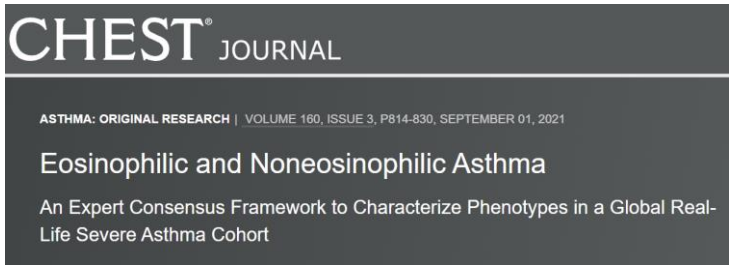
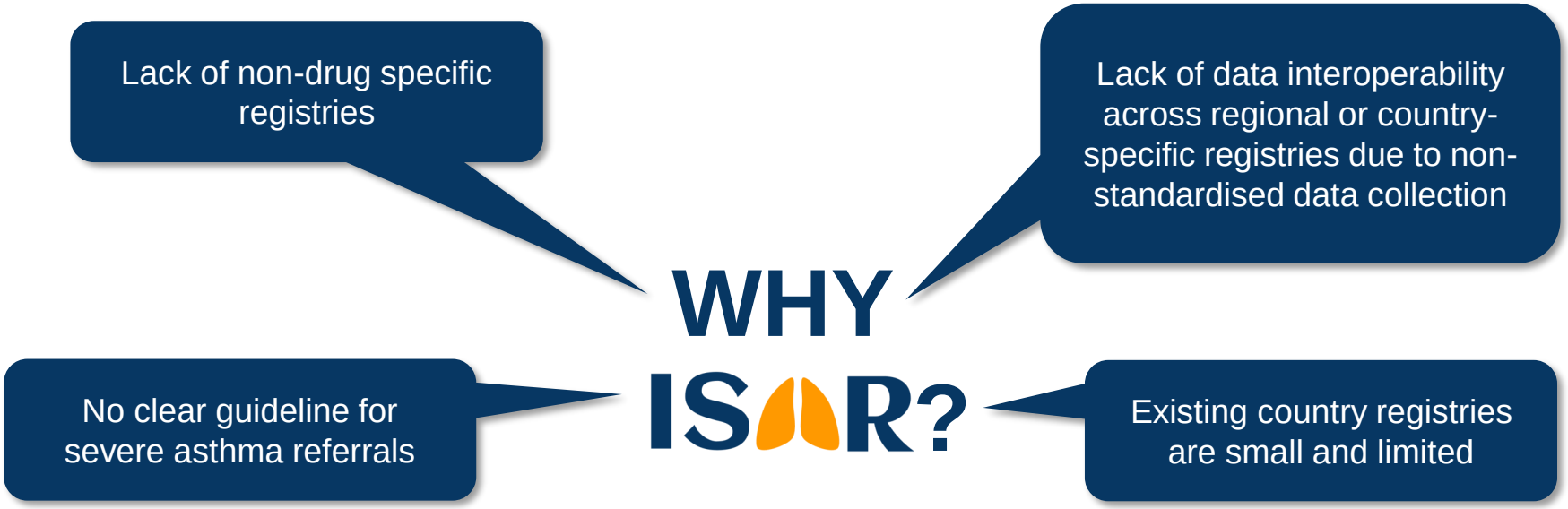
Characterization of the Eosinophilic Asthma Phenotype in a Global Real-Life Severe Asthma Cohort (International Severe Asthma Registry, ISAR) and Across All Asthma Severities in UK Primary Care



ISAR's overarching aim as a global adult severe asthma registry



ISAR provides statistical power to better understand severe asthma epidemiology, clinical management and outcomes internationally

ISAR = International Severe Asthma Registry
Canonica GW, Price DB et al. *CHEST* 2020;157(4):805-814

Why is characterization of the eosinophilic asthma phenotype important?

