ASMA, BPCO E ACOS: FACCIAMO CHIAREZZA

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Caso clinico (1)

- M.C., maschio, anni 68
- Riferisce da alcuni anni dispnea da sforzo di grado 1-2, tosse secca al mattino, e frequenti episodi invernali di tosse, espettorato colorato, costrizione toracica, dispnea a riposo e respiro sibilante, che tratta autonomamente con antibiotici e steroidi per bocca per alcuni giorni, ma con recupero molto lento
- Ex-fumatore da 5 anni (pack-years 44)
- Nell'infanzia e adolescenza, episodi di «bronchite asmatica», poi scomparsi con la pubertà
- Dai 15 ai 40 anni circa, rinite allergica primaverile
- Familiarità per asma (madre e una sorella)

Caso clinico (2)

- **Rx-torace (alcune settimane prima): accentuazione diffusa della trama bronco-vasale con immagini bronchiali a pareti ispessite; non altre alterazioni di rilievo**
- **Spirometria (quel giorno, in stabilità):**
  - **FEV1/FVC: 64%, FEV1 71%**
  - **Post-bronc: FEV1 + 310 ml, +16%**
- **Quale diagnosi ?**
  - **Asma**
  - **BPCO**
  - **«bronchite asmatica»?**
- **Quale terapia ?**
  - **ICS**
  - **LABA, LAMA o LABA/LAMA**
  - **ICS/LABA**

Caso clinico (3)

- Inizia Tiotropio polvere inalatoria, 1 inal. al mattino
- Torna dopo 8 settimane per visita non programmata
  - Riferisce miglioramento della dispnea da sforzo
  - Ha presentato un episodio di «bronchite» con dispnea e sibili che ha trattato come al solito, con parziale risultato
  - Da 5 giorni peggioramento della tosse con dispnea, costrizione toracica e sibili
- Esegue spirometria:
  - FEV1/FVC 57%, FEV1 58% (-14% rispetto al precedente)
- Quale diagnosi ?
  - ……..
- Quale terapia ?
  - ……..

Asthma-COPD overlap syndrome

Asthma

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation. [GINA 2014]

COPD

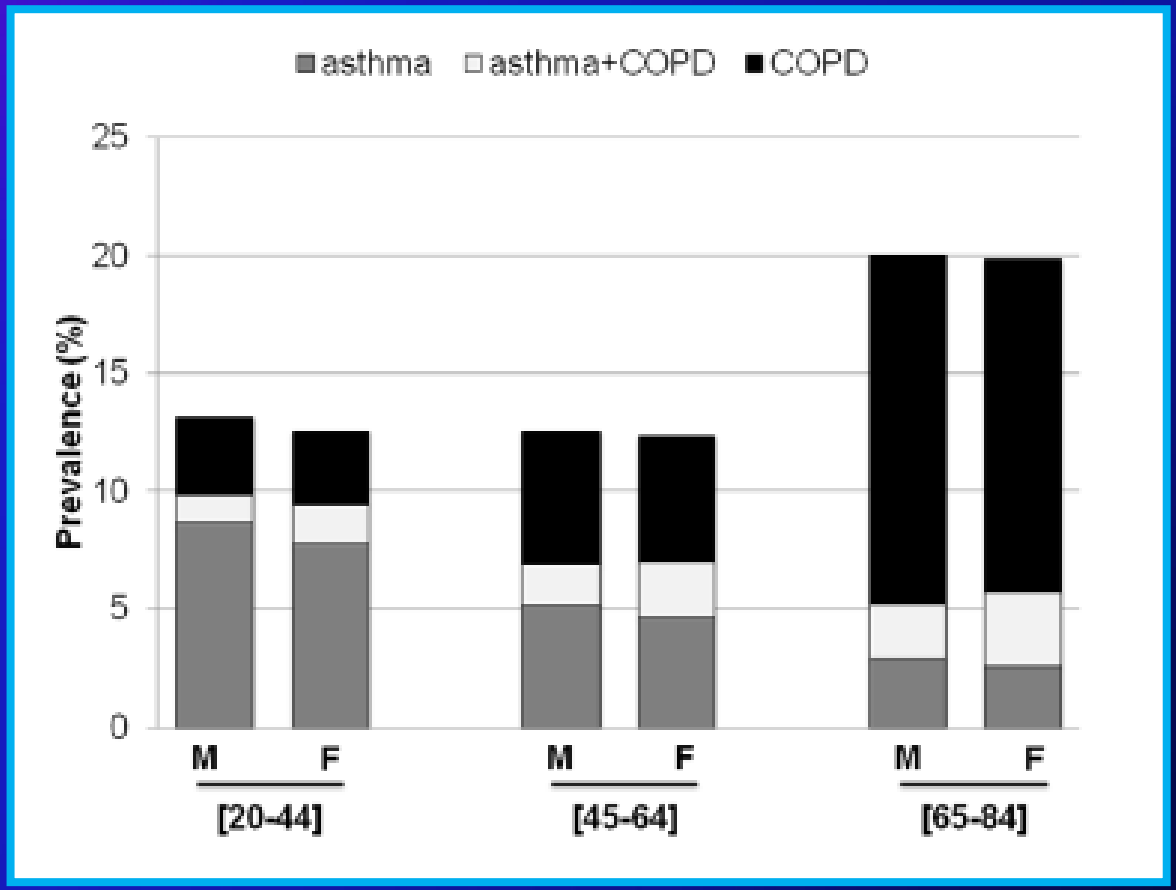
COPD is a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with enhanced chronic inflammatory responses in the airways and the lungs to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients. [GOLD 2014][21]

Asthma-COPD Overlap Syndrome (ACOS) – a description for clinical use

Asthma-COPD overlap syndrome (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.

GINA 2014

Prevalence of self-reported physician-diagnosed asthma and COPD



De Marco et al, PlosOne 2013

The clinical features of the overlap between COPD and asthma

Megan Hardin[1,2*], Edwin K Silverman[1,2], R Graham Barr[3], Nadia N Hansel[4], Joyce D Schroeder[5], Barry J Make[5], James D Crapo[5] and Craig P Hersh[1,2], for the COPDGene Investigators

