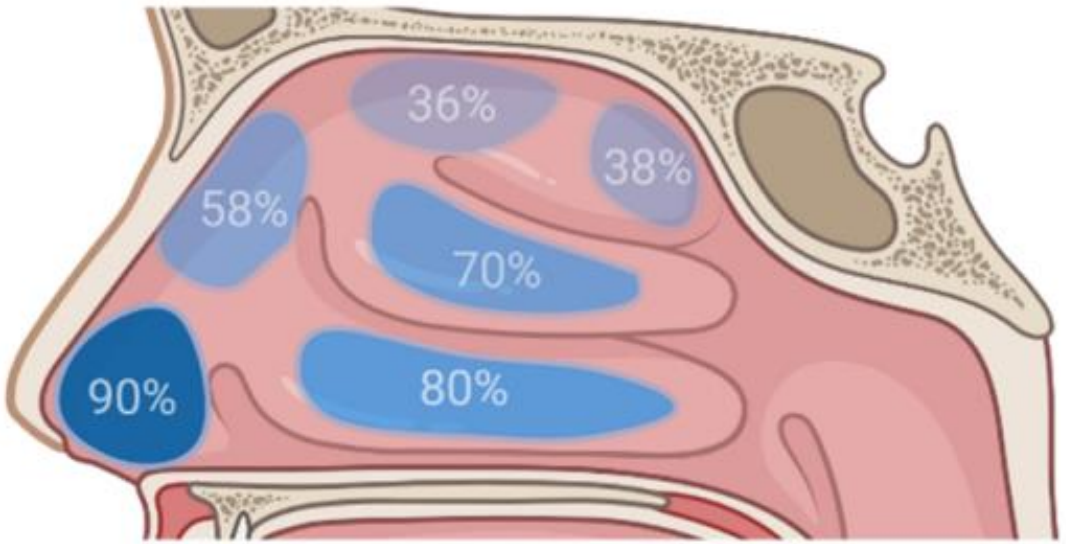
Oral steroid

Oral antibiotics

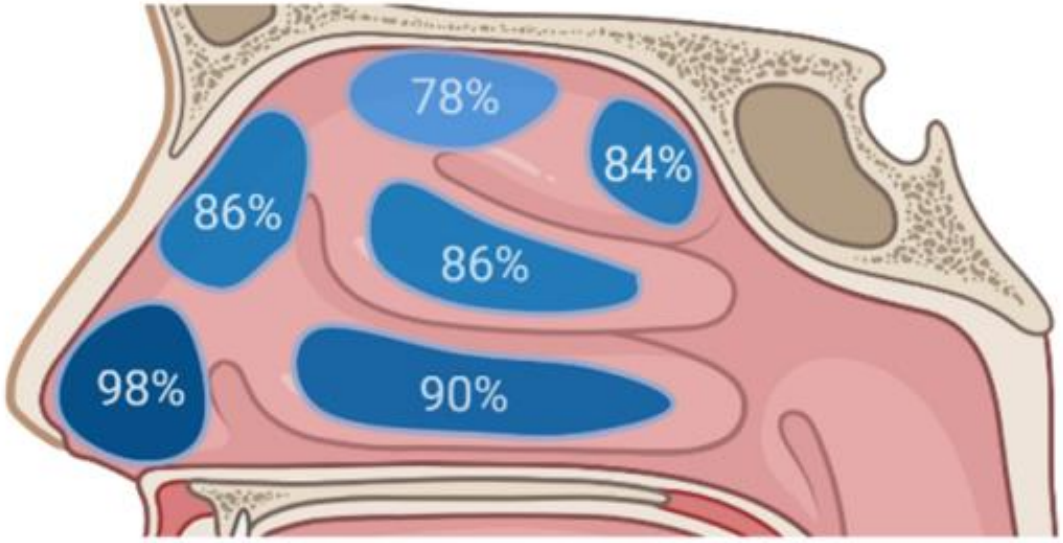
Antileukotriene agents

Refractory diseae: ESS, Biologics


ATOMISOR® - PURENEB®
A. Nasal drop
B. Nasal irrigation
C. Nasal spray
D. Sonic nebulization
E. Mucosal atomization device
F. Biomaterials
G. Sinus implant

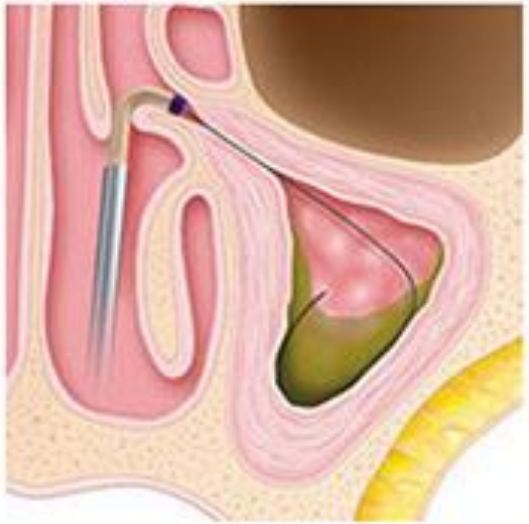


A. Nasal spray

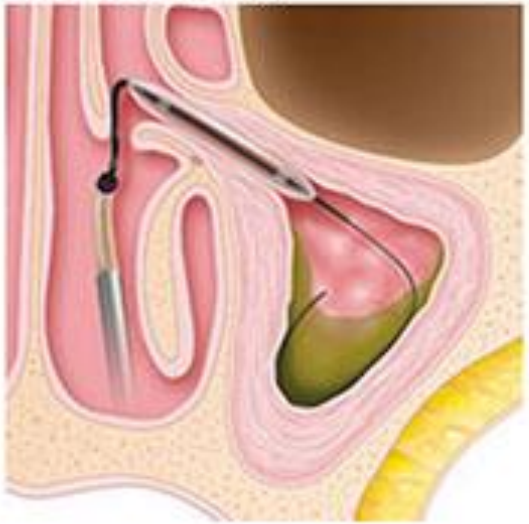


B. Nasal irrigation

Step 1. A balloon catheter is inserted into the inflamed sinus.



Step 2. The balloon is inflated to expand the sinus opening.

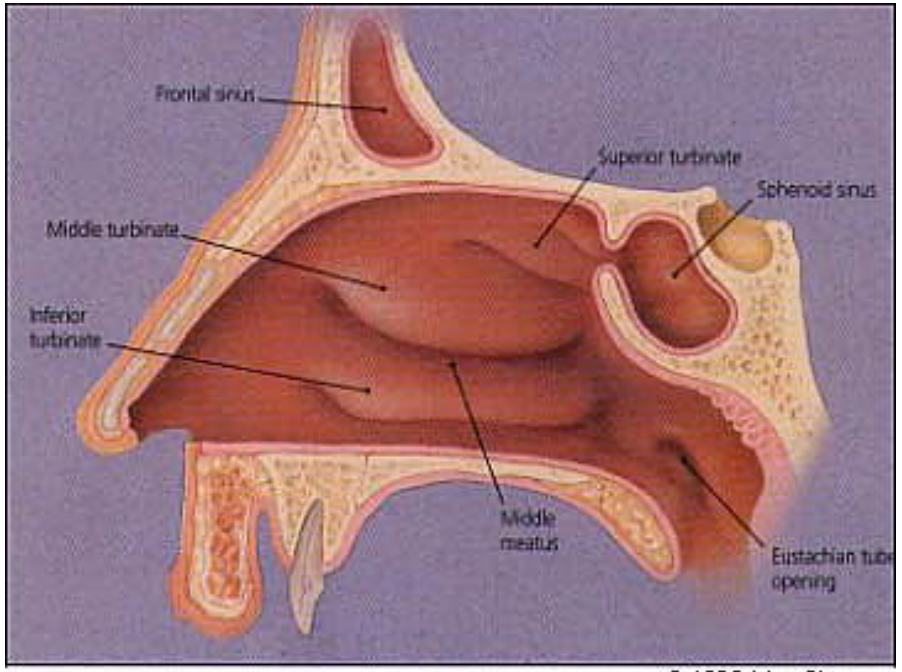


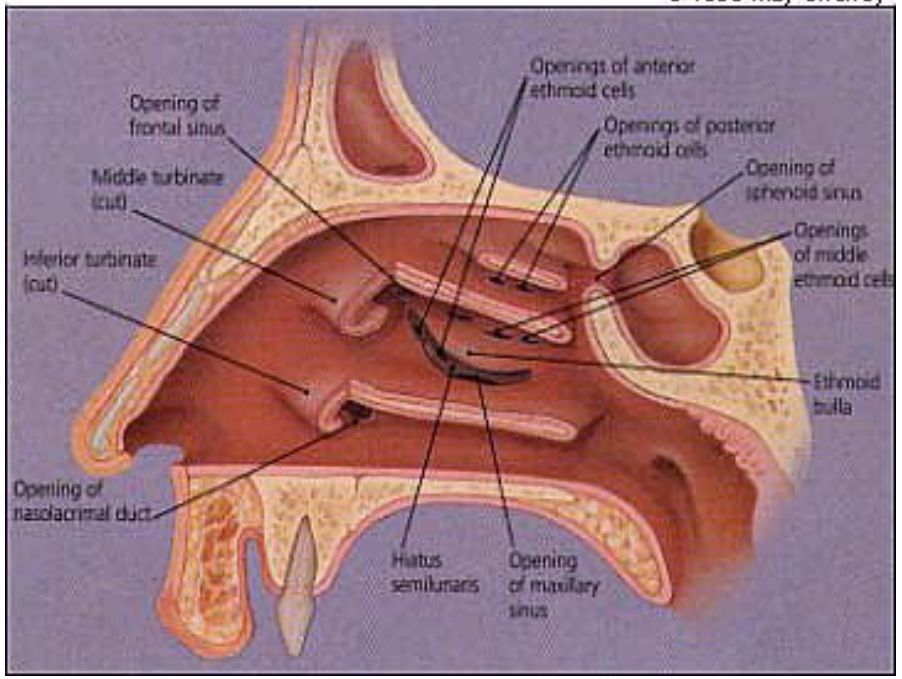
Step 3. Saline is sprayed into the inflamed sinus to flush out the pus and mucus.

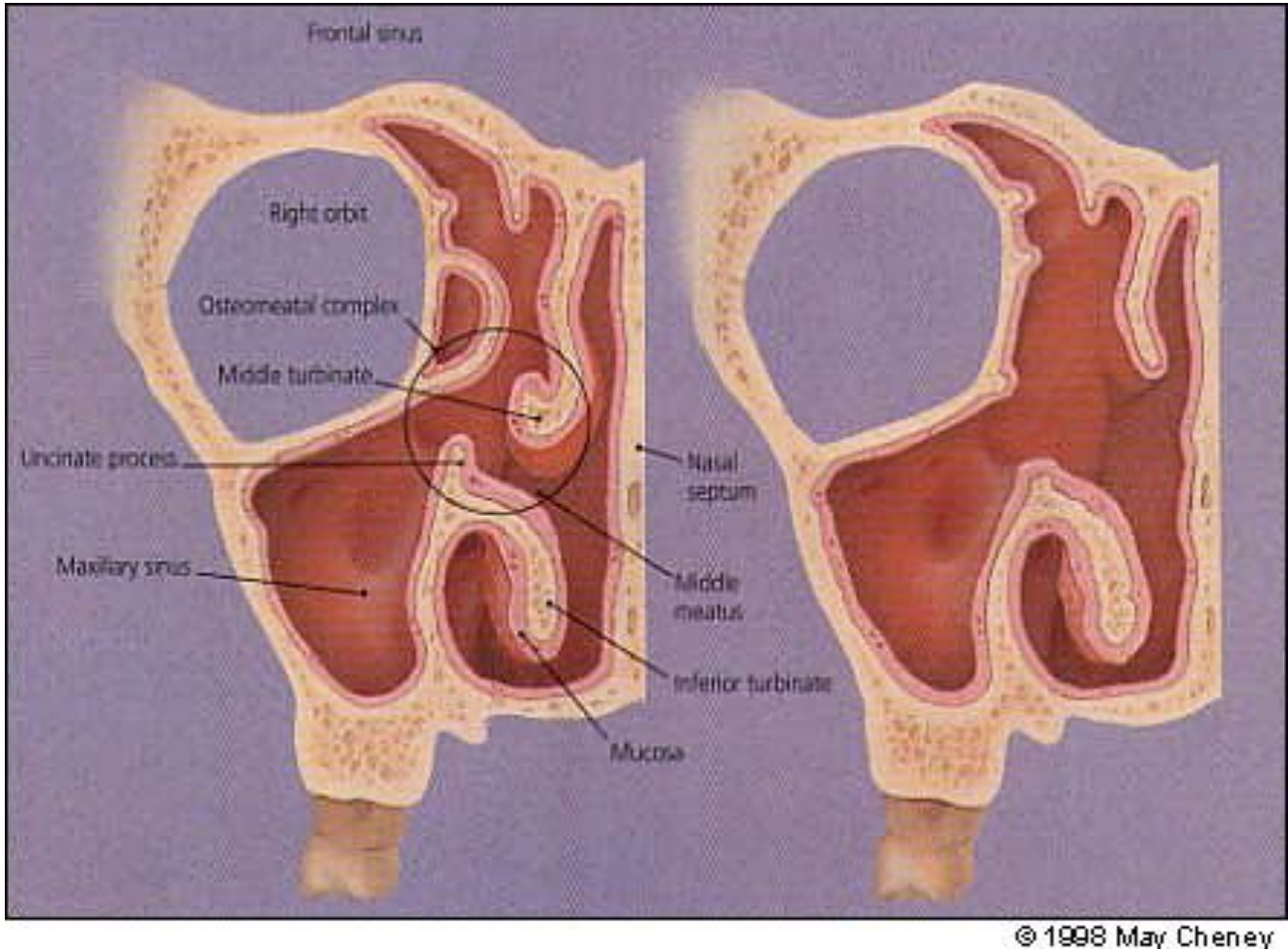
Step 4. The system is removed, leaving the sinuses open.

