



## **Severe asthma: A continuous challenge**

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## Conflicts [Honorarium fees]

- AstraZeneca Greece & Bulgaria & Poland
- Boehringer Ingelheim Greece& Europe
- Chiesi
- GlaxoSmithKline Greece & Denmark
- Elpen
- Menarini Hellas
- Novartis Hellas & Europe
- Pharmaten Hellas
- Vianex/MSD

# Design

- Starting from the definition

# Definition ATS/ERS task force 2014

Asthma which requires treatment with guidelines suggested medications for GINA steps 4-5 asthma (high dose ICS<sup>#</sup> and LABA or leukotriene modifier/theophylline) for the previous year or systemic CS for  $\geq 50\%$  of the previous year to prevent it from becoming "uncontrolled" or which remains "uncontrolled" despite this therapy

Uncontrolled asthma defined as at least one of the following:

- 1) Poor symptom control: ACQ consistently  $>1.5$ , ACT  $<20$  (or "not well controlled" by NAEPP/GINA guidelines)
- 2) Frequent severe exacerbations: two or more bursts of systemic CS ( $>3$  days each) in the previous year
- 3) Serious exacerbations: at least one hospitalisation, ICU stay or mechanical ventilation in the previous year
- 4) Airflow limitation: after appropriate bronchodilator withhold FEV<sub>1</sub>  $<80\%$  predicted (in the face of reduced FEV<sub>1</sub>/FVC defined as less than the lower limit of normal)

Controlled asthma that worsens on tapering of these high doses of ICS or systemic CS (or additional biologics)

Differential diagnosis  
Follow up properly



TASK FORCE REPORT  
ERS/ATS GUIDELINES ON SEVERE ASTHMA

International ERS/ATS guidelines on  
definition, evaluation and treatment of  
severe asthma

# ICS: The critical step: Defining the dose

TABLE 4 Definition of high daily dose of various inhaled corticosteroids in relation to patient age

Inhaled corticosteroid	Threshold daily dose in µg considered as high	
	Age 6-12 years	Age >12 years
Beclomethasone dipropionate	≥800 (DPI or CFC MDI) ≥320 (HFA MDI)	≥2000 (DPI or CFC MDI) ≥1000 (HFA MDI)
Budesonide	≥800 (MDI or DPI)	≥1600 (MDI or DPI)
Ciclesonide	≥160 (HFA MDI)	≥320 (HFA MDI)
Fluticasone propionate	≥500 (HFA MDI or DPI)	≥1000 (HFA MDI or DPI)
Mometasone furoate	≥500 (DPI)	≥800 (DPI)
Triamcinolone acetonide	≥1200	≥2000

Notes: 1) Designation of high doses is provided from manufacturers' recommendations where possible. 2) As chlorofluorocarbon (CFC) preparations are being taken from the market, medication inserts for hydrofluoroalkane (HFA) preparations should be carefully reviewed by the clinician for the equivalent correct dosage. DPI: dry powder inhaler; MDI: metered-dose inhaler.



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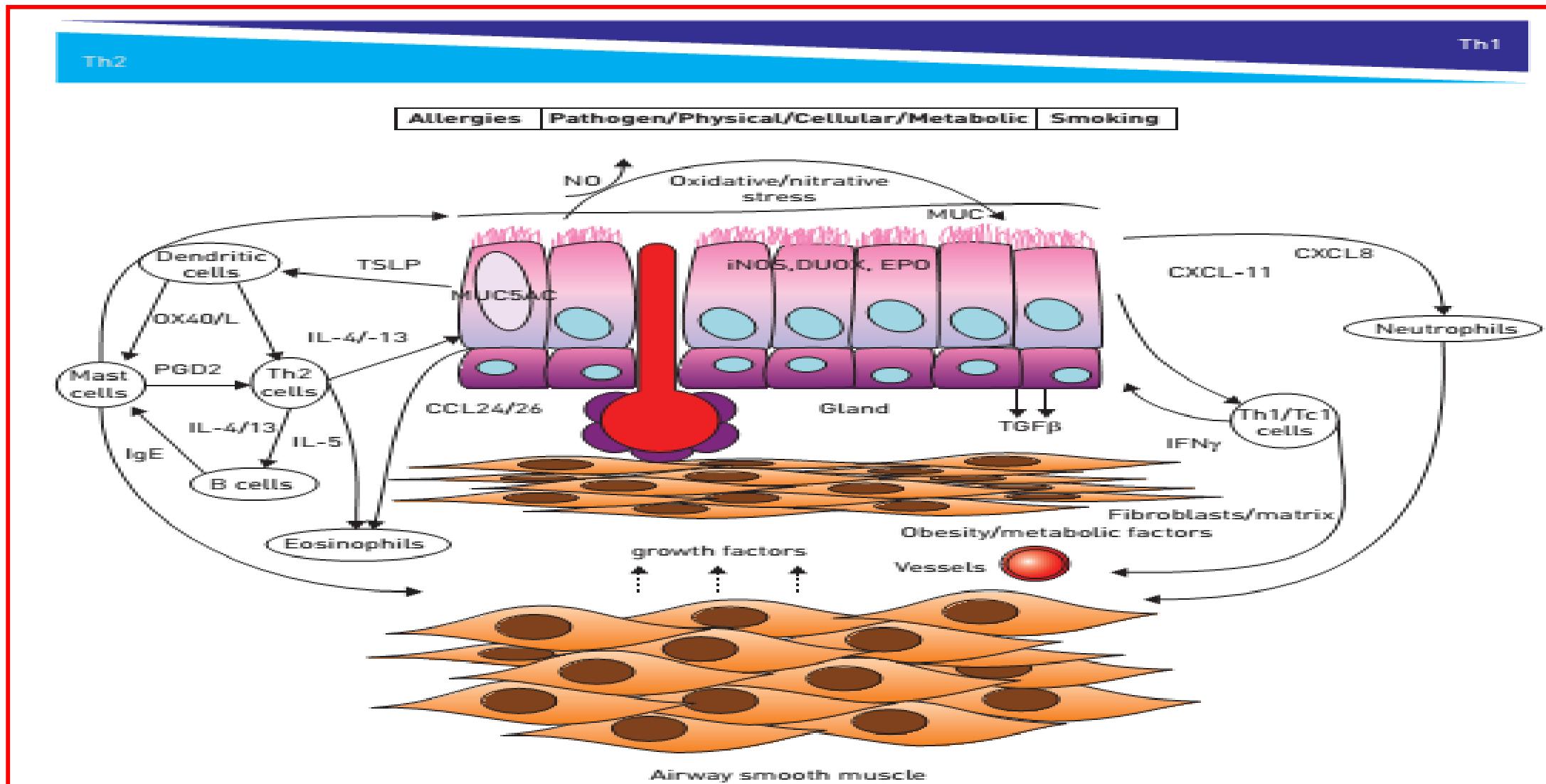
# The GINA perspective

Inhaled corticosteroid	Adults and adolescents			Children 6–11 years		
	Low	Medium	High	Low	Medium	High
Bclometasone dipropionate (CFC)*	200–500	>500–1000	>1000	100–200	>200–400	>400
Bclometasone dipropionate (HFA)	100–200	>200–400	>400	50–100	>100–200	>200
Budesonide (DPI)	200–400	>400–800	>800	100–200	>200–400	>400
Budesonide (nebuliser)				250–500	>500–1000	>1000
Ciclesonide (HFA)	80–160	>160–320	>320	80	>80–160	>160
Fluticasone furoate (DPI)	100	n.a.	200	n.a.	n.a.	n.a.
Fluticasone propionate (DPI)	100–250	>250–500	>500	100–200	>200–400	>400
Fluticasone propionate (HFA)	100–250	>250–500	>500	100–200	>200–500	>500
Mometasone furoate	110–220	>220–440	>440	110	≥220–<440	≥440
Triamcinolone acetonide	400–1000	>1000–2000	>2000	400–800	>800–1200	>1200

