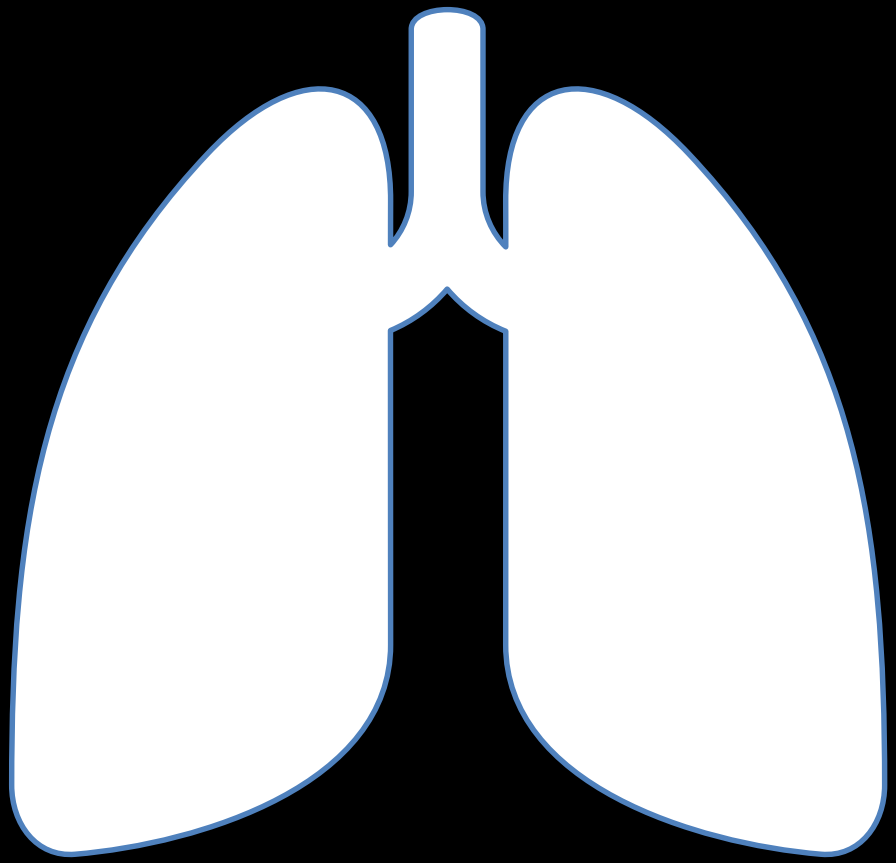
The Asthma COPD Overlap Syndrome

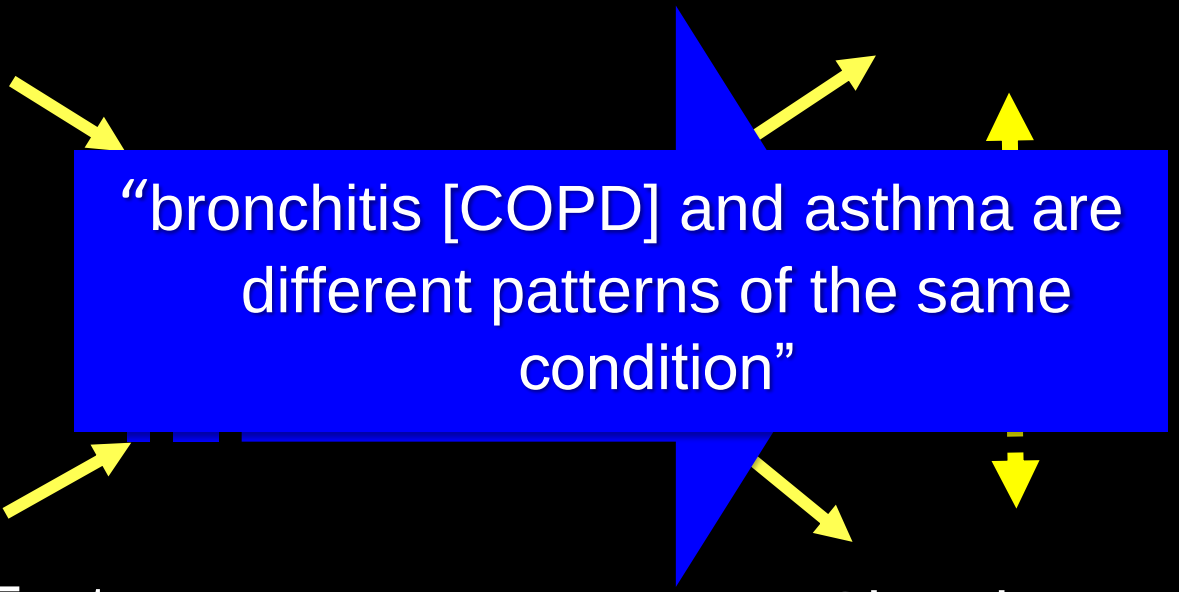


Joel E. Nieves Scharon, MD
Pulmonary and Critical Care Medicine
San Juan City Hospital
Instituto Neumologico de PR

The “Dutch” Hypothesis

Genetic susceptibility

Asthma



Environmental Factors
- Allergen
- Infection
- Smoking
- Air Pollution

Chronic Obstructive Pulmonary Disease

Orie, Sluter, DeVries, et al. The Host Factor In Bronchitis,
Orie, Sluiter, Eds. Bronchitis, Netherlands, Royal van Gorcumn Press, 1961

The reason why it is difficult to differentiate asthma from COPD

In 1995, the American Thoracic Society stated:

> … it may be impossible to differentiate patients with asthma whose airflow obstruction does not remit completely from persons with chronic bronchitis and emphysema with partially reversible airflow obstruction and bronchial hyperresponsiveness.[61]

Overlap: Why is it a problem?

1. It is common
2. Diagnostic uncertainty for doctors; confusion for patients
3. Severe form of CAO: natural history, treatment non-response (ICS and OCS), high resource use
4. Not covered in guidelines / strategy documents
5. Not studied in clinical trials

Suggested names for Asthma COPD Overlap

- Asthma-COPD phenotype
- Mixed asthma-COPD
- Mixed COPD-asthma
- Asthma with fixed airflow obstruction
- COPD with asthmatic component
- Eosinophilic COPD phenotype
- Hyper-reactive COPD phenotype

Coexistence of Asthma & COPD in young, middle-aged & elderly in general population

- Random general population: Gene Environment Interactions in Respiratory Diseases (GEIRD) study
  - Screening questionnaire
  - Doctor diagnosed asthma or COPD

Age class (years)	Asthma only % (95% CI)	Asthma + COPD % (95% CI)	COPD only % (95%CI)
20 - 44	8,2 (7.5-9.0)	1.6 % (1.3-2.0)	3.3 (2.8-3.8)
45 - 64	4.9 (4.0-5.9)	16.5%	5.7 (4.7-6.7)
65 - 84	2.9 (1.8-4.0)	21.7%	13.3 (11.1-15.5)

- Females (RR 1.63)
- More symptomatic: breathless, cough & wheeze
  - More exacerbations
  - More hospitalizations

De Marco R, et al, PLOS ONE 2013; 8:5.e62985

COPDGene Study: COPD with history of Asthma

- Poorer quality of life (SGRQ)
- Higher probability of exacerbation in past year
- More frequent exacerbations
  OR 3.55 (95% CI: 2.19-5.75) p<0.001
- More rapid lung function decline
- More refractory to ICS and OCS
- Higher OCS requirement

Hardin M, *et al, Respir Res* 2011;12:127.

POPE – COPD Phenotypes

Figure 2. **Recruitment of COPD subjects according participating countries (N = 3 745)**

Country	N (%)
Serbia	550 (14.7%)
Poland	477 (12.7%)
Czech Republic	453 (12.1%)
Hungary	407 (10.9%)
Russia	381 (10.2%)
Slovakia	370 (9.9%)
Croatia	362 (9.7%)
Austria	357 (9.5%)
Bulgaria	311 (8.3%)
Slovenia	70 (1.9%)
Latvia	7 (0.2%)

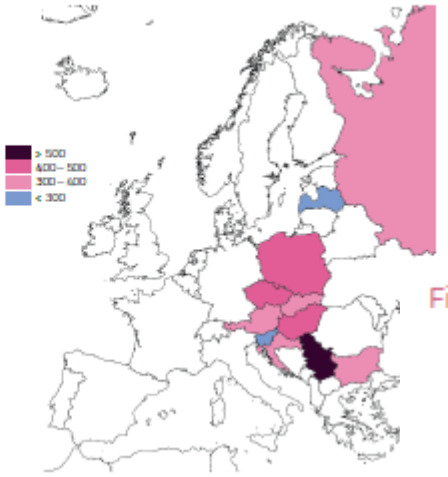
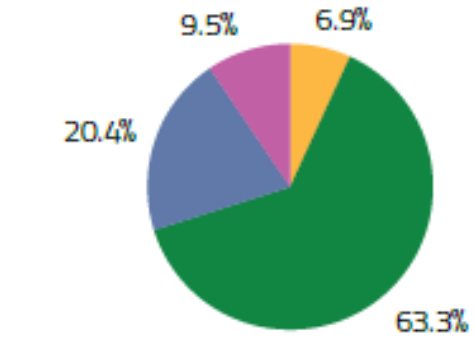


Figure 4. **Phenotypes of COPD (N = 3 366)**



- ACOS (N = 231)
- Non-exacerbator (N = 2 129)
- Frequent exacerbator with CB (N = 687)
- Frequent exacerbator without CB (N = 319)

Koblizek V, Milenkovic B, Barczyk A, et al. Eur Respir J 2017;49(5):

Population-based categorisation of patients with respiratory symptoms in New Zealand

Wellington Respiratory Survey: >50 years (N= 469) from random general population

Definitions used

Asthma

- post b.d ≥15% FEV_1, or
- PEF variability for 1 week, or
- physician diagnosis plus symptoms or reliever use in last 12 months