When the sinus balloon is inflated, it restructures and widens the walls of the sinus passageway while maintaining the integrity of the sinus lining.

https://www.entdoctor.co.za/functional-endoscopic-sinus-surgery







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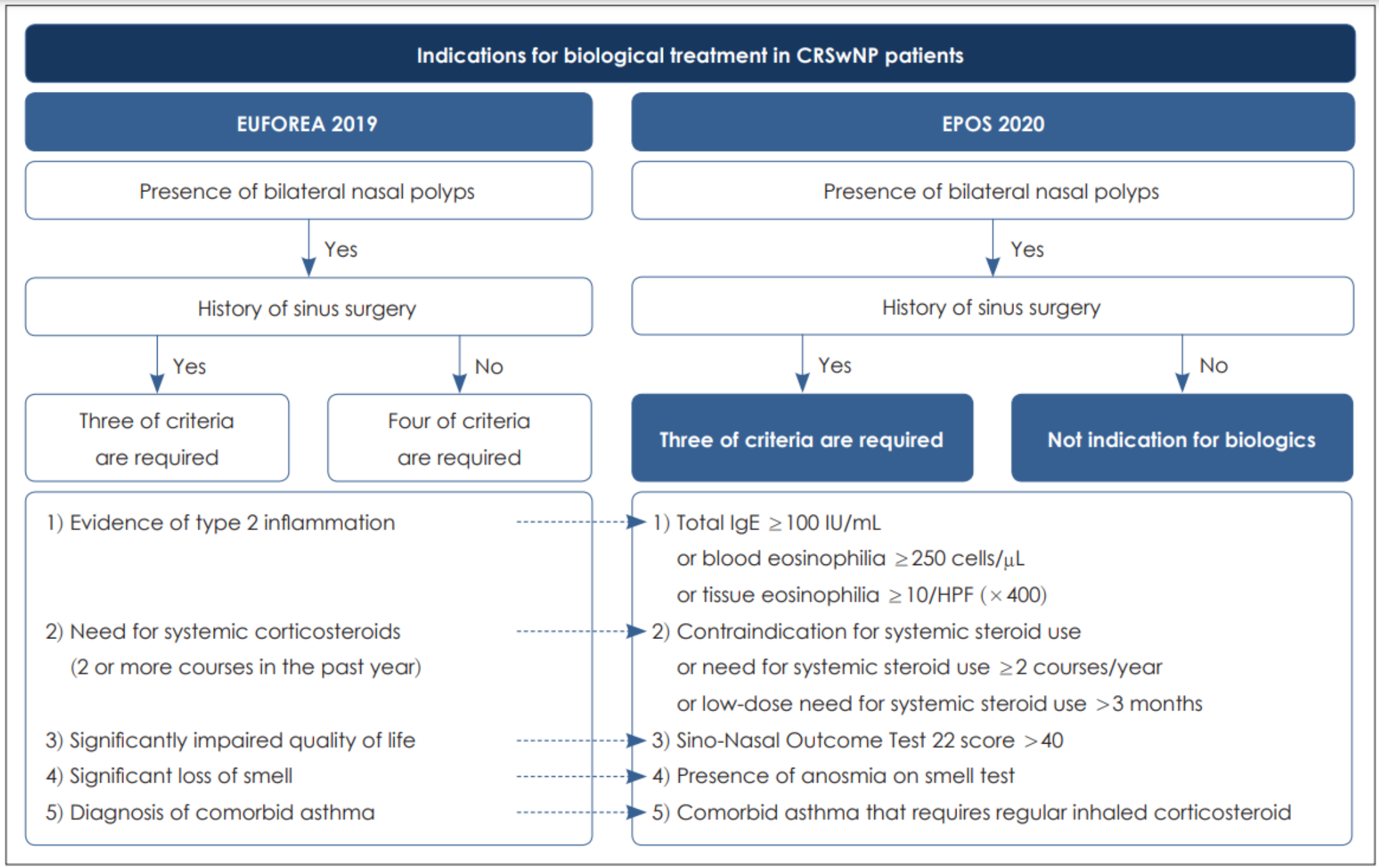


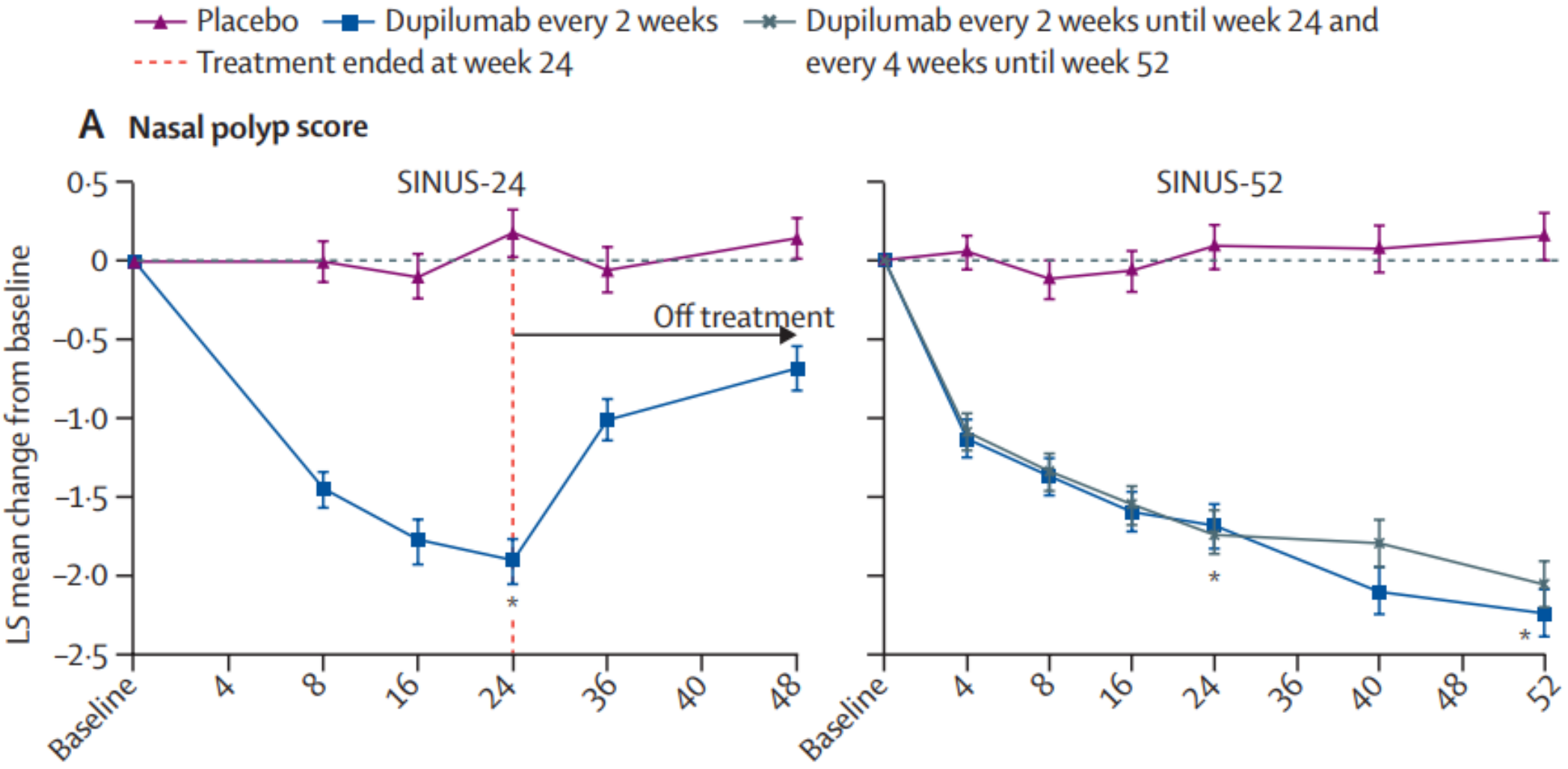
Korean J Otorhinolaryngol-Head Neck Surg 2021;64(10):693-702

Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials

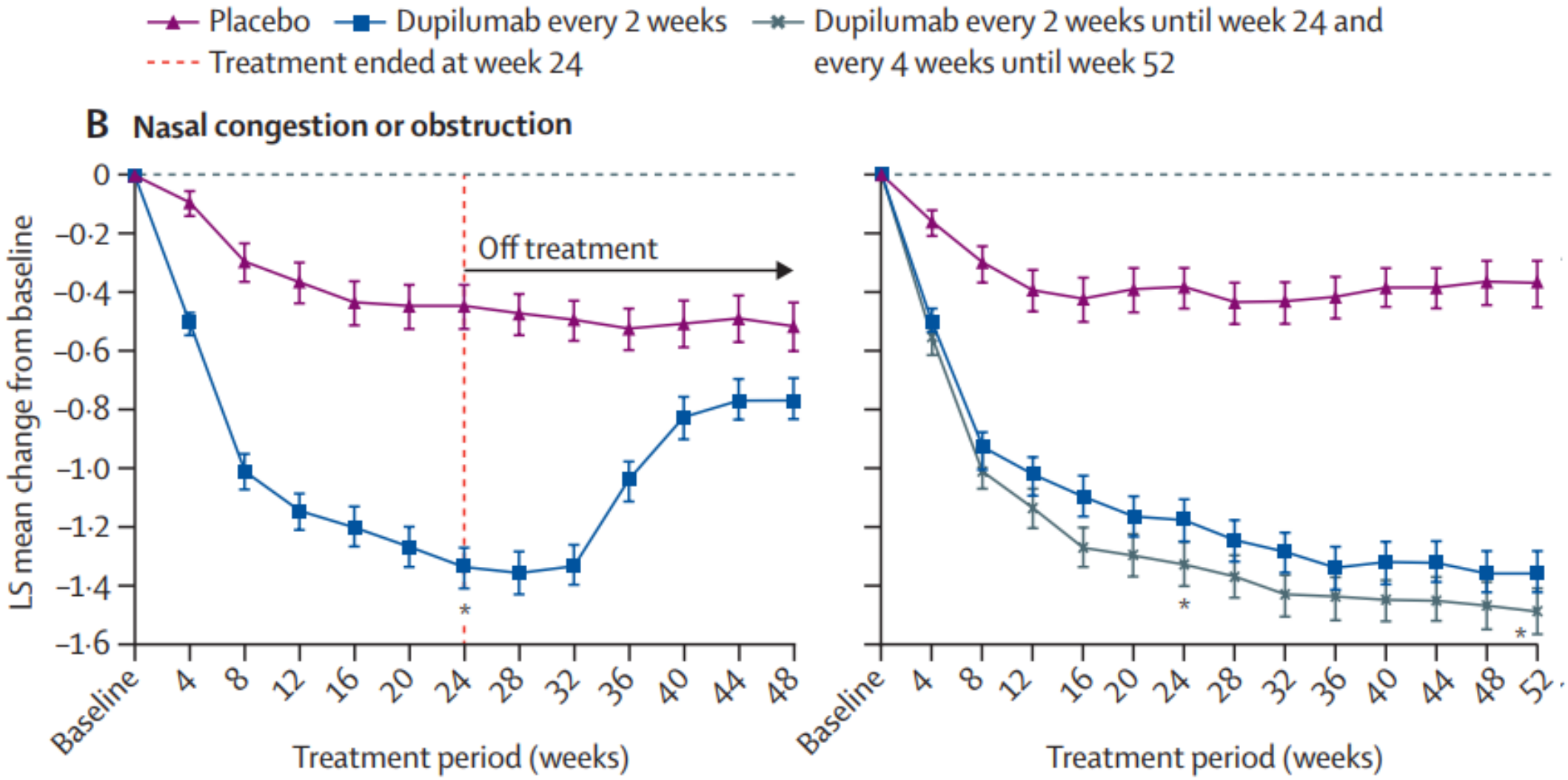
SINUS-24: 67 hospitals or clinical centres in 13 countries

SINUS-52: 117 hospitals or clinical centres in 14 countries

Lancet 2019; 394: 1638–50



Lancet 2019; 394: 1638–50



Lancet 2019; 394: 1638–50

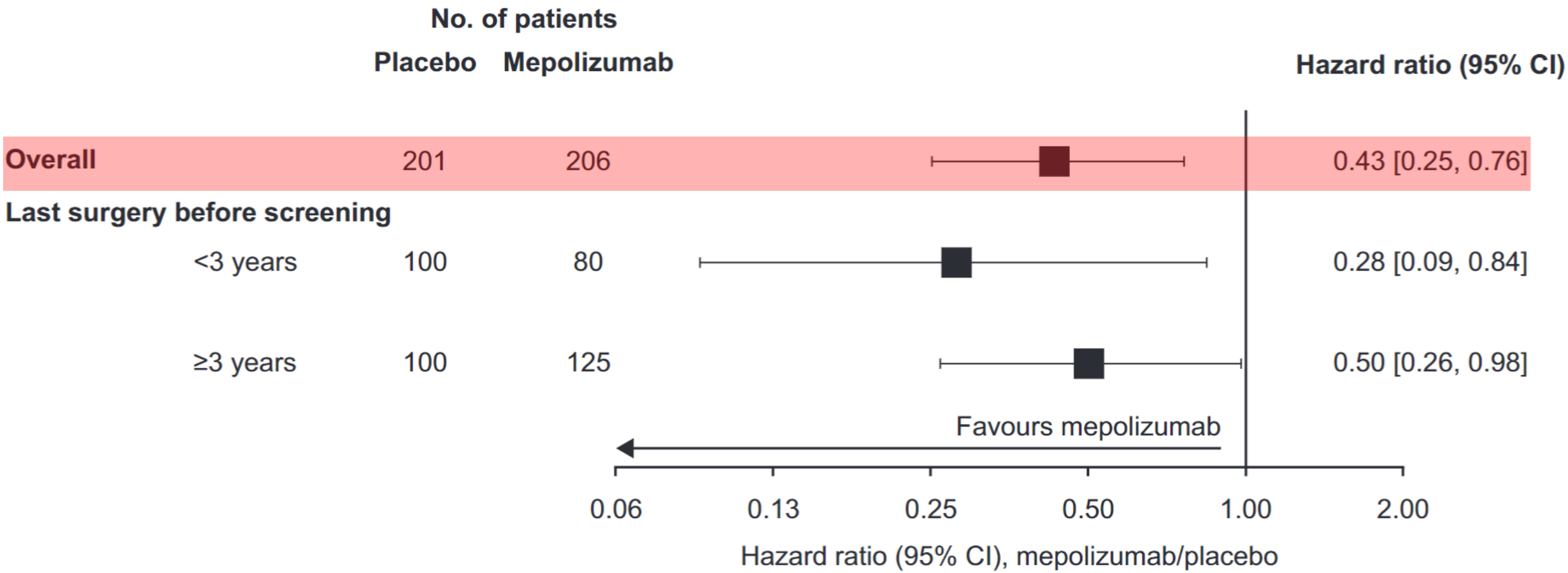
ORIGINAL ARTICLE

Allergen-Specific Immunotherapy and Biologics

Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): In-depth sinus surgery analysis

Wytske J. Fokkens[1] | Joaquim Mullol[2] | David Kennedy[3] | Carl Philpott[4,5] | Veronica Seccia[6] | Robert C. Kern[7] | André Coste[8] | Ana R. Sousa[9] | Peter H. Howarth[10,11] | Victoria S. Benson[12] | Bhabita Mayer[13] | Steve W. Yancey[14] | Robert Chan[9] | Simon B. Gane[15,16]

Allergy. 2023 Mar;78(3):812-821.


No. of patients
Placebo
Mepolizumab
Hazard ratio (95% CI)
Overall
201
206
0.43 [0.25, 0.76]
Last surgery before screening
<3 years
100
80
0.28 [0.09, 0.84]
≥3 years
100
125
0.50 [0.26, 0.98]
Favours mepolizumab
0.06
0.13
0.25
0.50
1.00
2.00
Hazard ratio (95% CI), mepolizumab/placebo

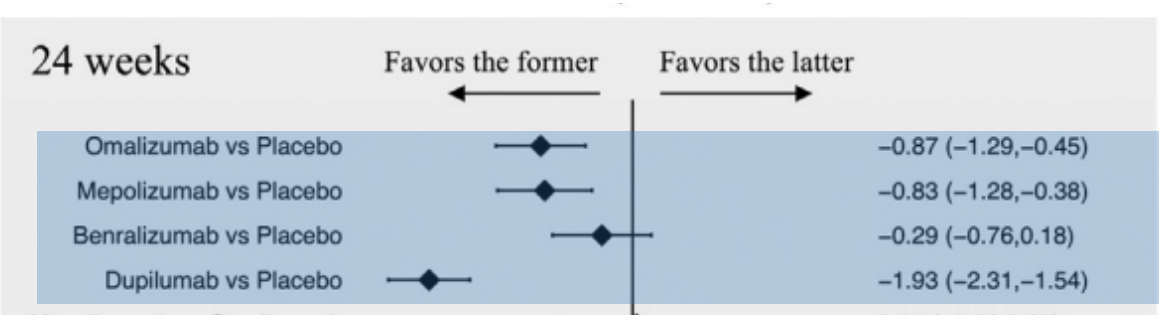
Original Article

Comparison of Different Biologics for Treating Chronic Rhinosinusitis With Nasal Polyps: A Network Analysis

Shiru Cai, BS[a,b,*], Shenglong Xu, BS[a,b,*], Hongfei Lou, MD, PhD[a,b,c], and Luo Zhang, MD, PhD[a,b,c,d] *Beijing, P.R. China*