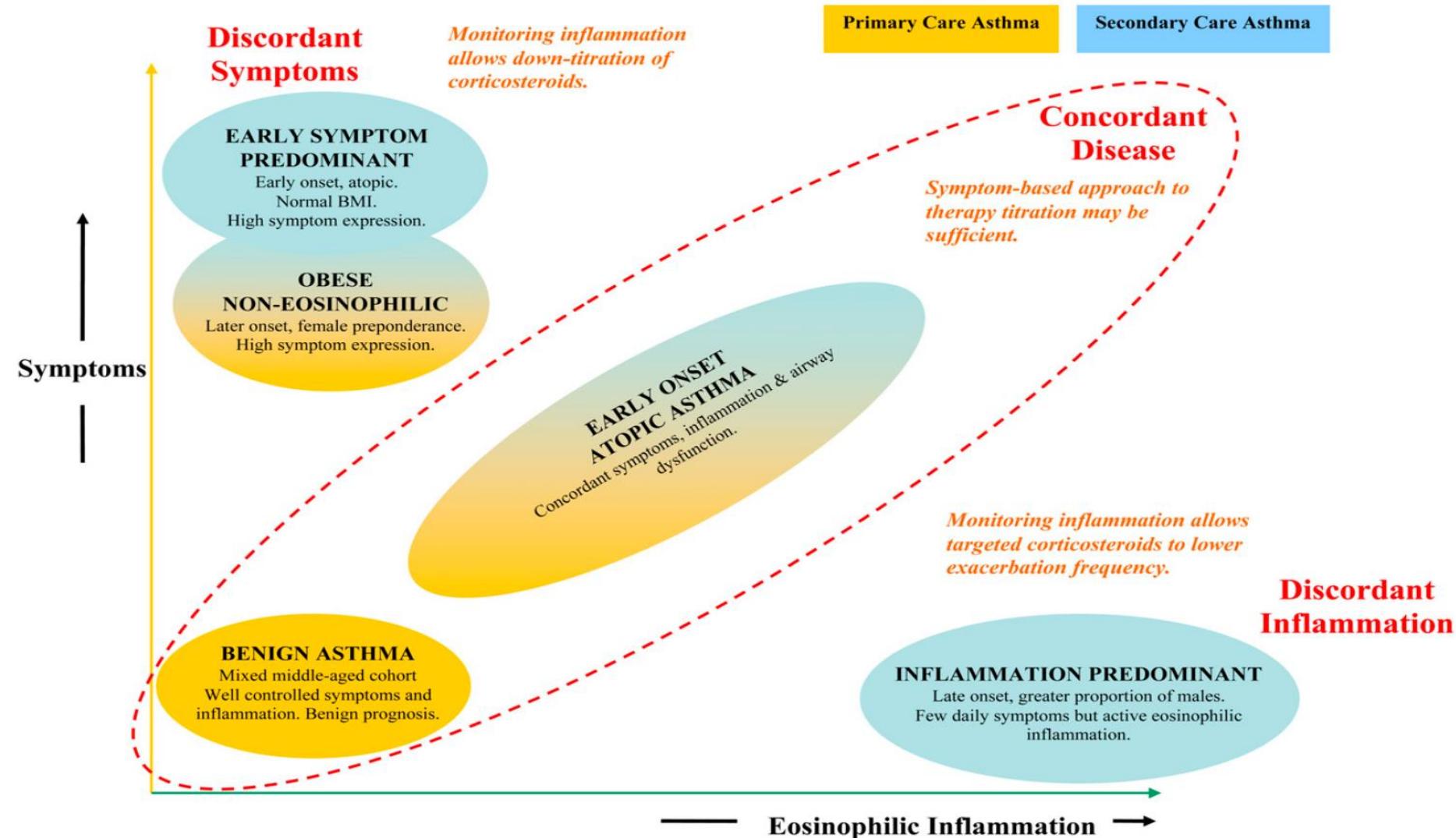
# Design

- Starting from the definition
- Inflammation

# Different or up-regulated?



# The clinical problem: Discrepancy between symptoms and inflammation.



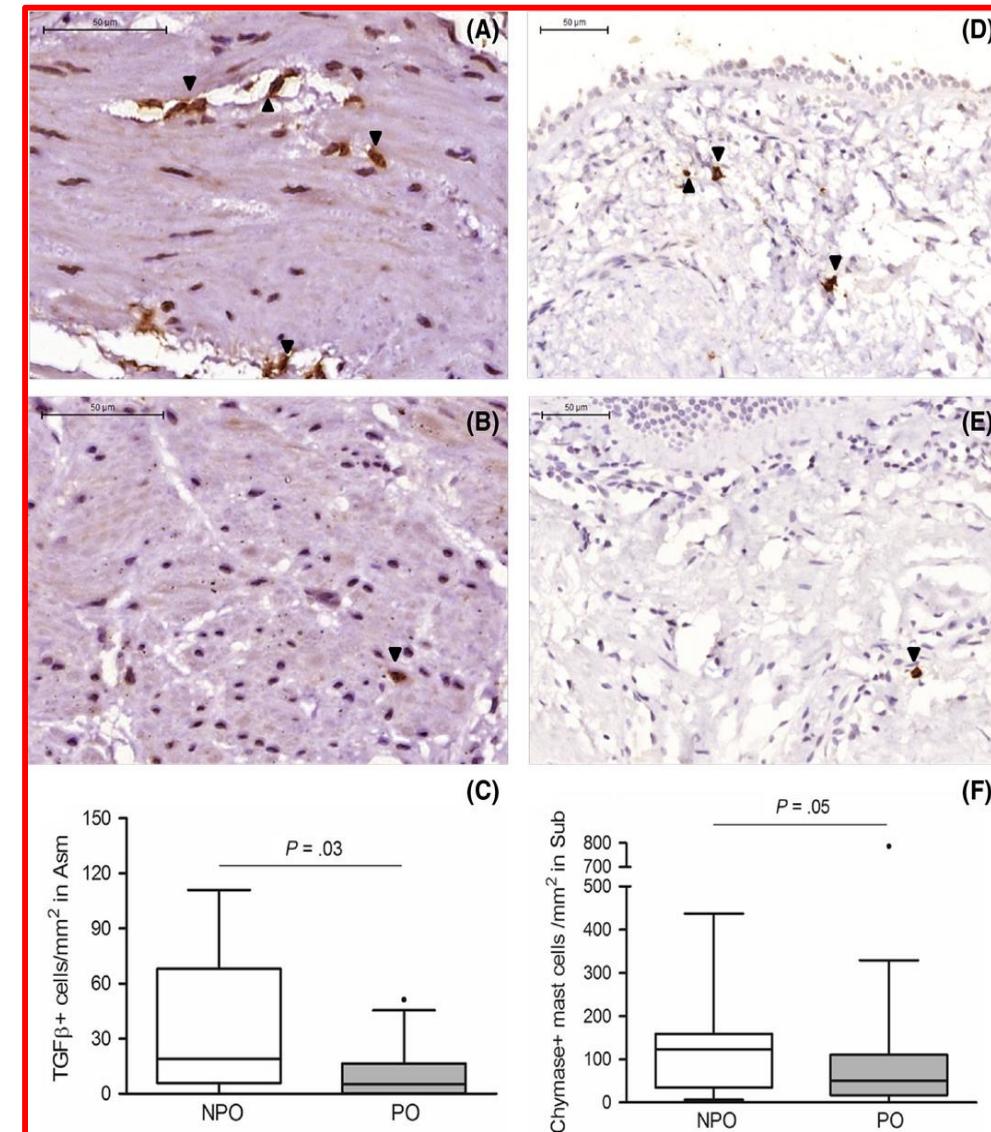
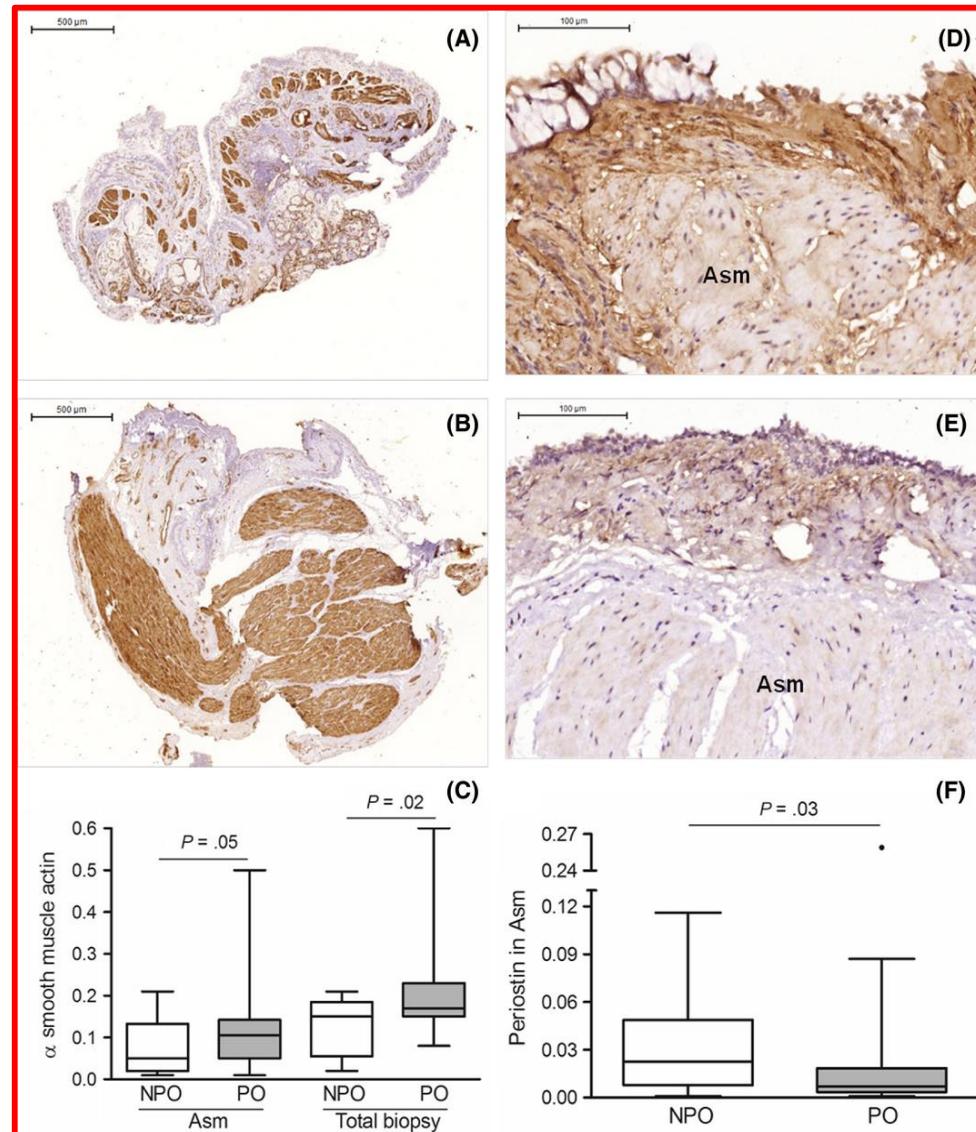
# The persistent airway obstruction

Table 2

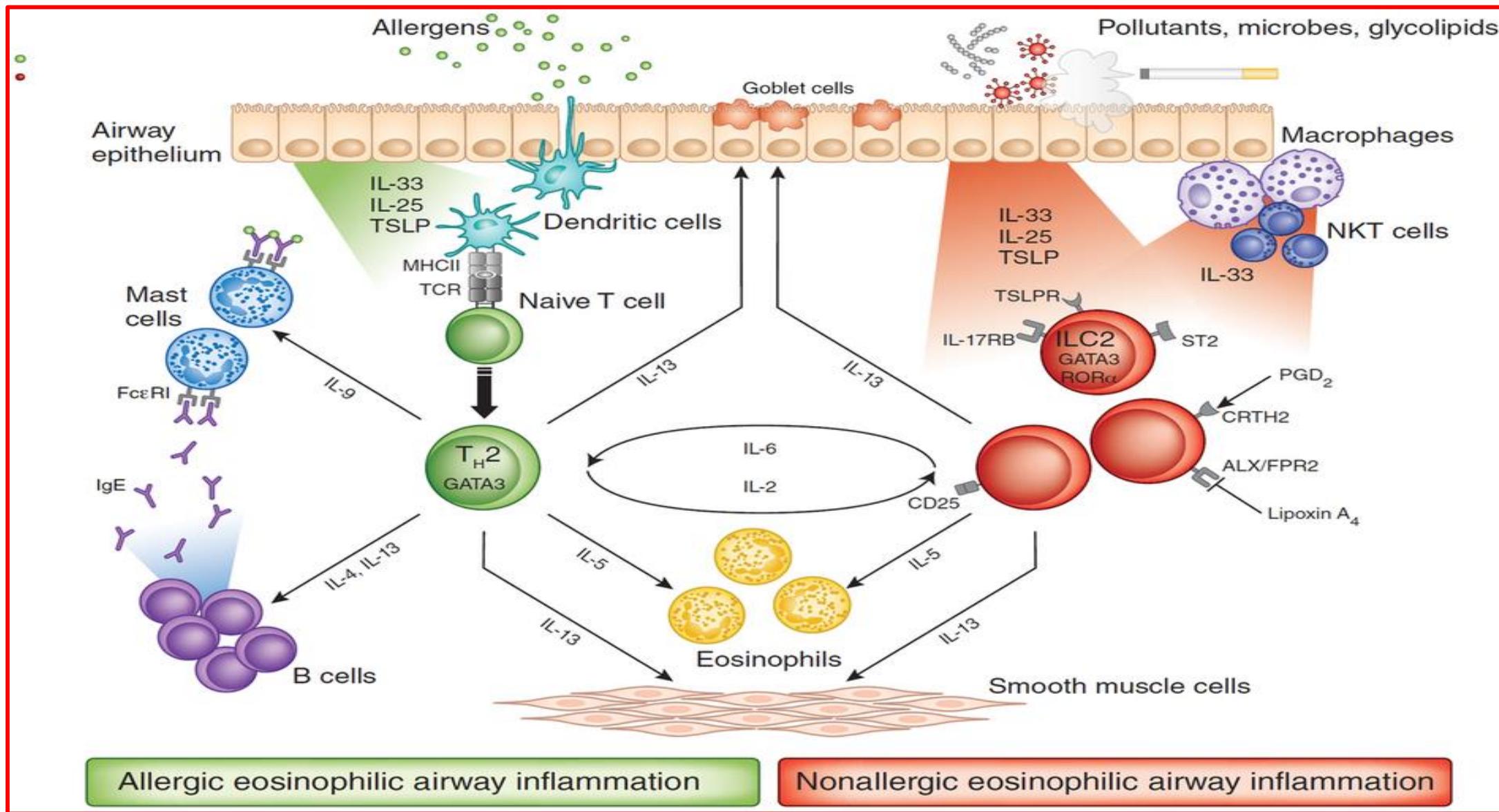
Characteristics of the three clusters of asthmatic patients and their relation to the presence of persistent airflow obstruction.

Cluster	Cluster 1	Cluster 2	Cluster 3
Size (%)	56 (32.9%)	53 (31.2%)	61 (35.9%)
Features	Low dose ICS (100%) No criteria for SRA (100%) No atopy (100%) No oral CS (100%) No persistent airflow obstruction (85.7%)	High dose ICS (100%) Criteria for SRA (90.6%) Atopy (54.7%) Oral CS (64.2%) Persistent airflow obstruction (83%)	Low dose ICS (100%) No criteria for SRA (100%) Atopy (100%) No oral CS (100%) No persistent airflow obstruction (86.9%)

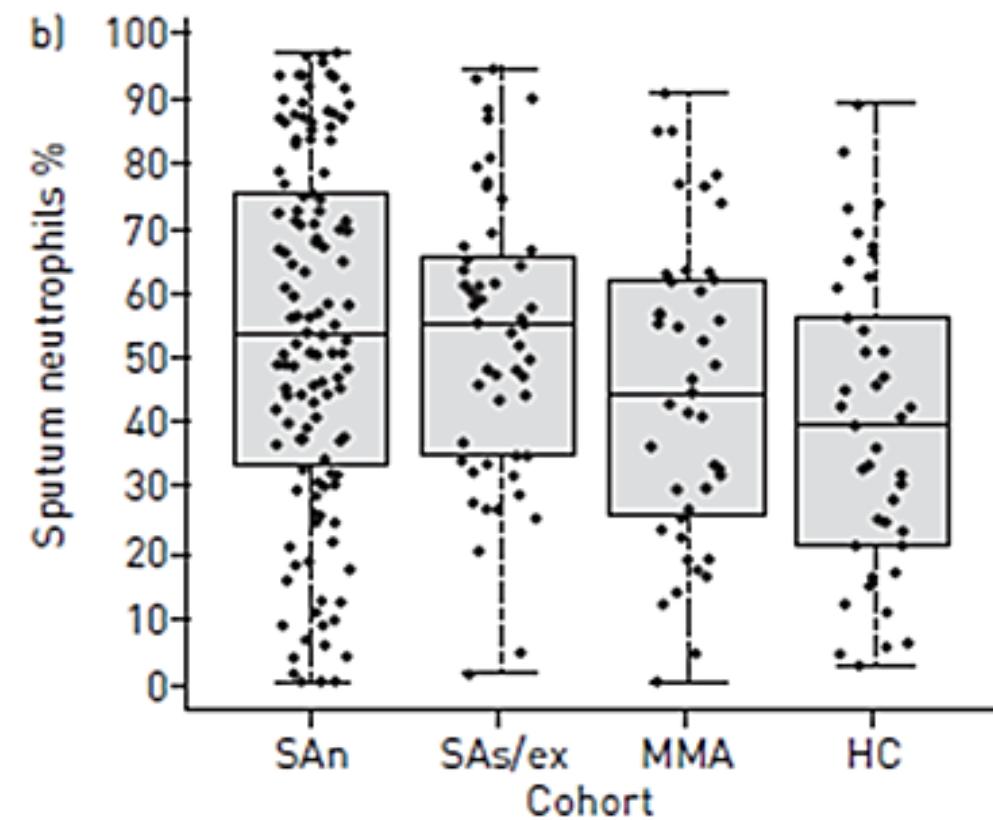
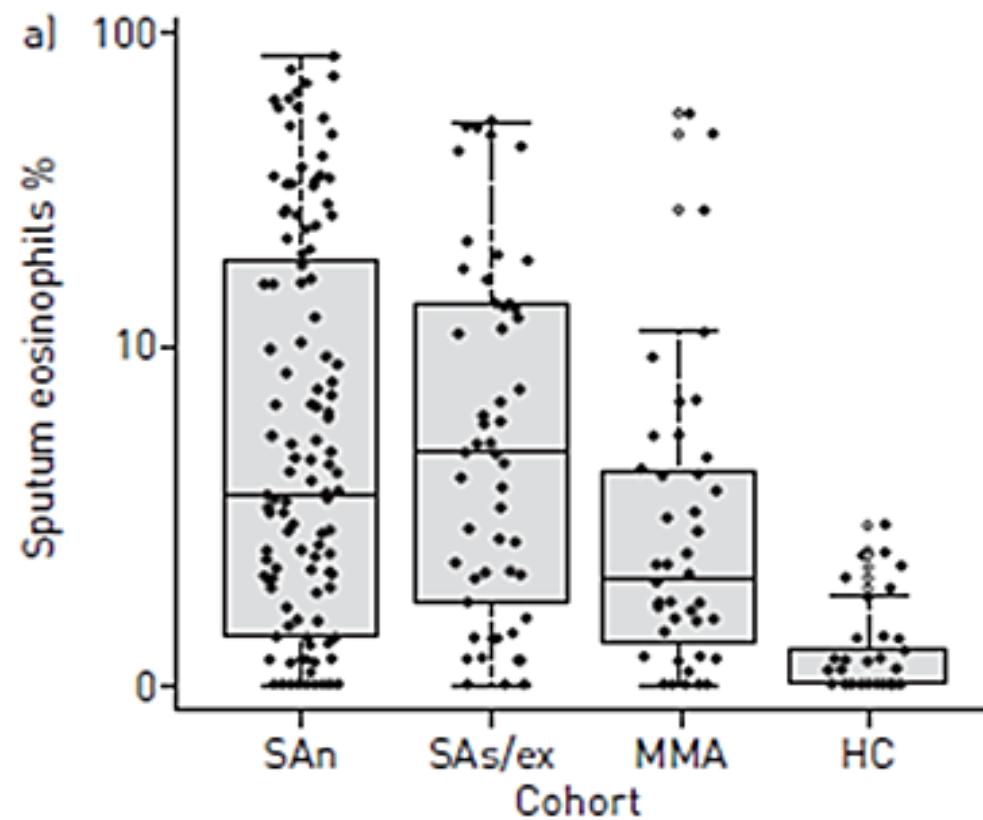
# Airway pathology in severe asthma is related to airflow obstruction but not symptom control