Respiratory Research 2011, **12**:127

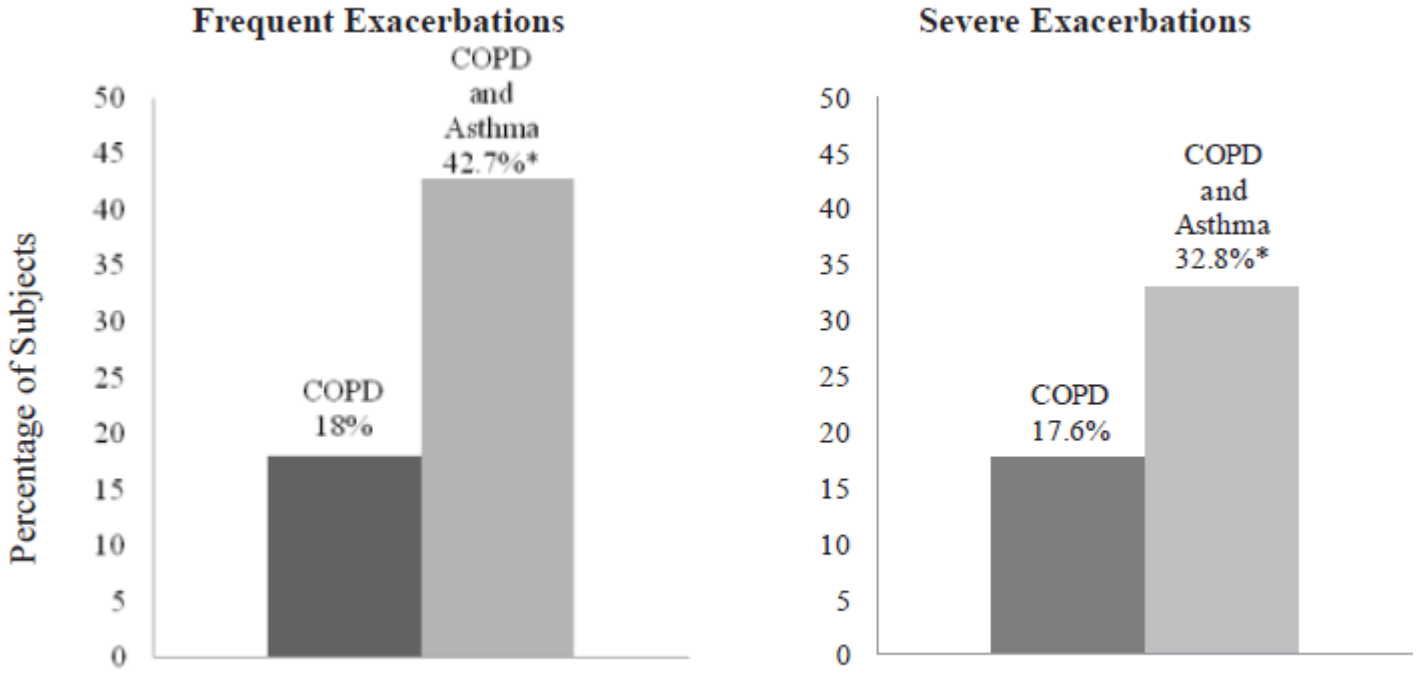


Figure 1 Exacerbations: Percentage of frequent and severe exacerbations among subjects with COPD compared to subjects with COPD and asthma. *$p < 0.0001$ for the difference between COPD and COPD with asthma.

Different pathogenesis

ASTHMA
Allergens

COPD
Sigarette smoke

Airway inflammation
T CD4+ Lymphocytes
Eosinophils

Airway and parenchimal inflammation
T CD8+ Lymphocytes
Macrophages, neutrophils

REVERSIBLE — AIRFLOW OBSTRUCTION — NOT REVERSIBLE

Which are the main characteristics of asthma ?

- Risk factors: atopy
- Clinical manifestation: complex of symptoms, variability over time
- Functional manifestations: normal lung function after treatment, large variability of FEV1 over time
- Biologic background: eosinophilic inflammation
- Response to treatment: good to ICS

A new definition of asthma (GINA 2014): a heterogeneous disease

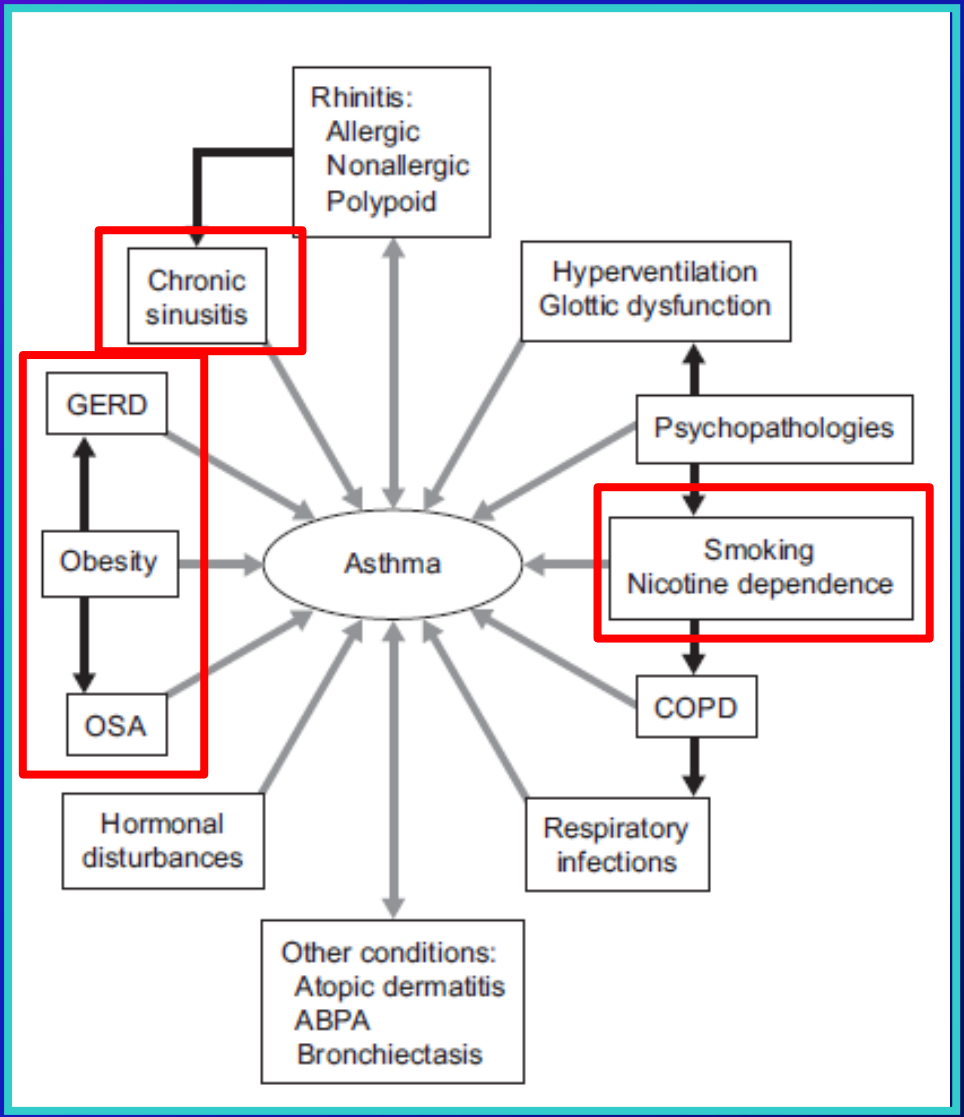
DEFINITION OF ASTHMA

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.