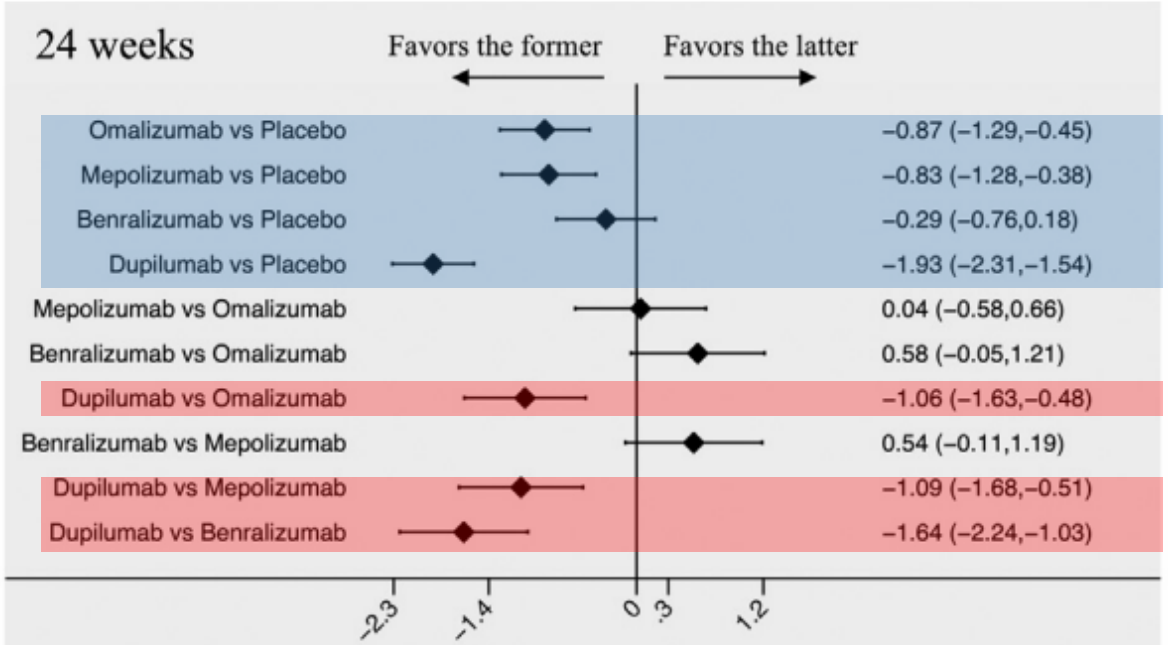
J Allergy Clin Immunol Pract 2022;10:1876-86

Mean difference in nasal polyp score



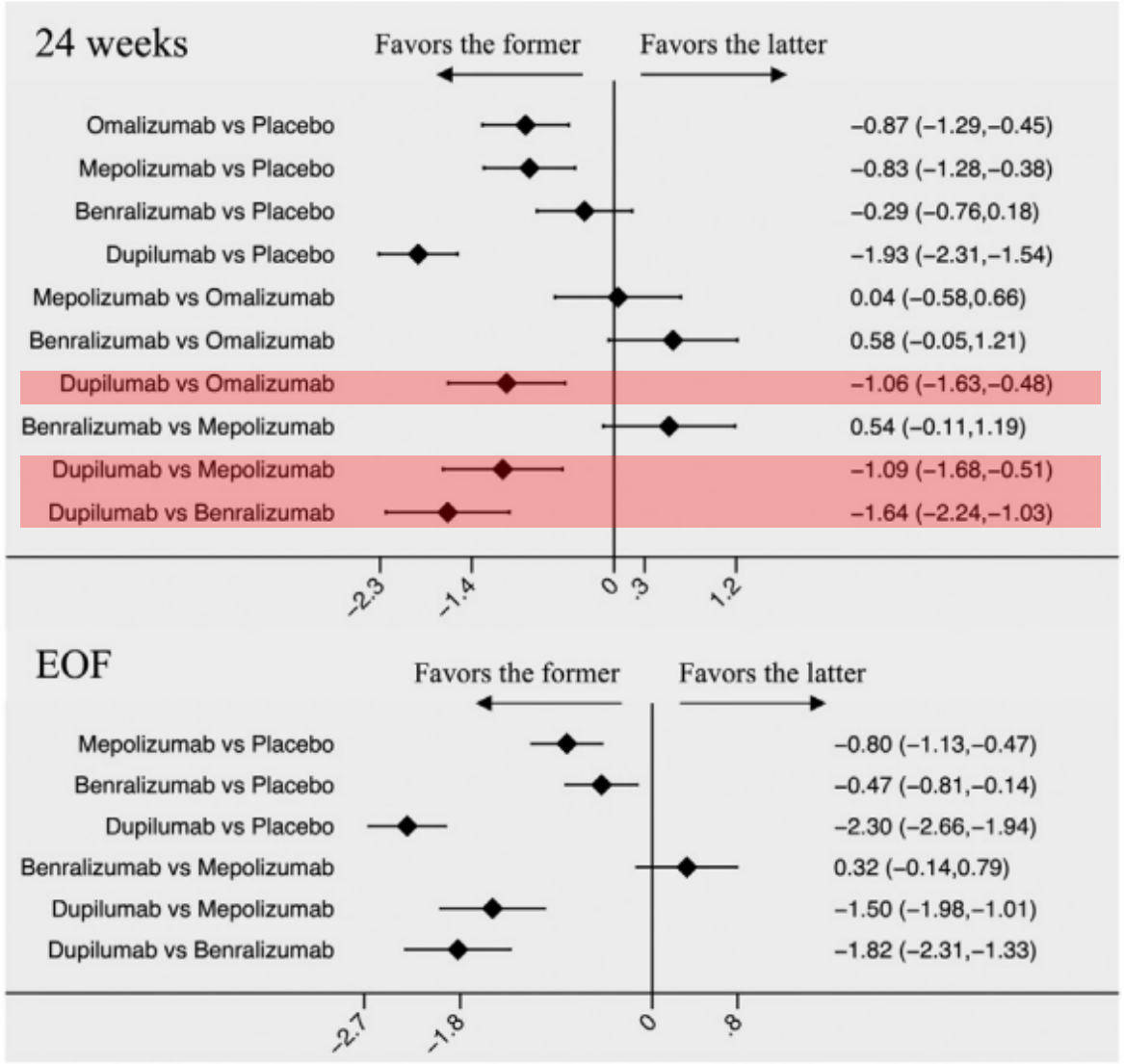
J Allergy Clin Immunol Pract 2022;10:1876-86

Mean difference in nasal polyp score

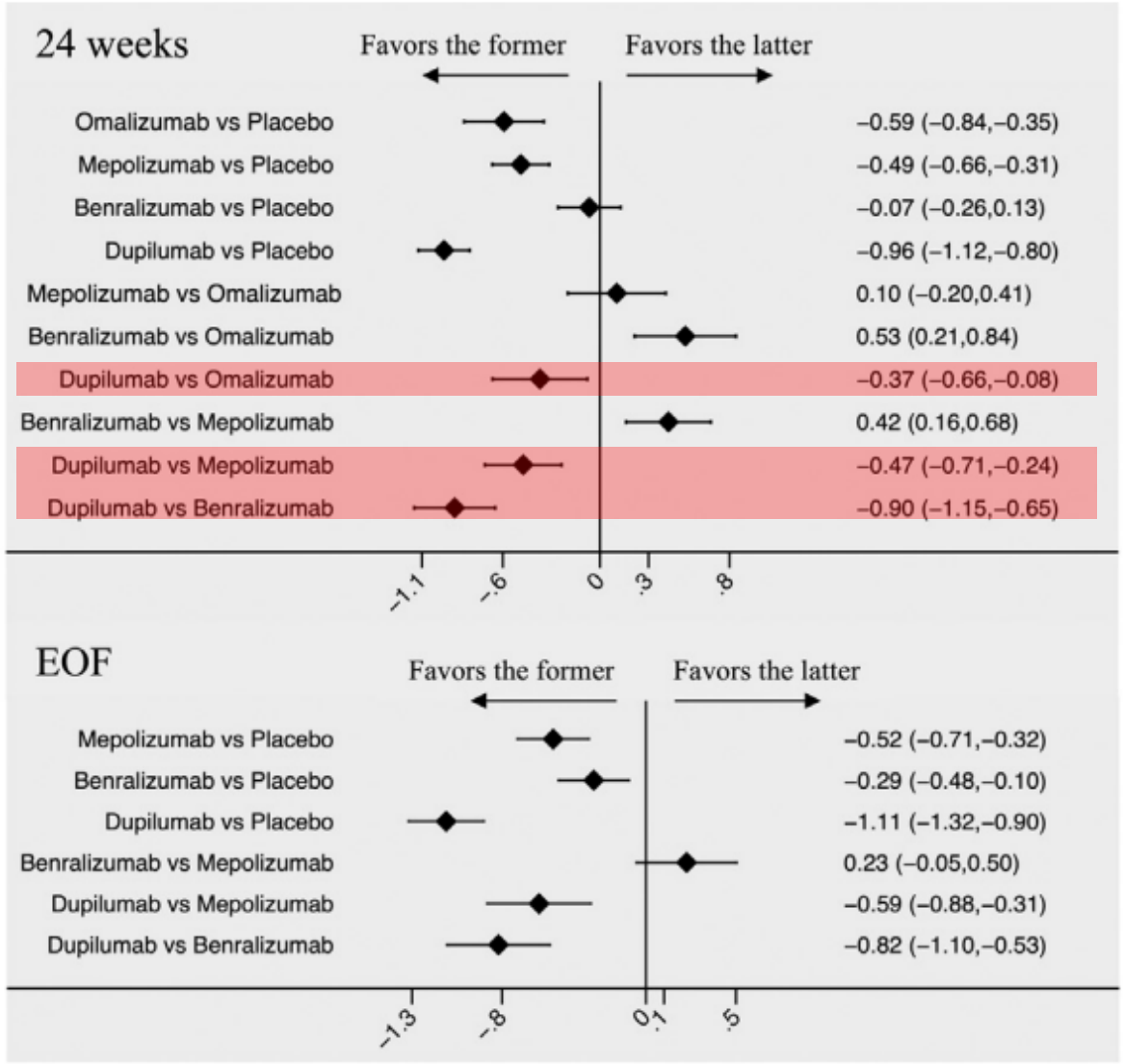


J Allergy Clin Immunol Pract 2022;10:1876-86

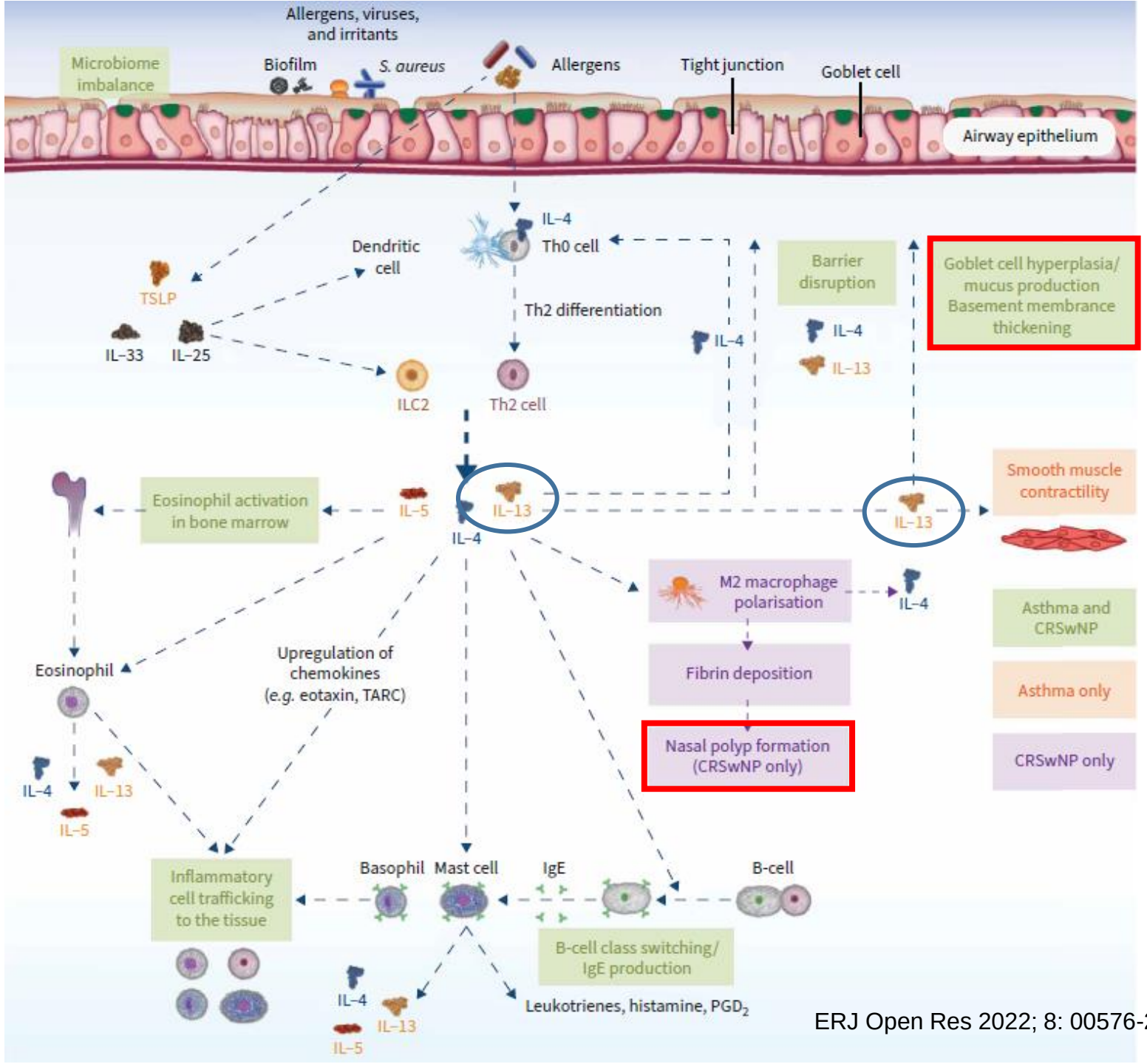
Mean difference in nasal polyp score



SMD in nasal congestion severity



J Allergy Clin Immunol Pract 2022;10:1876-86



ERJ Open Res 2022; 8: 00576-2021 [DOI: 10.1183/23120541.00576-2021]

Contents

Diagnostic criteria for ABPA

Predisposing conditions

Bronchial asthma, cystic fibrosis

Obligatory criteria (both should be present)

Type I *Aspergillus* skin test positive (immediate cutaneous hypersensitivity to *Aspergillus* antigen) or elevated IgE levels against *Aspergillus fumigatus*

Elevated total IgE levels (> 1000 IU/mL)[a]

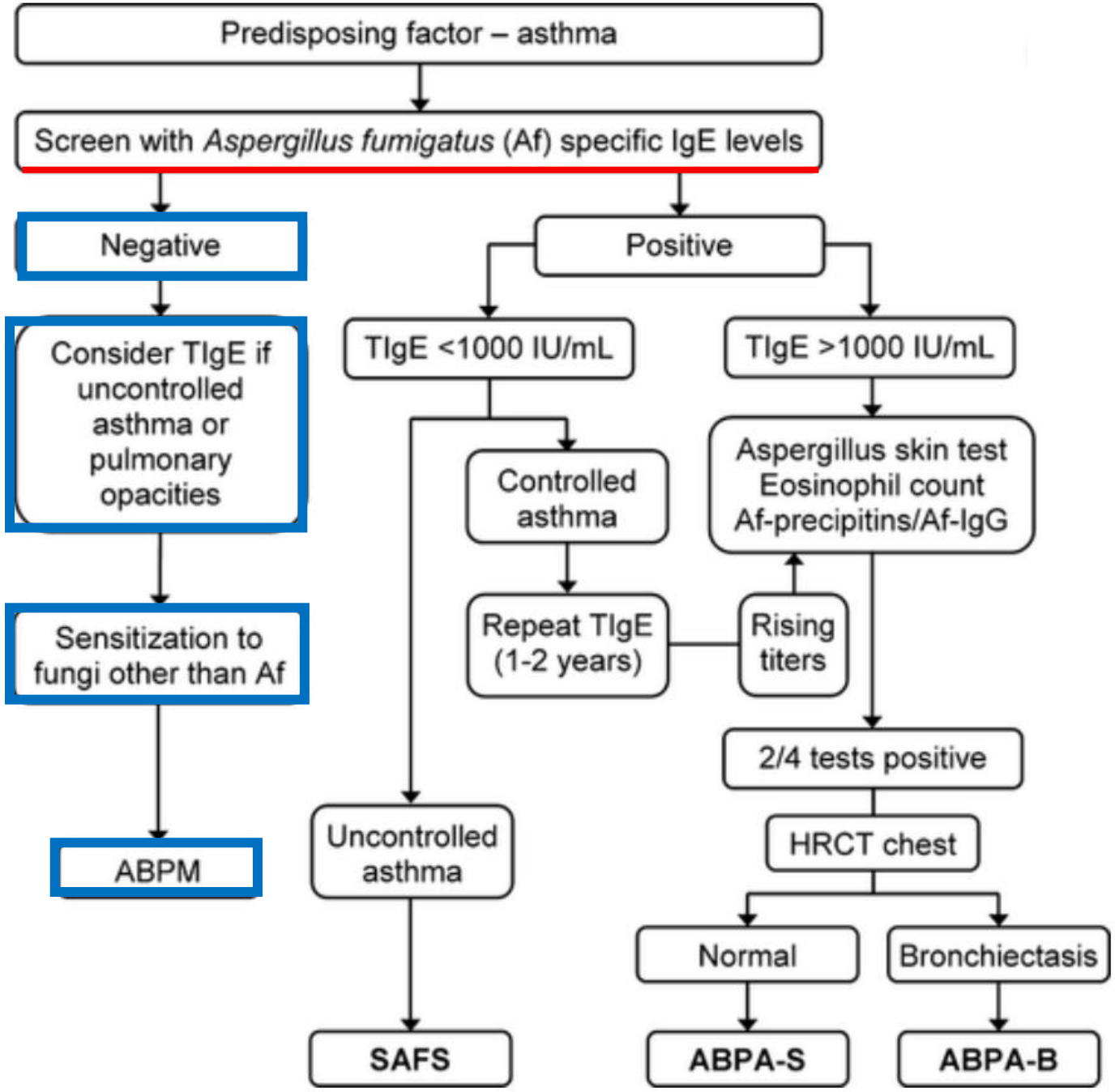
Other criteria (at least two of three)