# A different approach



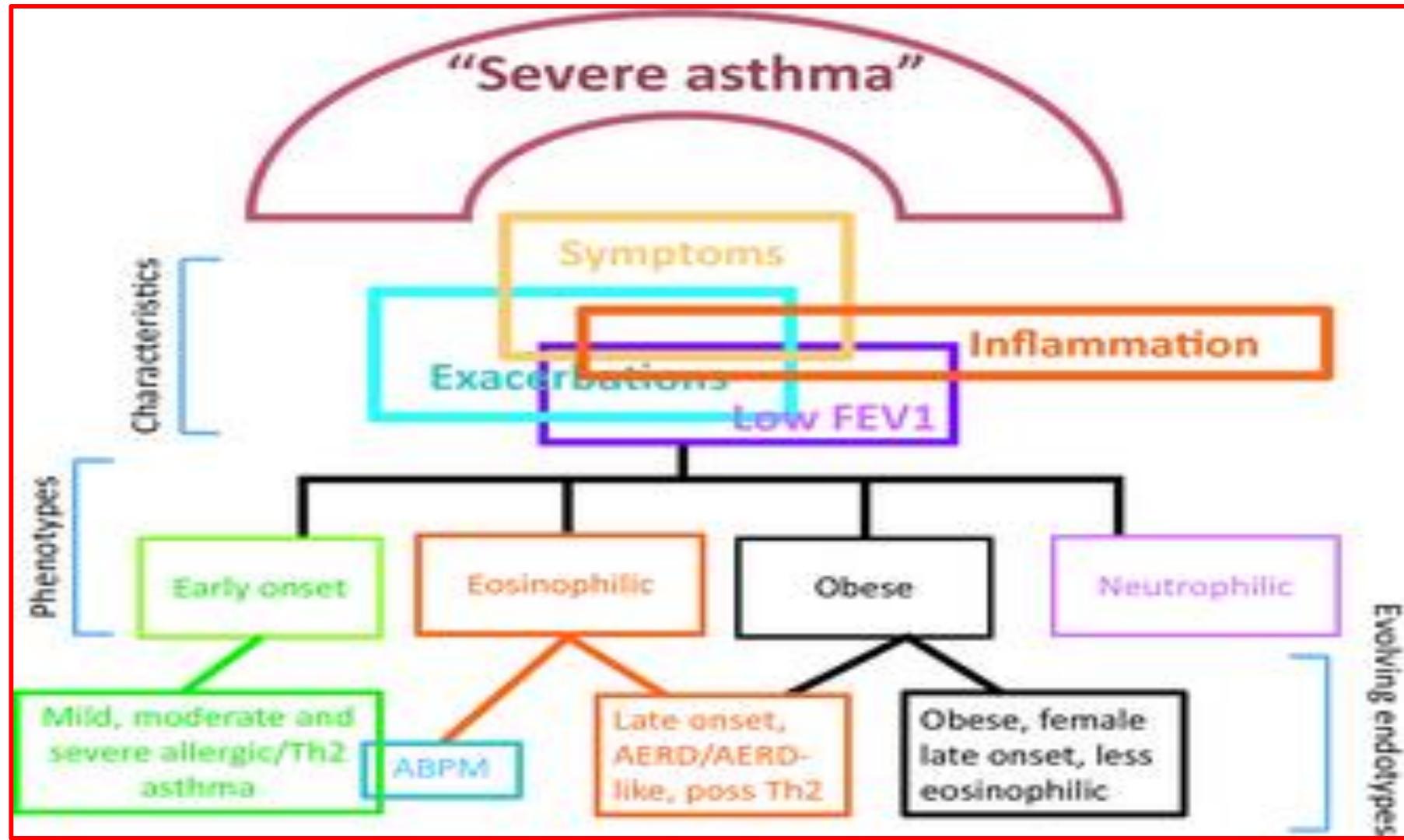
# Clinical and inflammatory characteristics of the European U-BIOPRED adult severe asthma cohort



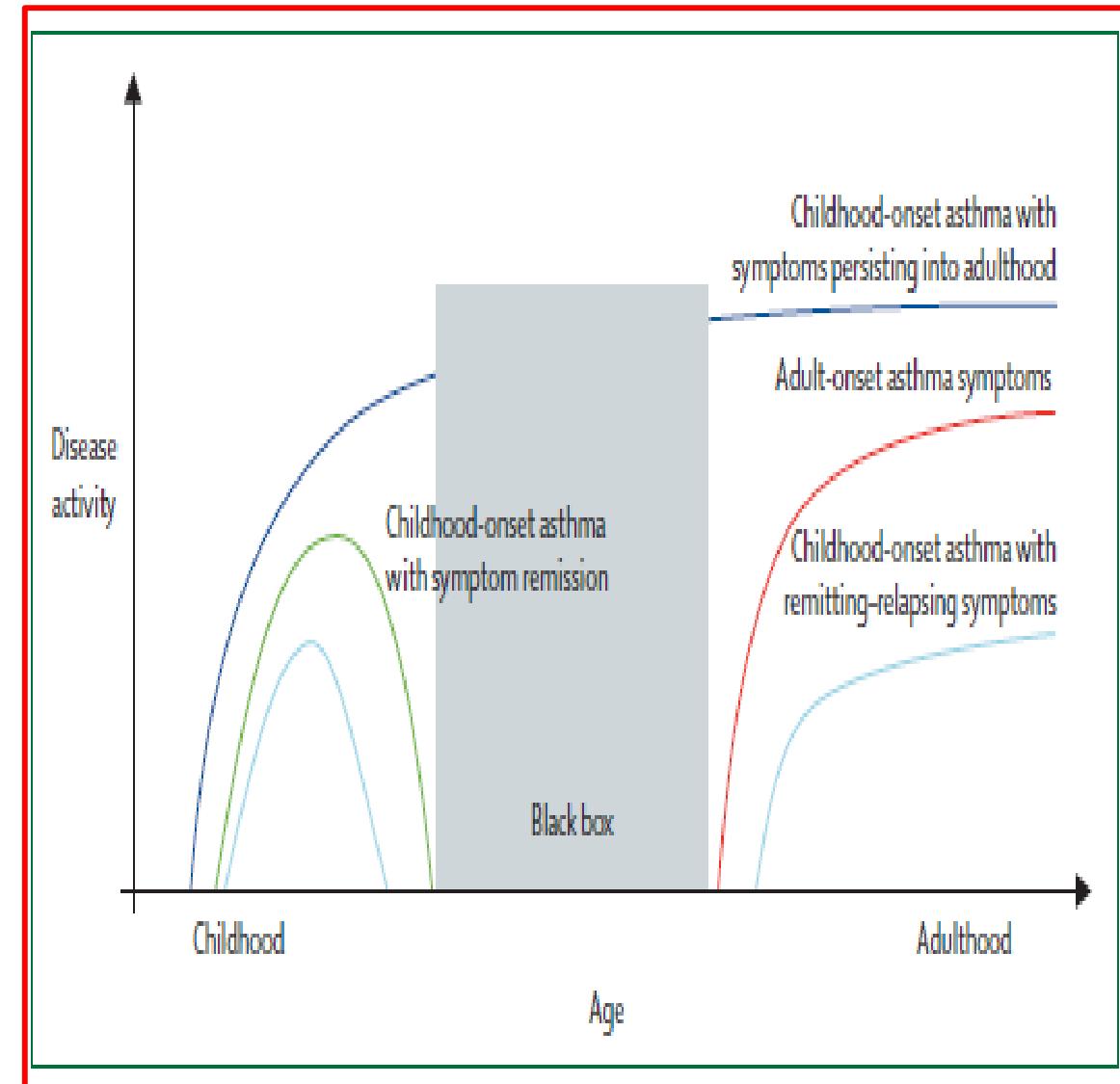
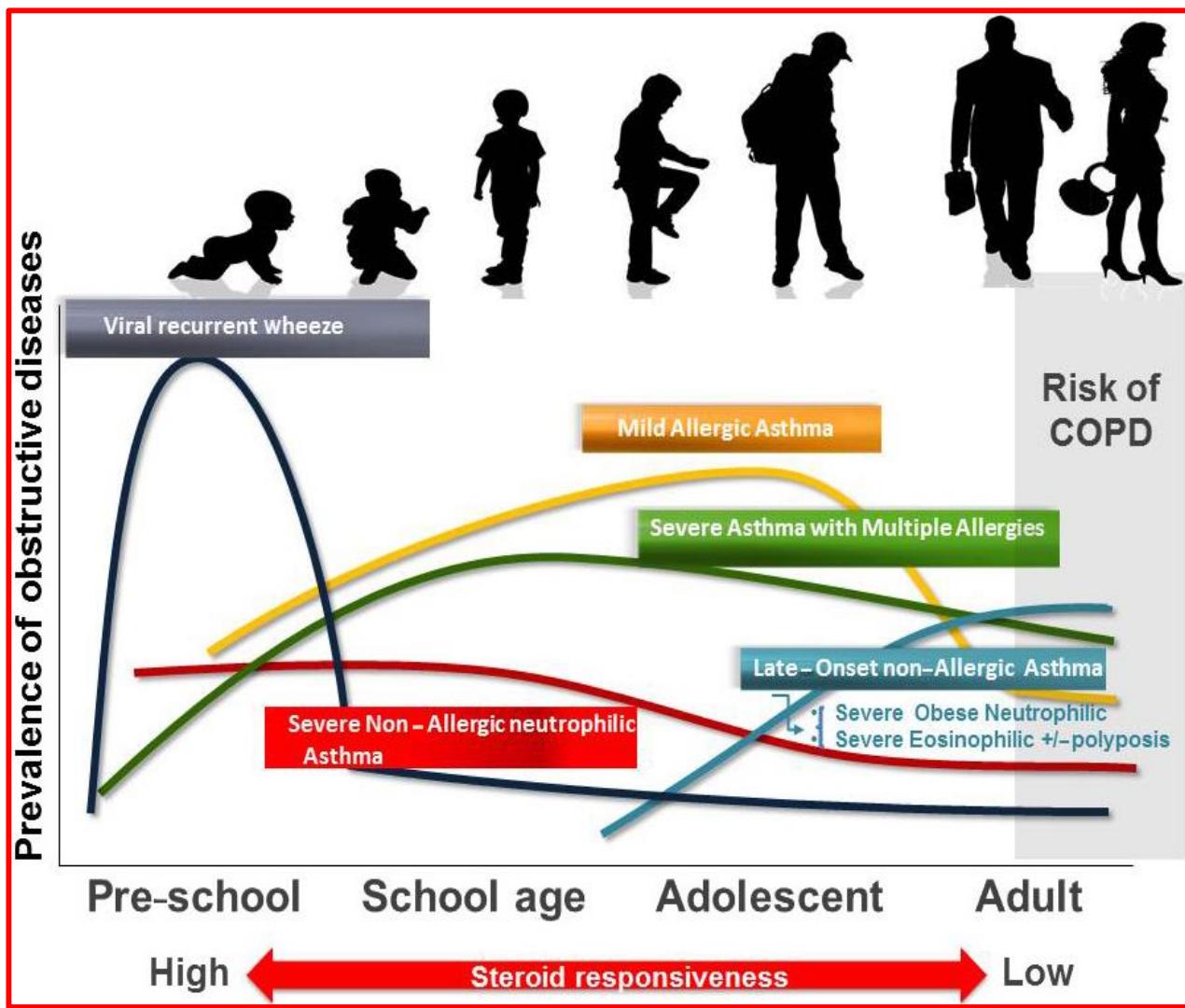
# Design