This definition was reached by consensus, based on consideration of the characteristics that are typical of asthma and that distinguish it from other respiratory conditions.

- *Allergic asthma*: this is the most easily recognized asthma phenotype, which often commences in childhood and is associated with a past and/or family history of allergic disease such as eczema, allergic rhinitis, or food or drug allergy. Examination of the induced sputum of these patients before treatment often reveals eosinophilic airway inflammation. Patients with this asthma phenotype usually respond well to inhaled corticosteroid (ICS) treatment.
- *Non-allergic asthma*: some adults have asthma that is not associated with allergy. The cellular profile of the sputum of these patients may be neutrophilic, eosinophilic or contain only a few inflammatory cells (paucigranulocytic). Patients with non-allergic asthma often respond less well to ICS.
- *Late-onset asthma*: some adults, particularly women, present with asthma for the first time in adult life. These patients tend to be non-allergic, and often require higher doses of ICS or are refractory to corticosteroid treatment.
- *Asthma with fixed airflow limitation*: some patients with long-standing asthma develop fixed airflow limitation that is thought to be due to airway wall remodeling.
- *Asthma with obesity*: some obese patients with asthma have prominent symptoms and little eosinophilic airway inflammation.

Several comorbidities may modify the clinical and biological features of asthma



Boulet, ERJ 2009

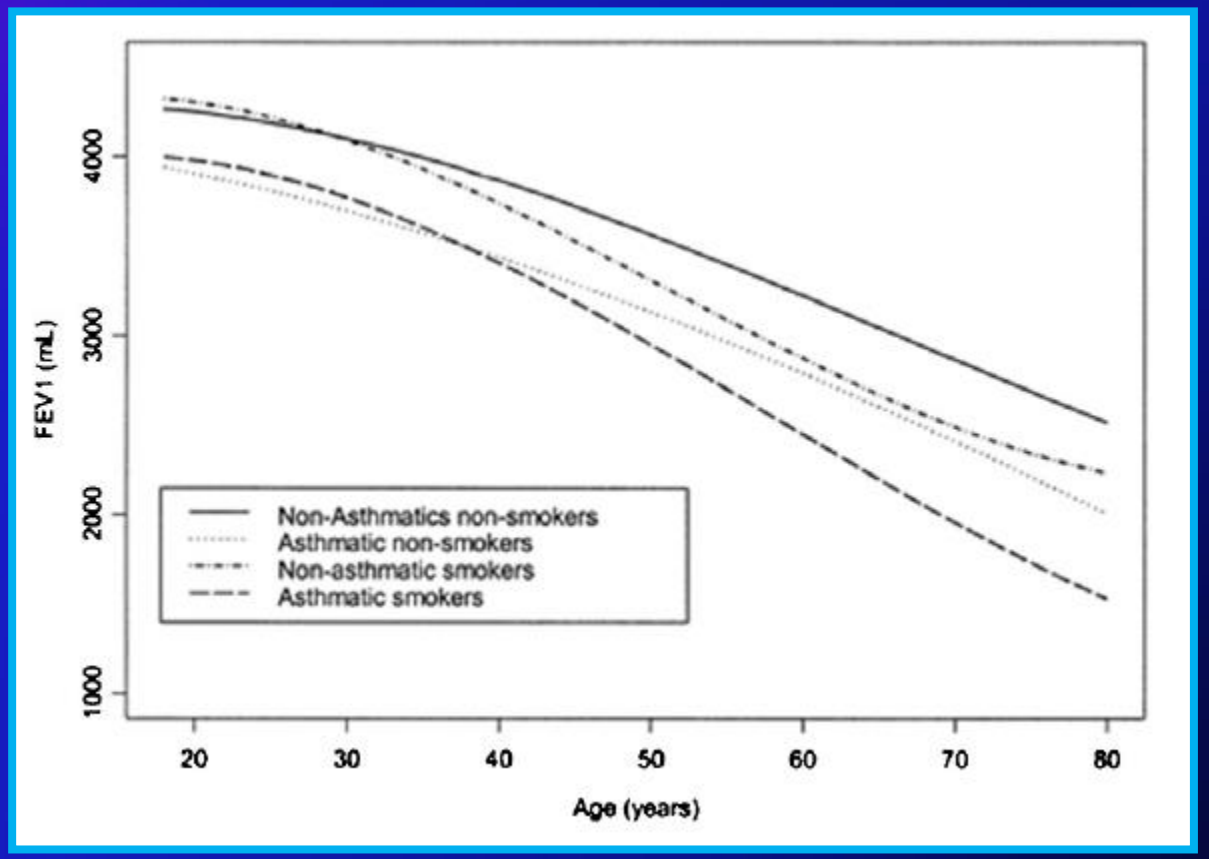
Asthma: a heterogeneous disease

- **Symptoms**
  - Non specific
  - Blunted by bronchodilators or poor perception
- **Risk factors**
  - Atopic vs non atopic
  - Young vs older patients
- **Mechanisms**
  - Different patterns of airway inflammation
  - Different mechanisms (non-inflammatory ?)
- **Importance of functional assessment**
  - Reversible obstruction
  - Bronchial hyperresponsiveness
  - Wide variability over time of pulmonary function

Asthma-COPD overlap syndrome: different possibilities

- **Asthma with fixed airway obstruction**
  - **Asthma progression in a subgroup of patients**
  - **Asthma phenotype ?**
- **Asthma and smoking habit**
  - **Asthma in childhood or adolescence (< 40 yrs)**
  - **Smoking habit**
  - **Funtional abnormalities of asthma and COPD**
- **COPD with large variability of airway obstruction**
  - **Eosinophilic component, good response to ICS**
  - **COPD phenotype ?**

Decline in FEV1 in asthmatics is greater than in non asthmatics



James et al, AJRCCM 2005

Fixed airflow limitation in asthma has some specific risk factors

A. Asthma symptom control

In the past 4 weeks, has the patient had:

		Level of asthma symptom control: Well controlled	Partly controlled	Uncontrolled
Daytime asthma symptoms more than twice/week?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
Any night waking due to asthma?	Yes☐ No☐			
Reliever needed more than twice/week?	Yes☐ No☐			
Any activity limitation due to asthma?	Yes☐ No☐			

B. Risk factors for poor outcomes

Measure FEV_1 at start of treatment, after 3–6 months of controller treatment to record the patient's personal best and then periodically for ongoing risk assessment

Potentially modifiable risk factors for exacerbations

- Uncontrolled asthma symptoms[36]
- Excessive SABA use (>1 x 200-dose canister/month)[37]
- Not taking ICS; incorrect inhaler technique; poor adherence[38]
- Low FEV_1, especially if <60% predicted[39,40]
- Major psychological or socioeconomic problems[41]
- Smoking,[40] obesity;[42] rhinosinusitis
- Food allergy;[43] allergen exposure if sensitized[40]
- Sputum or blood eosinophilia[44,45]