Presence of precipitating or IgG antibodies against *A. fumigatus* in serum

Radiographic pulmonary opacities consistent with ABPA[b]

Total eosinophil count > 500 cells/μL in steroid naïve patients (may be historical)

J Allergy Clin Immunol Pract 2014;2:703-8



J Allergy Clin Immunol Pract 2014;2:703-8

TABLE I. Fungi associated with ABPM

Organism	Study
Aspergillus fumigatus	Hinson et al, 1952[3]
Aspergillus ochraceus	Greenberger, 1988[4]
Aspergillus oryzae	Akiyama at al. 1987[5]
Aspergillus terreus	Elliott and Newman-Taylor, 1997[6]
Alternaria alternata	Chowdhary et al, 2012[7]
Bipolaris (Dreschleria) hawaiiensis	McAleer et al, 1981[8]
Candida albicans	Akiyama et al, 1984[9]
Cryptococcus neoformans	Arora and Huffnagle, 2005[10]
Curvularia lunata	Halwig et al, 1985[11]
Fusarium vasinfectum	Backman et al, 1995[12]
Geotricum candidum	Elliott and Newman-Taylor, 1997[6]
Helminthosporium species	Hendrich et al 1982[13]
Penicillium species	Elliott and Newman-Taylor, 1997[6]
Peudoallescheria boydii	Elliott and Newman-Taylor, 1997[6]
Sacchromycetes cerevisiae	Ogawa et al, 2004[14]
Schizophyllum commune	Kamei et al, 1994[15]
Stemphyllium lanuginosum	Benatar et al, 1980[16]
Torulopsus glabrata (now designated *Candida glabrata*)	Patterson et al, 1982[17]

J Allergy Clin Immunol Pract 2014;2:703-8

New clinical diagnostic criteria for allergic bronchopulmonary aspergillosis/mycosis and its validation

Koichiro Asano, MD,[a] Akira Hebisawa, MD, PhD,[b] Takashi Ishiguro, MD, PhD,[c] Noboru Takayanagi, MD, PhD,[c] Yasuhiko Nakamura, MD, PhD,[b] Junko Suzuki, MD,[d] Naoki Okada, MD,[a] Jun Tanaka, MD,[a] Yuma Fukutomi, MD, PhD,[e] Shigeharu Ueki, MD, PhD,[f] Koichi Fukunaga, MD, PhD,[g] Satoshi Konno, MD, PhD,[h] Hiroto Matsuse, MD,[i] Katsuhiko Kamei, MD,[j] Masami Taniguchi, MD,[e] Terufumi Shimoda, MD,[k] and Tsuyoshi Oguma, MD,[a] Japan ABPM Research Program

Kanagawa, Tokyo, Saitama, Akita, Sapporo, Chiba, and Fukuoka, Japan

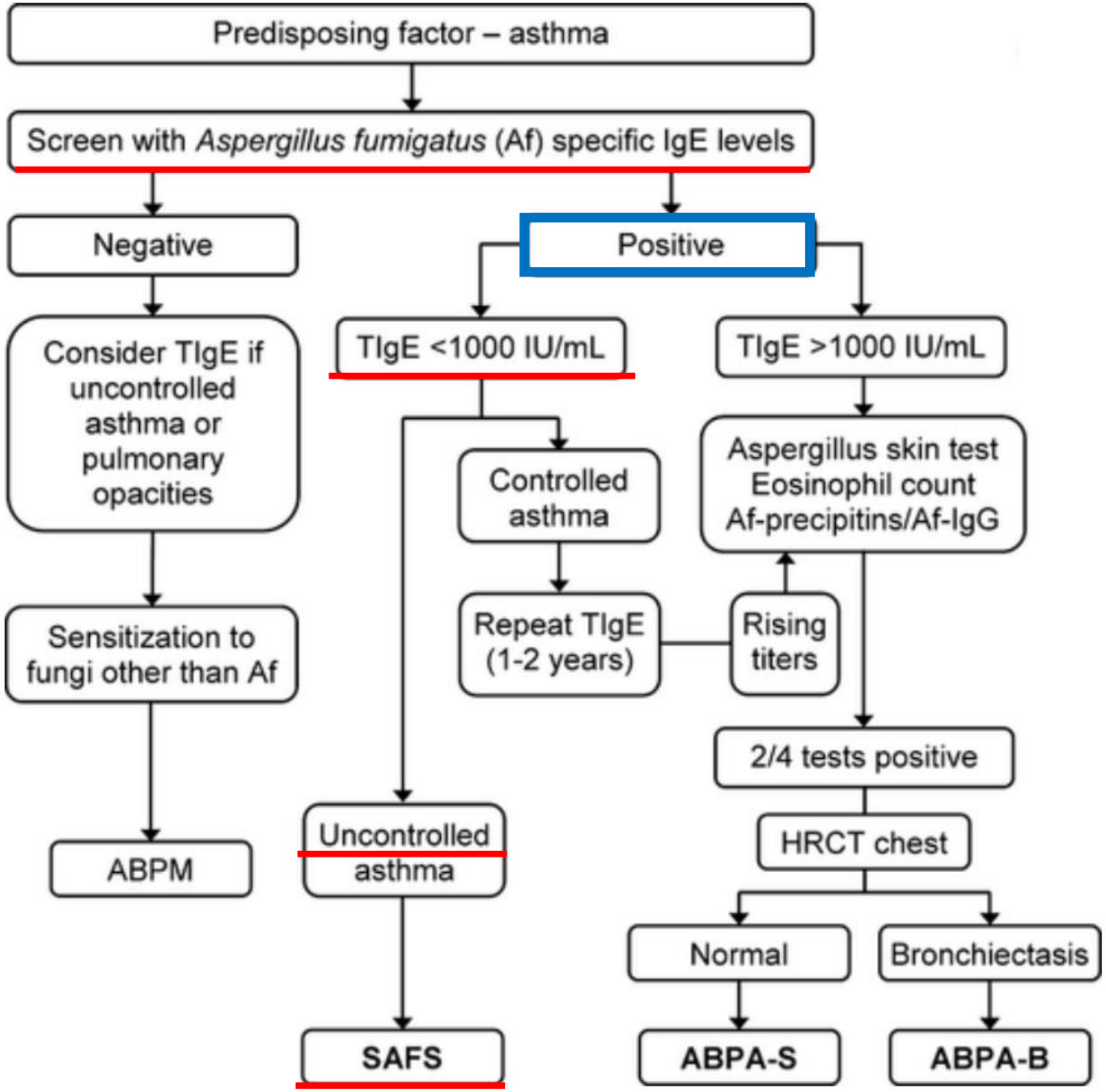
J Allergy Clin Immunol 2021;147:1261-68

TABLE I. Clinical diagnostic criteria for ABPM in patients without cystic fibrosis

1. Current or previous history of asthma or asthmatic symptoms
2. Peripheral blood eosinophilia (≥500 cells/mm^3)
3. Elevated total serum IgE levels (≥417 IU/mL)
4. Immediate cutaneous hypersensitivity or specific IgE for filamentous fungi
5. Presence of precipitins or specific IgG for filamentous fungi
6. Filamentous fungal growth in sputum cultures or bronchial lavage fluid
7. Presence of fungal hyphae in bronchial mucus plugs
8. Central bronchiectasis on CT
9. Presence of mucus plugs in central bronchi, based on CT/bronchoscopy or mucus plug expectoration history
10. High attenuation mucus in the bronchi on CT

Filamentous fungi in criteria 4 to 6 should be identical.

Patients that meet 6 or more of these criteria are diagnosed with ABPM.



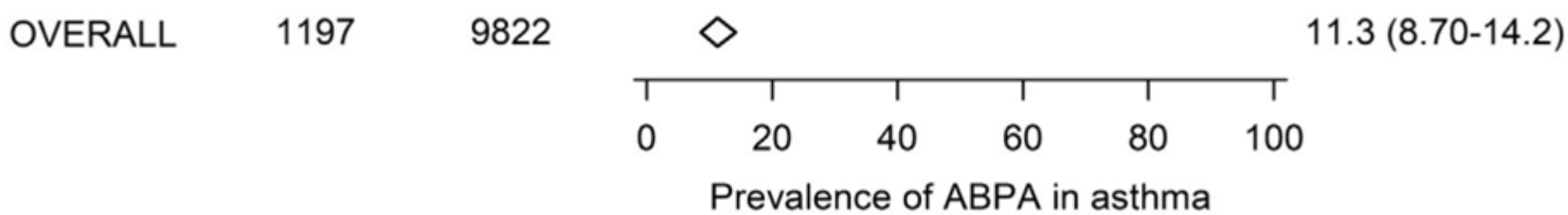
J Allergy Clin Immunol Pract 2014;2:703-8

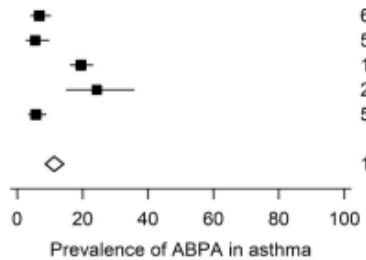
Original Article

Prevalence of Aspergillus Sensitization and Allergic Bronchopulmonary Aspergillosis in Adults With Bronchial Asthma: A Systematic Review of Global Data

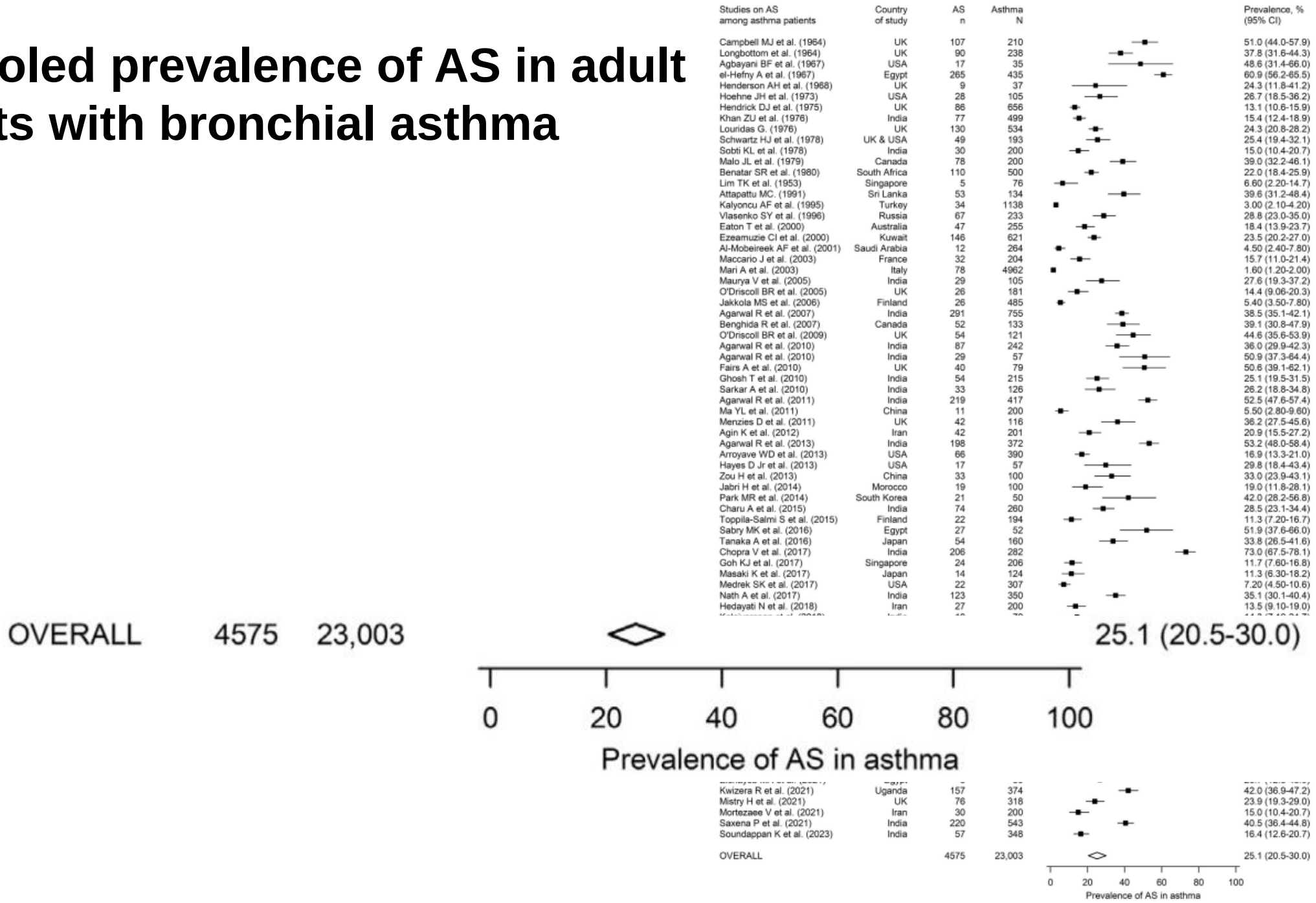
Ritesh Agarwal, MD, DM[a], Valliappan Muthu, MD, DM[a], Inderpaul Singh Sehgal, MD, DM[a], Sahajal Dhooria, MD, DM[a], Kuruswamy Thurai Prasad, MD, DM[a], Kathirvel Soundappan, MD[b], Shivaprakash Mandya Rudramurthy, MD[c], Ashutosh Nath Aggarwal, MD, DM[a], and Arunaloke Chakrabarti, MD[d] *Chandigarh and Haridwar, India*

Studies on ABPA among asthma patients	Country of study	ABPA n	Asthma N	Prevalence, % (95% CI)
Campbell MJ et al. (1964)	UK	87	210	41.4 (34.7-48.4)
Agbayani BF et al. (1967)	USA	1	53	1.90 (0.00-10.1)
Henderson AH et al. (1968)	UK	5	46	10.9 (3.60-23.6)
Hoehne JH et al. (1973)	USA	14	105	13.3 (7.50-21.4)
Khan ZU et al. (1976)	India	25	499	5.00 (3.30-7.30)
Sobti KL et al. (1978)	India	17	200	8.50 (5.00-13.3)
Benatar SR et al. (1980)	South Africa	8	500	1.60 (0.70-3.10)
Attapattu MC. (1991)	Sri Lanka	8	134	6.00 (2.60-11.4)
Eaton T et al. (2000)	Australia	9	35	25.7 (12.5-43.3)
Kumar R et al. (2000)	India	32	200	16.0 (11.2-21.8)
Al-Mobeireek AF et al. (2001)	Saudi Arabia	6	264	2.30 (0.80-4.90)
Maurya V et al. (2005)	India	8	105	7.60 (3.30-14.5)
Agarwal R et al. (2007)	India	155	755	20.5 (17.7-23.6)
O'Driscoll BR et al. (2009)	UK	1	121	0.80 (0.00-4.50)
Agarwal R et al. (2010)	India	54	242	22.3 (17.2-28.1)
Agarwal R et al. (2010)	India	22	57	38.6 (26.0-52.4)
Fairs A et al. (2010)	UK	4	79	5.10 (1.40-12.5)
Ghosh T et al. (2010)	India	15	215	7.00 (4.00-11.2)
Sarkar A et al. (2010)	India	9	126	7.10 (3.30-13.1)
Ma YL et al. (2011)	China	5	200	2.50 (0.80-5.70)
Menzies D et al. (2011)	UK	7	116	6.00 (2.50-12.0)
Agarwal R et al. (2013)	India	56	372	15.1 (11.6-19.1)
Park MR et al. (2014)	South Korea	3	50	6.00 (1.30-16.5)
Schleich F et al. (2014)	Belgium	11	350	3.10 (1.60-5.60)
Charu A et al. (2015)	India	64	260	24.6 (19.5-30.3)
Sabry MK et al. (2016)	Egypt	11	52	21.2 (11.1-34.7)
Tay TR et al. (2016)	Australia	47	297	15.8 (11.9-20.5)
Kozlova YI et al. (2017)	Russia	6	140	4.30 (1.06-9.10)
Nath A et al. (2017)	India	76	350	21.7 (17.5-26.4)
Woolnough KF et al. (2017)	UK	60	431	13.9 (10.8-17.6)
Kalaiyarasan et al. (2018)	India	9	70	12.9 (6.10-23.0)
Watai K et al. (2018)	Japan	2	118	1.70 (0.20-6.00)
Mistry H et al. (2021)	UK	21	311	6.80 (4.20-10.1)
Mortezaee V et al. (2021)	Iran	11	200	5.50 (2.80-9.60)
Saxena P et al. (2021)	India	106	543	19.5 (16.3-23.1)
Solidoro P et al. (2021)	Italy	18	74	24.3 (15.1-35.7)
Soundappan K et al. (2023)	India	20	348	5.70 (3.50-8.70)
OVERALL		1197	9822	11.3 (8.70-14.2)