2020 Guidelines

Type 2 inflammation is found in ~50% of people with severe asthma

Type 2 inflammation is often characterized by eosinophils or increased FeNO, and may be accompanied by atopy

GINA

2021 Guidelines

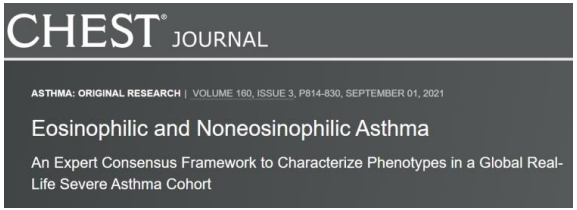
Type 2 inflammation is found in the majority of people with asthma

Type 2 targeted treatments are available, including non-biologics (ICS and add-on therapies like OCS) and biologics

FeNO = Fractional exhaled nitric oxide; GINA = Global Initiative for Asthma; ICS = Inhaled corticosteroids; OCS = Oral corticosteroids

GINA. Diagnosis and management of difficult-to-treat and severe asthma. https://ginasthma.org/severeasthma/. Accessed 30 September 2021.

Eosinophilic and Noneosinophilic Asthma:
An Expert Consensus Framework to Characterize Phenotypes in a Global Real-Life Severe Asthma Cohort



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Liam G. Heaney, Luis Perez de Llano, Mona Al-Ahmad, Vibeke Backer, John Busby, Giorgio Walter Canonica, George C. Christoff, Borja G. Cosio, J. Mark FitzGerald, Enrico Heffler, Takashi Iwanaga, David J. Jackson, Andrew N. Menzies-Gow, Nikolaos G. Papadopoulos, Andriana I. Papaioannou, Paul E. Pfeffer, Todor A. Popov, Celeste M. Porsbjerg, Chin Kook Rhee, Mohsen Sadatsafavi, Yuji Tohda, Eileen Wang, Michael E. Wechsler, Marianna Alacqua, Alan Altraja, Leif Bjermer, Unnur S. Björnsdóttir, Arnaud Bourdin, Guy G. Brusselle, Roland Buhl, Richard W. Costello, Mark Hew, Mariko Siyue Koh, Sverre Lehmann, Lauri Lehtimäki, Matthew Peters, Camille Taillé, Christian Taube, Trung N. Tran, James Zangrilli, Lakmini Bulathsinhala, Victoria A. Carter, Isha Chaudhry, Neva Eleangovan, Naeimeh Hosseini, Marjan Kerkhof, Ruth B. Murray, Chris A. Price, David B. Price

opc Global

Background and Objectives[1]

Background

- **Severe asthma consists of different phenotypes and endotypes that differ in their clinical presentation, underlying pathways and response to treatment[2]**
- Various classifications for the eosinophilic and non-eosinophilic phenotypes of severe asthma have been suggested; however, their clinical applicability in the real world is limited

Objectives

1. Develop an **algorithm** to characterize severe eosinophilic and non-eosinophilic asthma using both phenotypic characteristics and biomarkers
2. Quantify the **proportions** of patients with these phenotypes in ISAR
3. Describe and compare their **demographics** and **clinical characteristics**

ISAR = International Severe Asthma Registry

[1]Heaney LG, Price D et al. *CHEST* 2021;3:814-830; [2]Bakakos A, et al. *J Clin Med* 2019;8:1375

Study design

Historical registry study

Inclusion criteria

- Aged ≥18 years old
- Severe asthma diagnosis
- ≥1 BEC recorded

ISAR gradient eosinophilic algorithm

- Phenotypes of patients were classified as:
  - **Grade 3**: most likely eosinophilic
  - **Grade 2**: likely eosinophilic
  - **Grade 1**: least likely eosinophilic
  - **Grade 0**: non-eosinophilic