- Starting from the definition
- Inflammation
- Phenotypes and endotypes

# Multifactorial process

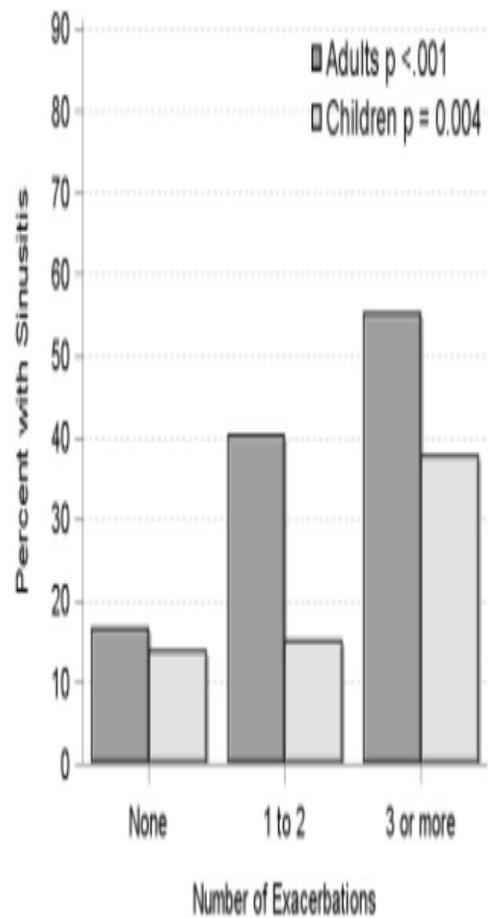


# Arising questions: From childhood to adulthood

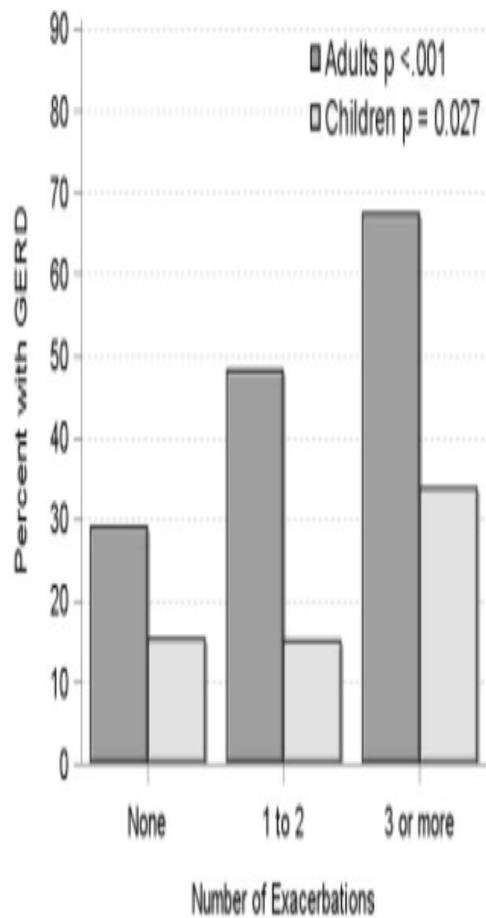


# The evidence : Frequent exacerbator

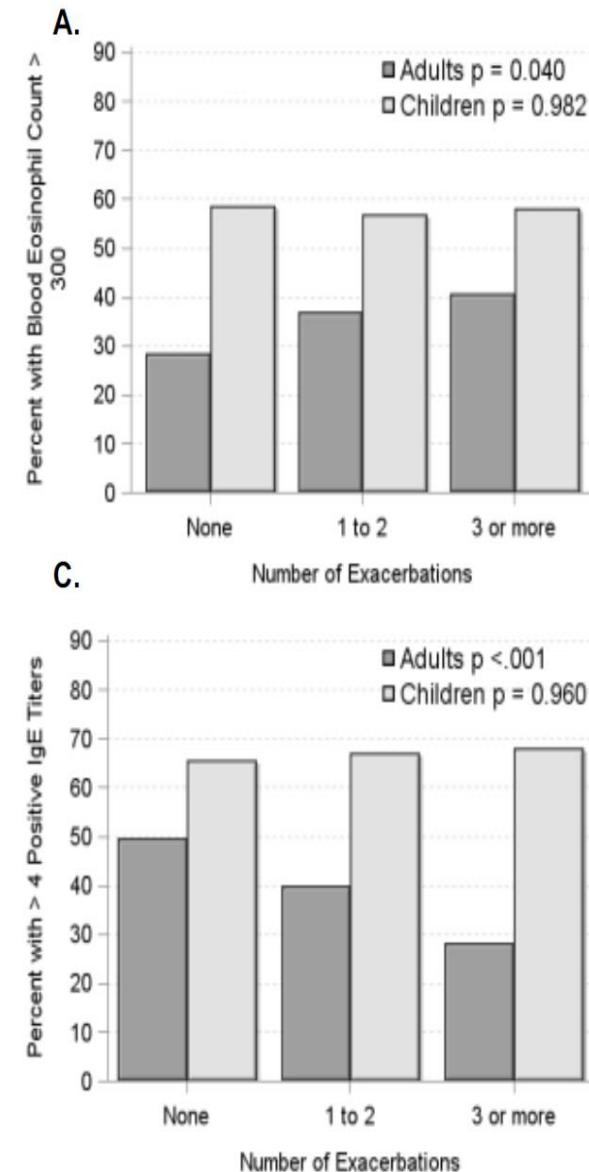
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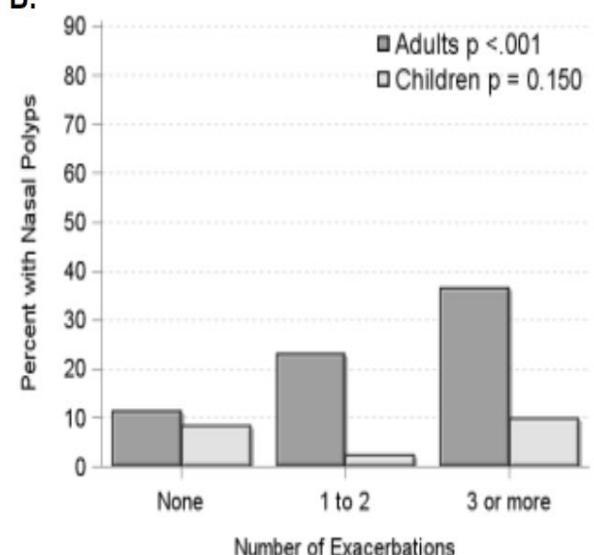
B.



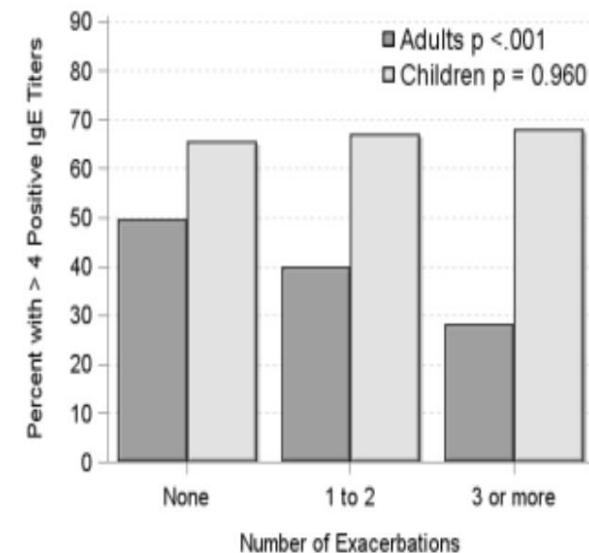
A.



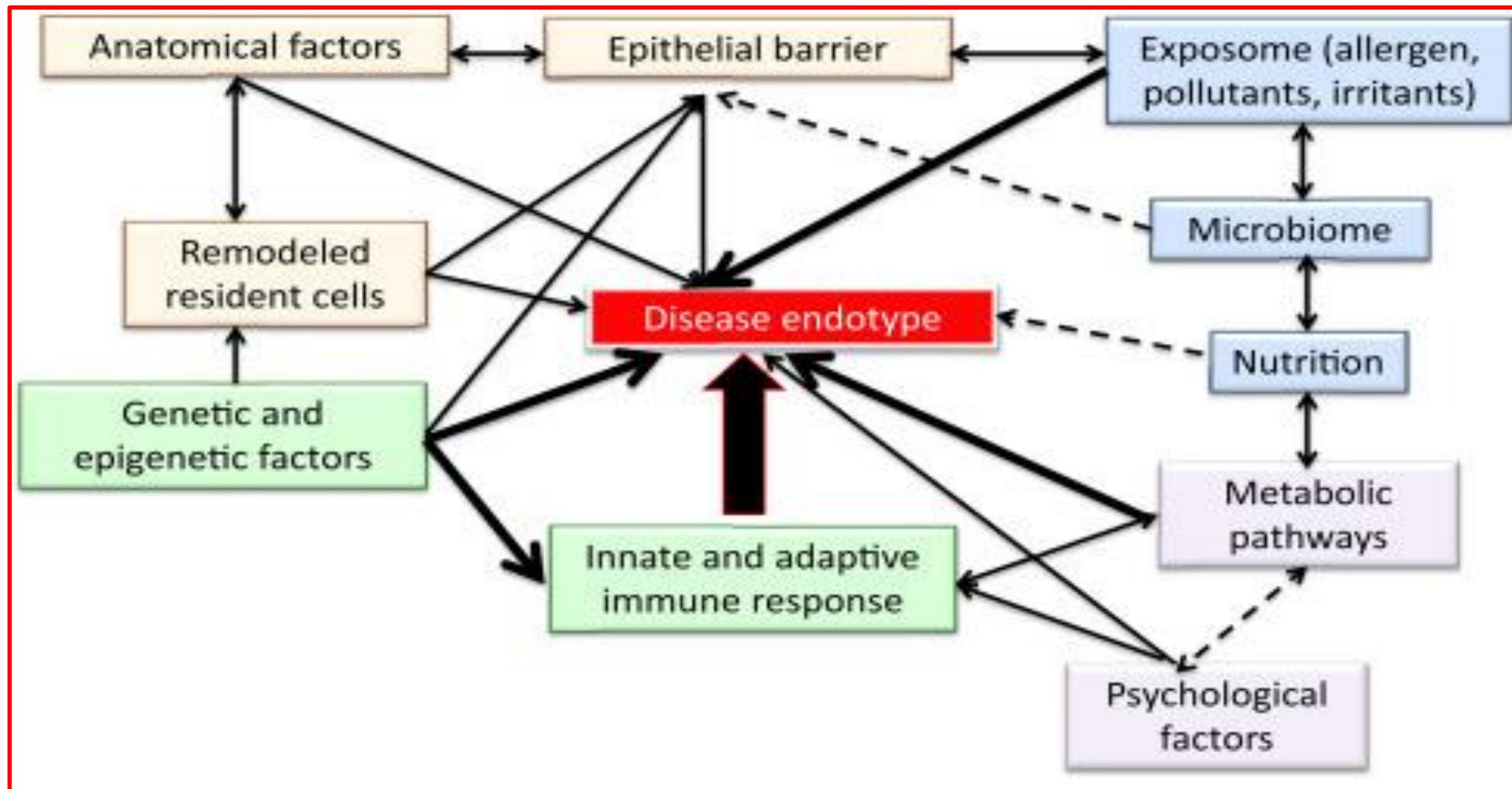
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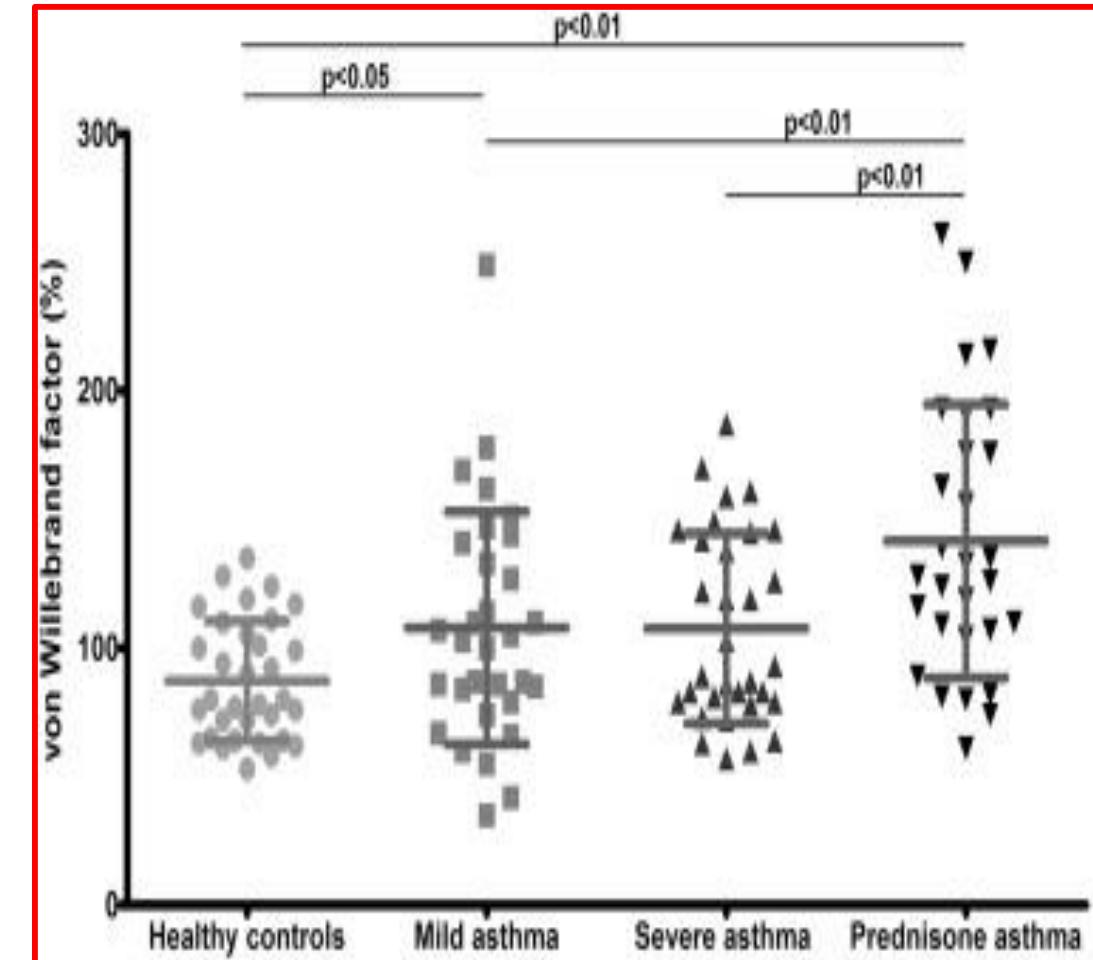
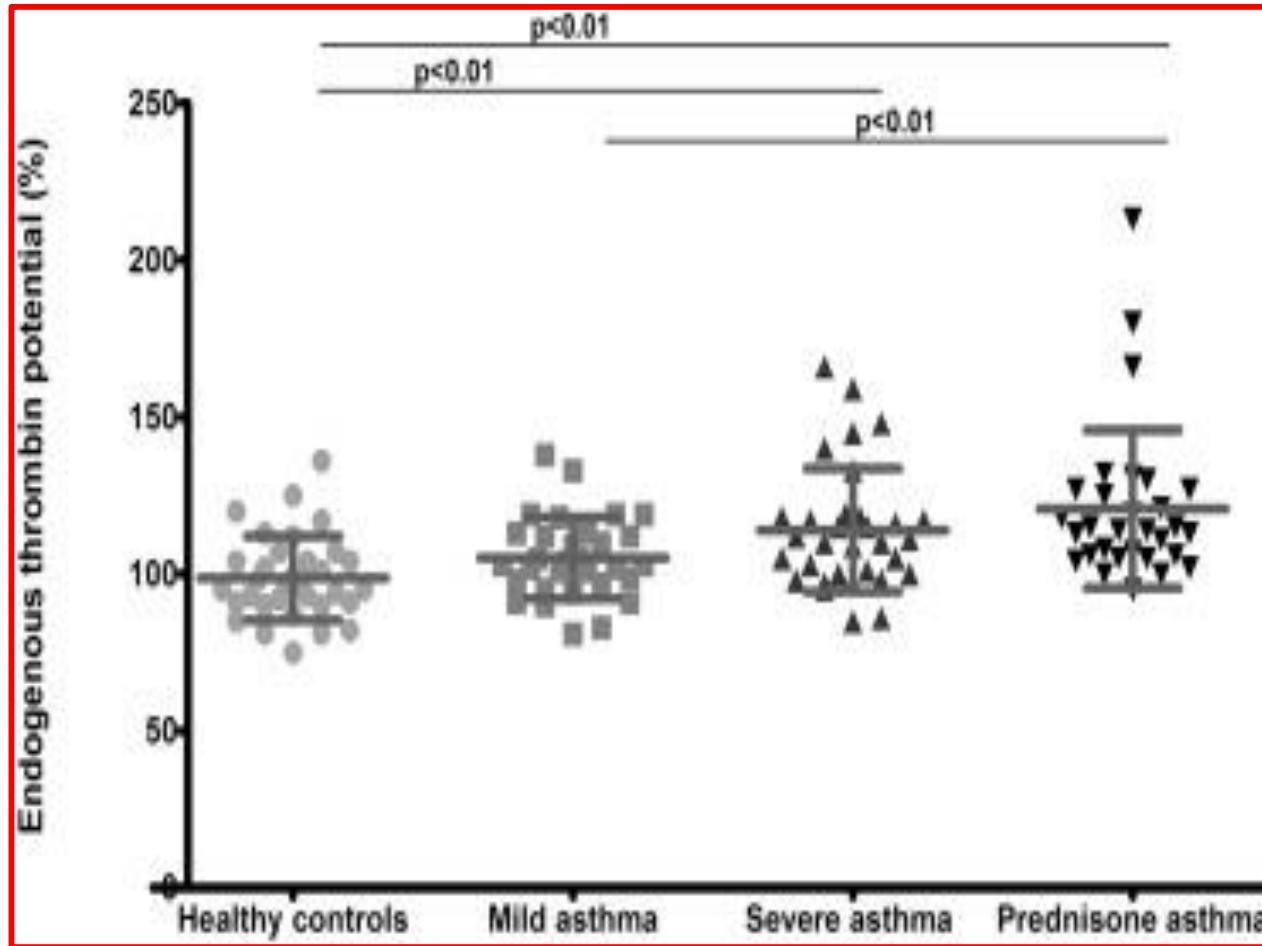
C.