Having one of these factors increases the risk of exacerbations even if symptoms are well controlled. Patients should be considered at high risk if more than one factor is present

Other key risk factors for exacerbations

- Ever intubated or in intensive care unit for asthma[46]
- ≥1 severe exacerbation in last 12 months[47]
- Pregnancy[48]

Risk factors for developing fixed airflow limitation

- Tobacco smoke;[49] noxious exposures; occupational asthma
- Low initial FEV_1;[50] chronic mucus hypersecretion;[49,50] sputum/blood eosinophilia (if available)[50]

Risk factors for medication side-effects

- *Systemic*: frequent OCS; long-term, high-dose/potent ICS; also taking P450 inhibitors[51]
- *Local*: high-dose or potent ICS;[51,52] poor inhaler technique[53]

BMJ Open

Sputum eosinophilia is a determinant of FEV1 decline in occupational asthma: results of an observational study

Donatella Talini,[1] Federica Novelli,[2] Elena Bacci,[2] Marialaura Bartoli,[2] Silvana Cianchetti,[2] Francesco Costa,[2] Federico L Dente,[2] Antonella Di Franco,[2] Manuela Latorre,[2] Laura Malagrinò,[2] Barbara Vagaggini,[2] Alessandro Celi,[2] Pierluigi Paggiaro[2]

BMJ Open 2015;5:e005748.

Table 3 Cha

Number of pat
Age, years, m
Gender, M/F
Smoke, No/Ex
Atopy, n (%)
LMWC/HMWC
FEV1, % pred
PD20FEV1, µ
Bronchial hyp
Reduction of e
Sputum eosin
Sputum neutr

*p<0.05 among
F, female; FEV1
molecular-weigh

.5 mL/year

-11.6

.8)

)+14.6*

6.9)
7)
)–24.4)
(19.4–96.0)

C, low-
d deviation.

Table 4 Results of the multivariate analysis on the main determinants of the FEV1 decline, including as independent variables only those variables significantly related to the FEV1 decline in the univariate analysis

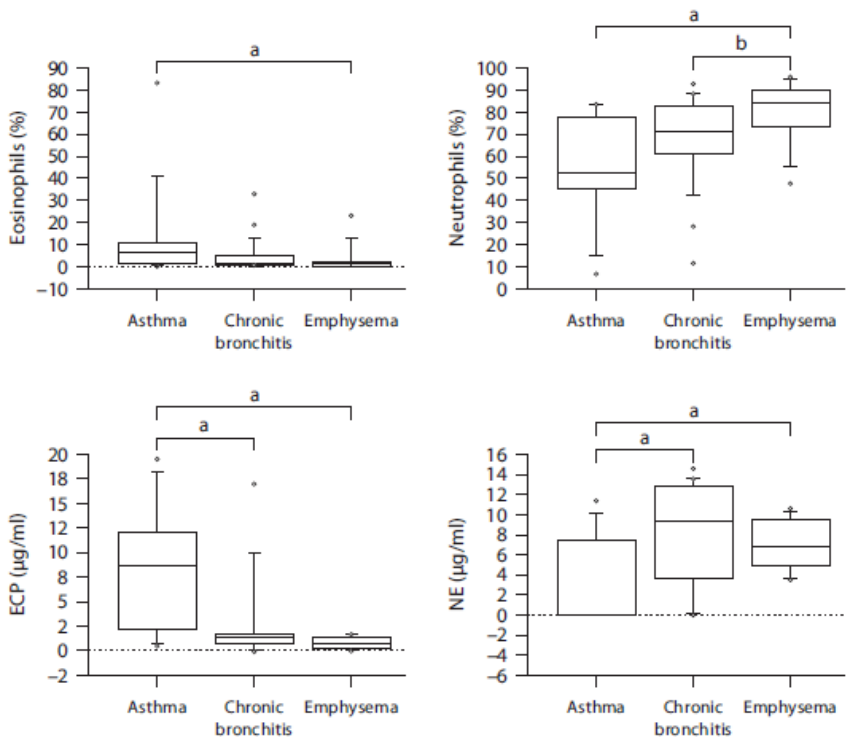
Variables	Odd ratios	95% CI Lower	95% CI Upper	p Value
Persistent exposure vs reduction	12.7	1.8	90.8	0.01
Sputum eosinophilia ≥3%	7.6	1.1	52.9	0.04
Baseline FEV1 (% of predicted)	1.06	0.99	1.13	0.06

FEV1, forced expiratory volume in the first second.

Biological Markers in Induced Sputum of Patients with Different Phenotypes of Chronic Airway Obstruction

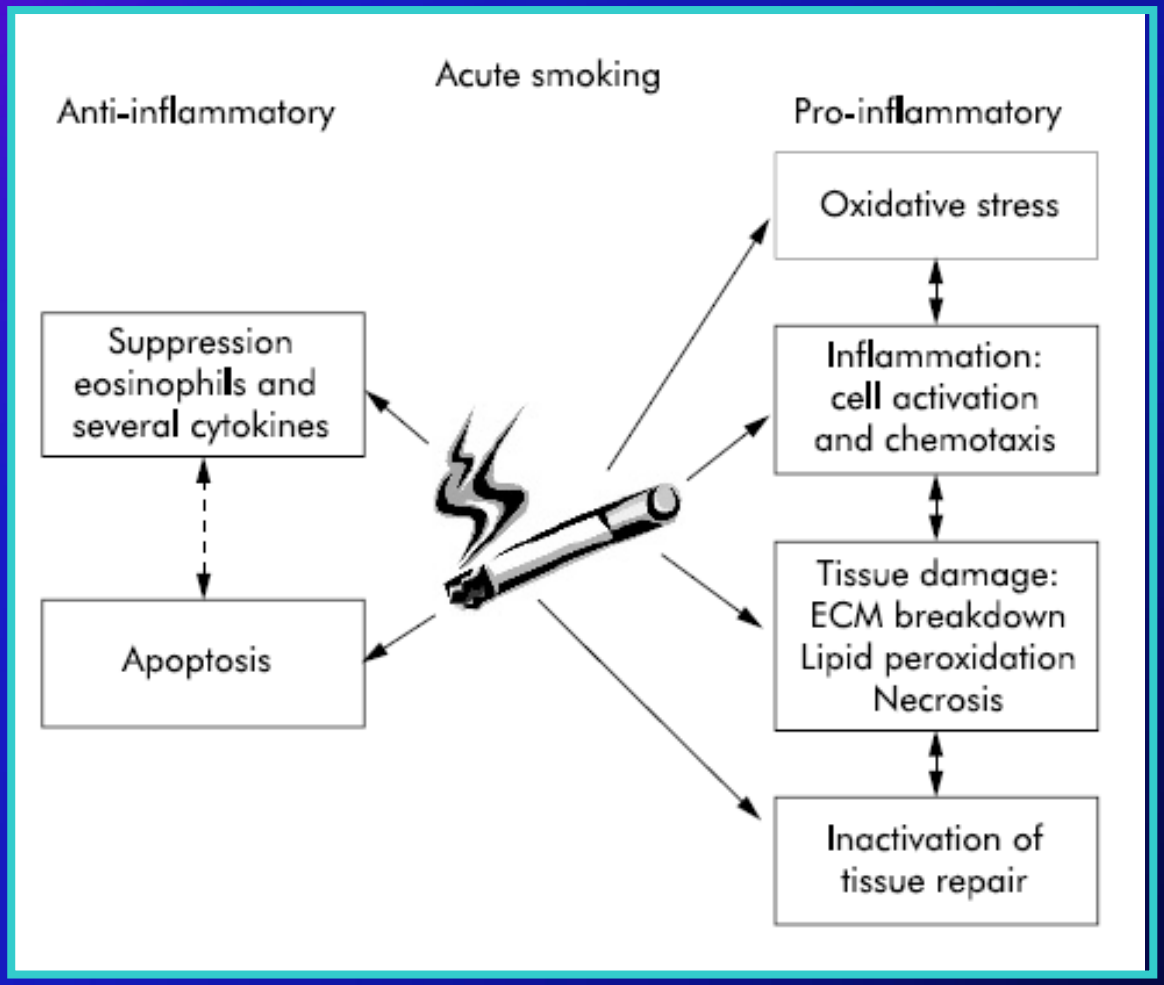
Maria Laura Bartoli Antonella Di Franco Barbara Vagaggini Elena Bacci
Silvana Cianchetti Federico Lorenzo Dente Monica Tonelli Pier Luigi Paggiaro