→

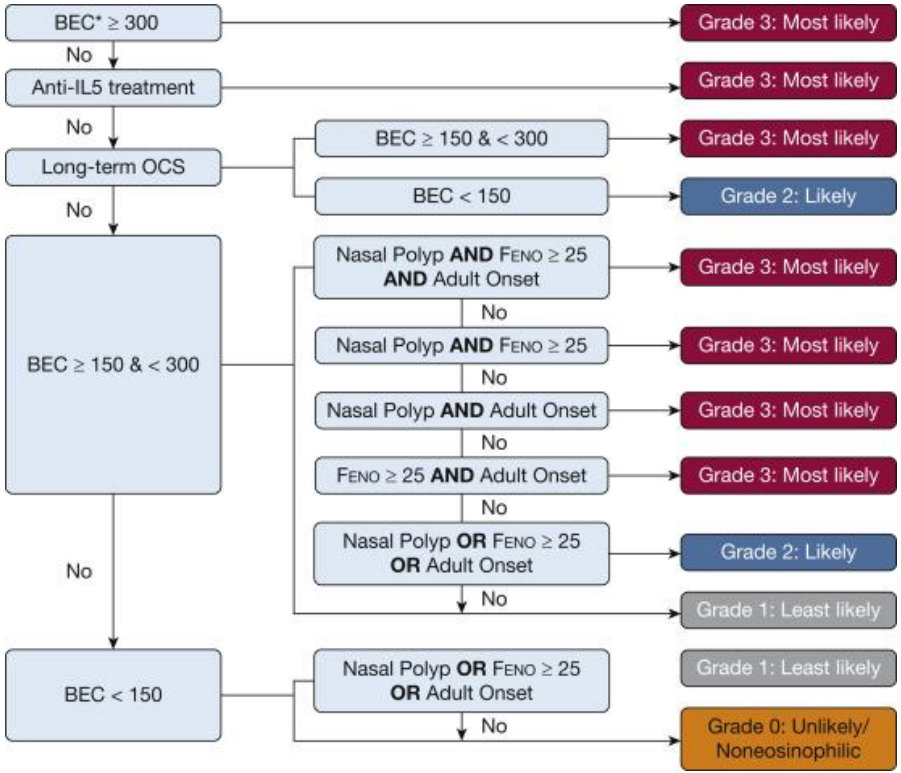
Analyses for each phenotype

- Demographic characteristics
- Clinical features
- Healthcare resource utilization

BEC = Blood eosinophil count; ISAR = International Severe Asthma Registry

Heaney LG, Price D et al. *CHEST* 2021;3:814-830

ISAR eosinophilic severe asthma phenotype algorithm



Anti-IL5 = Anti-interleukin 5; BEC = Blood eosinophil count; FeNO = Fractional exhaled nitric oxide; ISAR = International Severe Asthma Registry; OCS = Oral corticosteroids

Heaney LG, Price D et al. *CHEST* 2021;3:814-830

Prevalence of eosinophilic severe asthma phenotypes in ISAR

Highest BEC Available (cells/µL)[a]	Treatment or Clinical Characteristic	Eosinophilic Phenotype	Prospective ISAR Population (N = 1,716) [Original Algorithm]		Prospective ISAR Population (N = 1,716) [Original Algorithm Minus Age of Onset]		Prospective ISAR Population (N = 1,716) [Original Algorithm Minus FENO]	
			No. (%)	(%)	No. (%)	%	No. (%)	%
≥ 300		Grade 3: most likely	1,196 (69.7)	83.8	1,196 (69.7)	82.6	1,196 (69.7)	82.7
Anti-IL5		Grade 3: most likely	178[b] (10.4)		178[b] (10.4)		178[b] (10.4)	
≥ 150-< 300	Long-term OCS	Grade 3: most likely	37 (2.2)		37 (2.2)		37 (2.2)	
	Presence of ≥ 2 of the following: NP, FENO ≥ 25 ppb, or adult onset[c] (no long-term OCS)	Grade 3: most likely	27 (1.6)		7 (0.4)		8 (0.5)	
	Either NP, FENO ≥ 25 ppb or adult onset (no long-term OCS)	Grade 2: likely	67 (3.9)	3.9	45 (2.6)	2.6	71 (4.1)	4.1
	No NP, elevated FENO, adult onset, or long-term OCS	Grade 1: least likely	27 (1.6)	1.6	69 (4.0)	4.0	42 (2.4)	2.4
< 150	Long-term OCS	Grade 2: likely	75 (4.4)	4.4	75 (4.4)	4.4	75 (4.4)	4.4
	Either NP, FENO ≥ 25 ppb or adult onset (no long-term OCS)	Grade 1: least likely	81 (4.7)	4.7	40 (2.4)	2.4	64 (3.7)	3.7
	No NP, elevated FENO, adult onset, or long-term OCS	Grade 0: unlikely (non-eosinophilic)	28 (1.6)	1.6	69 (4.0)	4.0	45 (2.6)	2.6