The pooled prevalence of AS in adult subjects with bronchial asthma



Original Article

The Clinical Implications of *Aspergillus Fumigatus* Sensitization in Difficult-To-Treat Asthma Patients

Heena Mistry, MRCP[a,b,c,d,e,*], Hilda Maria Ajsivinac Soberanis, MSc[f,*], Mohammad Aref Kyyaly, PhD[a,e], Adnan Azim, MRCP[a,b,c], Clair Barber, BSc[a,b], Deborah Knight[b], Colin Newell, MSc[b], Hans Michael Haitchi, PhD[a,b,c,g], Tom Wilkinson, PhD[a,b], Peter Howarth, DM[a,b], Grégory Seumois, PhD[d], Pandurangan Vijayanand, PhD[a,d], S. Hasan Arshad, DM[a,b,c,e,g], and Ramesh J. Kurukulaaratchy, DM[a,b,c,e] *Southampton and Isle of Wight, United Kingdom; and La Jolla, Calif*

J Allergy Clin Immunol Pract. 2021 Dec;9(12):4254-4267.e10. doi: 10.1016/j.jaip.2021.08.038

TABLE I. Clinical characteristics of *A fumigatus*—sensitized vs nonsensitized patients

Variables	Overall	Sensitized	Nonsensitized	*P* value
Subjects N	318	76	242	
Demographic characteristics				
Sex, n (%)				
Female	204 (64.2)	38 (50.0)	166 (68.6)	**.003**
Male	114 (35.8)	38 (50.0)	76 (31.4)	
Age at enrollment (y)				
Median (IQR)	51.5 (25.0)	58.0 (16.0)	50.0 (26.0)	**.001**
Min-Max	17.0-85.0	18.0-81.0	17.0-85.0	
Ethnicity				
White	294 (92.5)	70 (92.1)	224 (92.6)	>.99
Not White	24 (7.5)	6 (7.9)	18 (7.4)	
Body mass index (kg/m^2)				
Median (IQR)	29.7 (9.7)	28.3 (7.4)	29.8 (10.5)	.349
Min-Max	17.6-53.3	19.2-53.3	17.6-52.3	
Smoking history, n (%)				
Never	163 (51.3)	33 (43.4)	130 (53.7)	.207
Current	16 (5.0)	3 (3.9)	13 (5.4)	
Ex	139 (43.7)	40 (52.6)	99 (40.9)	

TABLE I. Clinical characteristics of *A fumigatus*—sensitized vs nonsensitized patients

Variables	Overall	Sensitized	Nonsensitized	*P* value
Asthma-related history				
Age of asthma onset (y)				
Median (IQR)	19.0 (34.0)	12.0 (40.0)	21.0 (32.0)	.076
Min-Max	0-75.0	0-75.0	0-69.0	
Asthma duration (y)				
Median (IQR)	23.5 (25.0)	33.0 (31.0)	22.0 (24.0)	**<.001**
Min-Max	0-83.0	0-74.0	0-83.0	
Missing	14	1	13	
Health care utilization				
Asthma-related ICU visits				
Median (IQR)	0 (1)	0 (0)	0 (1)	.167
Min-Max	0-15	0-6	0-15	
Intubated ever, n (%)				
Yes	39 (12.3)	9 (11.8)	30 (12.4)	.898
Hospitalizations in past 12 mo				
Median (IQR)	0 (1)	0 (0)	0 (1)	**.001**
Min-Max	0-10	0-3	0-10	
Missing	2	0	2	
OCS courses in past 12 mo				
Median (IQR)	3.1 (4.0)	3.0 (3.0)	3.0 (4.0)	.511
Min-Max	3.2 0-16.0	0-12.0	0-16.0	
Missing	37	8	29	

TABLE I. Clinical characteristics of *A fumigatus*—sensitized vs nonsensitized patients

Variables	Overall	Sensitized	Nonsensitized	*P* value
Medication				
m-OCS, n/N (%)	94/314 (29.9)	29/73 (39.7)	65/241 (27.0)	**.037**
Biologics at enrollment, n (%)	56 (17.6)	21 (27.6)	34 (14.0)	**.006**
Biologics after enrollment, n (%)	86 (27.0)	24 (31.6)	69 (28.5)	.608
Itraconazole, n (%)	16 (5.0)	15 (19.7)	1 (0.4)	**<.001***
Macrolides, n (%)	68 (21.4)	14 (18.4)	54 (22.3)	.470
Doxycycline, n (%)	31 (9.7)	7 (9.2)	24 (9.9)	.856
Disease-related questionnaires				
ACQ6 score				
Median (IQR)	2.50 (2.00)	2.20 (1.70)	2.50 (2.00)	**.006**
Min-Max	0-6.00	0-5.70	0-6.00	
Missing	26	3	23	
ACQ6 score $\geq$ 1.50, n/N (%)	229/292 (78.4)	51/73 (69.9)	178/219 (81.3)	**.040**

TABLE II. Objective characteristics of *A fumigatus*—sensitized vs nonsensitized patients

Variables	Overall	Sensitized	Nonsensitized	*P* value
Subjects N	318	76	242	
Blood				
Log_{10} (total IgE+1) (±6 mo) (IU/L)				
Median (IQR)	1.96 (1.11)	2.43 (0.97)	1.78 (1.02)	**<.001**
Min, Max	0, 3.63	0, 3.51	0,3.63	
Missing	64	13	51	
Max blood eosinophils (10^9/L)				
Median (IQR)	0.40 (0.60)	0.60 (0.90)	0.40 (0.50)	**.017**
Min, Max	0, 4.50	0, 4.50	0, 3.80	
Airway inflammometry				
FENO (ppb)				
Median (IQR)	19.0 (29.4)	18.0 (28.8)	19.0 (30.2)	.901
Sputum eosinophils (%)				
Median (IQR)	1.50 (8.39)	2.56 (7.88)	1.50 (8.80)	.572
Sputum neutrophils (%)				
Median (IQR)	43.06 (42.72)	50.75 (40.90)	40.50 (35.75)	**.005**
HRCT chest imaging, n/N (%)				
Bronchiectasis	41/183 (22.4)	20/50 (40.0)	21/133 (15.8)	**.001**
Mucus plugging	20/183 (10.9)	10/50 (20.0)	10/133 (7.5)	**.016**
Ground glass shadowing	25/184 (13.6)	10/50 (20.0)	15/134 (11.2)	.121
Bronchial wall thickening	82/184 (44.6)	21/50 (42.0)	61/134 (45.5)	.740

- *A fumigatus*–sensitized
- *A fumigatus* nonsensitized

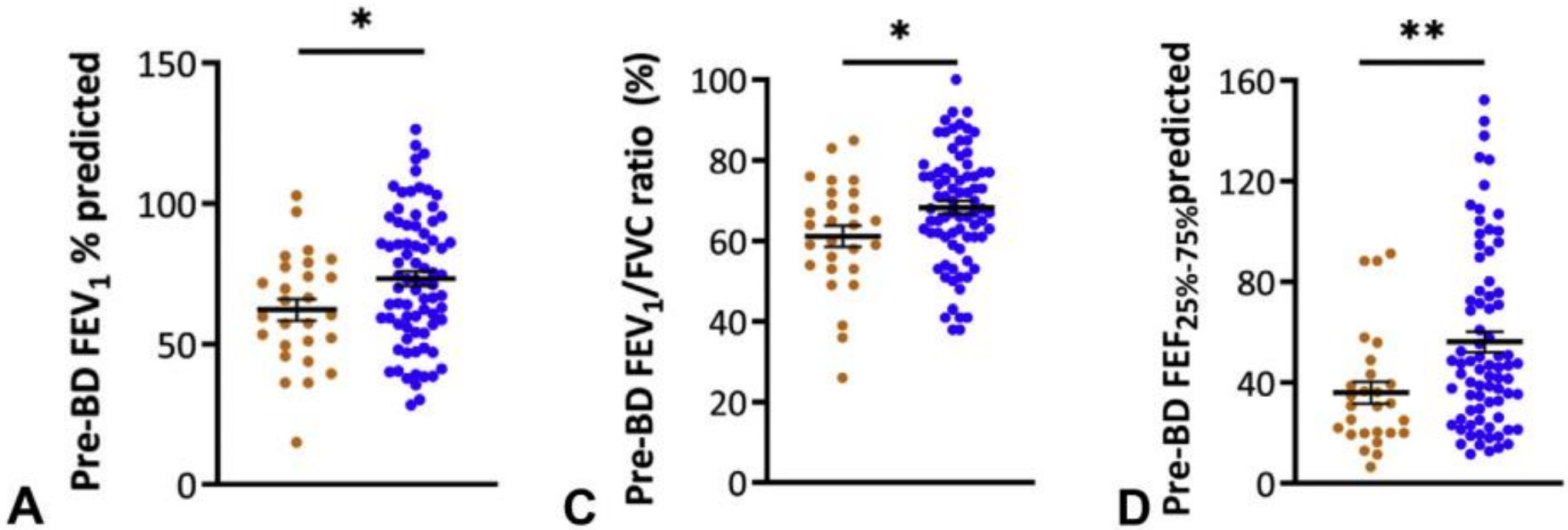


TABLE III. Logistic regression models assessing associated factors for *A fumigatus* sensitization and ABPA in difficult asthma

Comparisons	Models	Clinical variables	*P* value	OR	95% CI
1. *A fumigatus—sensitized* vs nonsensitized subjects	Model 1	m-OCS use	.011	3.34	1.32-8.49
		Maximum $\log_{10}$ total IgE+1	<.001	4.30	2.18-8.46
		Hospitalization in past 12 mo	.012	0.42	0.22-0.83
		Psychological comorbidity	.004	0.21	0.08-0.61
		Salicylate sensitivity	.011	0.13	0.03-0.63
	Model 2	m-OCS use	.023	2.32	1.12-4.77
		Maximum $\log_{10}$ total IgE+1	<.001	4.60	2.67-7.94
		Hospitalization in past 12 mo	.012	0.54	0.34-0.87
		Psychological comorbidity	.033	0.45	0.22-0.94
		Salicylate sensitivity	.004	0.19	0.06-0.59
2. Diagnosis of ABPA in WATCH cohort	Model 1	m-OCS use	.005	6.98	1.81-26.98
		Maximum $\log_{10}$ total IgE+1	.002	4.65	1.79-12.07
		Bronchiectasis on HRCT	.027	4.08	1.18-14.15
	Model 2	m-OCS use	<.001	9.42	2.80-19.68
		Maximum $\log_{10}$ total IgE+1	<.001	7.46	2.83-19.70
3. Diagnosis of ABPA in *A fumigatus*—sensitized subjects	Model 1	m-OCS use	.001	16.36	3.04-88.16
		Maximum $\log_{10}$ total IgE+1	.018	5.06	1.32-19.47
	Model 2	m-OCS use	<.001	13.30	3.17-55.72
		Maximum $\log_{10}$ total IgE+1	.006	5.21	1.59-17.05

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
R. AGARWAL ET AL.

A randomised trial of prednisolone *versus* prednisolone and itraconazole in acute-stage allergic bronchopulmonary aspergillosis complicating asthma

Eur Respir J 2022; 59: 2101787 DOI: 10.1183/13993003.01787-2021

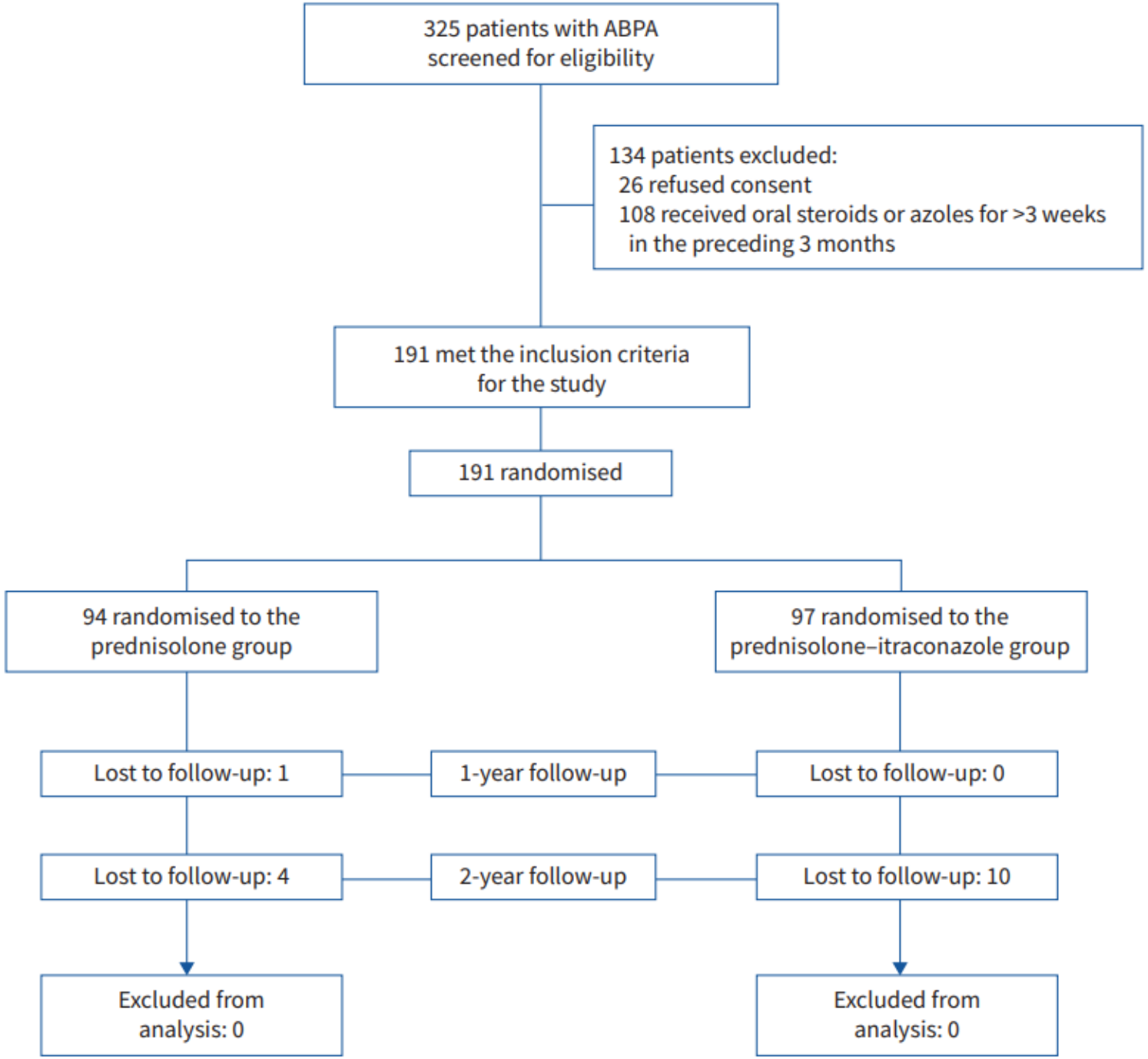
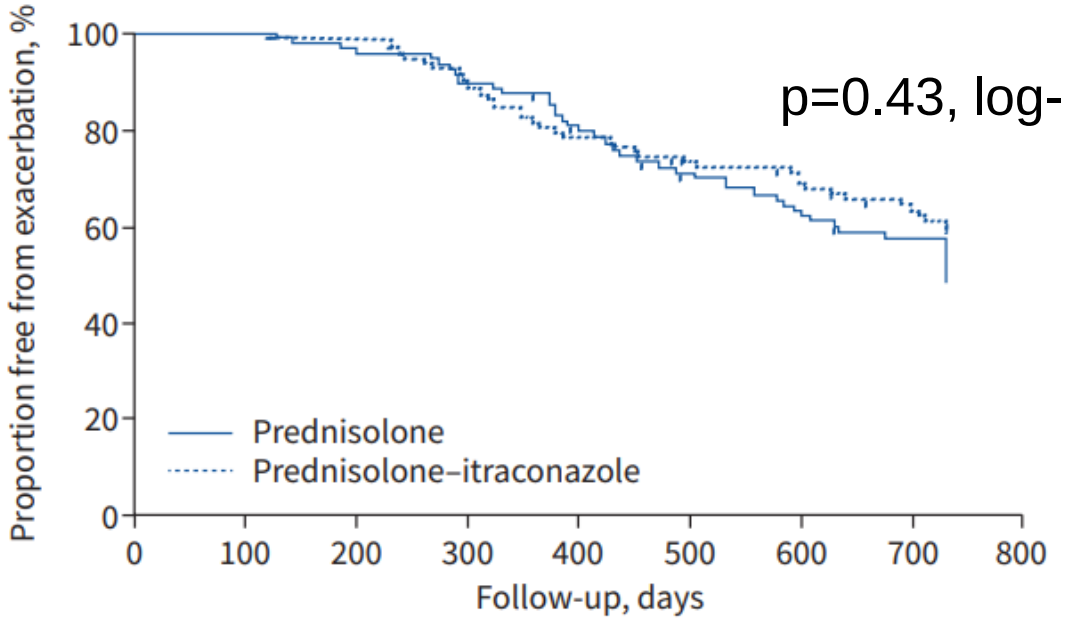