# Overcoming the simplicity



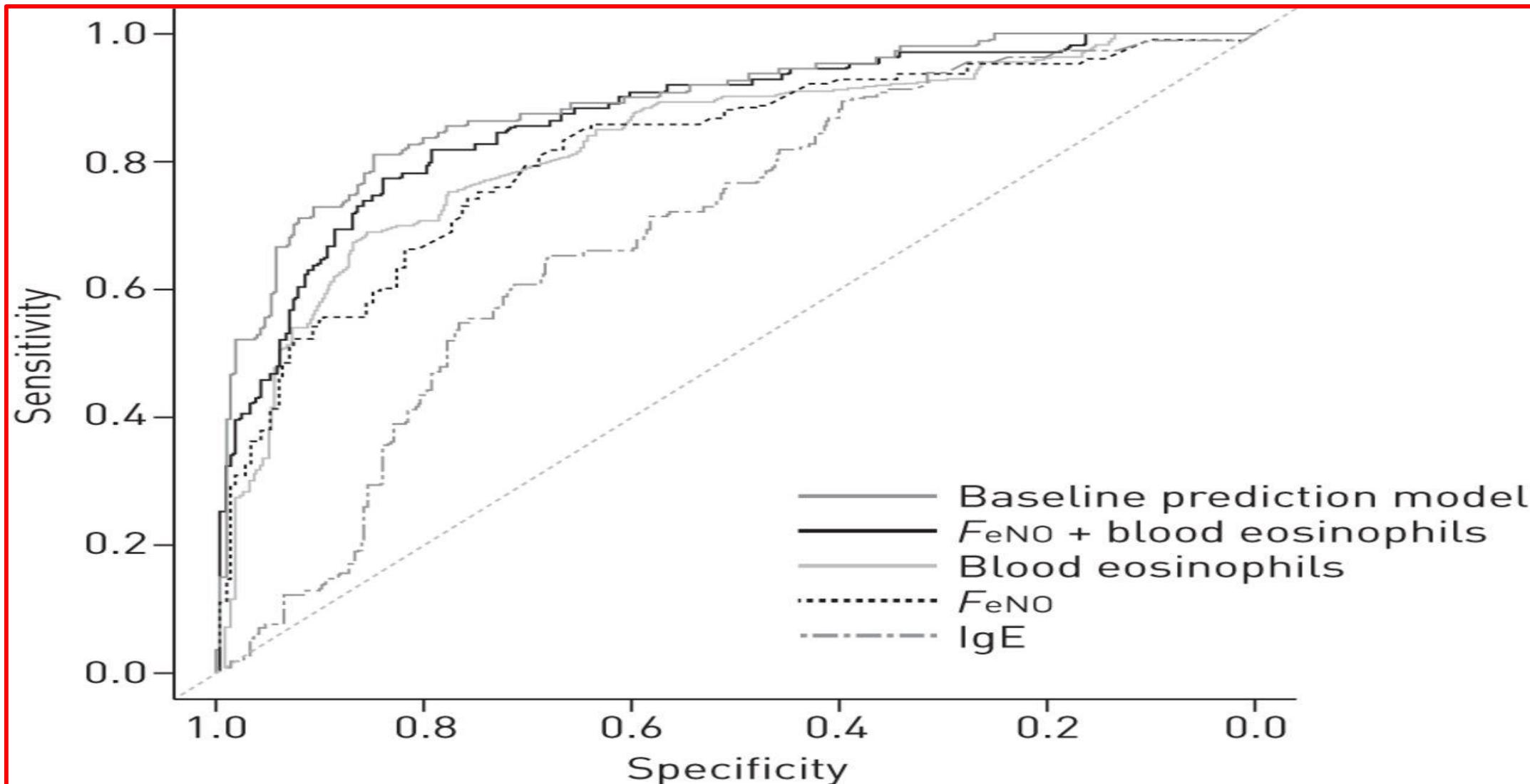
# An interesting endotype: Increased prothrombotic status



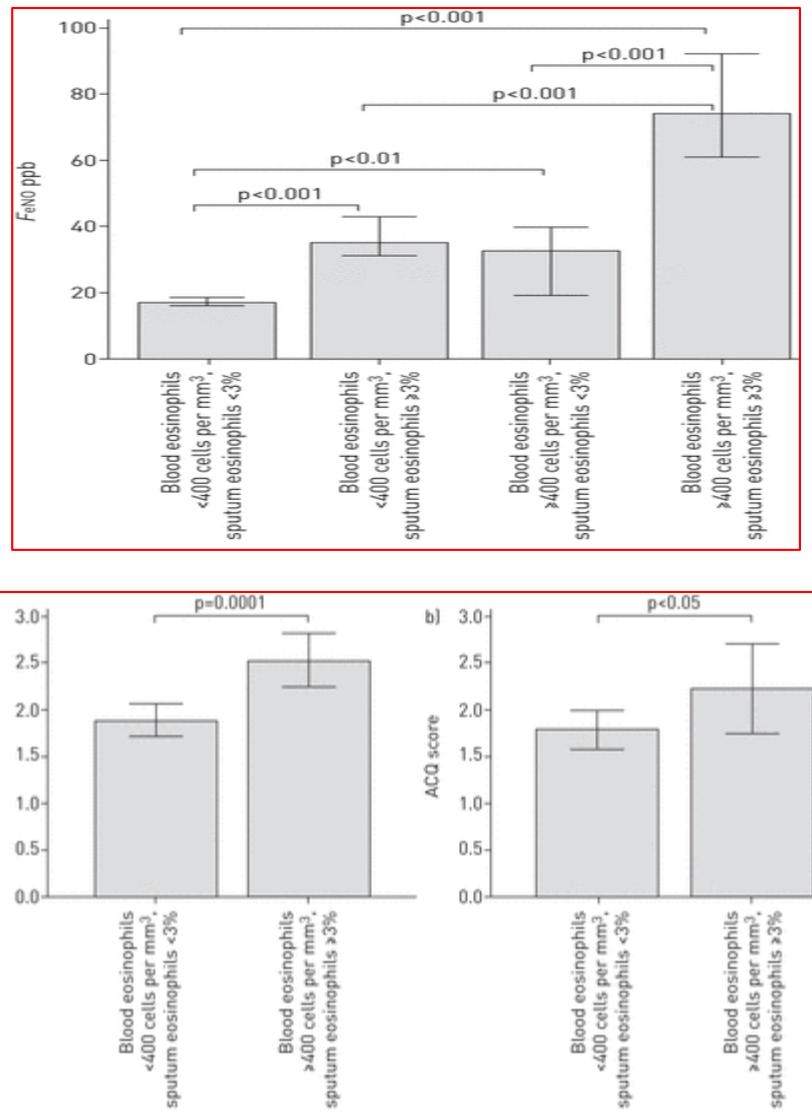
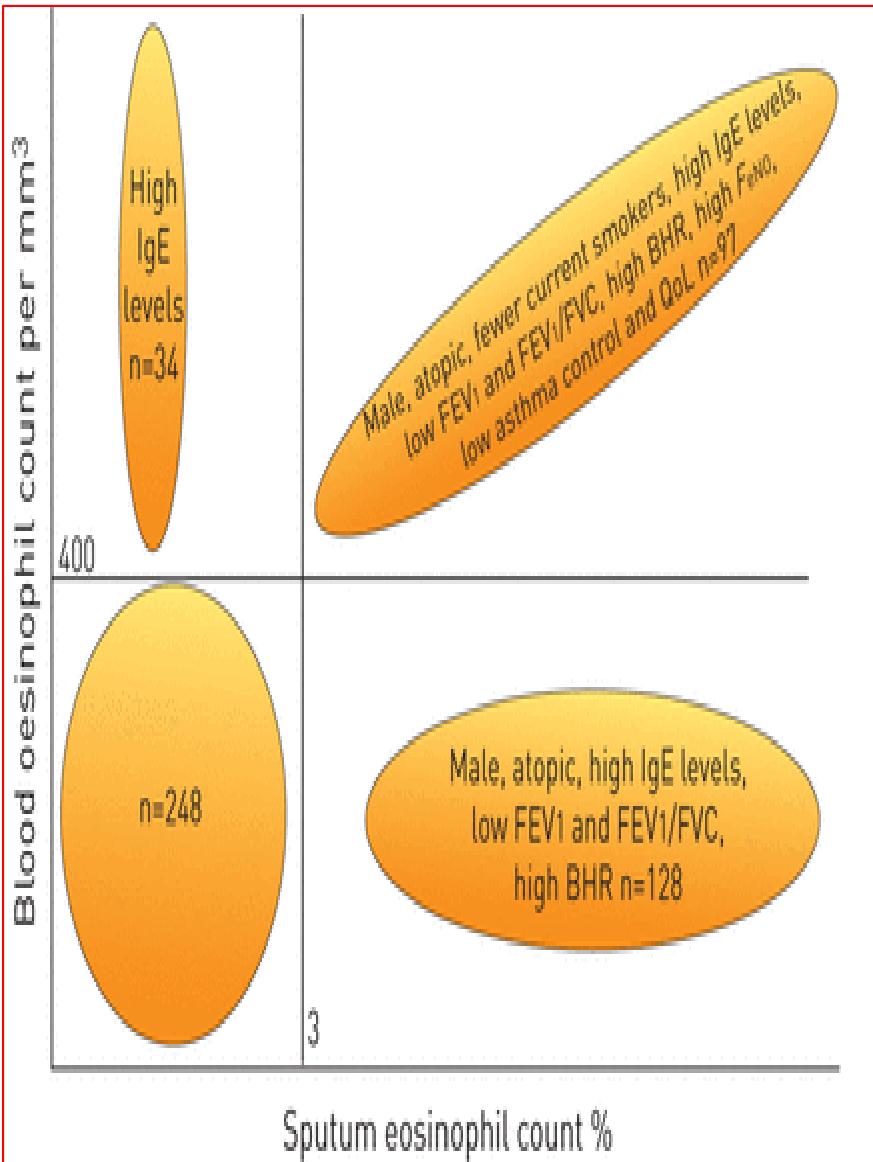
## Design

- Starting from the definition
- Inflammation
- Phenotypes and endotypes
- Inflammatory biomarkers