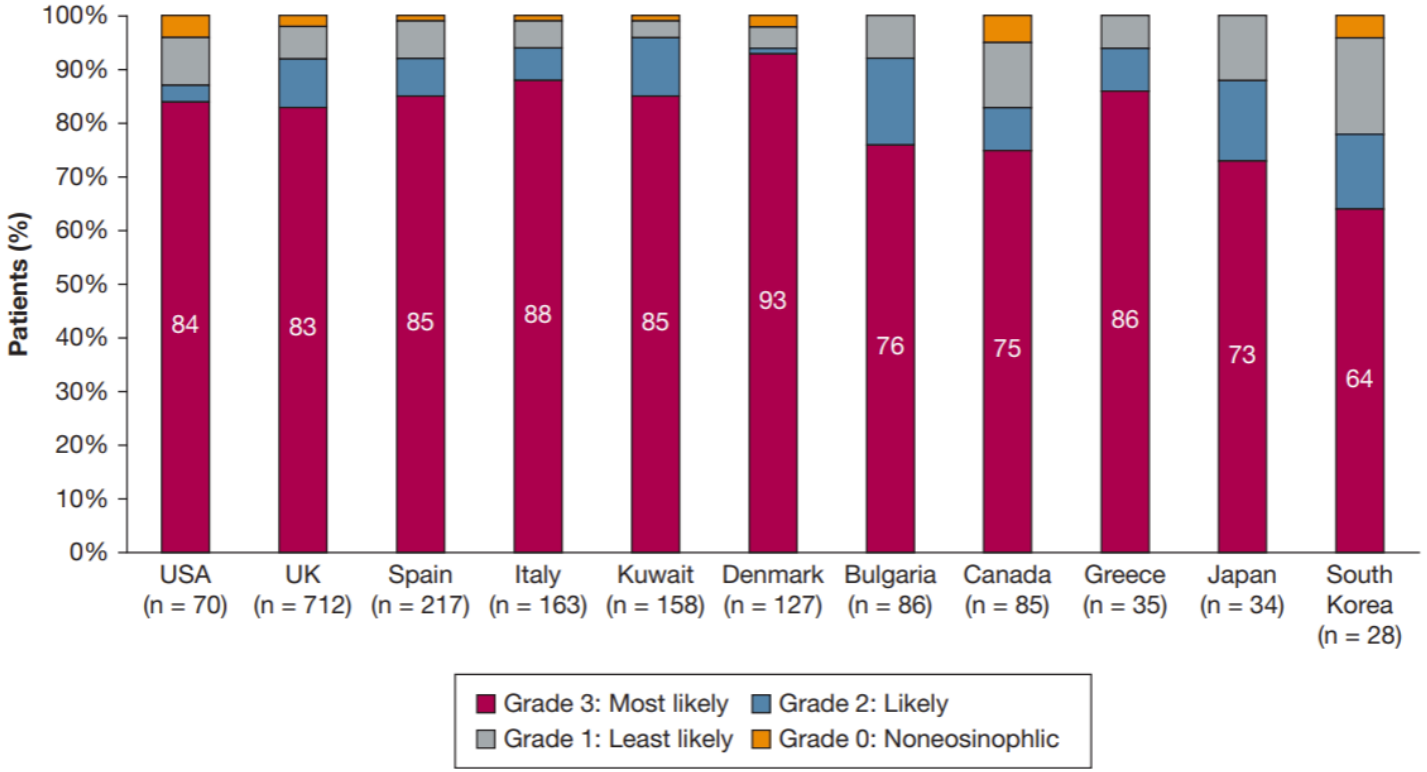
Most likely eosinophilic

Non-eosinophilic

Anti-IL5 = Anti-interleukin 5; BEC = Blood eosinophil count; FeNO = Fractional exhaled nitric oxide; ISAR = International Severe Asthma Registry; NP = Nasal polyps; ppb = parts per billion; OCS = Oral corticosteroids