Cardiothoracic and Vascular Department, University of Pisa, Pisa, Italy



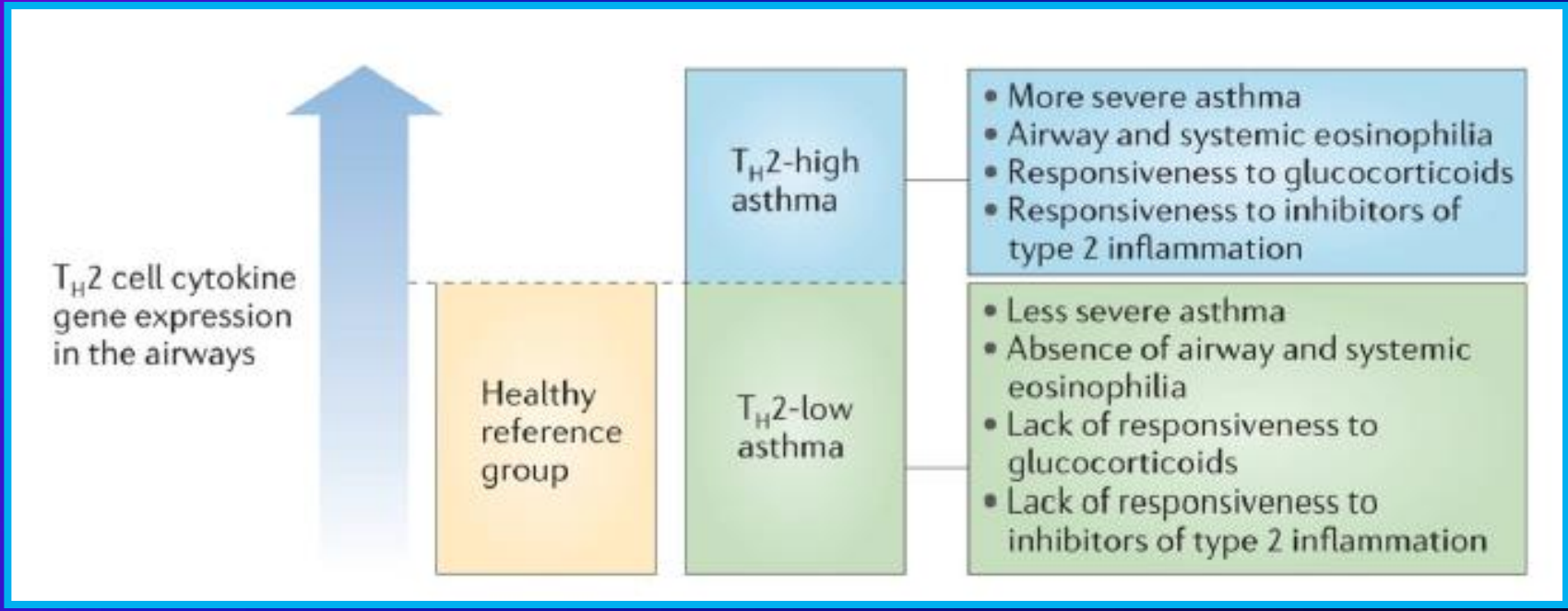
Respiration 2009;77:265–272
DOI: 10.1159/000176385

Cigarette smoke has different effects on airways



Van der Vaart et al, Thorax 2004

Type 2 inflammation in asthma — present in most, absent in many



Fahy, Nat Rev Immunol 2015

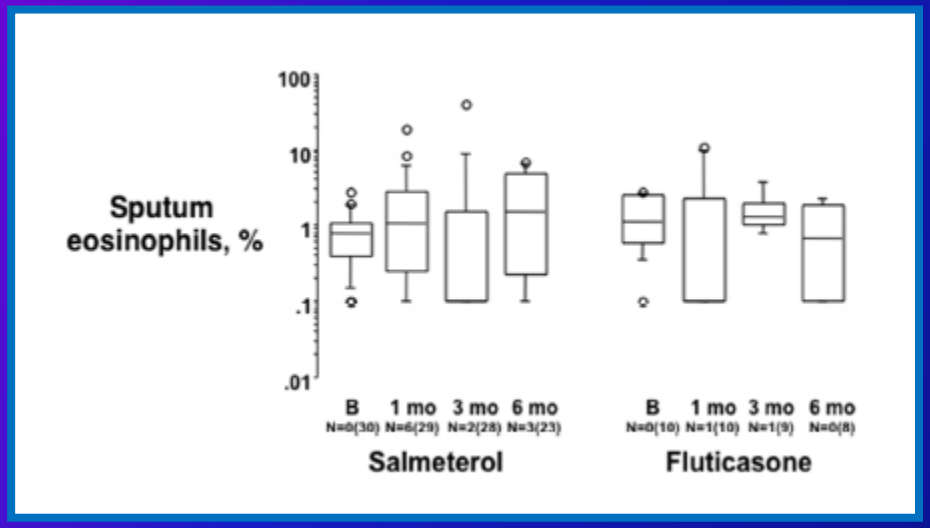
Absence of sputum eosinophilia in corticosteroid"naive" asthmatics predicts a poor short-term response to ICS