325 patients with ABPA screened for eligibility
134 patients excluded:
26 refused consent
108 received oral steroids or azoles for >3 weeks in the preceding 3 months
191 met the inclusion criteria for the study
191 randomised
94 randomised to the prednisolone group
97 randomised to the prednisolone–itraconazole group
Lost to follow-up: 1
1-year follow-up
Lost to follow-up: 0
Lost to follow-up: 4
2-year follow-up
Lost to follow-up: 10
Excluded from analysis: 0
Excluded from analysis: 0

TABLE 2 Outcomes of the study subjects (n=191) treated with prednisolone or prednisolone–itraconazole

	Prednisolone (n=94)	Prednisolone–itraconazole (n=97)	Estimate difference (95% CI)	p-value
Primary outcomes				
Subjects experiencing exacerbation after 1 year	31 (33.0)	20 (20.6)	12.3 (−0.2–24.5)	0.054
Subjects experiencing glucocorticoid-dependent ABPA after 2 years	0	0		



p=0.43, log-rank test

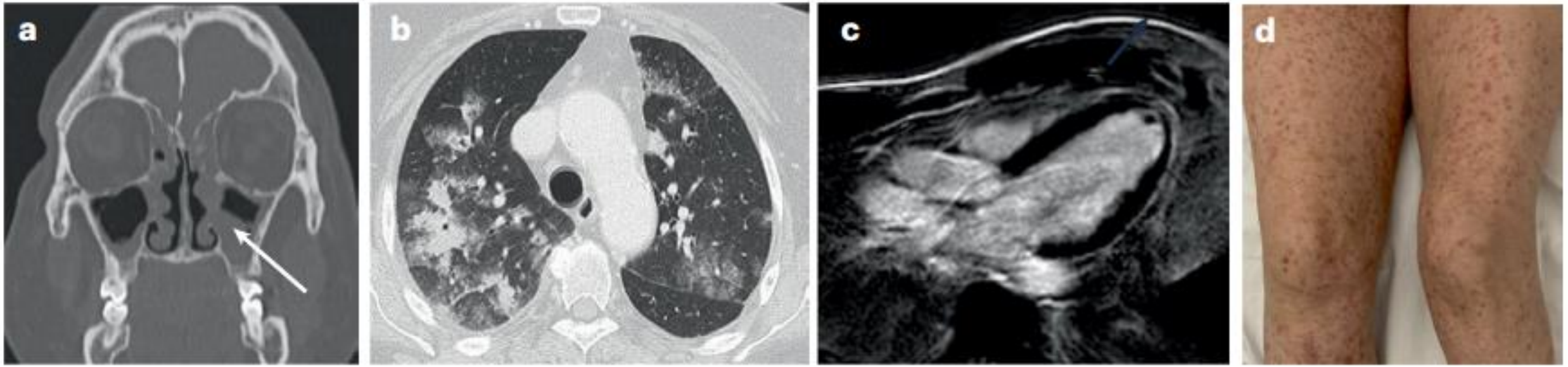
At risk, n:

Prednisolone	94	94	90	84	73	63	55	50	0
Prednisolone–itraconazole	97	97	96	87	76	68	62	55	0

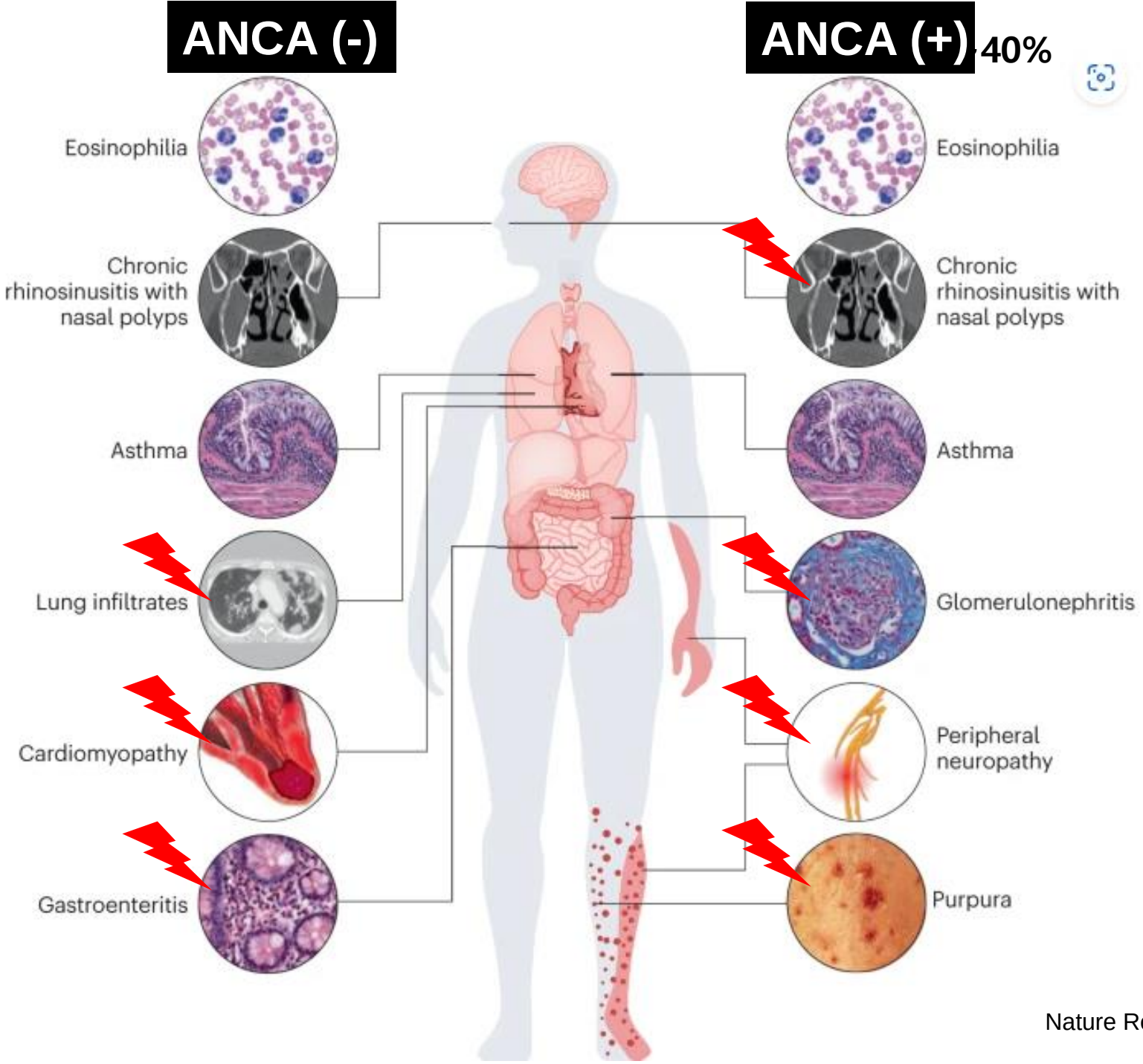
TABLE 2 Outcomes of the study subjects (n=191) treated with prednisolone or prednisolone–itraconazole

	Prednisolone (n=94)	Prednisolone–itraconazole (n=97)	Estimate difference (95% CI)	p-value
Primary outcomes				
Subjects experiencing exacerbation after 1 year	31 (33.0)	20 (20.6)	12.3 (−0.2–24.5)	0.054
Subjects experiencing glucocorticoid-dependent ABPA after 2 years	0	0		
Secondary outcomes				
Response after 6 weeks of treatment	94 (100)	97 (100)	0 (−0.04–0.04)	1.0
Decline in IgE after 6 weeks of treatment, %	47.6 (43.3–51.9)	45.6 (41.0–50.1)	2.0 (−4.2–8.2)	0.47
Mean time to first exacerbation, days	416.2 (371–461)	417.7 (365–470)	−1.5 (−45.3–42.3)	0.84
TEAEs				
Any TEAE	74 (78.7)	71 (73.2)	5.5 (−6.6–17.4)	0.37
Cushingoid facies	70 (74.5)	70 (72.2)	2.3 (−10.2–14.7)	0.19
Weight gain	37 (39.3)	36 (37.1)	2.2 (−11.3–15.8)	0.86
Deranged liver functions	6 (6.2)	21 (21.6)	15.4 (5.5–25.1)	0.001
Hypertension	2 (2.1)	1 (1.0)	1.1 (−3.7–6.5)	1.0
Hyperglycaemia	2 (2.1)	0	2.1 (−2.0–7.4)	0.50
Hirsutism	2 (2.1)	3 (3.1)	−1.0 (−6.8–4.7)	0.68
Emotional lability	1 (1.1)	1 (1.0)	0.1 (−4.6–4.8)	1.0

Contents



Nature Reviews Rheumatology volume 19, pages378–393 (2023)



Nature Reviews Rheumatology volume 19, pages378–393 (2023)

2022 AMERICAN COLLEGE OF RHEUMATOLOGY / EUROPEAN ALLIANCE OF ASSOCIATIONS FOR RHEUMATOLOGY

CLASSIFICATION CRITERIA FOR **EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS**

CONSIDERATIONS WHEN APPLYING THESE CRITERIA

- **These classification criteria should be applied to classify a patient as having eosinophilic granulomatosis with polyangiitis when a diagnosis of small- or medium-vessel vasculitis has been made**
- **Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria**

CLINICAL CRITERIA

Obstructive airway disease	+3
Nasal polyps	+3
Mononeuritis multiplex	+1

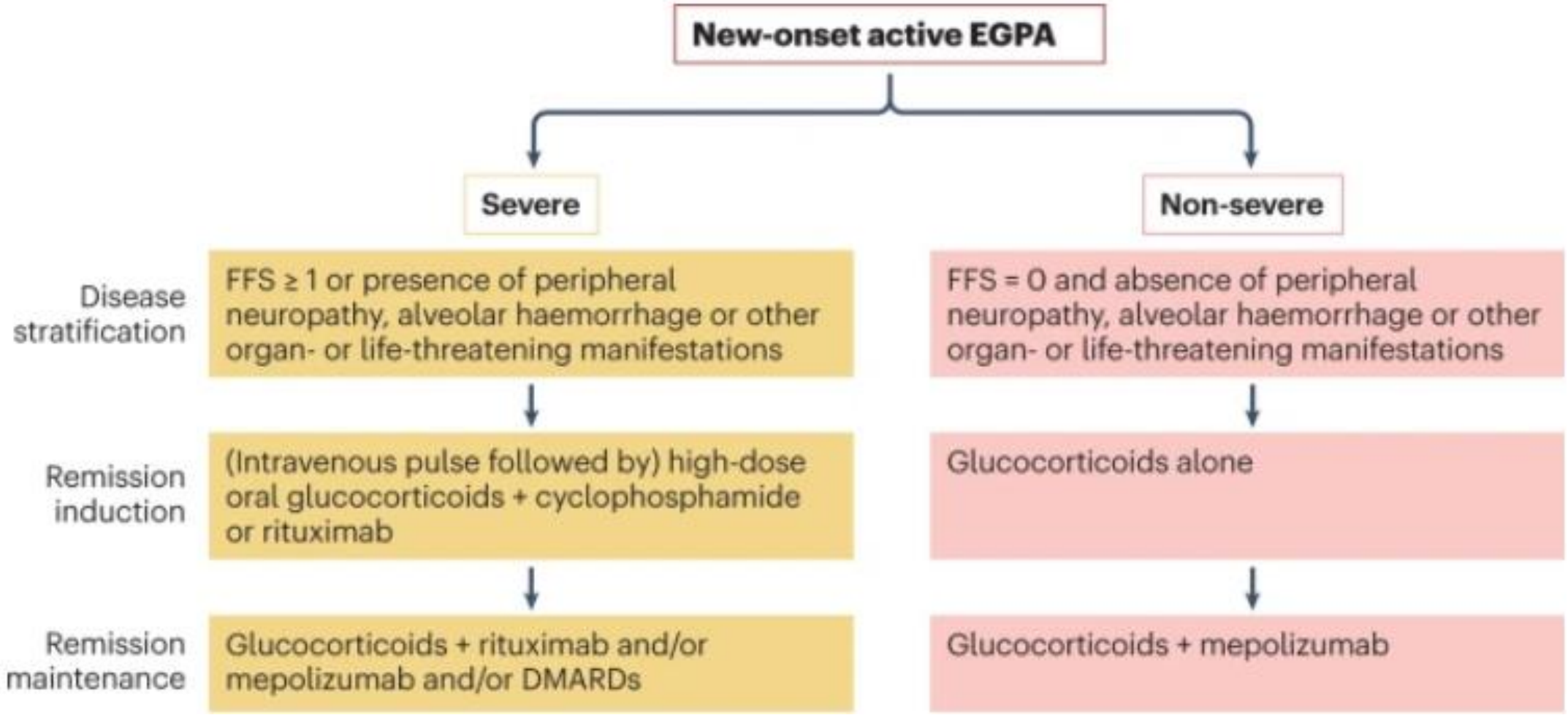
LABORATORY AND BIOPSY CRITERIA

Blood eosinophil count ≥ 1 x10^9/liter	+5
Extravascular eosinophilic-predominant inflammation on biopsy	+2
Positive test for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) or antiproteinase 3 (anti-PR3) antibodies	-3
Hematuria	-1

Sum the scores for 7 items, if present. A score of ≥ 6 is needed for classification of EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS.