# Blood eosinophils



# Does site matter?



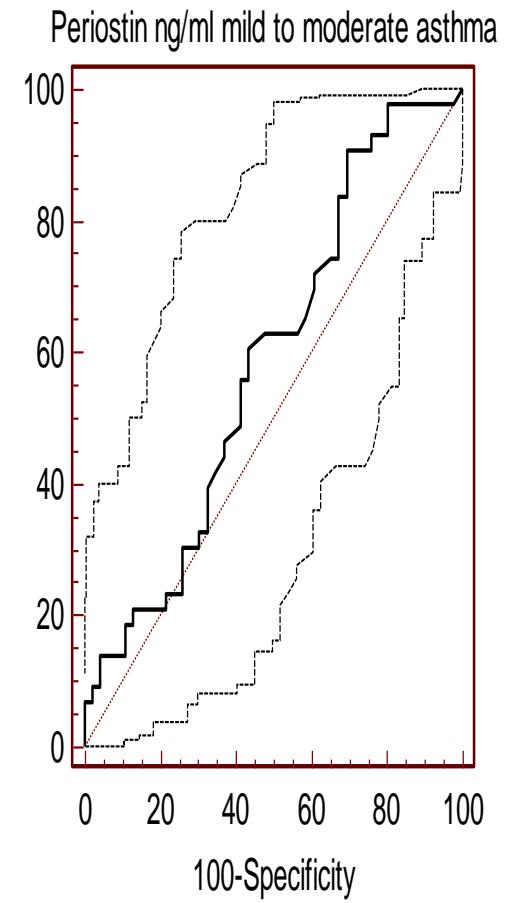
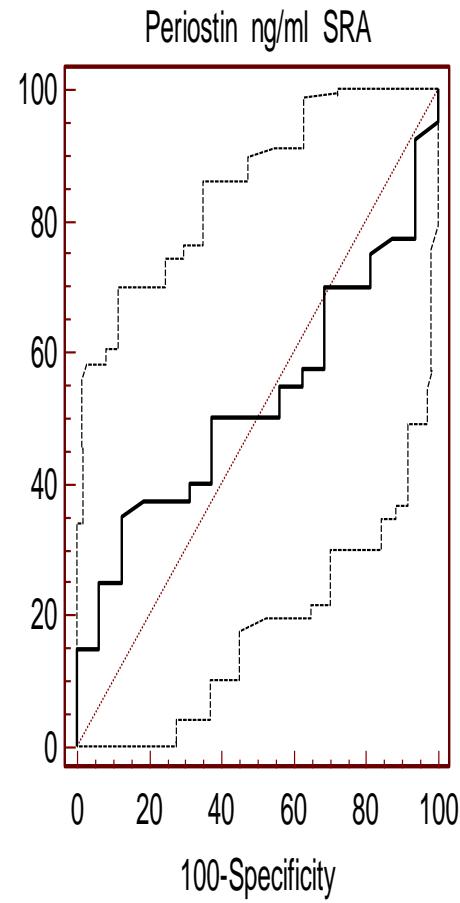
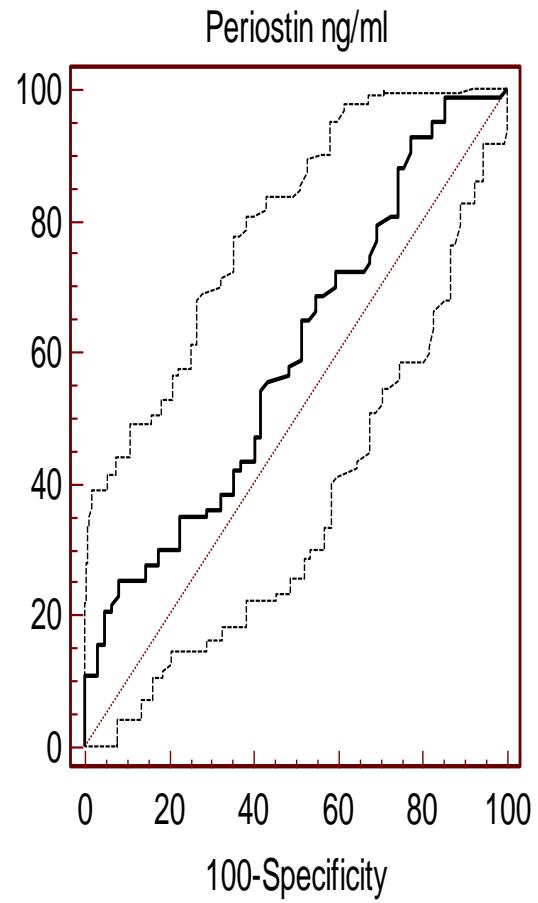
EDITORIAL  
ASTHMA



## Airway and systemic eosinophilia in asthma: does site matter?

Konstantinos Kostikas, Eleftherios Zervas and Mina Gaga

# Periostin and Th2 composite index



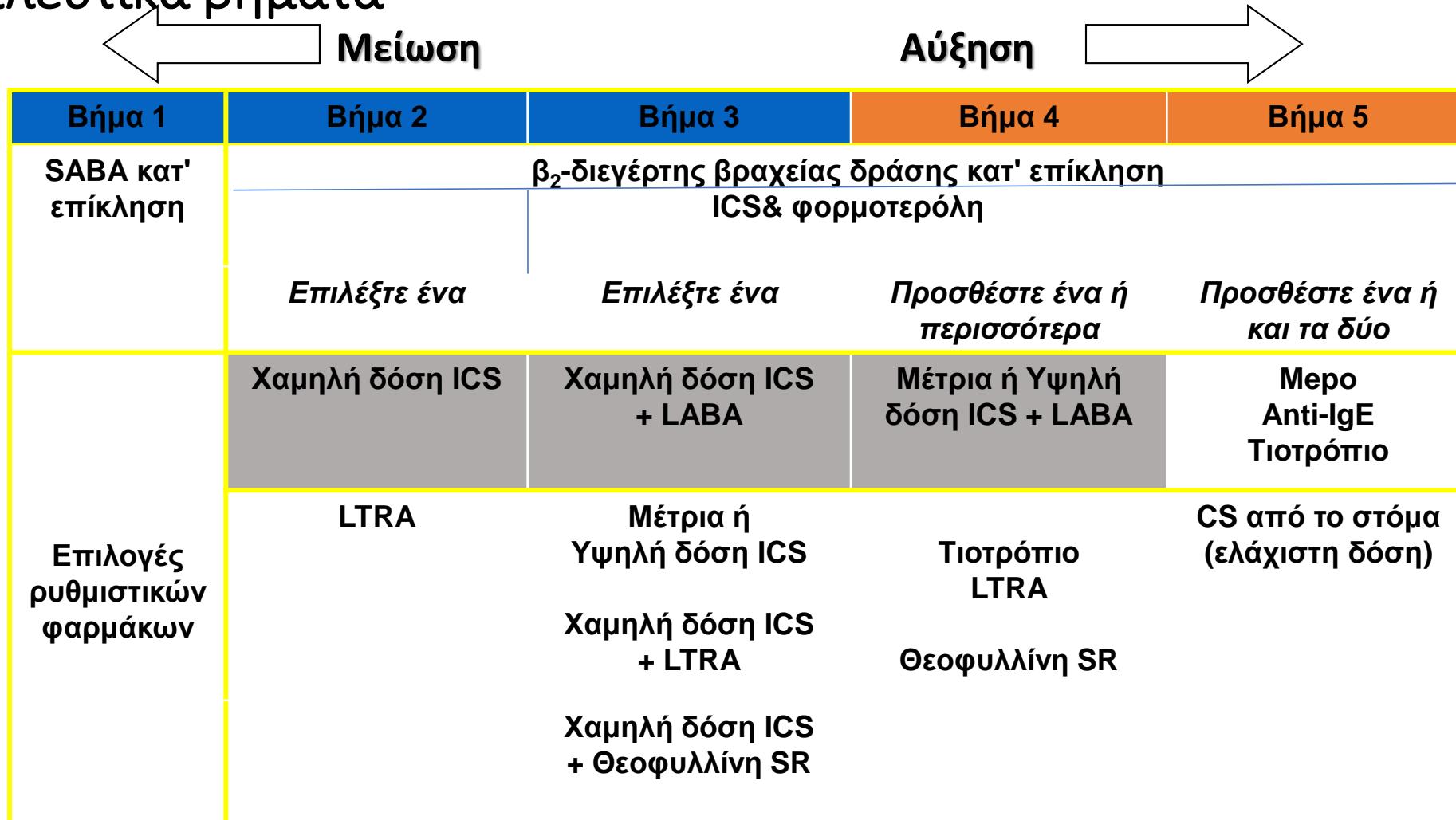
## Design

- Starting from the definition
- Inflammation
- Phenotypes and endotypes
- Inflammatory biomarkers
- Treatment options



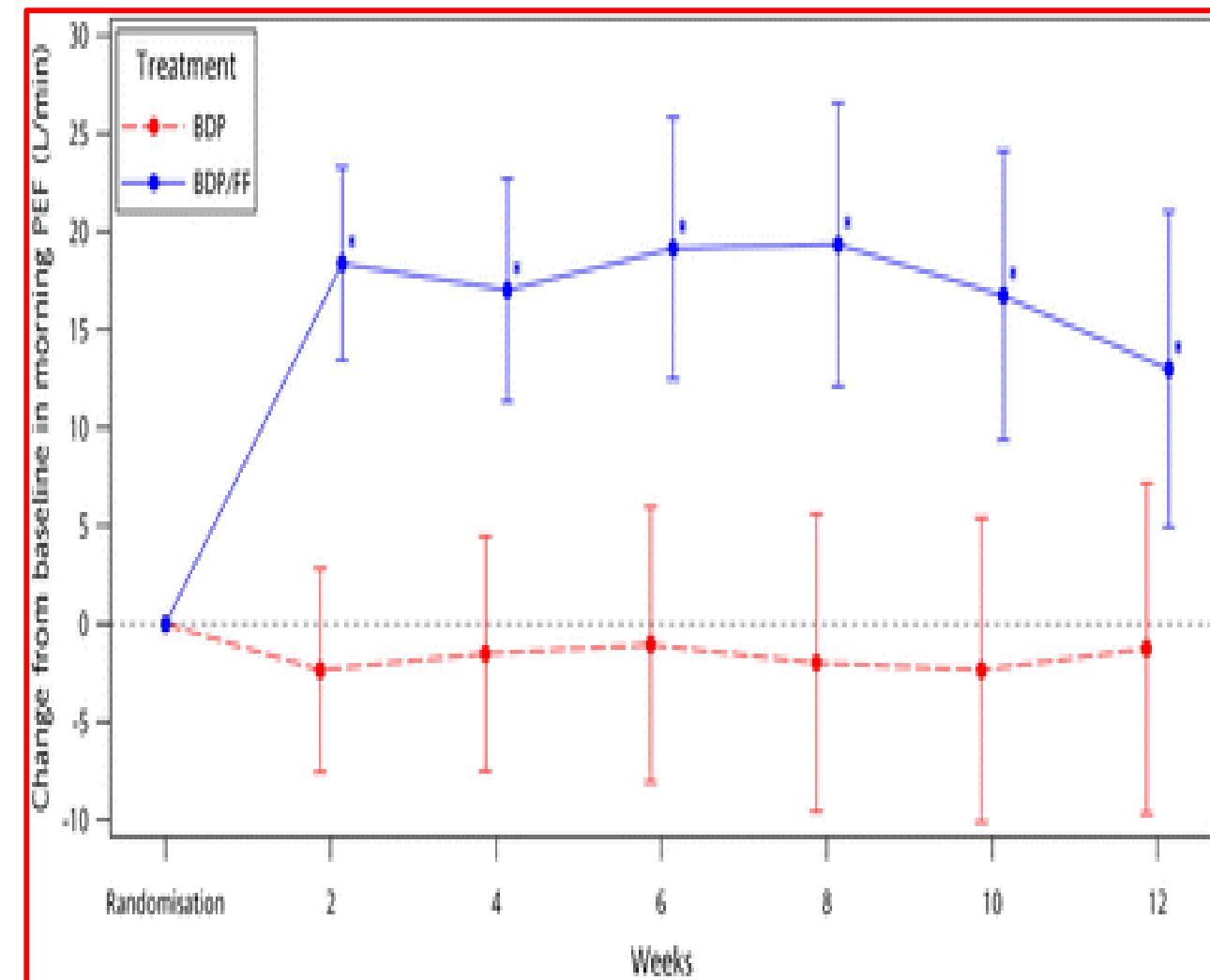
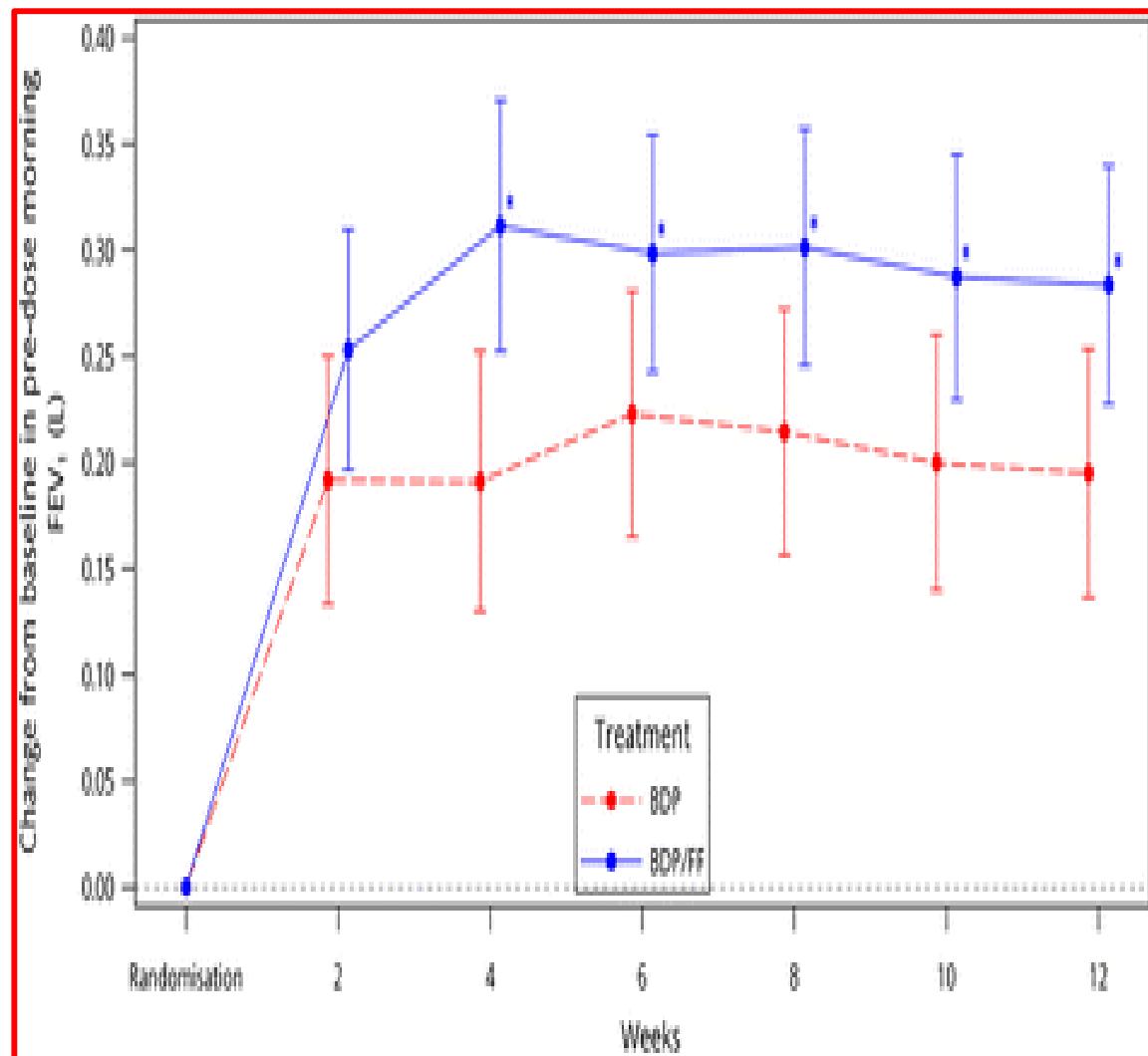
# GINA 2017