Emphysema

- Macroscopic emphysema on CT, or
- AFO with TLCO/V_A <LLN

Chronic Bronchitis

- British MRC definition

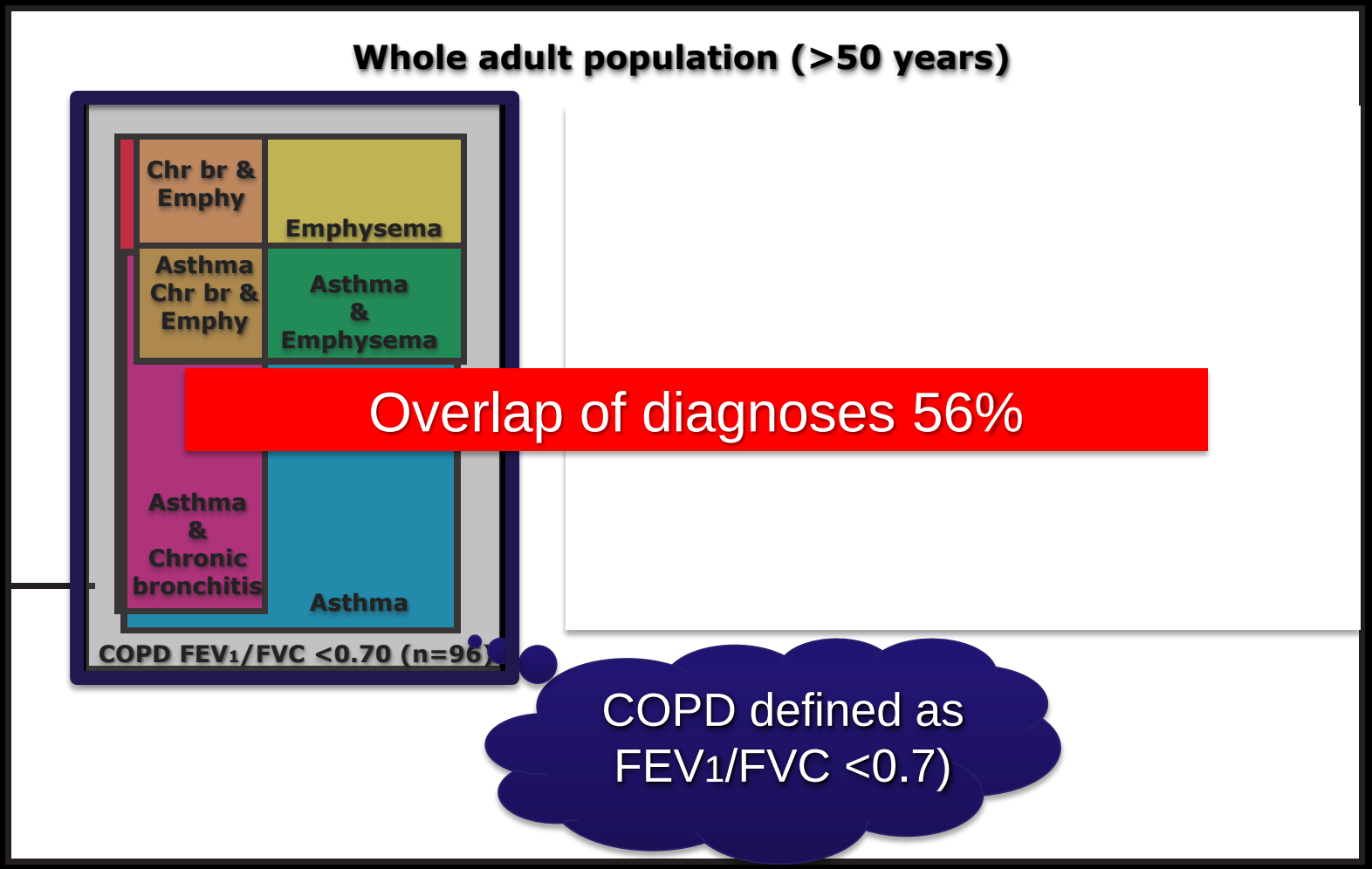
COPD

- FEV_1/FVC <0.7

Marsh SE, *et al. Thorax* 2008;63:761-7.

Population-based classification of patients aged 50 years and older

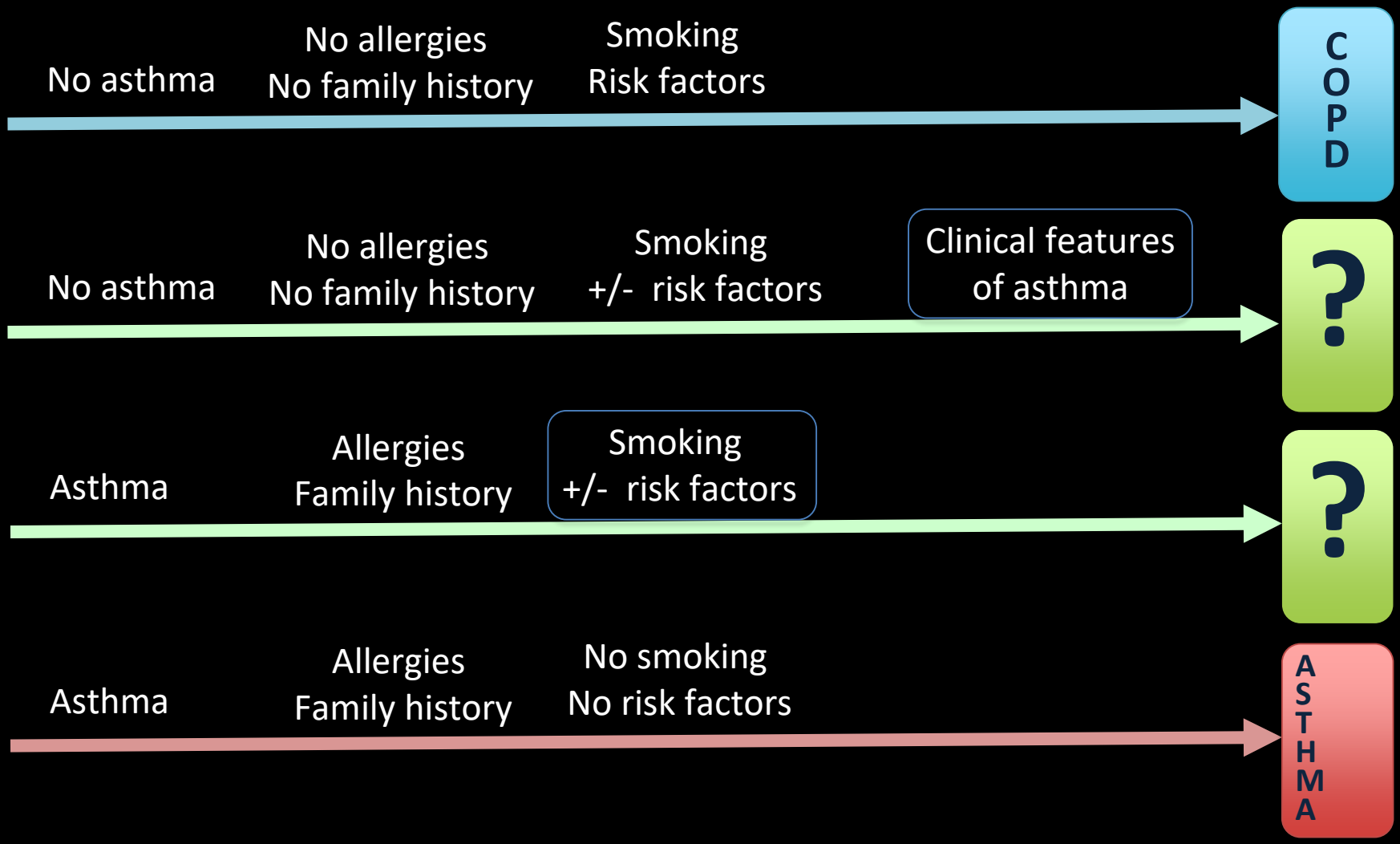
Wellington Respiratory Survey: >50 years (N= 469) from random general population



Axis-aligned proportional rectangles

Based on Marsh SE, *et al. Thorax* 2008;63:761-7.

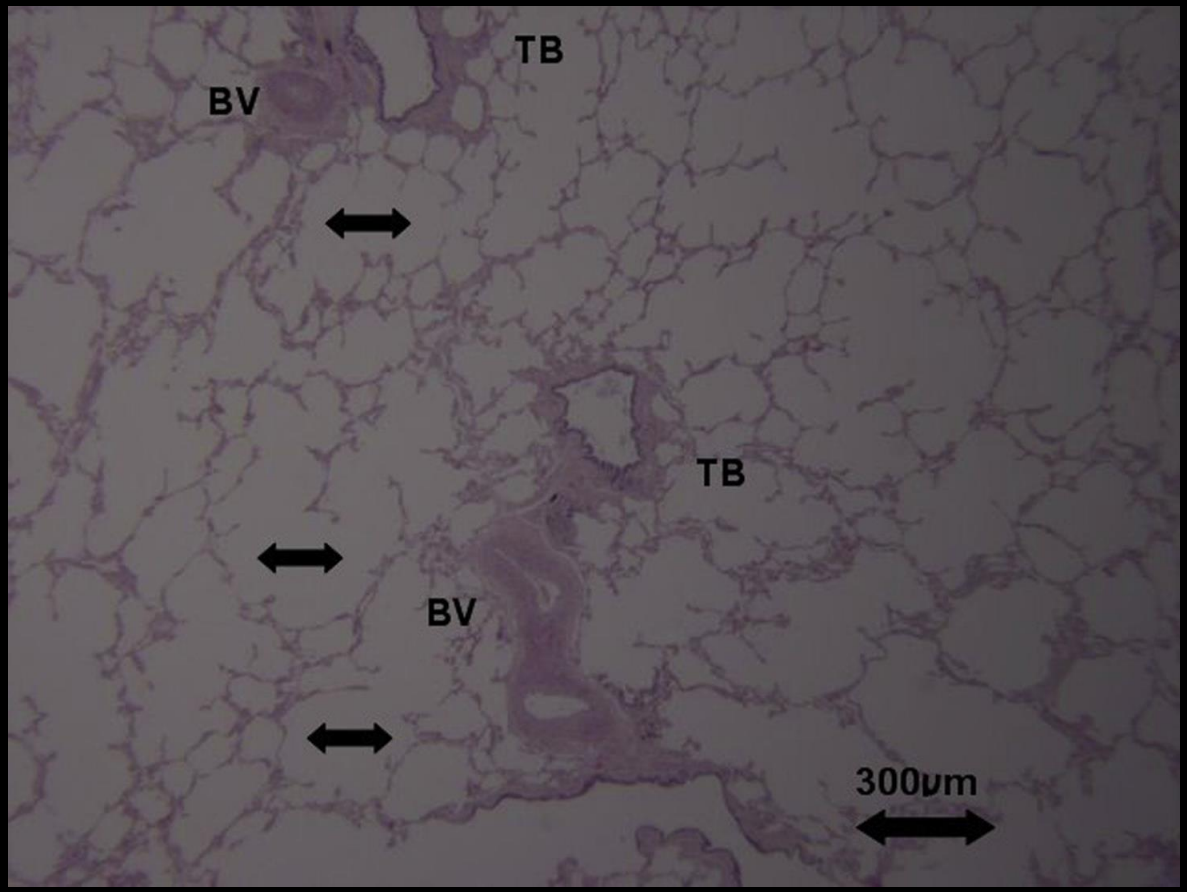
Pathways to Chronic Airflow Obstruction



Unexpected mild emphysema in non-smoking asthma with persistent AFO

72-year-old women non-smoker, lifelong asthma

- Mild centrilobular emphysema, fractured alveolar septae
- Mucin in terminal bronchioles
- Neutrophils predominate



Gelb AJ, et al. J Allergy Clin Immunol 2014; 133:265-267.