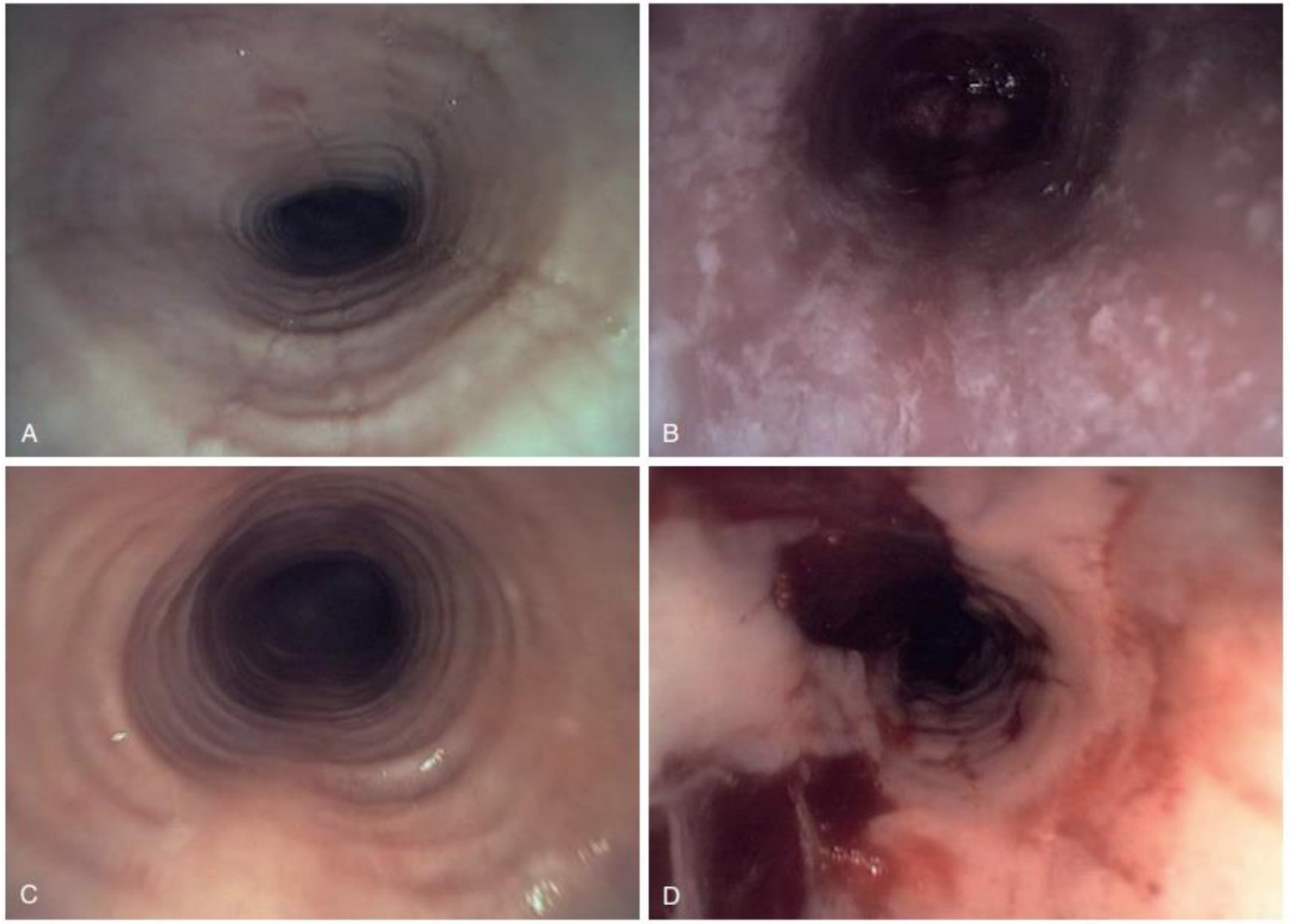
Ann Rheum Dis 2022;81:309–314

Proposed treatment algorithm for EGPA



Contents

Eosinophilic Esophagitis



Eosinophilic Esophagitis is a Late Manifestation of the Allergic March

David A. Hill, MD, PhD[a,b,*], **Robert W. Grundmeier, MD**[c,*], **Mark Ramos, BS**[c], and **Jonathan M. Spergel, MD, PhD**[a,b]

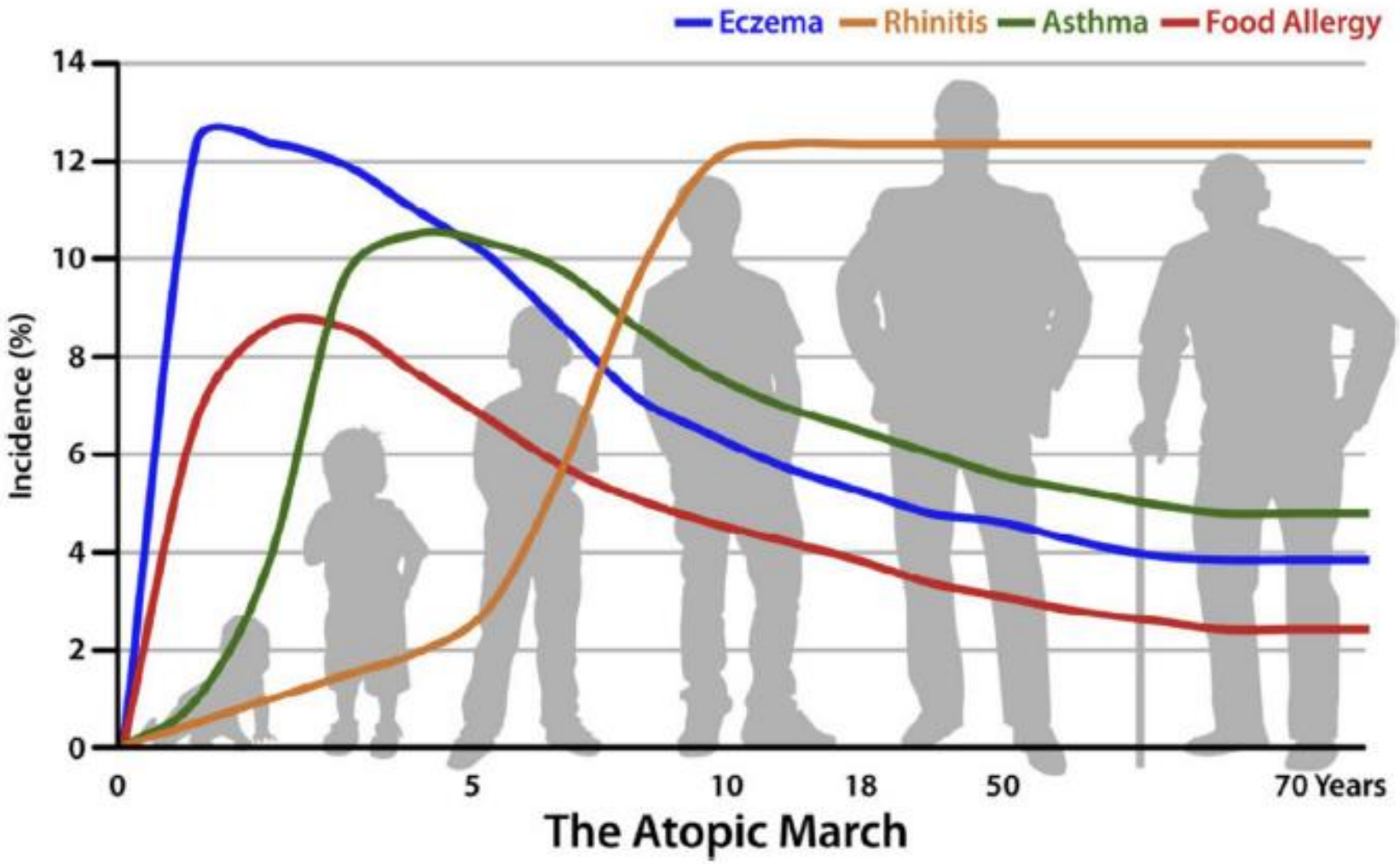
[a]Institute for Immunology, Perelman School of Medicine at the University of Pennsylvania

[b]Department of Pediatrics, Division of Allergy and Immunology

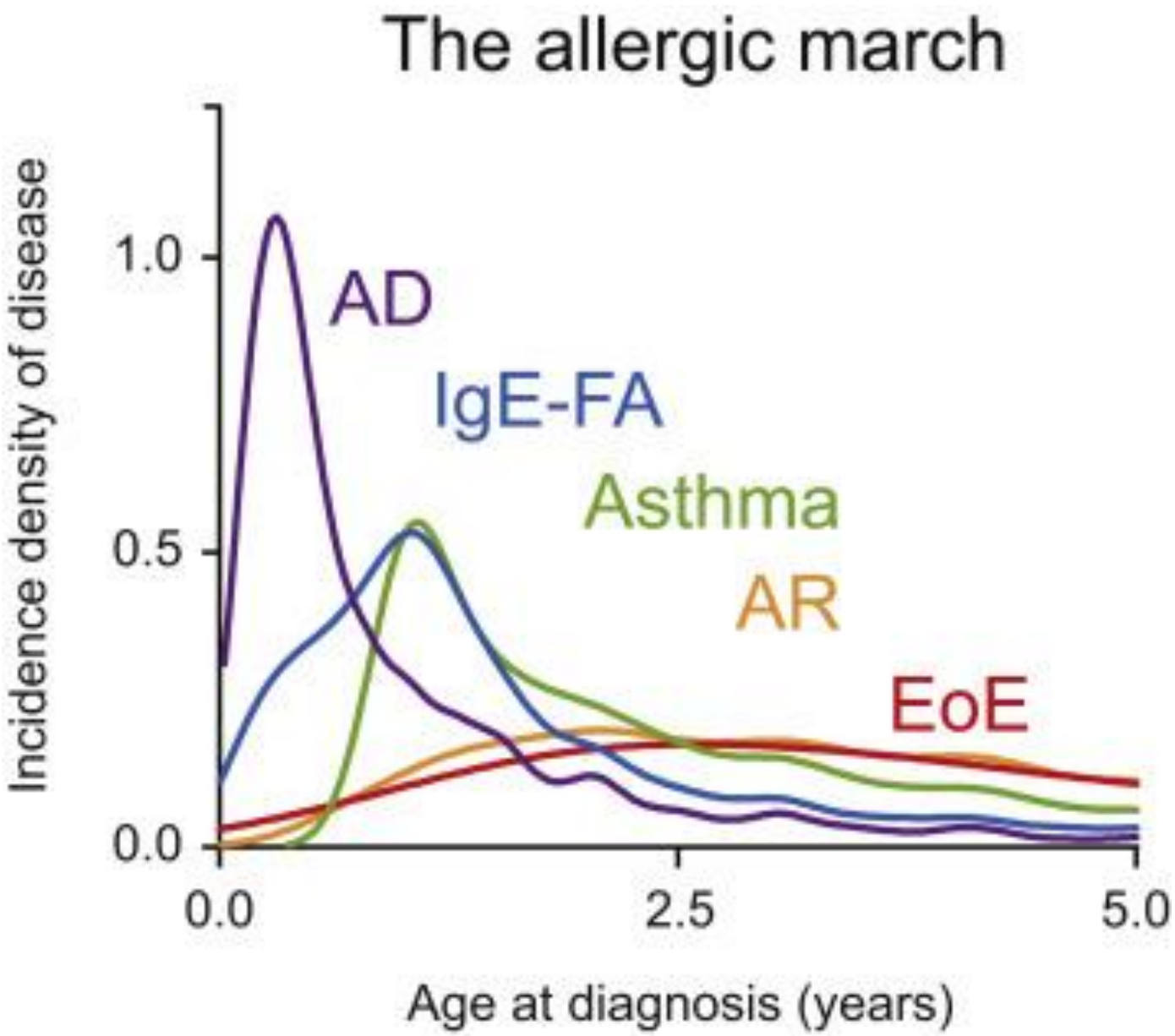
[c]Department of Biomedical and Health Informatics, Children's Hospital of Philadelphia, Philadelphia, PA, USA

J Allergy Clin Immunol Pract. 2018 ; 6(5): 1528–1533. doi:10.1016/j.jaip.2018.05.010.

The Atopic March

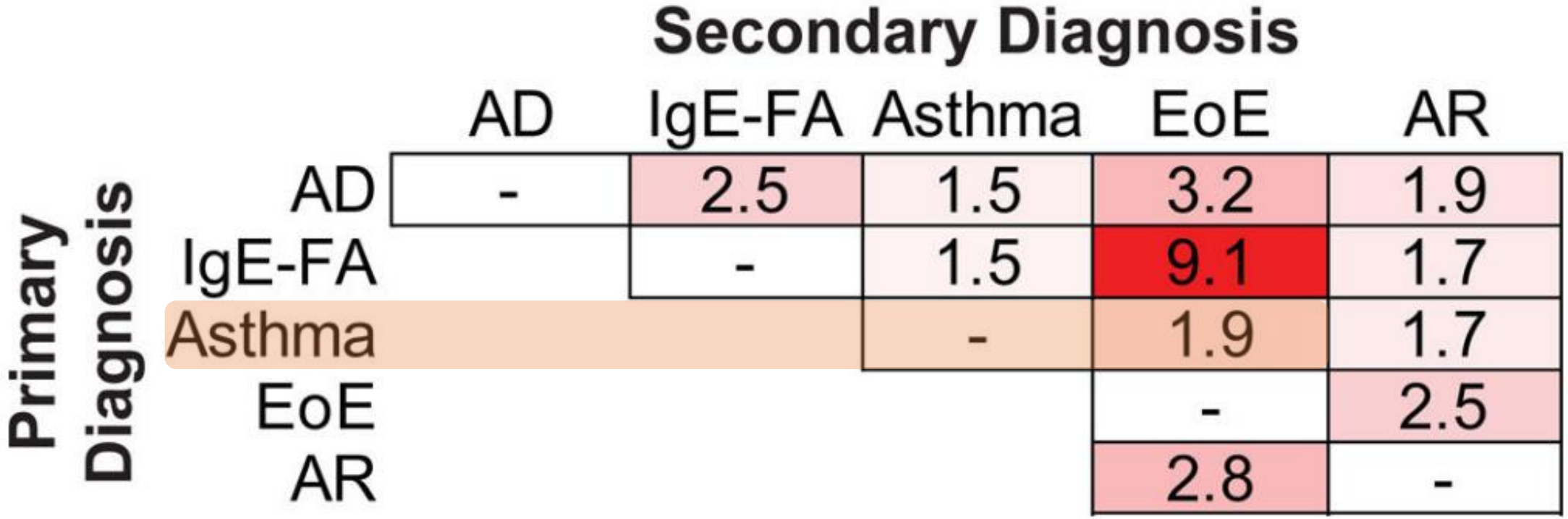


J Allergy Clin Immunol Pract 2021;9:3862-6



J Allergy Clin Immunol Pract. 2018 Sep-Oct;6(5):1528-1533.

Allergic march hazard ratios



J Allergy Clin Immunol Pract. 2018 Sep-Oct;6(5):1528-1533.