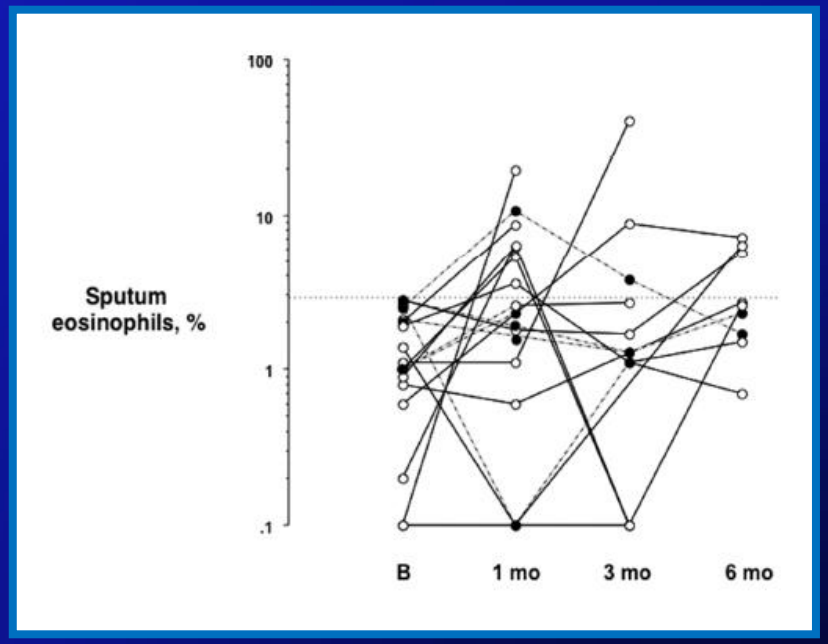
Table 4—*Negative and Positive Predictive Values, and Sensitivity and Specificity of Some Baseline Indices in Predicting Two Different Outcomes (FEV_1 Increase ≥ 12% and PD_{20} Doubling Dose) After Corticosteroid Treatment*

Variables	Predictive Value, %		Sensitivity, %	Specificity, %
	Negative	Positive		
FEV_1 increase ≥ 12%				
Sputum eosinophils				
≤ 3%	100		100	
> 3%		34		34
Baseline FEV_1				
≥ 80%	86		59	
< 80%		56		84
PD_{20}				
≥ 400 μg	82		80	
< 400 μg		18		20
Daily symptom score				
<1	87		87	
≥ 1		27		27
PD_{20} doubling dose				
Sputum eosinophils				
≤ 3%	73		84	
> 3%		43		28
Baseline FEV_1				
≥ 80%	59		11	
< 80%		33		86
PD_{20}				
≥ 400 μg	75		89	
< 400 μg		42		21
Daily symptom score				
< 1	54		68	
≥ 1		38		25

Bacci et al, Chest 2006

Steroid-naif symptomatic noneosinophilic asthma may remain stable over 6 months





Bacci et al, Respirology 2012

Assessment of asthma (vs COPD)

- Complete resolution of airway obstruction
  - Spontaneously or after treatment
- Diffusing capacity
  - Normal or increased
- Chest imaging
  - Chest X-ray
    - » Not useful
  - Chest tomography
    - » No emphysema findings

Which are the main characteristics of COPD ?

- Risk factors: smoke
- Clinical manifestations: dyspnea on exercise, chronic cough and sputum
- Functional manifestations: non competely reversible airway obstruction
- Biologic background: neutrophilic inflammation
- Response to treatment: mild and heterogeneous to ICS

DEFINITION OF COPD

OVERALL KEY POINTS:

- *Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.*

- *The most common respiratory symptoms include dyspnea, cough and/or sputum production. These symptoms may be under-reported by patients.*

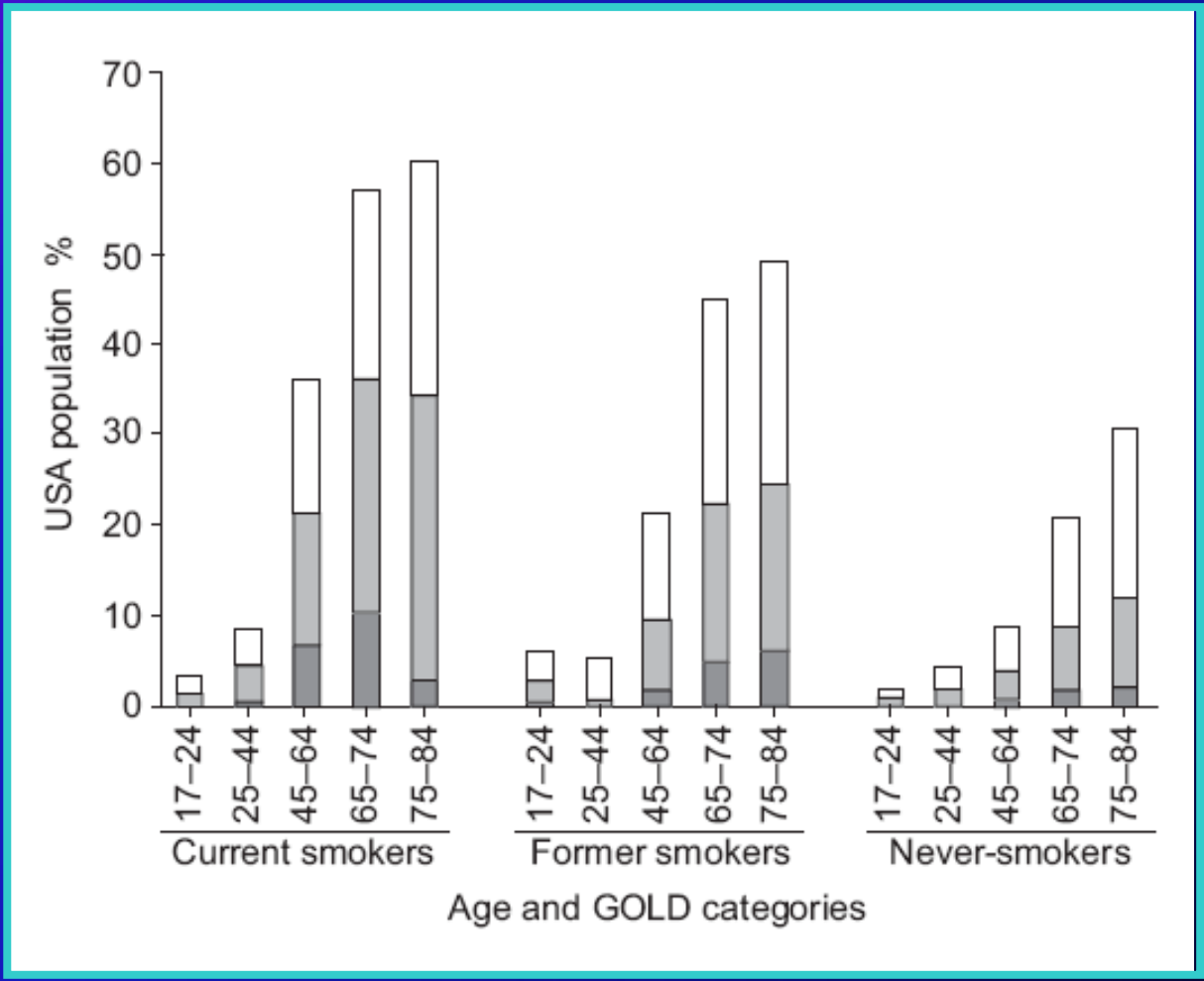
- *The main risk factor for COPD is tobacco smoking but other environmental exposures such as biomass fuel exposure and air pollution may contribute. Besides exposures, host factors predispose individuals to develop COPD. These include genetic abnormalities, abnormal lung development and accelerated aging.*