Inflammatory cells in airway walls in COPD and asthma with fixed airflow obstruction

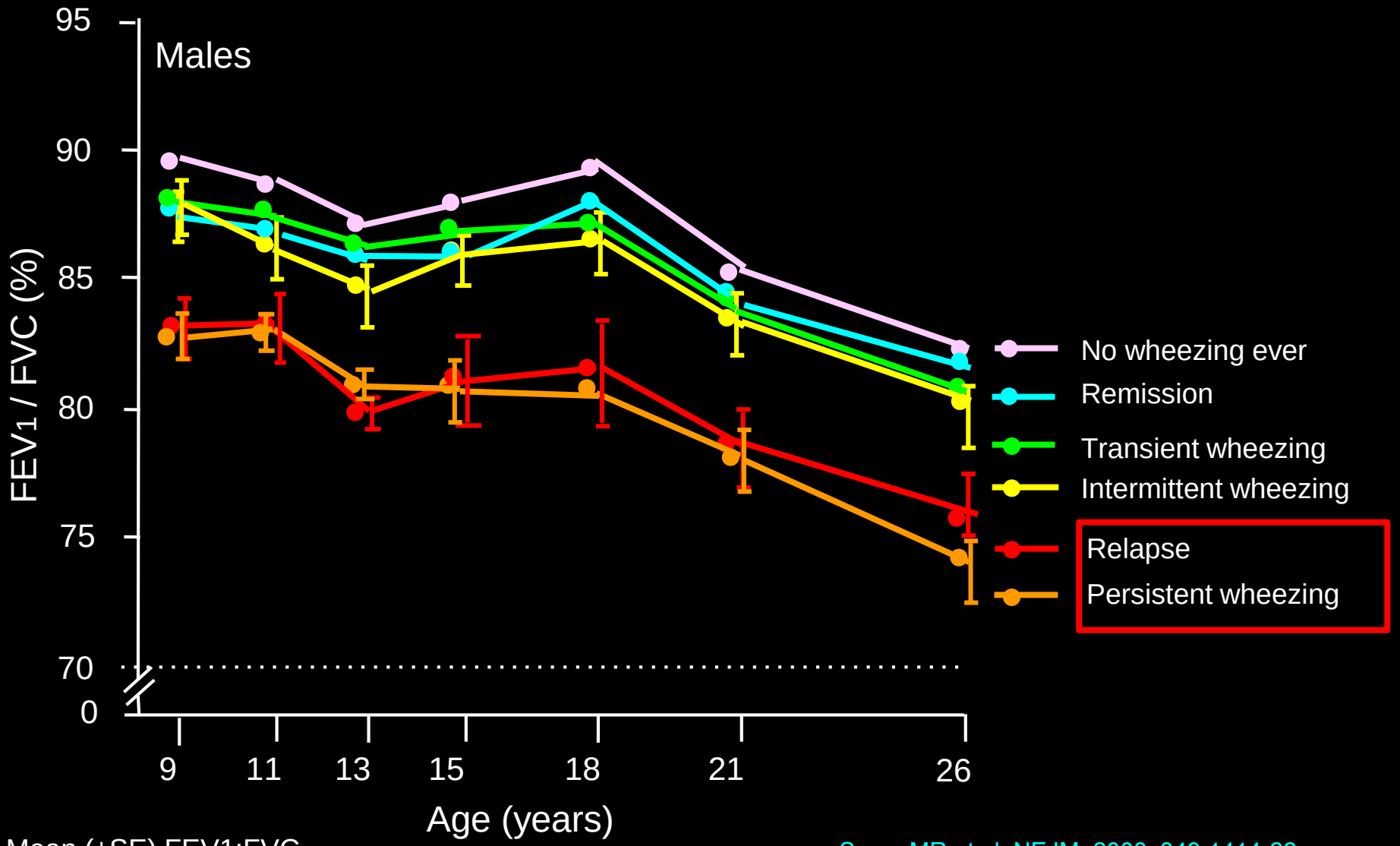
Inflammatory cells in the lamina propria

Cells (cells/mm^2)	Fixed airflow obstruction (n=21)	History of COPD (n=11)	History of asthma (n=10)
Macrophages	91.3 (47.0–102.0)	99.4 (65.0–105.6)	86.0 (41.0–97.7)
Neutrophils	109.5 (71.0–180.0)	88.5 (43.0–156.0)	157.0 (99.0–183.0)
Eosinophils	30.0 (5.0–57.5)	5.0 (2.3–33.0)	50.0 (10.0–280.0)**
Mast cells	45.0 (13.5–70.0)	40.0 (18.7–65.0)	53.0 (9.2–120.0)
$CD4^+$	142.0 (65.0–210.0)	109.0 (18.0–138.2)	218.0 (110.7–372.2)*
$CD8^+$	45.0 (25.2–102.0)	72.5 (36.5–145.0)	40.0 (15.2–71.5)
$CD4^+/CD8^+$	2.0 (0.97–7.75)	1.2 (0.27–3.15)	7.0 (2.0–21.0)

Medians with interquartile range
Versus COPD patients: *p<0.05, **p<0.01

Fabbri LM, et al. AJRCCM 2003;167:418-424.

Longitudinal asthma cohort: Lung function decline



Mean (±SE) FEV1:FVC

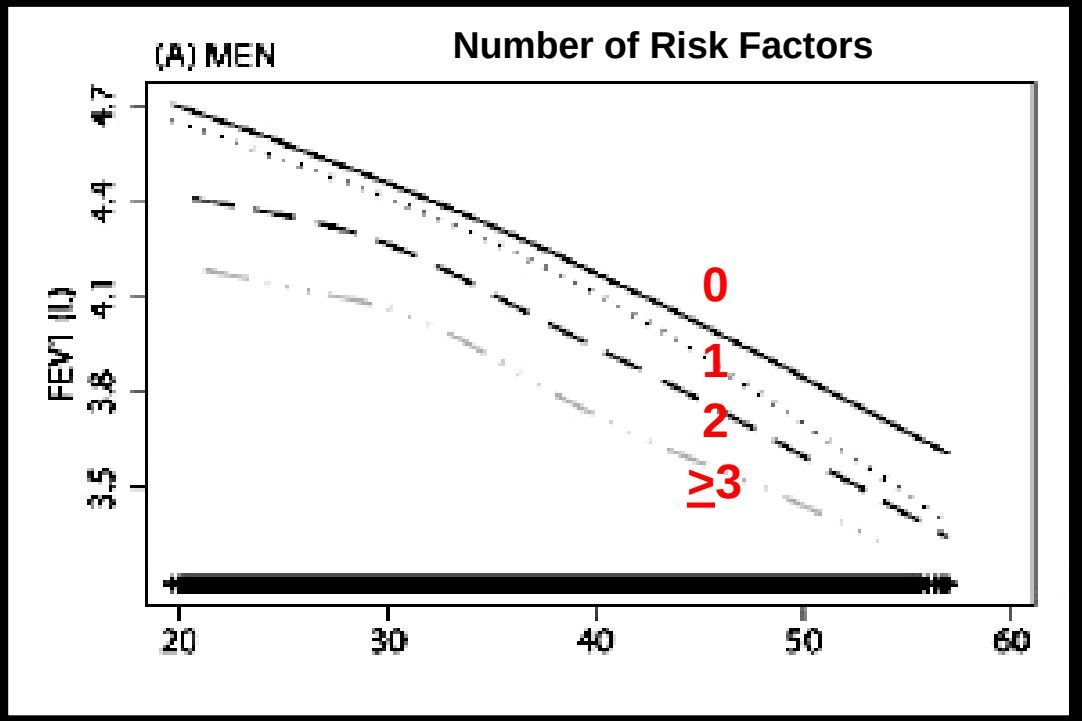
Sears MR et al, NEJM 2003; 349:1414-22.

Evidence for early-life origins of COPD risk

European Community Respiratory Health study

1993 13 359 20-45 year olds

Follow-up 9 years later on 7738



Risk factors for FEV1 decline

- Maternal asthma
- Paternal asthma
- Childhood asthma
- Maternal smoking
- Childhood respiratory infections

Early childhood disadvantage associated with:

- **Lower lung function**
  - **No catch-up**
- **Faster rate of decline**
- **Higher risk of COPD**

Svanes C, *et al. Thorax*. 2010;65:14-20.

COPD clinical phenotypes (Spanish guidelines - GesEPOC)

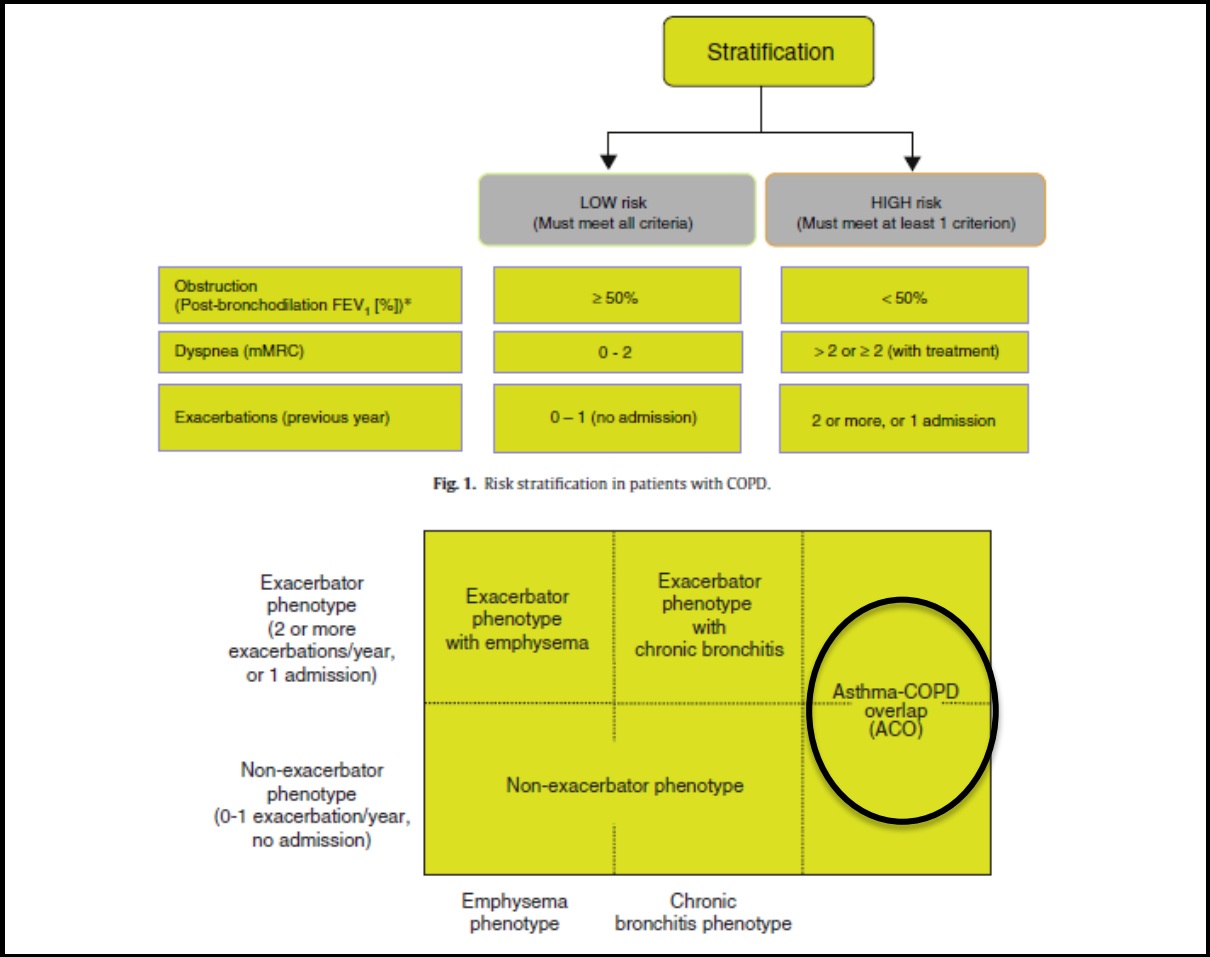


Fig. 1. Risk stratification in patients with COPD.