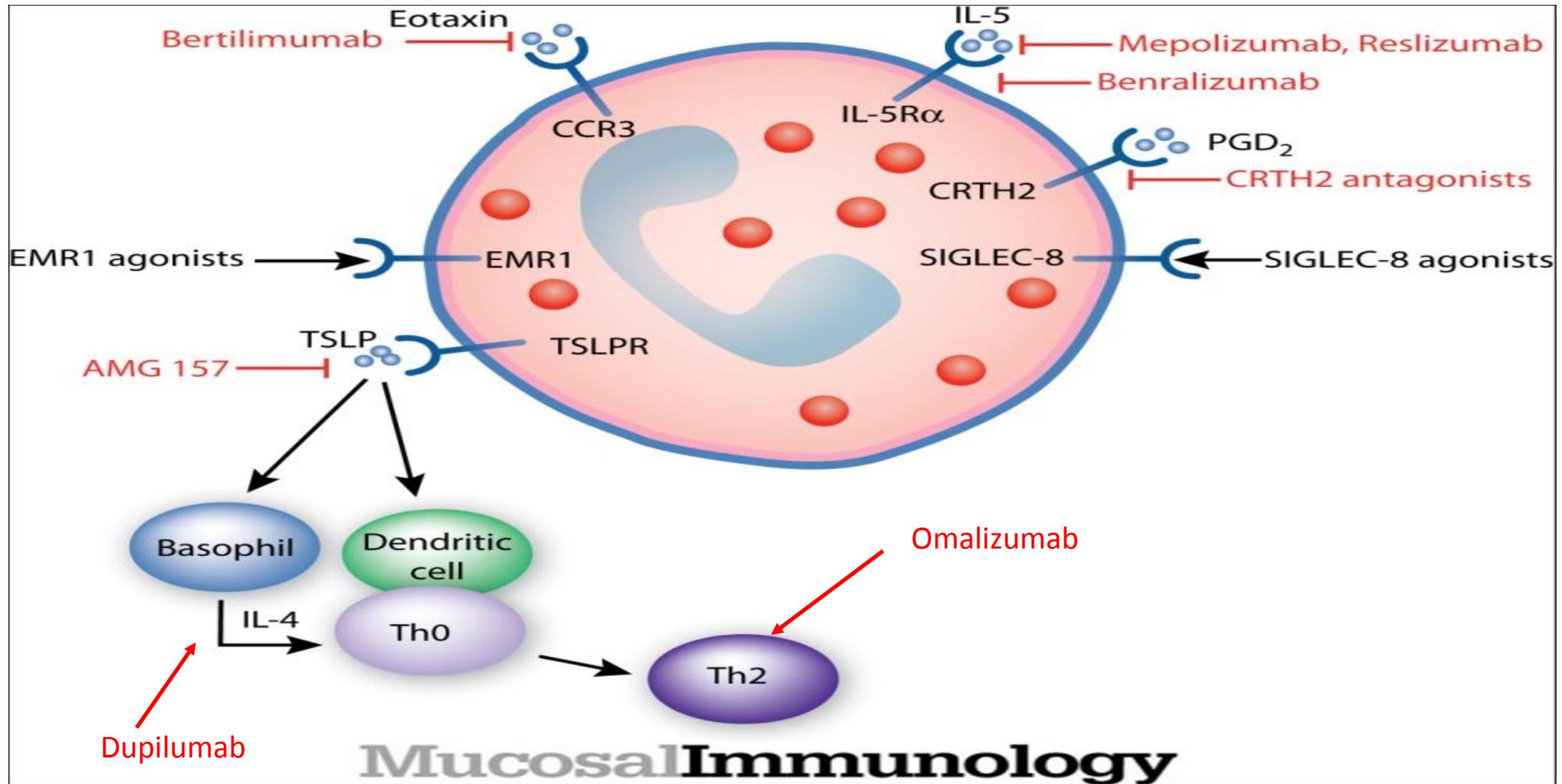
## Θεραπευτικά βήματα



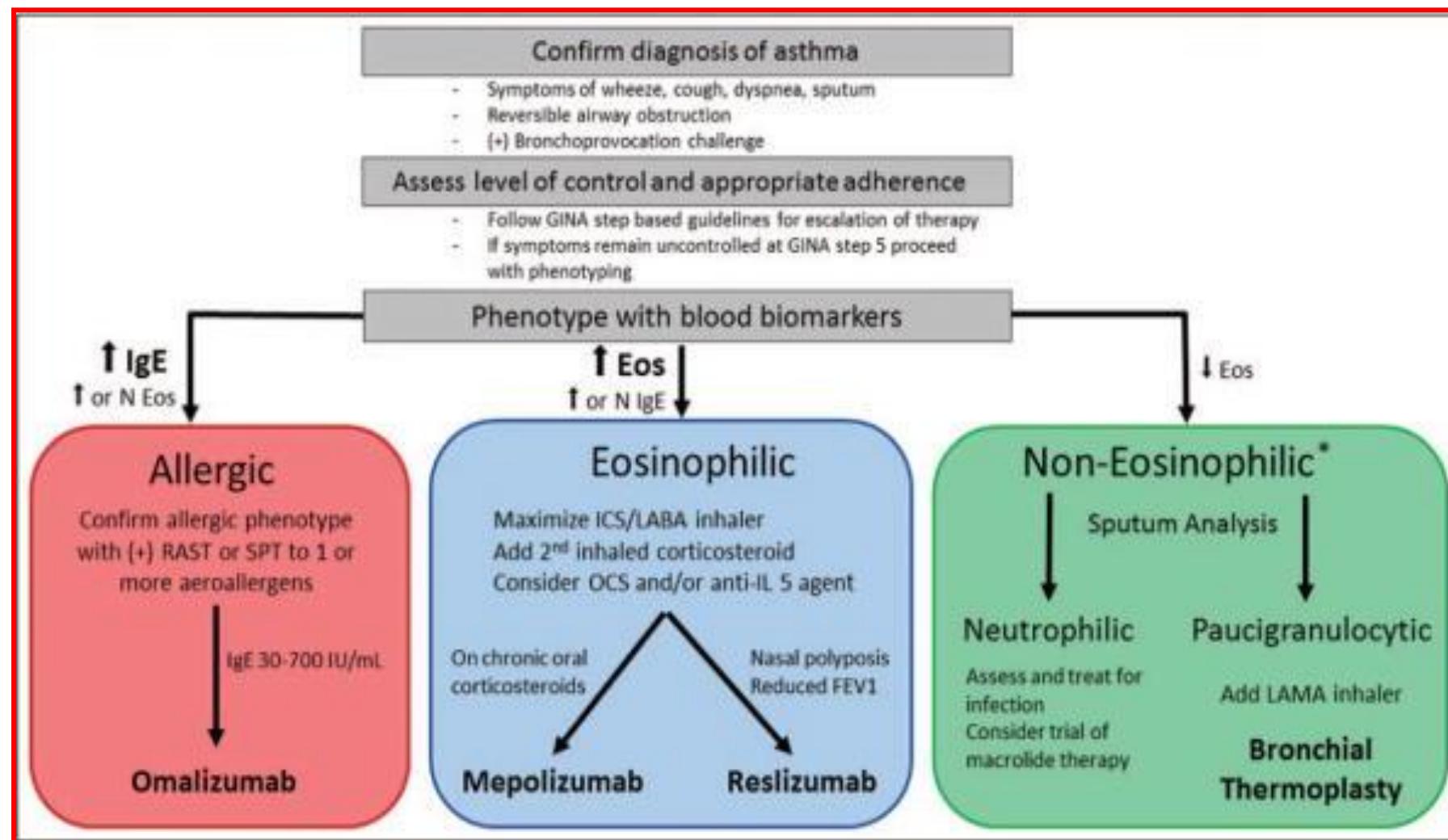
SABA: β<sub>2</sub>-διεγέρτης βραχείας δράσης, LABA: β<sub>2</sub>-διεγέρτης μακράς δράσης, ICS: εισπνεόμενα κορτικοστεροειδή, LTRA: ανταγωνιστές υποδοχέων λευκοτριενίων, CS: κορτικοστεροειδή, SR: βραδείας αποδέσμευσης  
Ανακουφιστικά: SABA, anticholinergics, formoterol, short-acting oral β<sub>2</sub>-agonists, short-acting theophylline