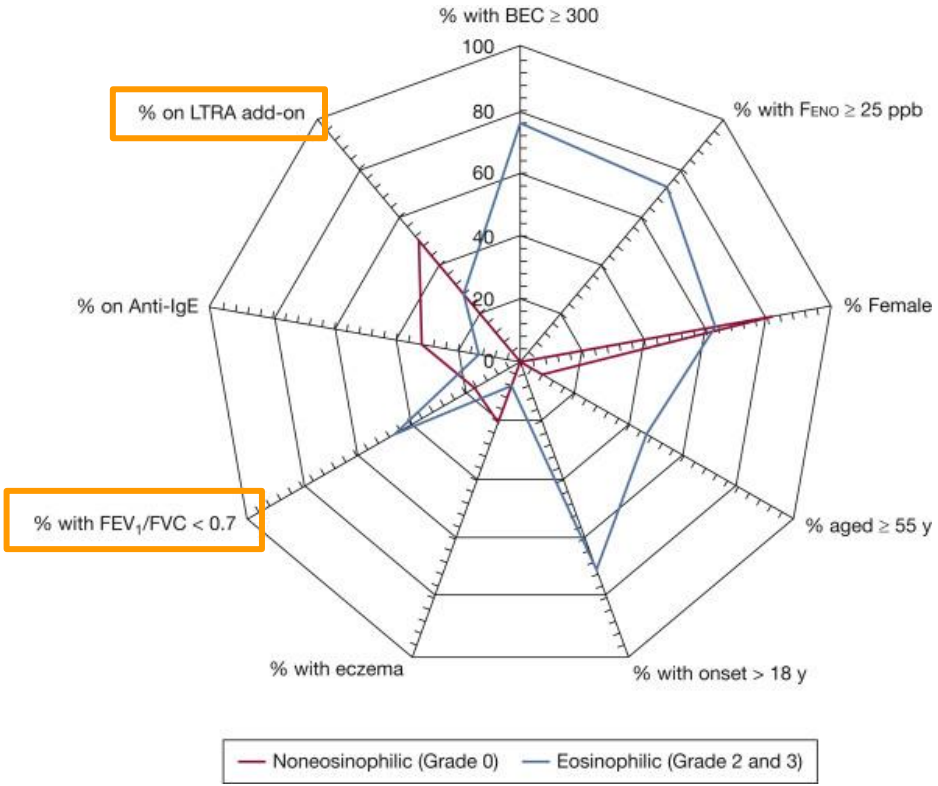
Heaney LG, Price D et al. *CHEST* 2021;3:814-830

Eosinophilic severe asthma was the most common phenotype globally



Heaney LG, Price D et al. *CHEST* 2021;3:814-830

Patients with eosinophilic severe asthma were more likely to have poorer lung function and adult-onset asthma



Anti-IgE = Anti-immunoglobulin E; BEC = Blood eosinophil count; FeNO = Fractional exhaled nitric oxide; FEV1/FVC = ratio of forced expiratory volume in one second to forced vital capacity; LRTA = leukotriene receptor antagonist; ppb = parts per billion

Heaney LG, Price D et al. *CHEST* 2021;3:814-830

Conclusions

- **The ISAR eosinophil phenotype algorithm was developed by expert consensus to characterize and quantify the eosinophilic and non-eosinophilic phenotypes of severe asthma patients in ISAR**
- **The eosinophilic phenotype was predominant in severe asthma**
  - 83.8% of patients were most likely eosinophilic and 1.6% of patients were non-eosinophilic
  - Eosinophilic severe asthma was the most common phenotype globally
- **Patients with eosinophilic severe asthma were more likely to have poorer lung function and adult-onset asthma than those with non-eosinophilic severe asthma**
- **Asthma eosinophilic phenotyping can potentially lead to the identification of treatable traits and delivery of precision medicine in patients with severe asthma**

ISAR = International Severe Asthma Registry
Heaney LG, Price D et al. *CHEST* 2021;3:814-830

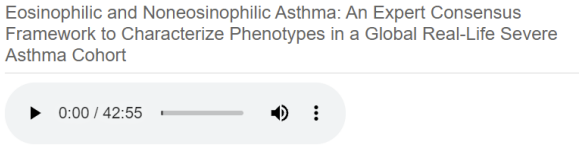
Editorial and Podcast in *CHEST*

Editorial

Click here for the editorial

Ramesh J. Kurukulaaratchy and Heena Mistry discussed the clinical importance of the ISAR eosinophilic gradient algorithm in characterizing severe asthma phenotypes in the real-world setting.[1]

Podcast



Click here for the podcast

David B. Price and Ramesh J. Kurukulaaratchy, together with the *CHEST* podcast moderator Dominique Pepper, discussed the prevalence and characterization of eosinophilic and non-eosinophilic severe asthma phenotypes.[2]

ISAR = International Severe Asthma Registry

[1]Kurukulaaratchy RJ and Mistry H. *CHEST* 2021;160:P789-790; [2]*CHEST*. Podcasts: September 2021. https://journal.chestnet.org/podcast-archive-2021. Accessed 30 September 2021.