Miravitlles M, et al. Arch Bronconeumol. 2017;53(6):324–335

Review Article

The Asthma-COPD Overlap Syndrome: A Common Clinical Problem in the Elderly

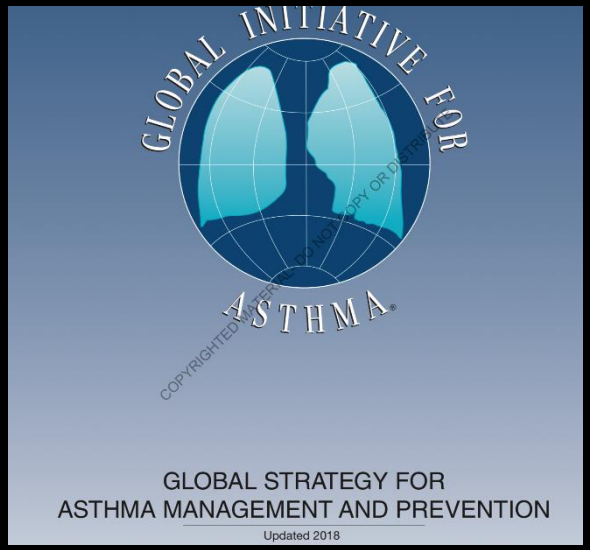
Amir A. Zeki,[1,2] Michael Schivo,[1,2] Andrew Chan,[1,3] Timothy E. Albertson,[1,3] and Samuel Louie[1]

Two Clinical Defintions (phenotype):

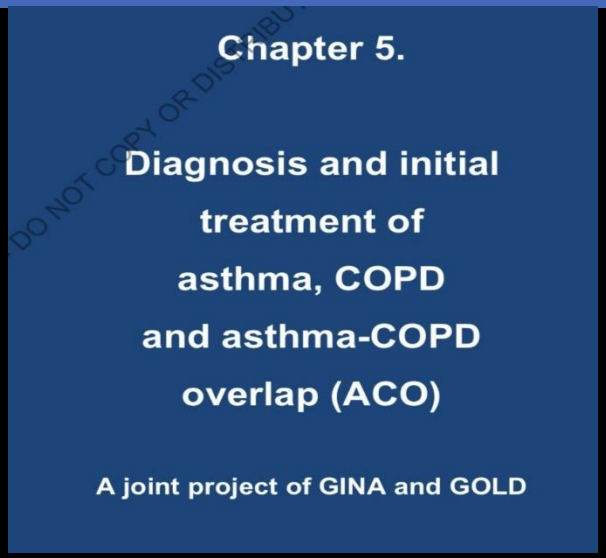
1. Asthma with partially reversible airflow obstruction, with or without emphysema or DLCO <80% pred.

2. COPD with emphysema accompanied by reversible or partially reversible airflow obstruction, with or without environmental allergies or DLCO <80% pred.

Zeki AA, et al, J Allergy (Cairo) 2011:861926.



Stepwise approach to diagnosis and initial treatment



*www.ginasthma.org &
www.goldcopd.org

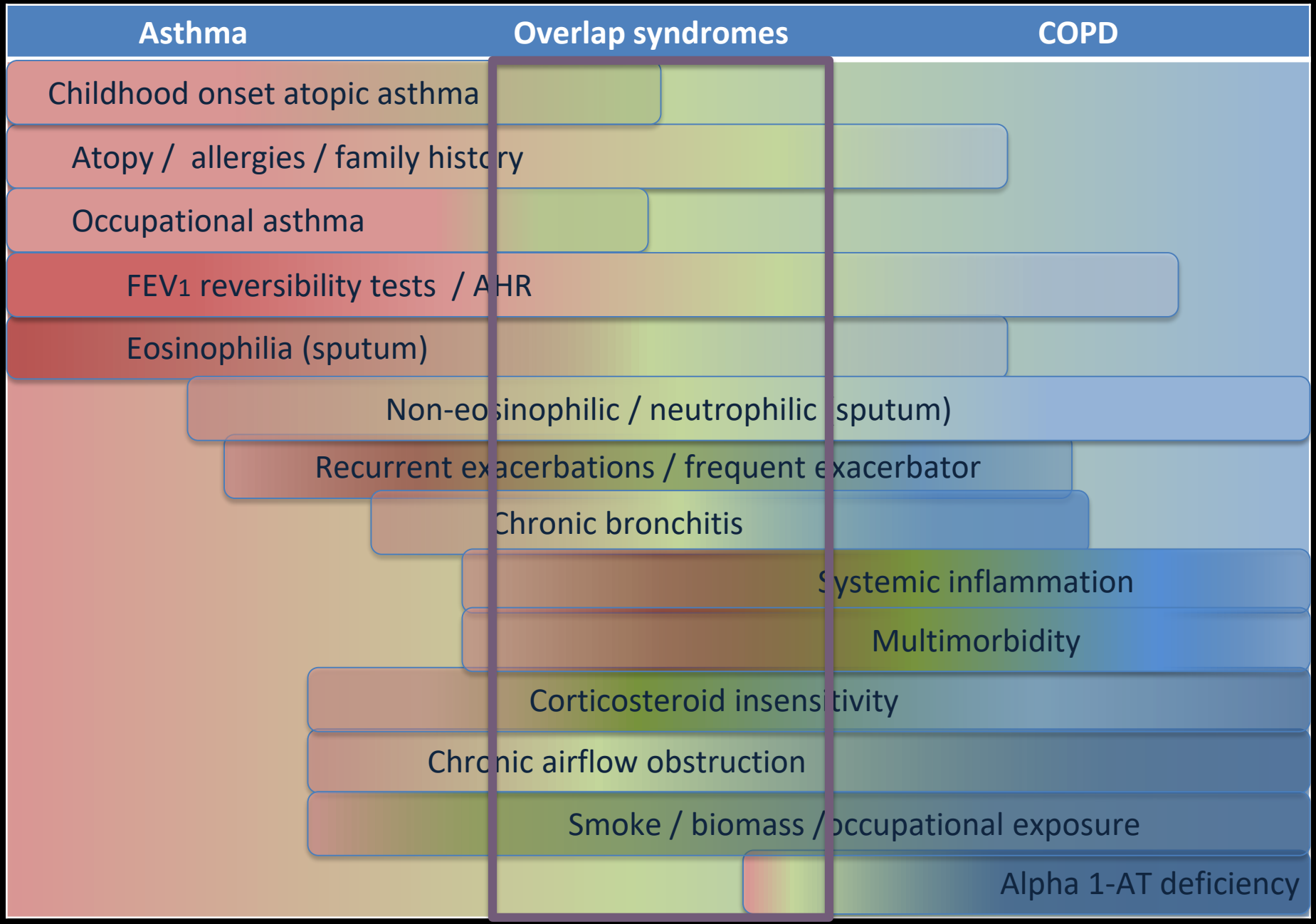
Diagnosing Asthma, COPD and ACOS

- There are no pathognomic features for asthma, COPD or ACOS

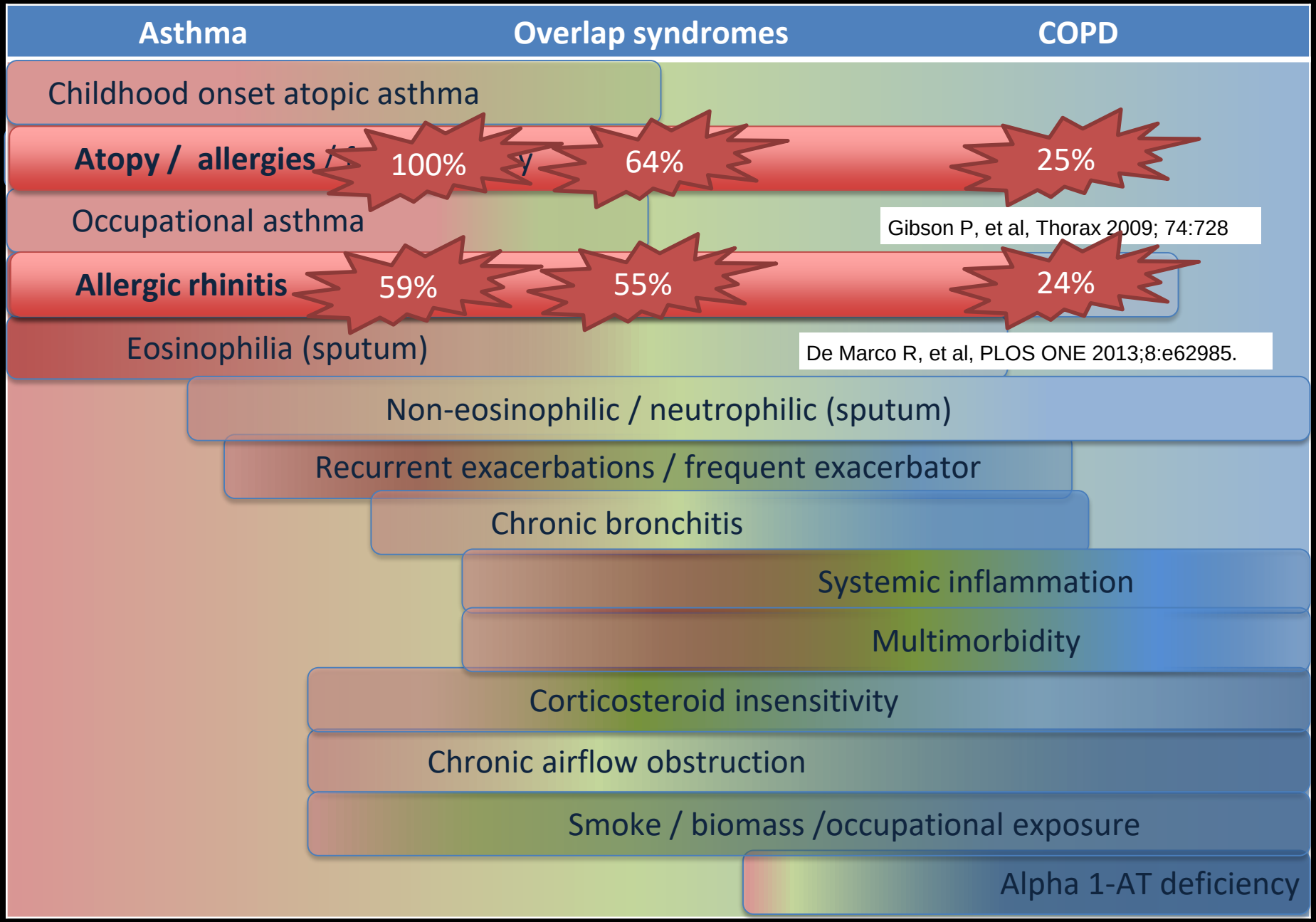
- Phenotypic features / risk factors present the likelihood (probability) of a diagnosis