# Diagnosis confirmed: Start high doses of ICS

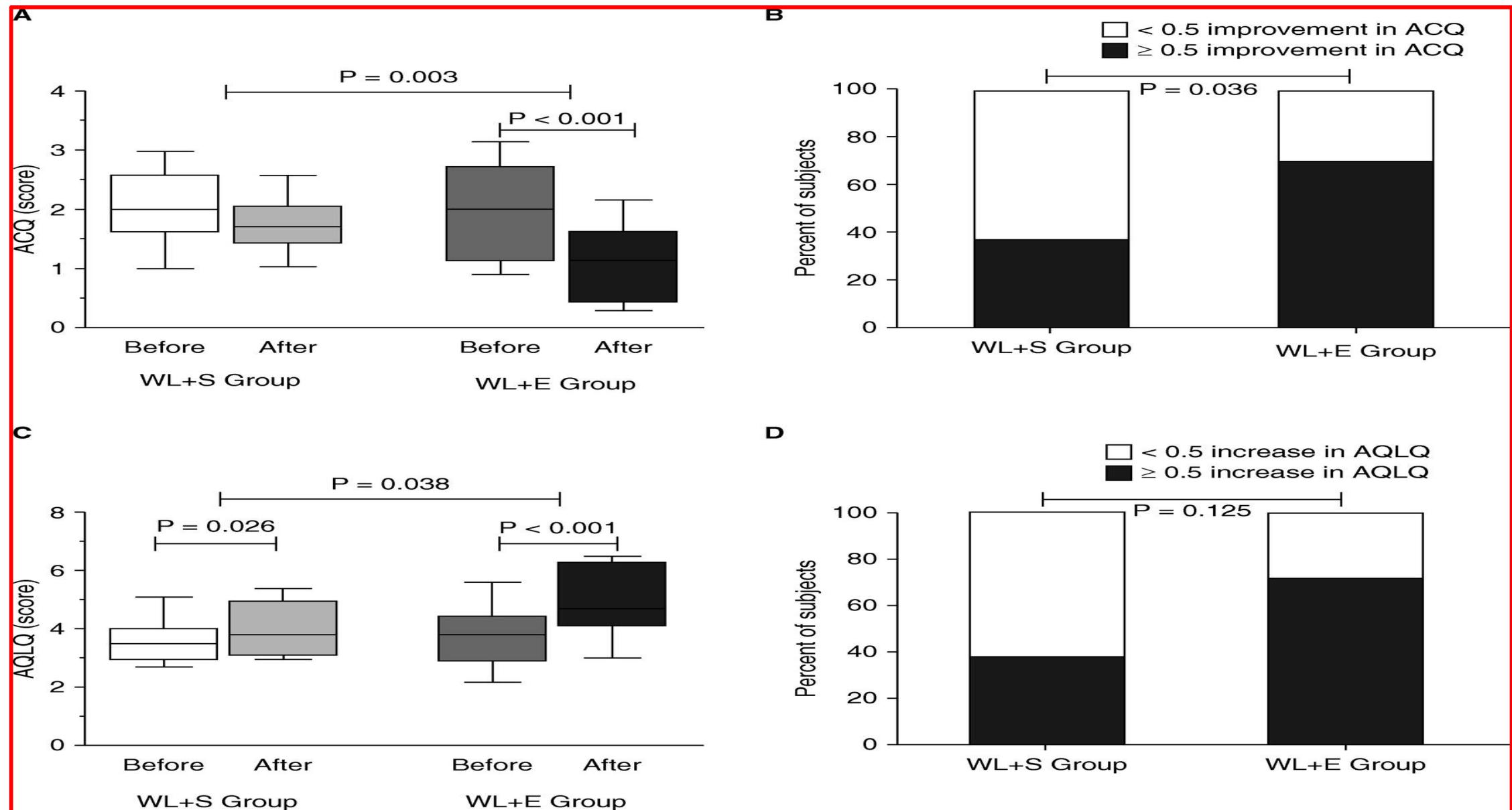




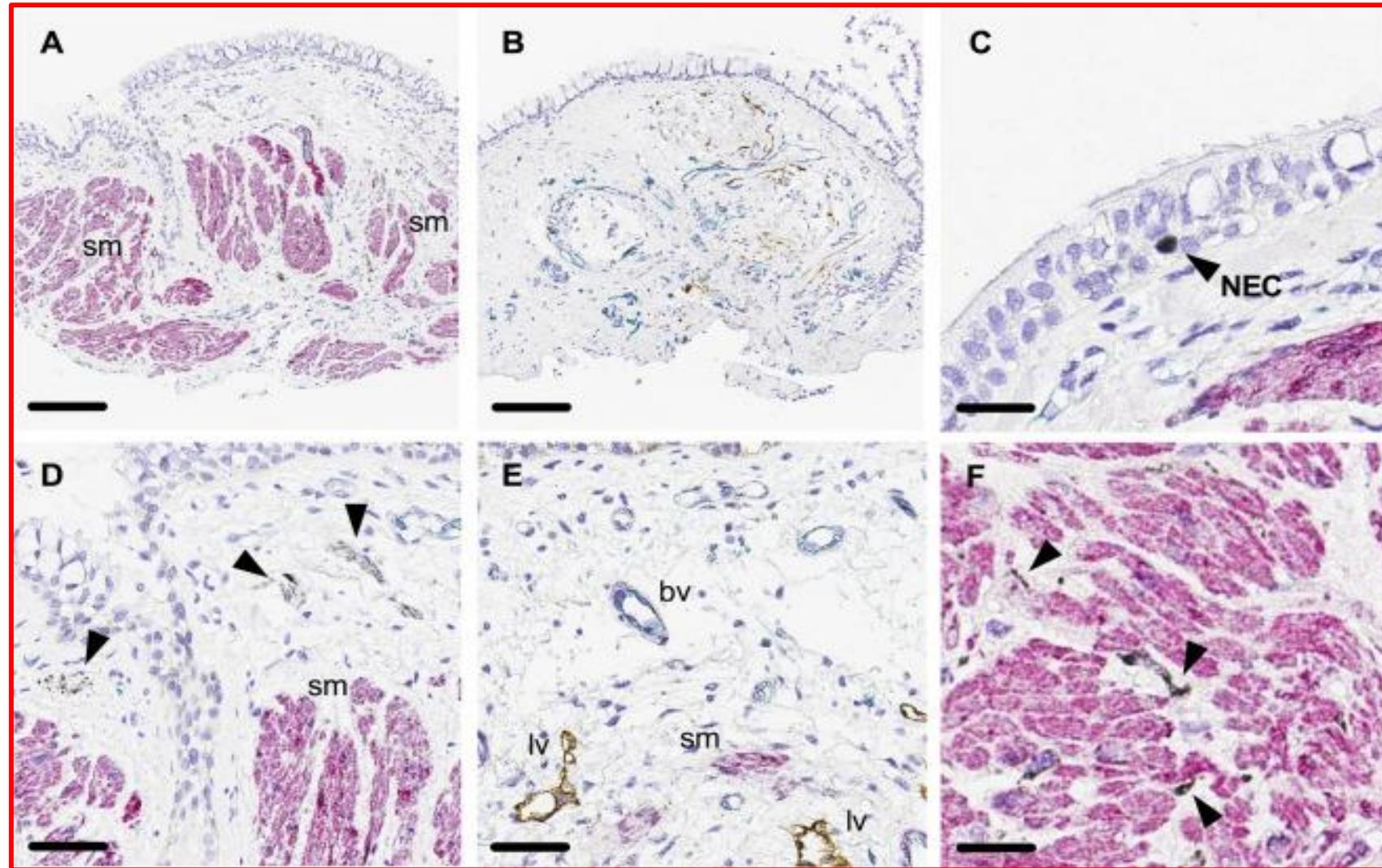
# Searching the specific endotype-establishing precision medicine...



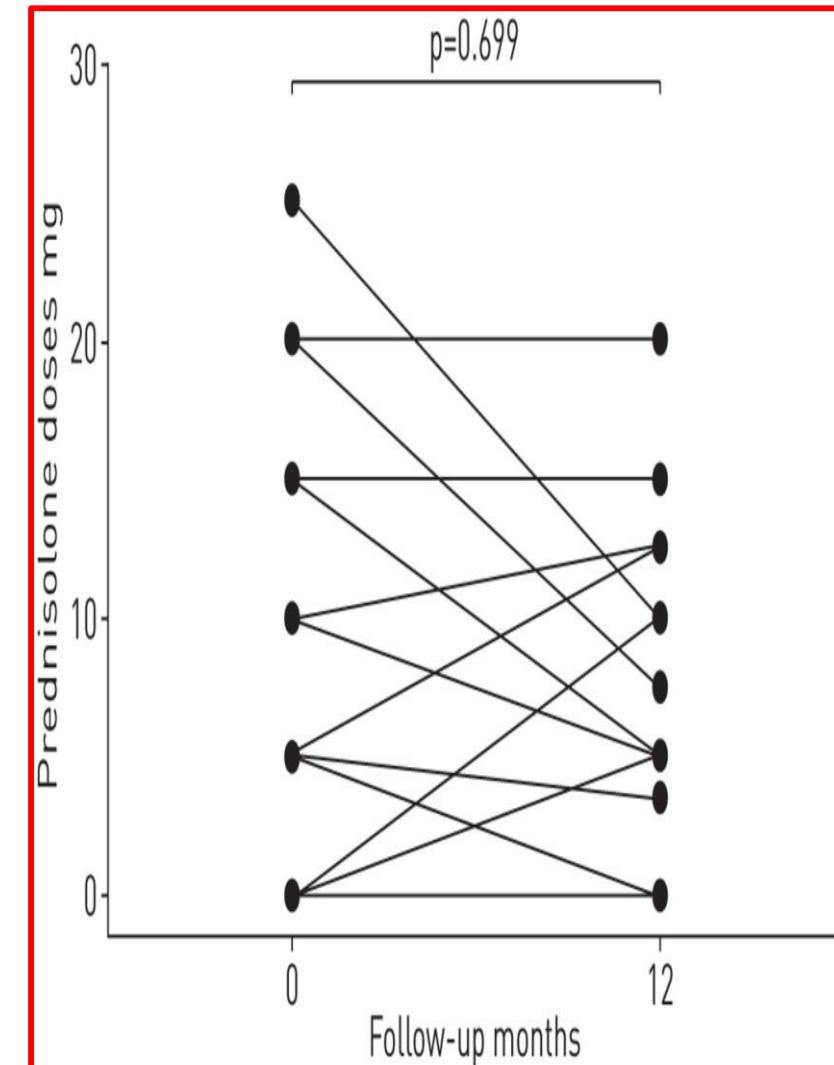
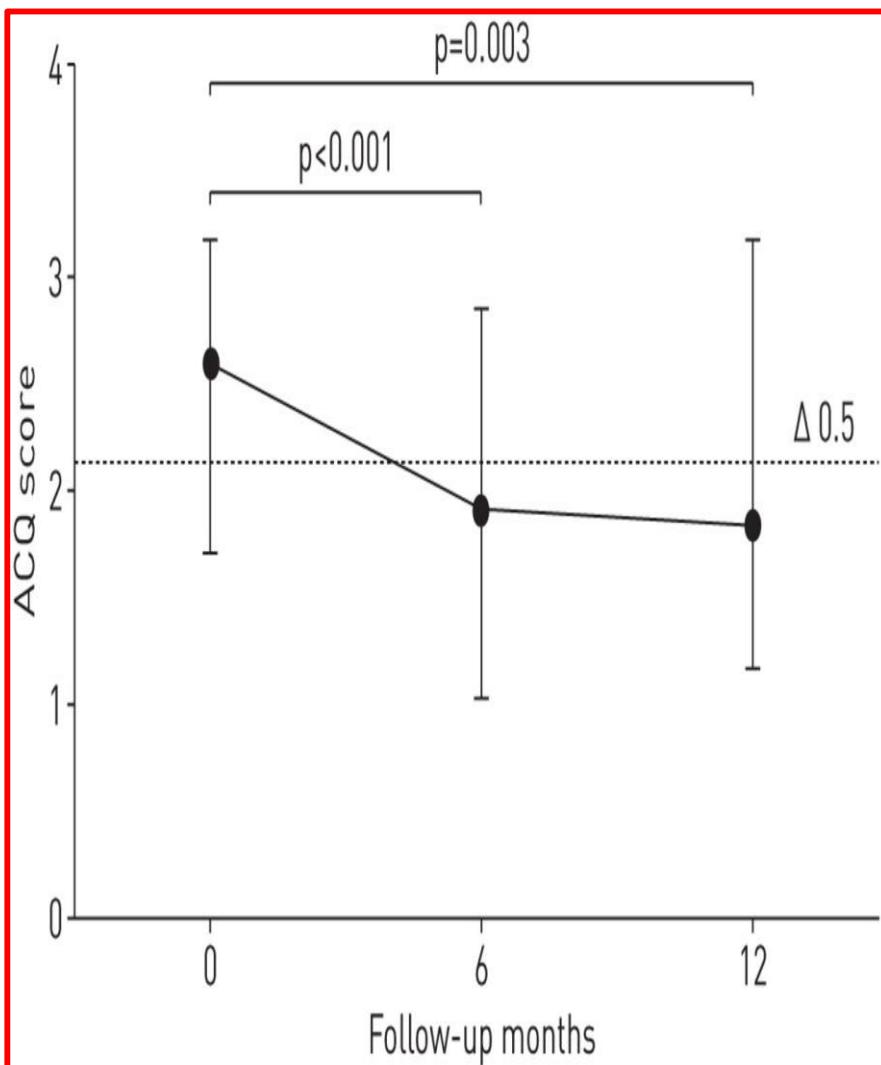
# A Life style personalized approach



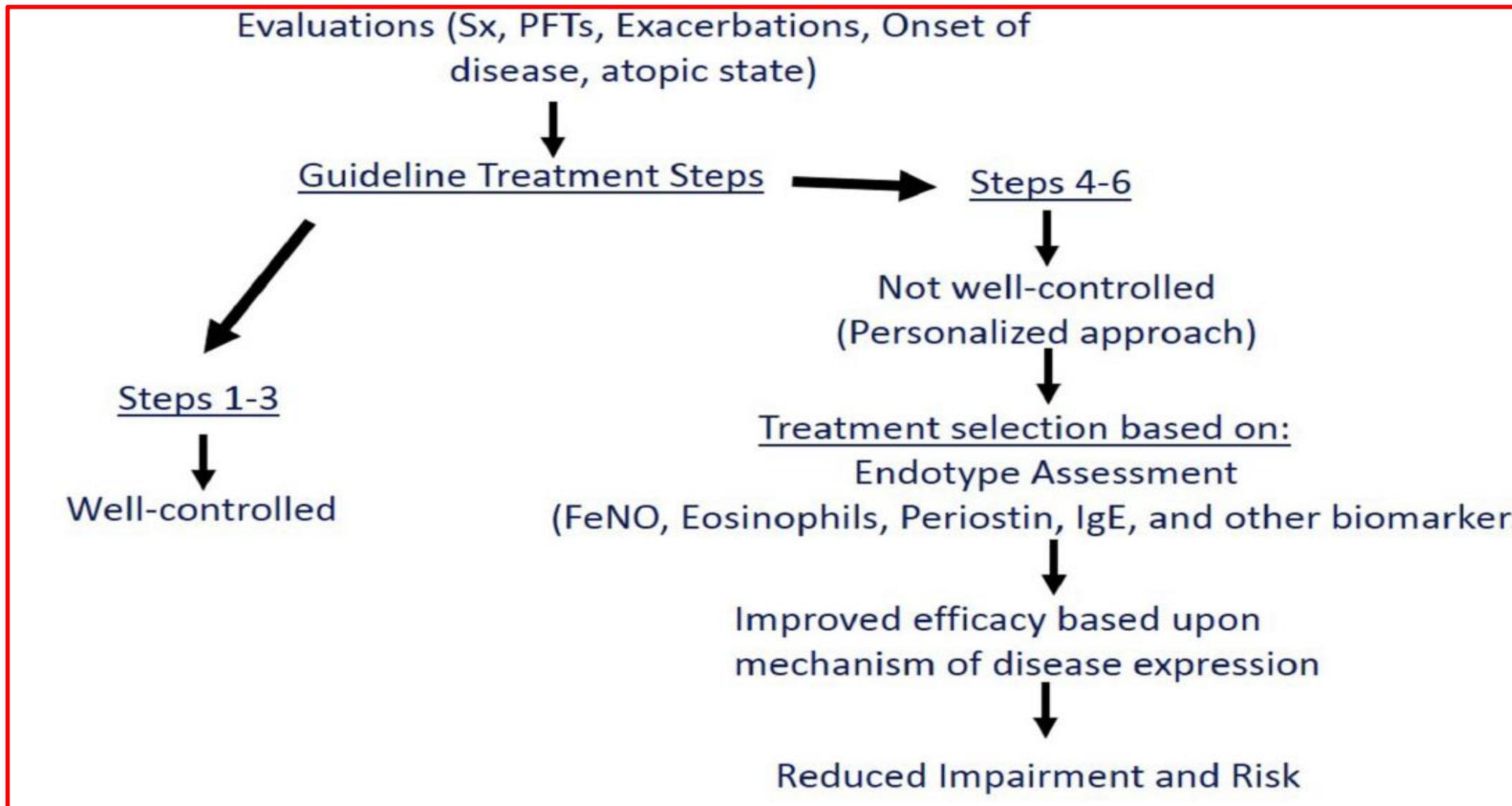
# Bronchial thermoplasty: Targeting ASM irrespective of the inflammatory process?



## SRA ask for specialists



# A different approach



## Messages

- Confirm the diagnosis
- Use the criteria
- Start with ICS
- Consider endotypes and precision medicine
- Future ... always promising