Asthma Phenotyping in Primary Care:
Applying the International Severe Asthma Registry Eosinophil Phenotype Algorithm Across All Asthma Severities

Marjan Kerkhof, Trung N. Tran, Riyad Allehebi, G. Walter Canonica, Liam G. Heaney, Mark Hew, Luis Perez de Llano, Michael E. Wechsler, Lakmini Bulathsinhala, Victoria A. Carter, Isha Chaudhry, Neva Eleangovan, Ruth B. Murray, Chris A. Price, David B. Price

Click here for the article

Background and Objectives[1]

Background

- **Asthma types should be characterized using phenotypic characteristics and biomarkers, to potentially identify treatable traits and deliver precision treatment**
- Various classifications of asthma phenotypes in primary care have been proposed; however, they used variables that were not readily accessible in routine clinical practice or lacked characterization of underlying inflammatory disease pathways

Objectives

1. Apply the **ISAR eosinophil phenotype gradient algorithm[2]** across all asthma severities in a UK primary care cohort
2. **Quantify** and **characterize** the eosinophilic and non-eosinophilic phenotypes in this cohort
3. Study the association between the likelihood of eosinophilic asthma phenotype severity and **healthcare resource utilization**

ISAR = International Severe Asthma Registry

[1]Kerkhof M, Price D et al. *J Allergy Clin Immunol* 2021; doi: 10.1016/j.jaip.2021.07.056; [2]Heaney LG, Price D et al. *CHEST* 2021;3:814-830

Study design

OPTIMUM PATIENT CARE RESEARCH DATABASE

Clinical Practice Research Datalink

Historical cohort study

Inclusion criteria

- Aged ≥13 years old
- Active asthma diagnosis
- ≥1 BEC recorded

ISAR gradient eosinophilic algorithm

- Phenotypes of patients were classified as:
  - **Grade 3**: most likely eosinophilic
  - **Grade 2**: likely eosinophilic
  - **Grade 1**: least likely eosinophilic
  - **Grade 0**: non-eosinophilic

→

Analyses for each phenotype

- Demographic characteristics
- Clinical features
- Healthcare resource utilization

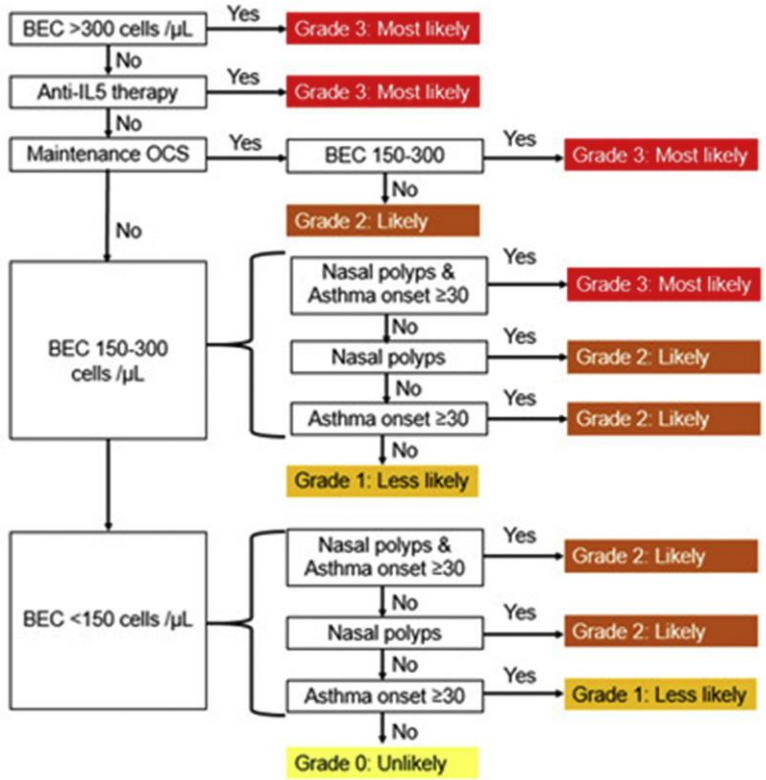
BEC = Blood eosinophil count; ISAR = International Severe Asthma Registry