- Pooling probabilities strengthens diagnosis

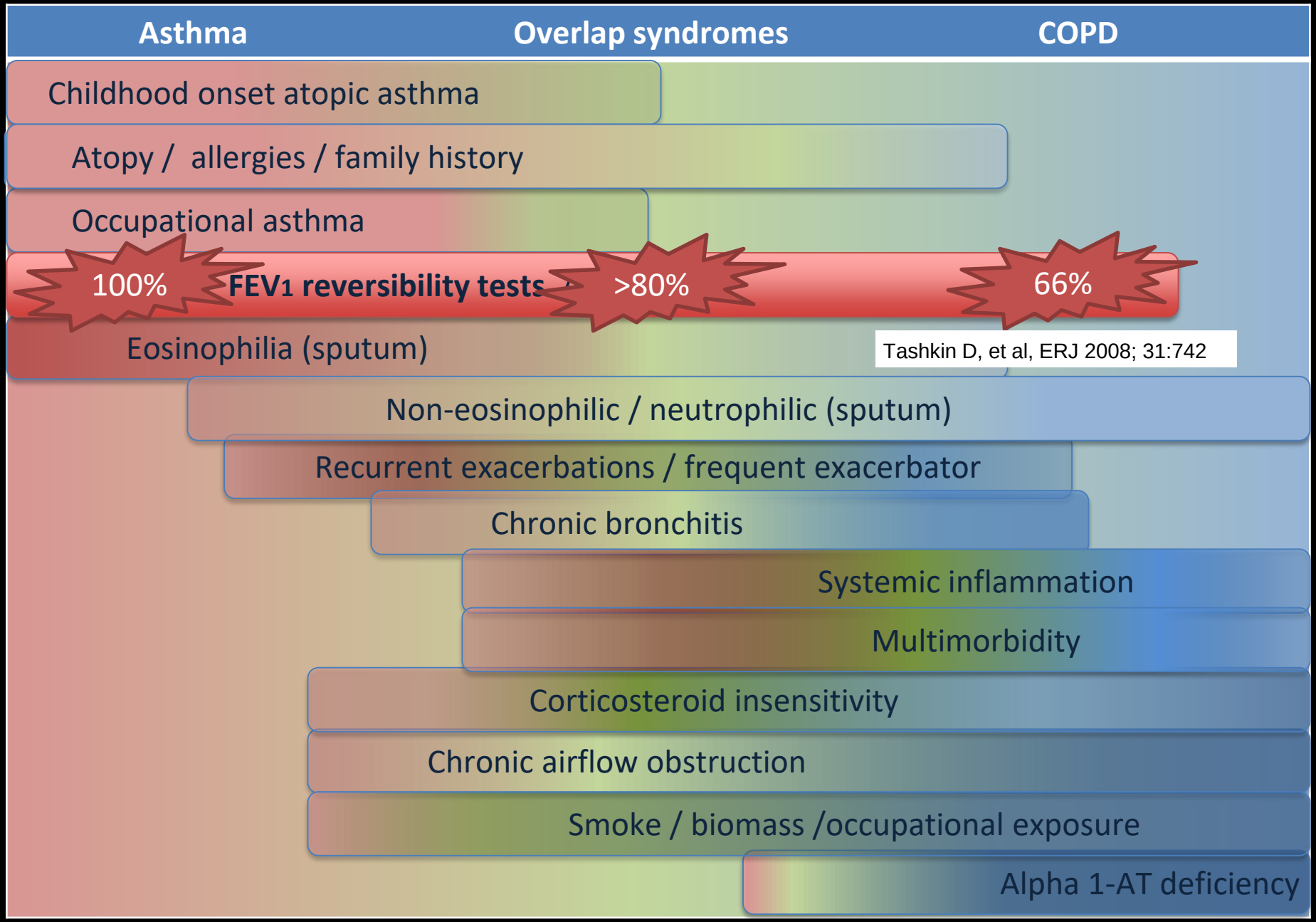
Phenotypic features of asthma and COPD in adults



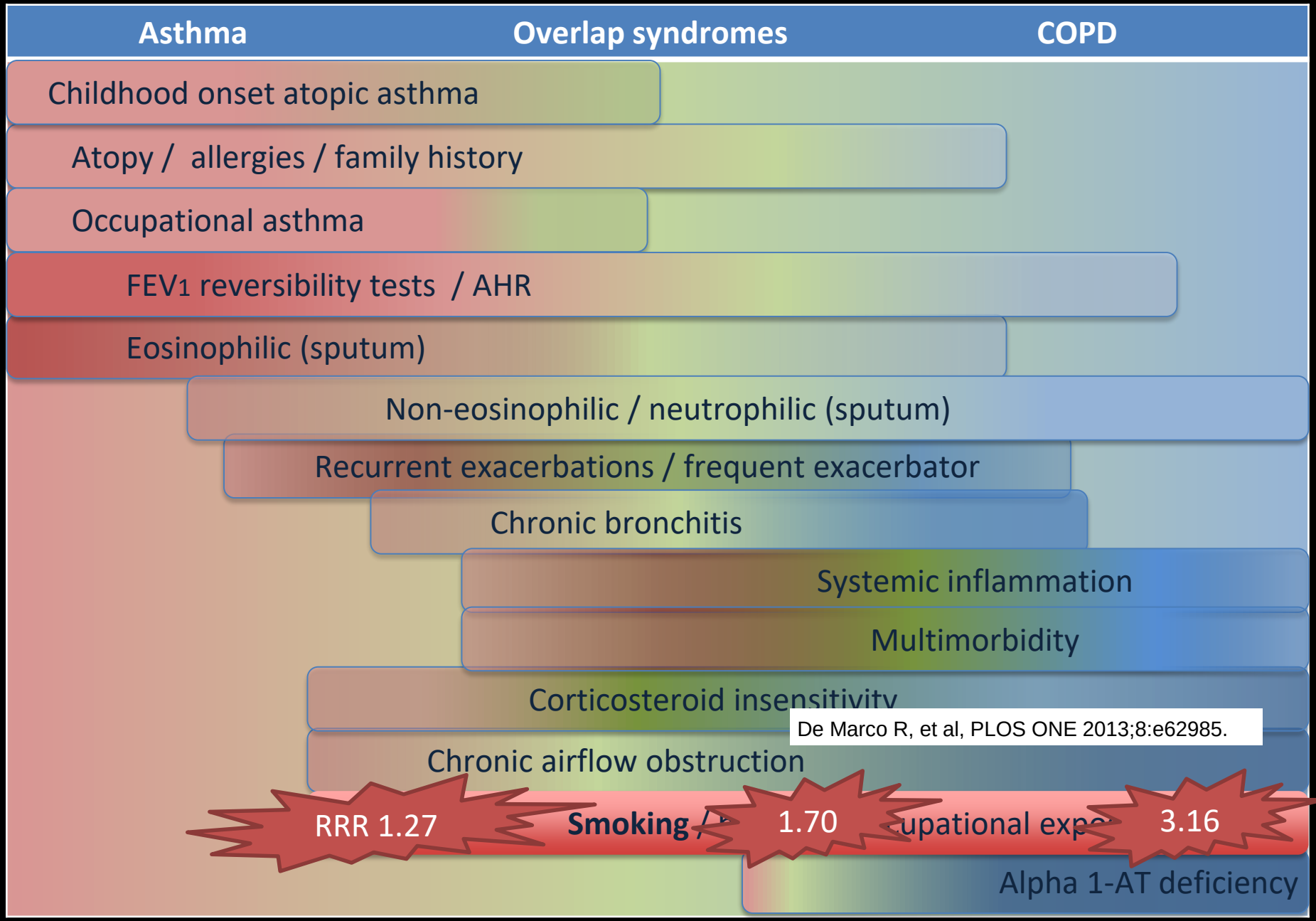
Phenotypic features of asthma and COPD in adults