Prevalence of Eosinophilic Esophagitis in an Adult Population Undergoing Upper Endoscopy: A Prospective Study

GANESH R. VEERAPPAN,* JOSEPH L. PERRY,* TIMOTHY J. DUNCAN,* THOMAS P. BAKER,‡
CORINNE MAYDONOVITCH,* JASON M. LAKE,* ROY K. H. WONG,* and ERIC M. OSGARD*

Gastroenterology Service and ‡Department of Pathology, Walter Reed Army Medical Center, Washington, DC

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2009;7:420 – 426

gitis in an Adult Population Undergoing tudy

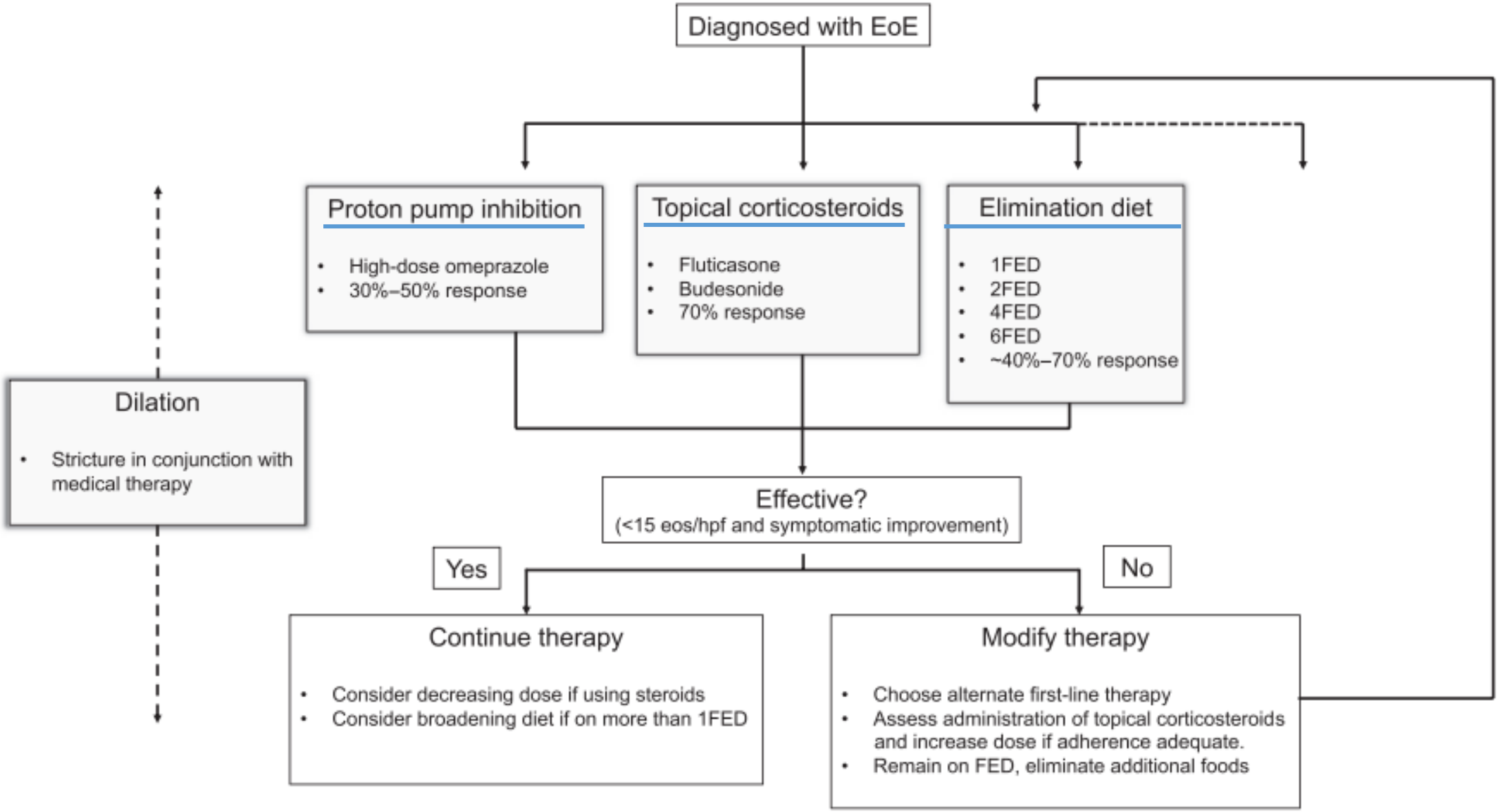
J. DUNCAN,* THOMAS P. BAKER,‡
H. WONG,* and ERIC M. OSGARD*

Medical Center, Washington, DC

	Total	EoE (+)	EoE (−)
No. of patients	385	25	360
Demographics			
Male	193 (50.1%)	20 (80%)[a]	173 (48.1%)
Age, median (*y*) (range)	50 (19–92)	41 (27–92)	52 (19–89)
Age <50 y	194 (50.4%)	18 (72%)[a]	7 (28%)
Race			
Caucasian	214 (55.6%)	15 (60%)	199 (55.3%)
African American	107 (27.8%)	10 (40%)	97 (26.9%)
Asian	20 (5.2%)	0 (0%)	20 (5.6%)
Hispanic	34 (8.8%)	0 (0%)	34 (9.4%)
Other	10 (2.6%)	0 (0%)	10 (2.8%)
Medical history			
Asthma	47 (12.2%)	8 (32%)[a]	39 (10.8%)
Food impactions	40 (10.4%)	8 (32%)[a]	32 (8.9%)
Dermatitis	28 (7.3%)	4 (16%)	24 (6.7%)
Seasonal allergies	153 (39.7%)	11 (44%)	142 (39.4%)
Food allergies	34 (8.8%)	4 (16%)	30 (8.3%)
GERD	212 (55%)	14 (56%)	198 (55%)
Peptic ulcer disease	36 (9.4)	2 (8%)	34 (9.4%)
PPI use	254 (66%)	15 (60%)	239 (66.4%)
Months on PPI (mean ± SD)	24 ± 29	23 ± 26	24 ± 29
Symptoms			
Dysphagia	153 (39.7%)	16 (64%)[a]	137 (38.1%)
Heartburn	243 (63.1%)	16 (64%)	227 (63.1%)
Belching	159 (41.3%)	9 (36%)	150 (41.6%)
Chest pain	147 (38.2%)	11 (44%)	136 (37.8%)
Regurgitation	159 (41.3%)	10 (40%)	149 (41.4%)
Night symptoms	158 (41.0%)	11 (44%)	147 (40.8%)
Nausea	138 (35.8%)	7 (28%)	131 (36.4%)
Abdominal pain	176 (45.7%)	10 (40%)	166 (46.2%)

Odds ratio [OR], 4.48

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2009;7:420 – 426



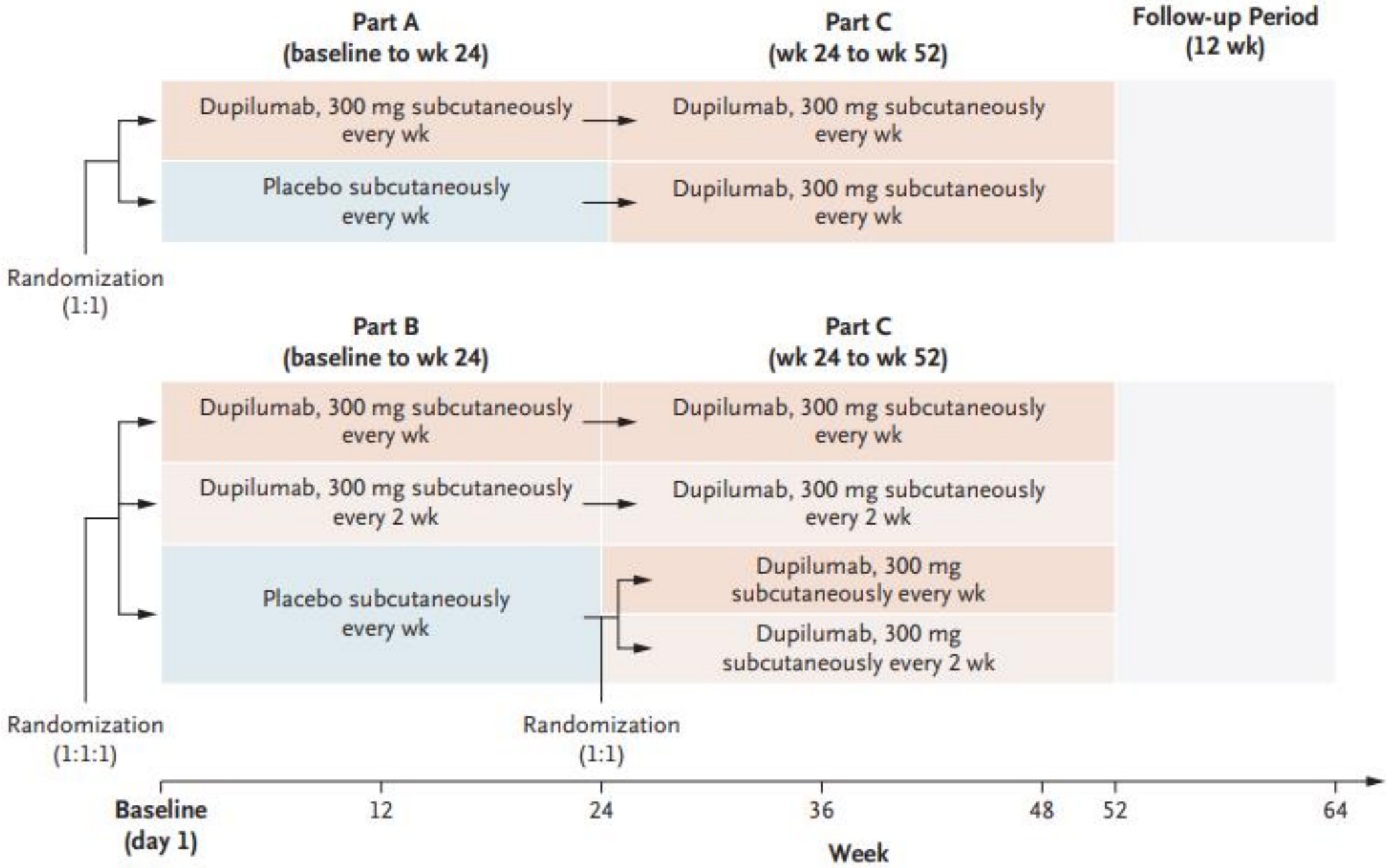
J Allergy Clin Immunol Pract 2023;11:2654-63

The NEW ENGLAND JOURNAL of MEDICINE

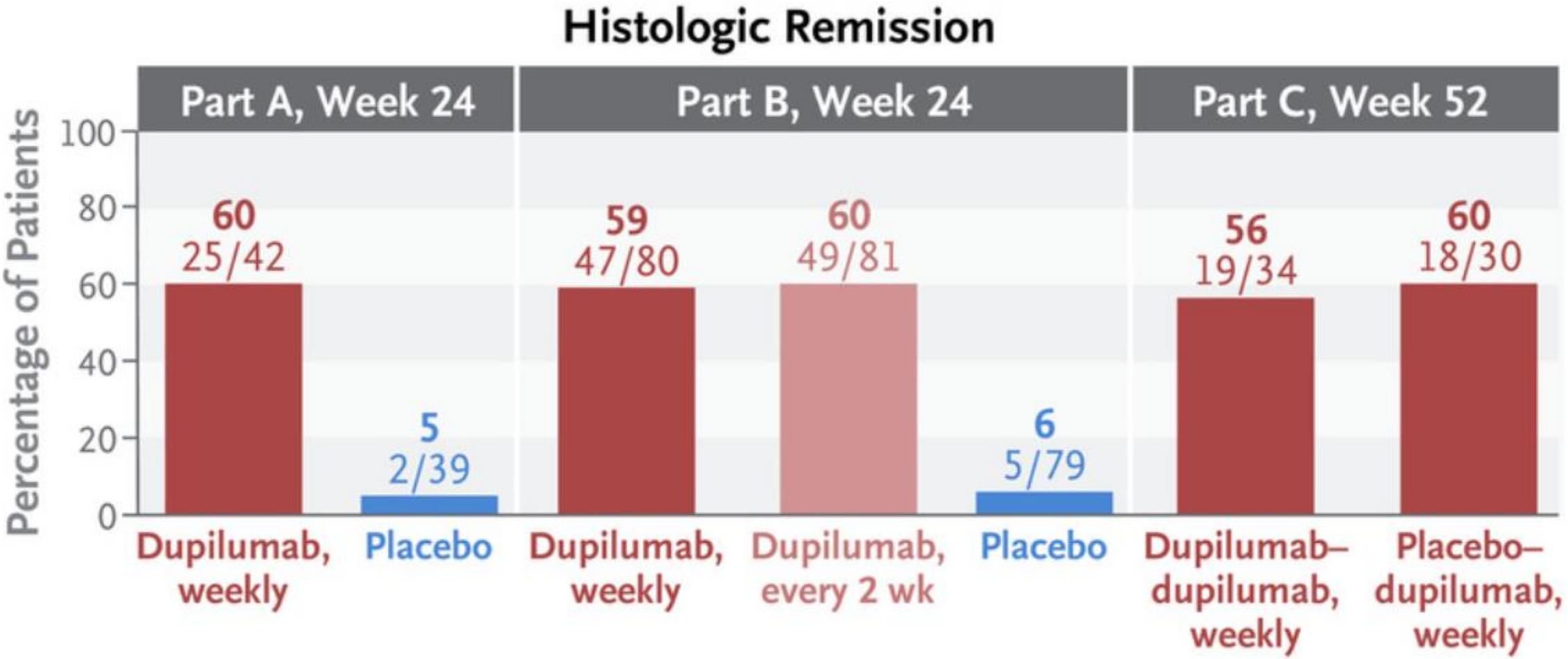
ORIGINAL ARTICLE

Dupilumab in Adults and Adolescents with Eosinophilic Esophagitis

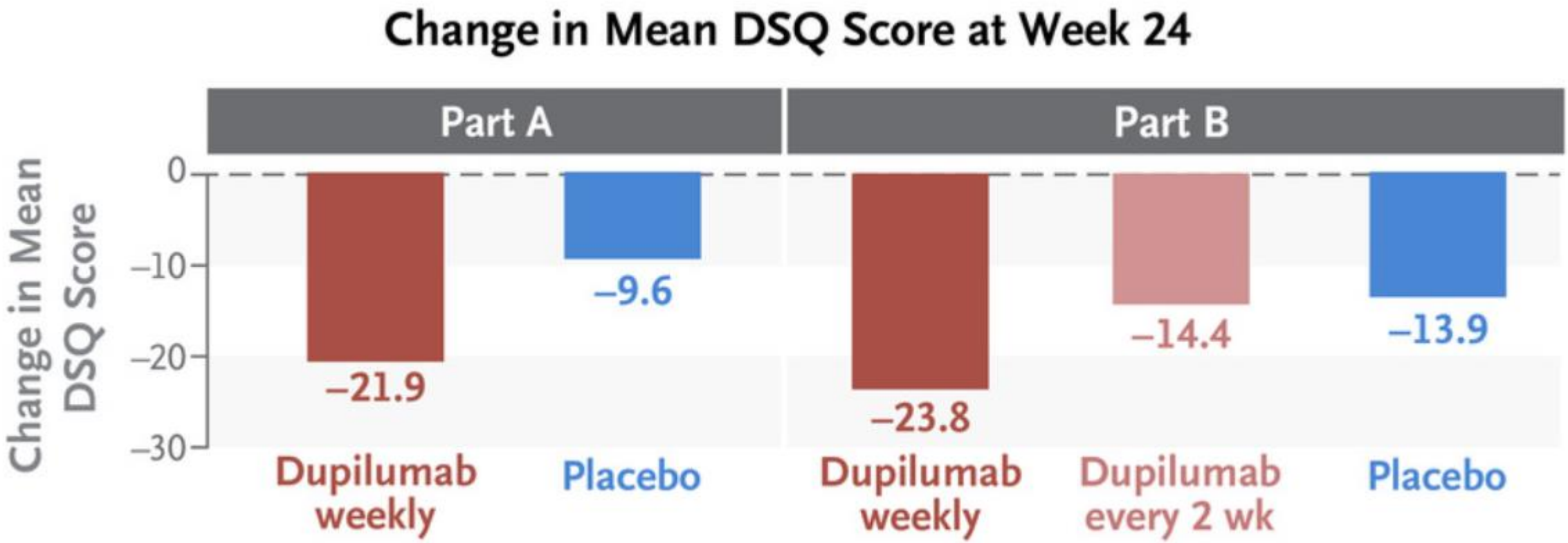
N Engl J Med 2022;387:2317-30.


Part A
(baseline to wk 24)
Part C
(wk 24 to wk 52)
Follow-up Period
(12 wk)
Dupilumab, 300 mg subcutaneously every wk
Dupilumab, 300 mg subcutaneously every wk
Placebo subcutaneously every wk
Dupilumab, 300 mg subcutaneously every wk
Randomization (1:1)
Part B
(baseline to wk 24)
Part C
(wk 24 to wk 52)
Dupilumab, 300 mg subcutaneously every wk
Dupilumab, 300 mg subcutaneously every wk
Dupilumab, 300 mg subcutaneously every 2 wk
Dupilumab, 300 mg subcutaneously every 2 wk
Placebo subcutaneously every wk
Dupilumab, 300 mg subcutaneously every wk
Dupilumab, 300 mg subcutaneously every 2 wk
Randomization (1:1:1)
Randomization (1:1)
Baseline (day 1)
12
24
36
48
52
64
Week

Histologic Remission at Weeks 24 and 52.



ES Dellon et al. N Engl J Med 2022;387:2317-2330.


Change in Mean DSQ Score at Week 24
Part A
Part B
Change in Mean DSQ Score
0
−10
−20
−30
−21.9
−9.6
−23.8
−14.4
−13.9
Dupilumab weekly
Placebo
Dupilumab weekly
Dupilumab every 2 wk
Placebo

경청해 주셔서 진심으로 감사드립니다.