Kerkhof M, Price D et al. *J Allergy Clin Immunol* 2021; doi: 10.1016/j.jaip.2021.07.056

ISAR eosinophil phenotype algorithm applied to a UK primary care asthma cohort

Overall distribution

Grade 3: Most likely	N=121,313 (50.3%)
Grade 2: Likely	N=53,431 (22.2%)
Grade 1: Less Likely	N=52,741 (21.9%)
Grade 0: Unlikely	N=13,521 (5.6%)

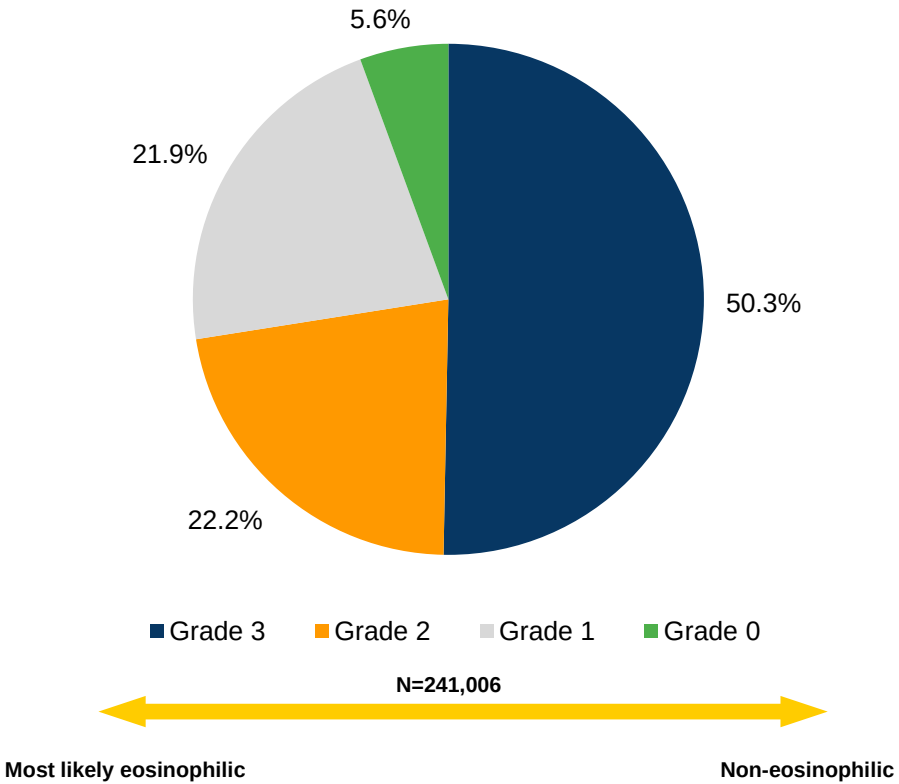


Number (%)
119,447 (49.6)
0 (0.0)
458 (0.2)
97 (0.0)
1,408 (0.6)
656 (0.3)
52,298 (21.7)
36,901 (15.3)
230 (0.1)
150 (0.1)
15,840 (6.6)
13,521 (5.6)

Anti-IL5 = Anti-interleukin 5; BEC = Blood eosinophil count; ISAR = International Severe Asthma Registry; OCS = Oral corticosteroids

Kerkhof M, Price D et al. *J Allergy Clin Immunol* 2021; doi: 10.1016/j.jaip.2021.07.056