Phenotypic features of asthma and COPD in adults

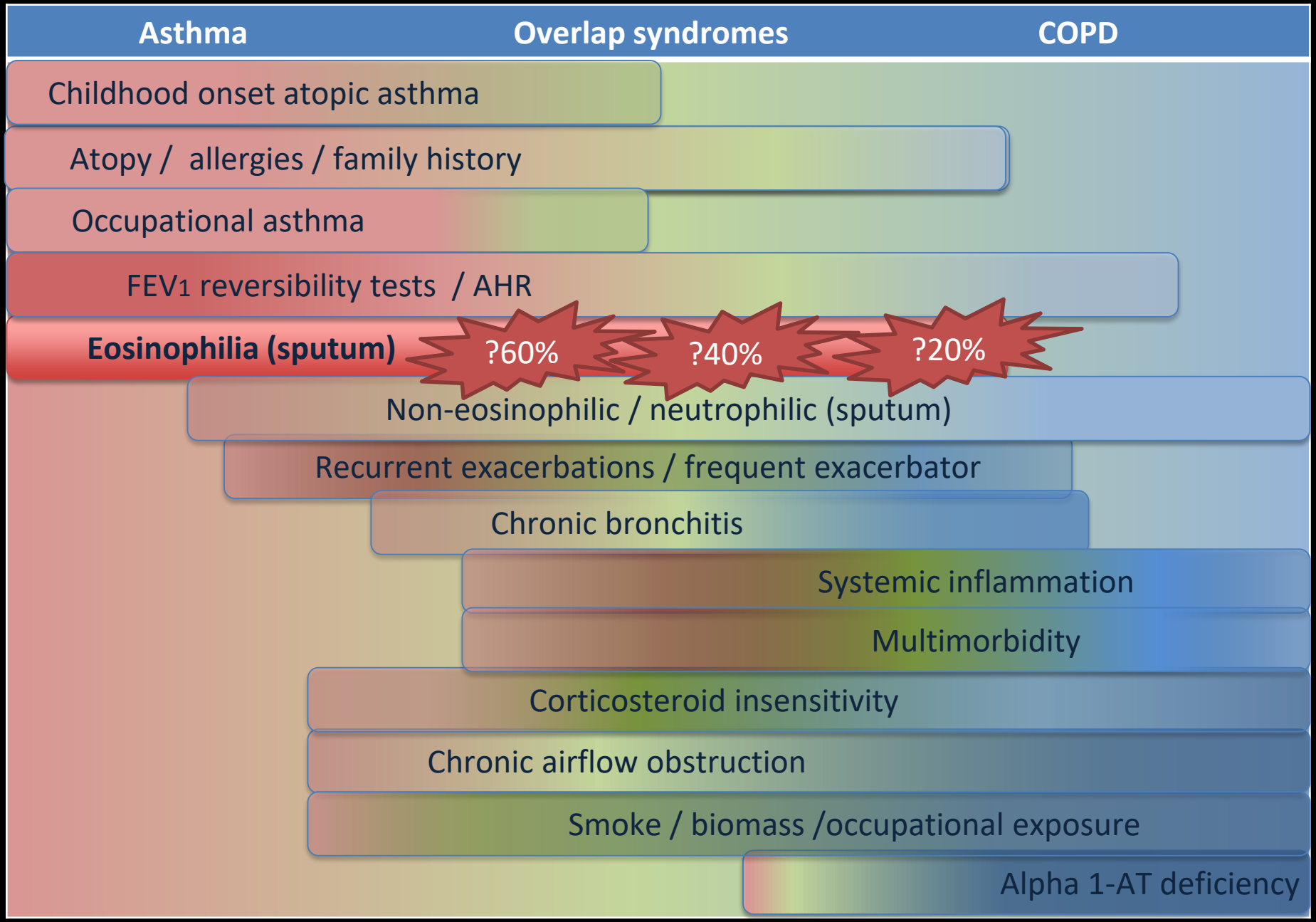


Phenotypic features of asthma and COPD in adults

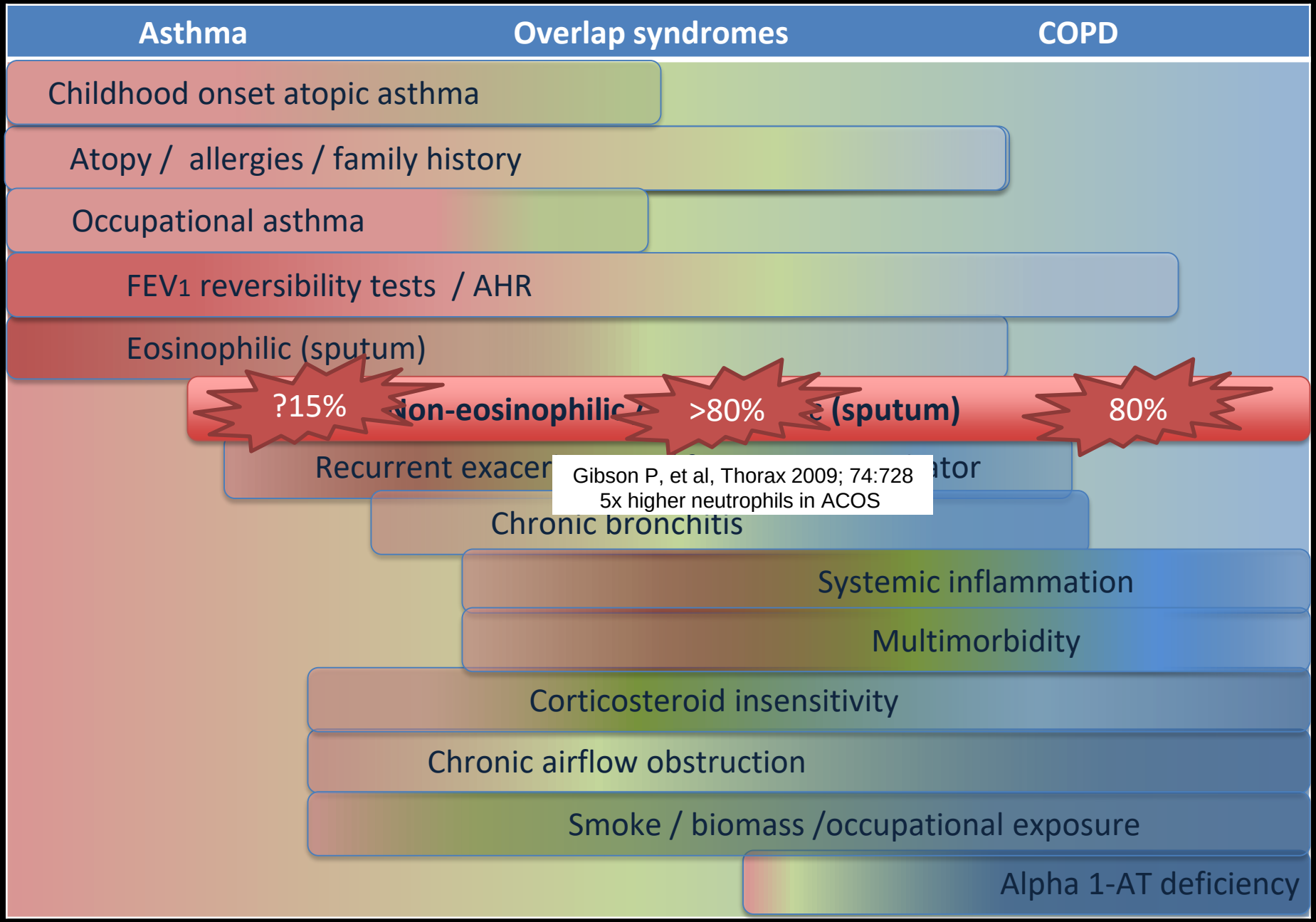


De Marco R, et al, PLOS ONE 2013;8:e62985.

Phenotypic features of asthma and COPD in adults

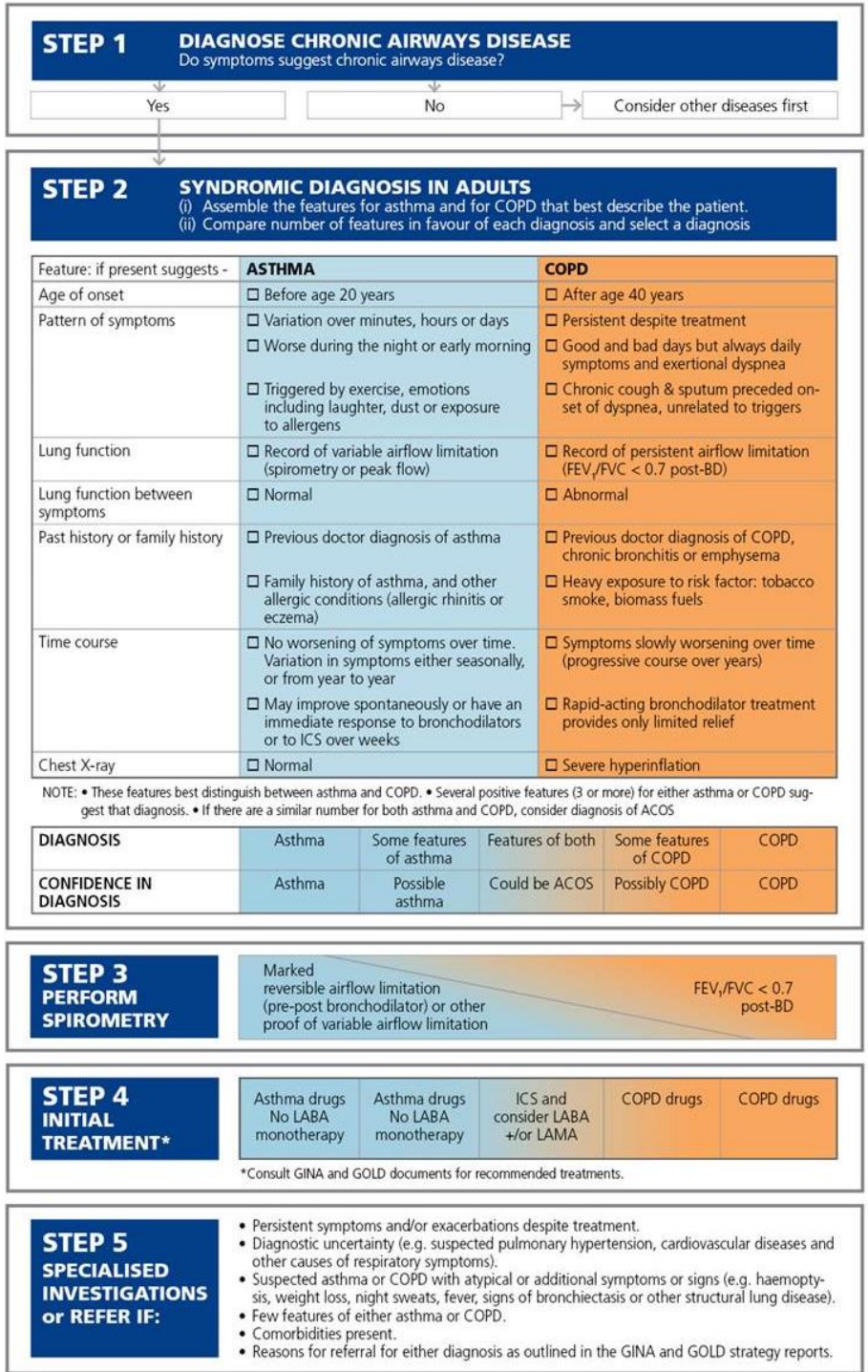


Phenotypic features of asthma and COPD in adults



Usual features of ACOS

Age of onset	Age >40 years, but may have symptoms in childhood or early adulthood
Pattern of respiratory symptoms	Symptoms, including exertional dyspnea, are persistent but variability may be predominant
Lung function	Airflow limitation is not fully reversible, but often with current or historical variability
Lung function between symptoms	Persistent airflow limitation
Past or family history	Frequently a history of doctor-diagnosed asthma (current or previous), allergies and a family history of asthma and/or history of noxious exposures
Time course	Symptoms are partly but significantly reduced by treatment. Progression is usual and treatment needs are high
Chest X-ray	May have hyperinflation and other changes of COPD
Exacerbations	More common than in COPD but are reduced by treatment. Comorbidities can contribute to impairment
Typical airway inflammation	Eosinophils and/or neutrophils in sputum



STEP 1 DIAGNOSE CHRONIC AIRWAYS DISEASE
Do symptoms suggest chronic airways disease?

Yes → **STEP 2**

No → Consider other diseases first

STEP 2 SYNDROMIC DIAGNOSIS IN ADULTS
(i) Assemble the features for asthma and for COPD that best describe the patient.
(ii) Compare number of features in favour of each diagnosis and select a diagnosis

Feature: if present suggests -	ASTHMA	COPD
Age of onset	☐ Before age 20 years	☐ After age 40 years
Pattern of symptoms	☐ Variation over minutes, hours or days ☐ Worse during the night or early morning ☐ Triggered by exercise, emotions including laughter, dust or exposure to allergens	☐ Persistent despite treatment ☐ Good and bad days but always daily symptoms and exertional dyspnea ☐ Chronic cough & sputum preceded onset of dyspnea, unrelated to triggers
Lung function	☐ Record of variable airflow limitation (spirometry or peak flow)	☐ Record of persistent airflow limitation ($FEV_1/FVC < 0.7$ post-BD)
Lung function between symptoms	☐ Normal	☐ Abnormal
Past history or family history	☐ Previous doctor diagnosis of asthma ☐ Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)	☐ Previous doctor diagnosis of COPD, chronic bronchitis or emphysema ☐ Heavy exposure to risk factor: tobacco smoke, biomass fuels
Time course	☐ No worsening of symptoms over time. Variation in symptoms either seasonally, or from year to year ☐ May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks	☐ Symptoms slowly worsening over time (progressive course over years) ☐ Rapid-acting bronchodilator treatment provides only limited relief
Chest X-ray	☐ Normal	☐ Severe hyperinflation

NOTE: • These features best distinguish between asthma and COPD. • Several positive features (3 or more) for either asthma or COPD suggest that diagnosis. • If there are a similar number for both asthma and COPD, consider diagnosis of ACOS

DIAGNOSIS	Asthma	Some features of asthma	Features of both	Some features of COPD	COPD
CONFIDENCE IN DIAGNOSIS	Asthma	Possible asthma	Could be ACOS	Possibly COPD	COPD

STEP 3 PERFORM SPIROMETRY

Marked reversible airflow limitation (pre-post bronchodilator) or other proof of variable airflow limitation

$FEV_1/FVC < 0.7$ post-BD

STEP 4 INITIAL TREATMENT*

Asthma drugs No LABA monotherapy	Asthma drugs No LABA monotherapy	ICS and consider LABA +/or LAMA	COPD drugs	COPD drugs

*Consult GINA and GOLD documents for recommended treatments.

STEP 5 SPECIALISED INVESTIGATIONS or REFER IF:

- Persistent symptoms and/or exacerbations despite treatment.
- Diagnostic uncertainty (e.g. suspected pulmonary hypertension, cardiovascular diseases and other causes of respiratory symptoms).
- Suspected asthma or COPD with atypical or additional symptoms or signs (e.g. haemoptysis, weight loss, night sweats, fever, signs of bronchiectasis or other structural lung disease).
- Few features of either asthma or COPD.
- Comorbidities present.
- Reasons for referral for either diagnosis as outlined in the GINA and GOLD strategy reports.