- *COPD may be punctuated by periods of acute worsening of respiratory symptoms, called exacerbations.*

- *In most patients, COPD is associated with significant concomitant chronic diseases, which increase morbidity and mortality.*

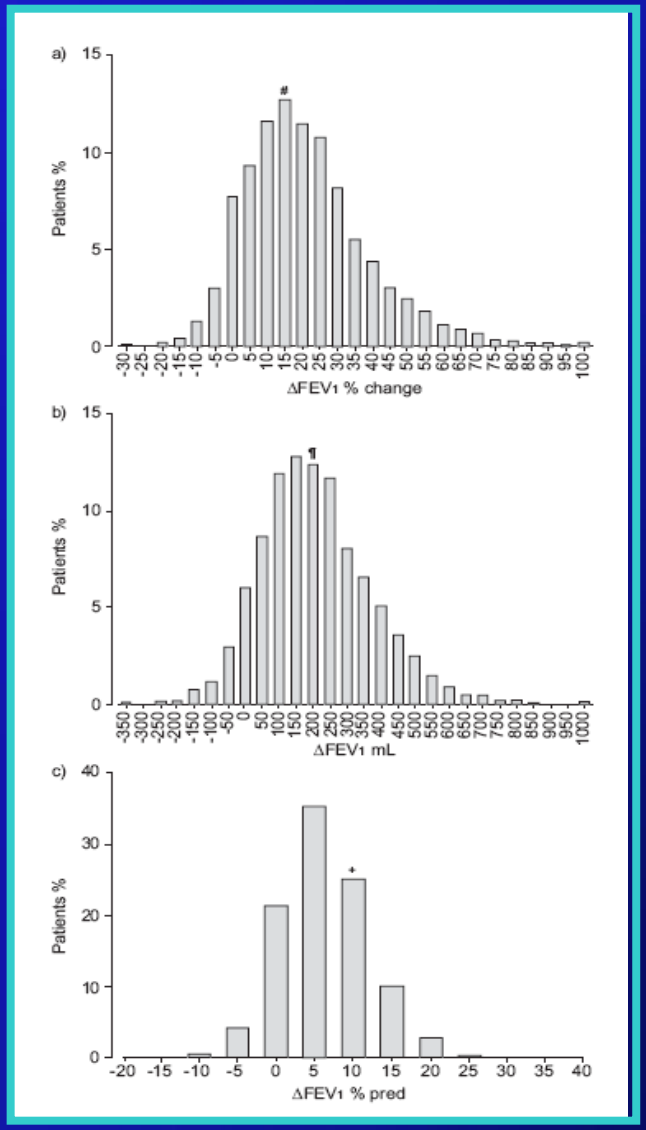
GOLD document 2017

In the general population, a consistent percentage of COPD is represented by non smokers



Mannino et al, ERJ 2006

Partial but relevant reversibility of airway obstruction is frequent in COPD patients

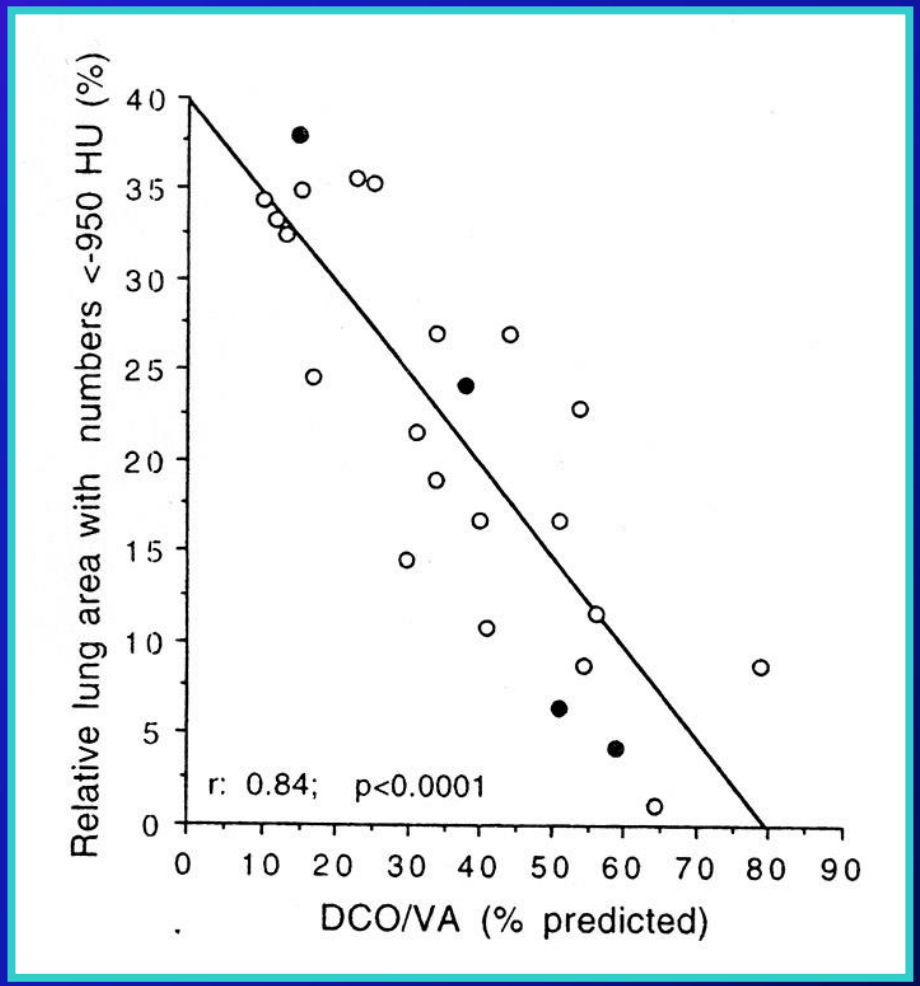


Tashkin et al,
ERJ 2008

Assessment of COPD (vs asthma)