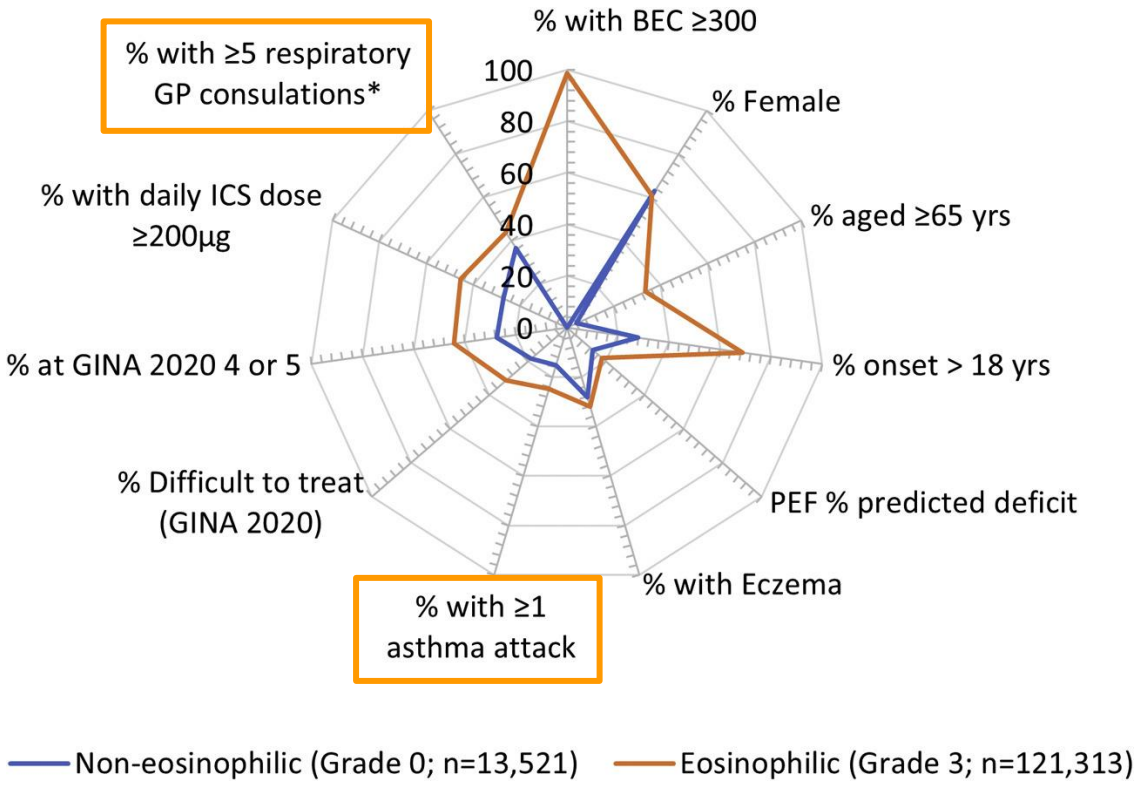
Prevalence of phenotypes across all asthma severities in UK primary care



Many patients in primary care had ‘most likely eosinophilic’ asthma, irrespective of disease severity

Kerkhof M, Price D et al. *J Allergy Clin Immunol* 2021; doi: 10.1016/j.jaip.2021.07.056

Characterization of phenotypes across all asthma severities in UK primary care



Eosinophilic patients were more likely to have poorer asthma control and greater healthcare utilization than non-eosinophilic patients

BEC = Blood eosinophil count; GINA = Global Initiative for Asthma; GP = General practice; ICS = Inhaled corticosteroid; PEF = Peak expiratory flow

Kerkhof M, Price D et al. *J Allergy Clin Immunol* 2021; doi: 10.1016/j.jaip.2021.07.056

Conclusions

- **The eosinophilic phenotype was predominant across all asthma severities in UK primary care**
  - 72.5% of patients had most likely or likely eosinophilic phenotypes
  - 5.6% of patients were non-eosinophilic
- **Patients with most likely eosinophilic asthma tended to have more comorbidities, poorer asthma control, and greater healthcare resource use than those with non-eosinophilic asthma**
  - **28.2%** of patients with most likely eosinophilic asthma versus **6.9%** of patients with non-eosinophilic asthma had a Charlson comorbidity index of ≥2
  - **24.8%** of patients with most likely eosinophilic asthma versus **15.3%** of patients with non-eosinophilic asthma experienced ≥1 asthma attacks
- **Asthma eosinophilic phenotyping should become part of routine clinical practice in primary care**
  - Patients with eosinophilic asthma phenotypes may benefit from earlier intervention with Type 2 targeted treatments, including ICS and steroid-sparing therapies such as biologics

ICS = Inhaled corticosteroids

Kerkhof M, Price D et al. *J Allergy Clin Immunol* 2021; doi: 10.1016/j.jaip.2021.07.056