For an adult who presents with respiratory symptoms:

1. Does the patient have chronic airways disease?
2. Syndromic diagnosis of asthma, COPD and ACOS
3. Spirometry
4. Commence initial therapy
5. Referral for specialized investigations (if necessary)

ACOS - A description for clinical use

ACOS is characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. ACOS is therefore identified by the features that it shares with both asthma and COPD.

STEP 2 SYNDROMIC DIAGNOSIS IN ADULTS

(i) Assemble the features for asthma and for COPD that best describe the patient.
(ii) Compare number of features in favour of each diagnosis and select a diagnosis

Feature: if present suggests -	ASTHMA	COPD
Age of onset	☐ Before age 20 years	☐ After age 40 years
Pattern of symptoms	☐ Variation over minutes, hours or days ☐ Worse during the night or early morning ☐ Triggered by exercise, emotions including laughter, dust or exposure to allergens	☐ Persistent despite treatment ☐ Good and bad days but always daily symptoms and exertional dyspnea ☐ Chronic cough & sputum preceded onset of dyspnea, unrelated to triggers
Lung function	☐ Record of variable airflow limitation (spirometry or peak flow)	☐ Record of persistent airflow limitation ($FEV_1/FVC < 0.7$ post-BD)
Lung function between symptoms	☐ Normal	☐ Abnormal
Past history or family history	☐ Previous doctor diagnosis of asthma ☐ Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)	☐ Previous doctor diagnosis of COPD, chronic bronchitis or emphysema ☐ Heavy exposure to risk factor: tobacco smoke, biomass fuels
Time course	☐ No worsening of symptoms over time. Variation in symptoms either seasonally, or from year to year ☐ May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks	☐ Symptoms slowly worsening over time (progressive course over years) ☐ Rapid-acting bronchodilator treatment provides only limited relief
Chest X-ray	☐ Normal	☐ Severe hyperinflation

NOTE: • These features best distinguish between asthma and COPD. • Several positive features (3 or more) for either asthma or COPD suggest that diagnosis. • If there are a similar number for both asthma and COPD, consider diagnosis of ACOS

DIAGNOSIS	Asthma	Some features of asthma	Features of both	Some features of COPD	COPD
CONFIDENCE IN DIAGNOSIS	Asthma	Possible asthma	Could be ACOS	Possibly COPD	COPD

Accuracy of Syndromic Diagnosis of COPD (vs asthma) in patients with cough and difficult breathing:

Combining positive & negative features (n=800)

Diagnostic feature For COPD	FEATURE PRESENT Adjusted likelihood ratio	FEATURE ABSENT Adjusted likelihood ratio
Smoking ≥20 P-yrs	1.97 (1.42-2.71)	0.59 (0.46-0.76)
Symptoms worsen slowly	1.84 (1.40-2.45)	0.54 (0.41-0.73)
Onset of symptoms >40 yr	1.54 (1.22-0.96)	0.57 (0.42-0.79)
No previous diagnosis of asthma	4.08 (3.05-5.38)	0.28 (0.22-0.36)
No day to day variability	1.99 (1.43-2.76)	0.58 (0.46-0.78)
Male	1.40 (1.02-1.88)	0.72 (0.54-0.98)
	Combination of features:	
7 features	135.5 (44.8-315.8)	0.02 (0.01-0.03)
4 features	10.72	0.19
ROC for 4 features	0.95	0.95

English R, *et al, In preparation*.

Accuracy of Syndromic Diagnosis of ASTHMA (vs COPD) on history in patients with cough and difficult breathing:

Combining positive & negative features (n=800)

Diagnostic feature For ASTHMA	FEATURE PRESENT Adjusted likelihood ratio	FEATURE ABSENT Adjusted likelihood ratio
Previous diagnosis of asthma	4.03 (3.03-5.18)	0.21 (0.16-0.28)
Audible wheeze	1.48 (1.08-2.00)	0.72 (0.56-0.94)
Day to day variability of symptoms	1.73 (1.37-2.22)	0.49 (0.37-0.67)
No worsening of symptoms over time	2.17 (1.62-2.91)	0.46 (0.35-0.61)
Smoking <20 p-yrs	1.80 (1.31-2.48)	0.48 (0.36-0.70)
Female	1.42 (1.05-1.85)	0.70 (0.53-0.95)
	Combination of features:	
7 features	58.0 (32.2-105.1)	0.01 (0.01-0.20)
4 features	11.9	0.14
ROC for 4 features	0.95	0.95

English R, *et al, In preparation*.

Step 2 – Syndromic diagnosis of asthma, COPD and ACOS

- Assemble the features that, **when present**, most favor a diagnosis of asthma or COPD
- Compare the number of features on each side
  - If the patient has **≥3 features** of either asthma or COPD, there is a strong likelihood that this is the correct diagnosis
- Consider the level of certainty around the diagnosis
  - Diagnoses are made on the weight of evidence
  - The absence of any of these typical features does not rule out either diagnosis, e.g. absence of atopy does not rule out asthma
  - **When a patient has a similar number of features of both asthma and COPD, consider the diagnosis of ACOS**

Step 2

Box 5-2a. Usual features of asthma, COPD and asthma-COPD overlap

Feature	Asthma	COPD	Asthma-COPD overlap
Age of onset	Usually childhood onset but can commence at any age.	Usually > 40 years of age	Usually age ≥40 years, but may have had symptoms in childhood or early adulthood
Pattern of respiratory symptoms	Symptoms may vary over time (day to day, or over longer periods), often limiting activity. Often triggered by exercise, emotions including laughter, dust or exposure to allergens	Chronic usually continuous symptoms, particularly during exercise, with 'better' and 'worse' days	Respiratory symptoms including exertional dyspnea are persistent but variability may be prominent
Lung function	Current and/or historical variable airflow limitation, e.g. BD reversibility, AHR	FEV_1 may be improved by therapy, but post-BD $FEV_1/FVC < 0.7$ persists	Airflow limitation not fully reversible, but often with current or historical variability
Lung function between symptoms	May be normal between symptoms	Persistent airflow limitation	Persistent airflow limitation
Past history or family history	Many patients have allergies and a personal history of asthma in childhood, and/or family history of asthma	History of exposure to noxious particles and gases (mainly tobacco smoking and biomass fuels)	Frequently a history of doctor-diagnosed asthma (current or previous), allergies and a family history of asthma, and/or a history of noxious exposures
Time course	Often improves spontaneously or with treatment, but may result in fixed airflow limitation	Generally, slowly progressive over years despite treatment	Symptoms are partly but significantly reduced by treatment. Progression is usual and treatment needs are high
Chest X-ray	Usually normal	Severe hyperinflation & other changes of COPD	Similar to COPD
Exacerbations	Exacerbations occur, but the risk of exacerbations can be considerably reduced by treatment	Exacerbations can be reduced by treatment. If present, comorbidities contribute to impairment	Exacerbations may be more common than in COPD but are reduced by treatment. Comorbidities can contribute to impairment
Airway inflammation	Eosinophils and/or neutrophils	Neutrophils ± eosinophils in sputum, lymphocytes in airways, may have systemic inflammation	Eosinophils and/or neutrophils in sputum.

Box 5-2b. Features that if present favor asthma or COPD

More likely to be asthma if several of ...*	More likely to be COPD if several of...*
☐ Onset before age 20 years	☐ Onset after age 40 years
☐ Variation in symptoms over minutes, hours or days	☐ Persistence of symptoms despite treatment
☐ Symptoms worse during the night or early morning	☐ Good and bad days but always daily symptoms and exertional dyspnea
☐ Symptoms triggered by exercise, emotions including laughter, dust or exposure to allergens	☐ Chronic cough and sputum preceded onset of dyspnea, unrelated to triggers
☐ Record of variable airflow limitation (spirometry, peak flow)	☐ Record of persistent airflow limitation (post-bronchodilator $FEV_1/FVC < 0.7$)
☐ Lung function normal between symptoms	☐ Lung function abnormal between symptoms
☐ Previous doctor diagnosis of asthma	☐ Previous doctor diagnosis of COPD, chronic bronchitis or emphysema
☐ Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)	☐ Heavy exposure to a risk factor: tobacco smoke, biomass fuels
☐ No worsening of symptoms over time. Symptoms vary either seasonally, or from year to year	☐ Symptoms slowly worsening over time (progressive course over years)
☐ May improve spontaneously or have an immediate response to BD or to ICS over weeks	☐ Rapid-acting bronchodilator treatment provides only limited relief.
☐ Normal	☐ Severe hyperinflation

Syndromic diagnosis of airways disease: how to use Box 5-2b

Shaded columns list features that, <u>when present</u>, best identify patients with typical asthma and COPD. For a patient, count the number of check boxes in each column. If three or more boxes are checked for either asthma or COPD, the patient is likely to have that disease. If there are similar numbers of checked boxes in each column, the diagnosis of ACO should be considered. See Step 2 for more details.

Step 3 - Spirometry

Spirometric variable	Asthma	COPD	ACOS
Normal FEV_1/FVC pre- or post-BD	Compatible with asthma	Not compatible with diagnosis (GOLD)	Not compatible unless other evidence of chronic airflow limitation
Post-BD FEV_1/FVC <0.7	Indicates airflow limitation; may improve	Required for diagnosis by GOLD criteria	Usual in ACOS
FEV_1 =80% predicted	Compatible with asthma (good control, or interval between symptoms)	Compatible with GOLD category A or B if post-BD FEV_1/FVC <0.7	Compatible with mild ACOS
FEV_1 <80% predicted	Compatible with asthma. A risk factor for exacerbations	Indicates severity of airflow limitation and risk of exacerbations and mortality	Indicates severity of airflow limitation and risk of exacerbations and mortality
Post-BD increase in FEV_1 >12% and 200mL from baseline (reversible airflow limitation)	Usual at some time in course of asthma; not always present	Common in COPD and more likely when FEV_1 is low, but consider ACOS	Common in ACOS, and more likely when FEV_1 is low
Post-BD increase in FEV_1 >12% and 400mL from baseline	High probability of asthma	Unusual in COPD. Consider ACOS	Compatible with diagnosis of ACOS

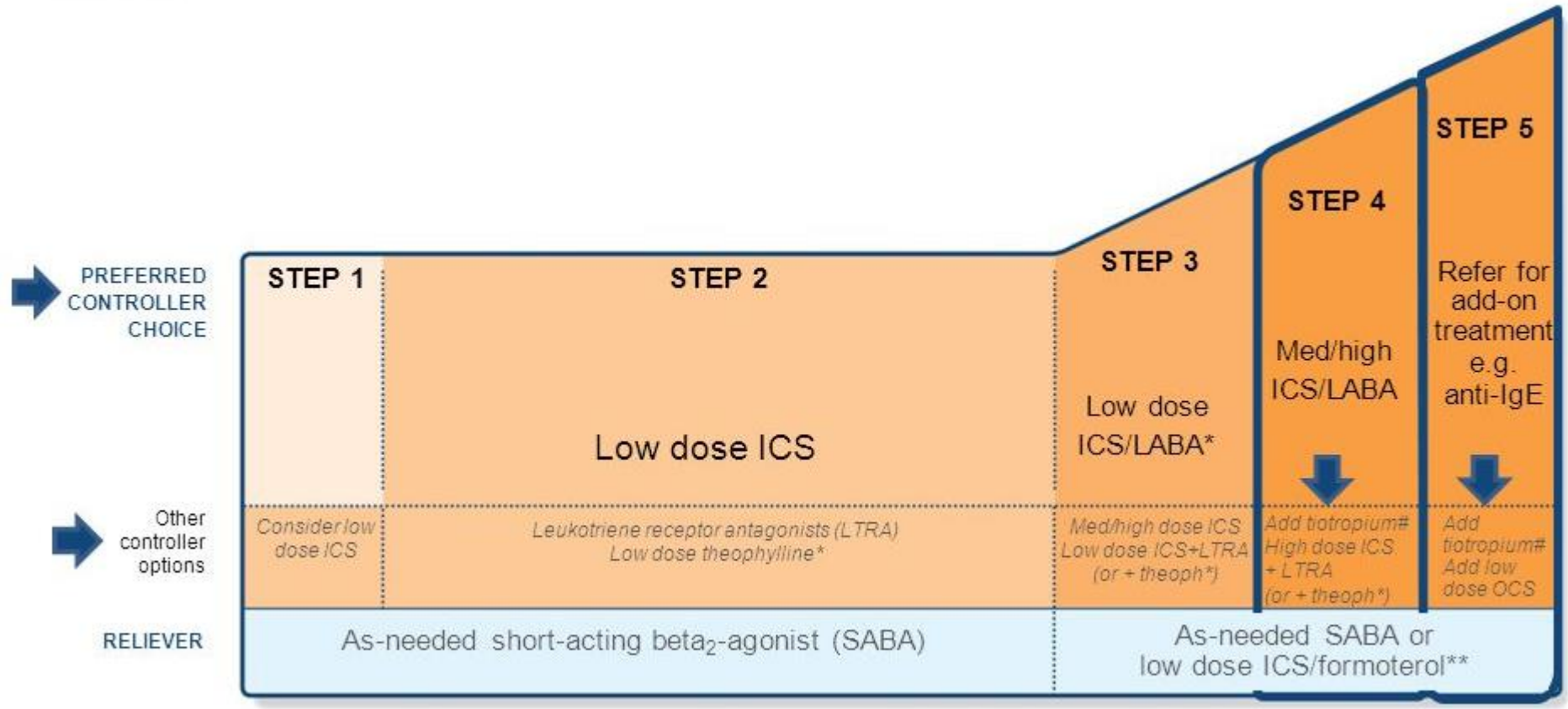
Step 4 Initial Therapy

If **asthma**→ treat asthma, avoid LABA monotherapy

If **COPD**→ LABA/LAMA +/- ICS

If **ACO** (equal balance of features)

- ICS low/medium dose and use asthma step up treatment approach



Step 4 PLUS

two or more controllers + as-needed inhaled reliever

- LAMA
- Roflumilast (PDE4-inhibitor)
- Theophylline
- Omalizumab? Bronchial thermoplasty??

STEP 1 DIAGNOSE CHRONIC AIRWAYS DISEASE

Do symptoms suggest chronic airways disease?

Yes → proceed to STEP 2

No → Consider other diseases first

STEP 2 SYNDROMIC DIAGNOSIS IN ADULTS

(i) Assemble the features for asthma and for COPD that best describe the patient.
(ii) Compare number of features in favour of each diagnosis and select a diagnosis

Feature: if present suggests -	ASTHMA	COPD
Age of onset	☐ Before age 20 years	☐ After age 40 years
Pattern of symptoms	☐ Variation over minutes, hours or days ☐ Worse during the night or early morning ☐ Triggered by exercise, emotions including laughter, dust or exposure to allergens	☐ Persistent despite treatment ☐ Good and bad days but always daily symptoms and exertional dyspnea ☐ Chronic cough & sputum preceded onset of dyspnea, unrelated to triggers
Lung function	☐ Record of variable airflow limitation (spirometry or peak flow)	☐ Record of persistent airflow limitation ($FEV_1/FVC < 0.7$ post-BD)
Lung function between symptoms	☐ Normal	☐ Abnormal
Past history or family history	☐ Previous doctor diagnosis of asthma ☐ Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)	☐ Previous doctor diagnosis of COPD, chronic bronchitis or emphysema ☐ Heavy exposure to risk factor: tobacco smoke, biomass fuels
Time course	☐ No worsening of symptoms over time. Variation in symptoms either seasonally, or from year to year ☐ May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks	☐ Symptoms slowly worsening over time (progressive course over years) ☐ Rapid-acting bronchodilator treatment provides only limited relief
Chest X-ray	☐ Normal	☐ Severe hyperinflation

NOTE: • These features best distinguish between asthma and COPD. • Several positive features (3 or more) for either asthma or COPD suggest that diagnosis. • If there are a similar number for both asthma and COPD, consider diagnosis of ACOS

DIAGNOSIS	Asthma	Some features of asthma	Features of both	Some features of COPD	COPD
CONFIDENCE IN DIAGNOSIS	Asthma	Possible asthma	Could be ACOS	Possibly COPD	COPD

STEP 3 PERFORM SPIROMETRY

Marked reversible airflow limitation (pre-post bronchodilator) or other proof of variable airflow limitation → $FEV_1/FVC < 0.7$ post-BD

STEP 4 INITIAL TREATMENT*

Asthma drugs No LABA monotherapy	Asthma drugs No LABA monotherapy	ICS and consider LABA +/or LAMA	COPD drugs	COPD drugs

*Consult GINA and GOLD documents for recommended treatments.

STEP 5 SPECIALISED INVESTIGATIONS or REFER IF:

- Persistent symptoms and/or exacerbations despite treatment.
- Diagnostic uncertainty (e.g. suspected pulmonary hypertension, cardiovascular diseases and other causes of respiratory symptoms).
- Suspected asthma or COPD with atypical or additional symptoms or signs (e.g. haemoptysis, weight loss, night sweats, fever, signs of bronchiectasis or other structural lung disease).
- Few features of either asthma or COPD.
- Comorbidities present.
- Reasons for referral for either diagnosis as outlined in the GINA and GOLD strategy reports.

Specialized investigations

	Asthma	COPD
Lung function tests		
DLCO	Normal (or slightly elevated).	Often reduced.
Arterial blood gases	Normal between exacerbations	May be chronically abnormal between exacerbations in more severe forms of COPD
Airway hyperresponsiveness (AHR)	Not useful on its own in distinguishing asthma from COPD, but higher levels of AHR favor asthma	
Imaging		
High resolution CT Scan	Usually normal but air trapping and increased bronchial wall thickness may be observed.	Low attenuation areas denoting either air trapping or emphysematous change can be quantitated; bronchial wall thickening and features of pulmonary hypertension may be seen.
Inflammatory biomarkers		
Test for atopy (specific IgE and/or skin prick tests)	Modestly increases probability of asthma; not essential for diagnosis	Conforms to background prevalence; does not rule out COPD
FENO	A high level (>50 ppb) in non-smokers is associated with eosinophilic airway inflammation	Usually normal. Low in current smokers.
Blood eosinophilia	Supports diagnosis of eosinophilic airway inflammation	May be present in COPD including during exacerbations
Sputum inflammatory cell analysis	Role in differential diagnosis is not established in large populations	

DLCO: diffusing capacity of the lungs for carbon monoxide; FENO: fractional concentration of exhaled nitric oxide; IgE: immunoglobulin E

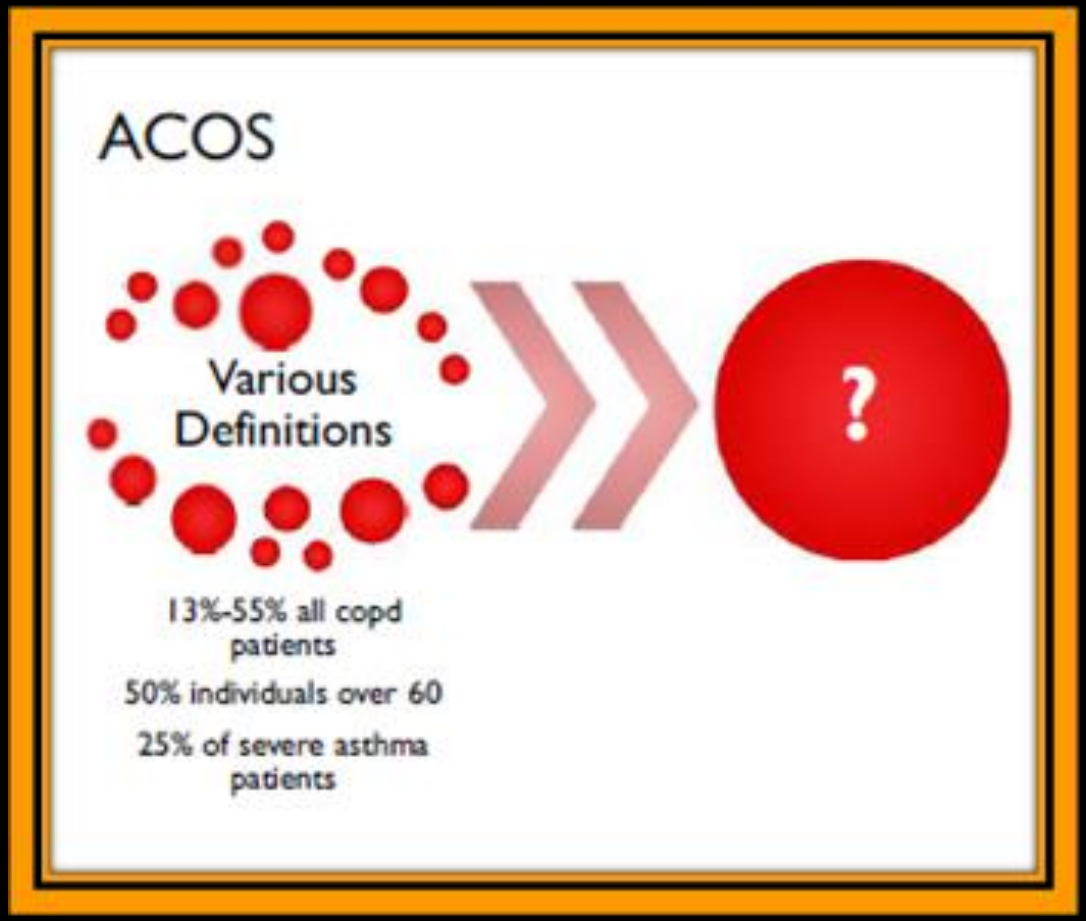
Asthma, COPD and Asthma COPD Overlap Syndrome
Perspectives

1. A problem of definitions
2. Asthma and COPD may coexist and share risk factors
3. An approach to diagnosis & initial treatment
   - GINA/GOLD (2018)
4. Future research:
   - ➢ Phenotyping & mechanisms of disease
   - ➢ Clinical trials of treatment

Conclusion

- We must treat patients by personalizing therapy on the basis of these treatable traits present in each subject.

Conclusion


ACOS
Various Definitions
?
13%-55% all copd patients
50% individuals over 60
25% of severe asthma patients

Conclusion


Treatment
• In General
COPD
LAMA +/- LABA/ICS
Asthma
ICS
ACOS
ICS +
◦ THERAPY MAY BETTER DIRECTED IF BASED ON PHENOTYPE THAN SEVERITY.

Conclusion

Take Home Points

- Clinically an overlap appears apparent
- Different phenotypes driven by various endotypes of diseases
- Now more scientific evidence
- ICS treatment can lead to clinical and spirometric improvement and decrease in exacerbations if based on eosinophilic inflammation

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