- **Static lung volumes**
  - **Hyperinflation: present in emphysema, sometines in acute and chronic severe asthma**
- **Diffusing capacity**
  - **Reduced in COPD (mainly in emphysema)**
- **Chest imaging**
  - **Chest X-ray**
    - » **Low sensitivity in mild COPD patients**
  - **Chest tomography**
    - » **Qualitative vs quantitative (%HU < -950)**

Diffusing capacity is the best functional test related to the severity of emphysema

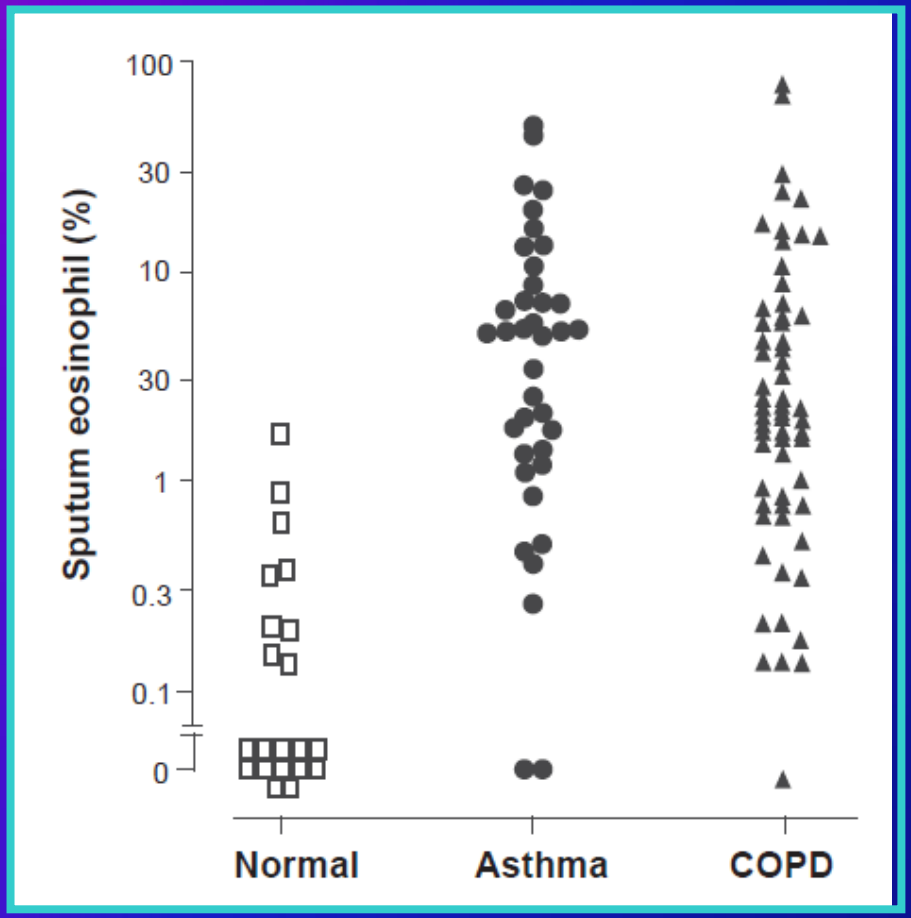


Baldi et al, AJRCCM 2000

Asthma-COPD overlap syndrome: different possibilities

- Asthma with fixed airway obstruction
  - Asthma progression in a subgroup of patients
  - Asthma phenotype ?
- Asthma and smoking habit
  - Asthma in childhood or adolescence (< 40 yrs)
  - Smoking habit
  - Funtional abnormalities of asthma and COPD
- COPD with large variability of airway obstruction
  - Eosinophilic component, good response to ICS
  - COPD phenotype ?

High frequency of sputum eosinophils in COPD patients

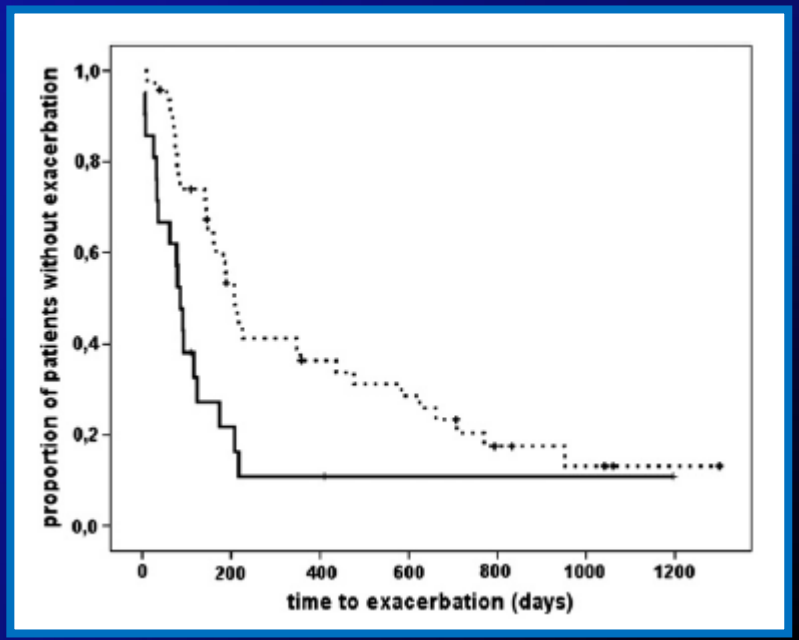


The origin of eosinophilic airway inflammation in COPD is unclear, although it is widely assumed that it indicates an asthmatic component to the fixed airways obstruction (Barnes 1998). This is unlikely to be the case, as most studies on patients with COPD rigorously exclude subjects with variable airflow obstruction and those with clinical features suggesting asthma. It is more likely that smoking and other mechanisms that recruit neutrophils into the airway mucosa in COPD may in turn cause a minor degree of eosinophil influx. However, it is difficult to explain the very high levels of sputum eosinophilia observed in some of our subjects. An alternative and intriguing possibility is that eosinophilic COPD starts as eosinophilic bronchitis.

Eosinophilic inflammation and response to ICS in COPD

- **Eosinophilic inflammation**
  - **Is frequent in several COPD patients**
  - **Mainly in acute mild-moderate exacerbations**
- **Response to ICS is better in eosinophilic than in non eosinophilic patients**
  - **Increase in FEV1**
  - **Prevention of exacerbations**
- **Exacerbation recurrence after ICS withdrawal is higher in eosinophilic COPD pts**

(Liesker, RespMed 2011)



FORWARD data: exacerbations

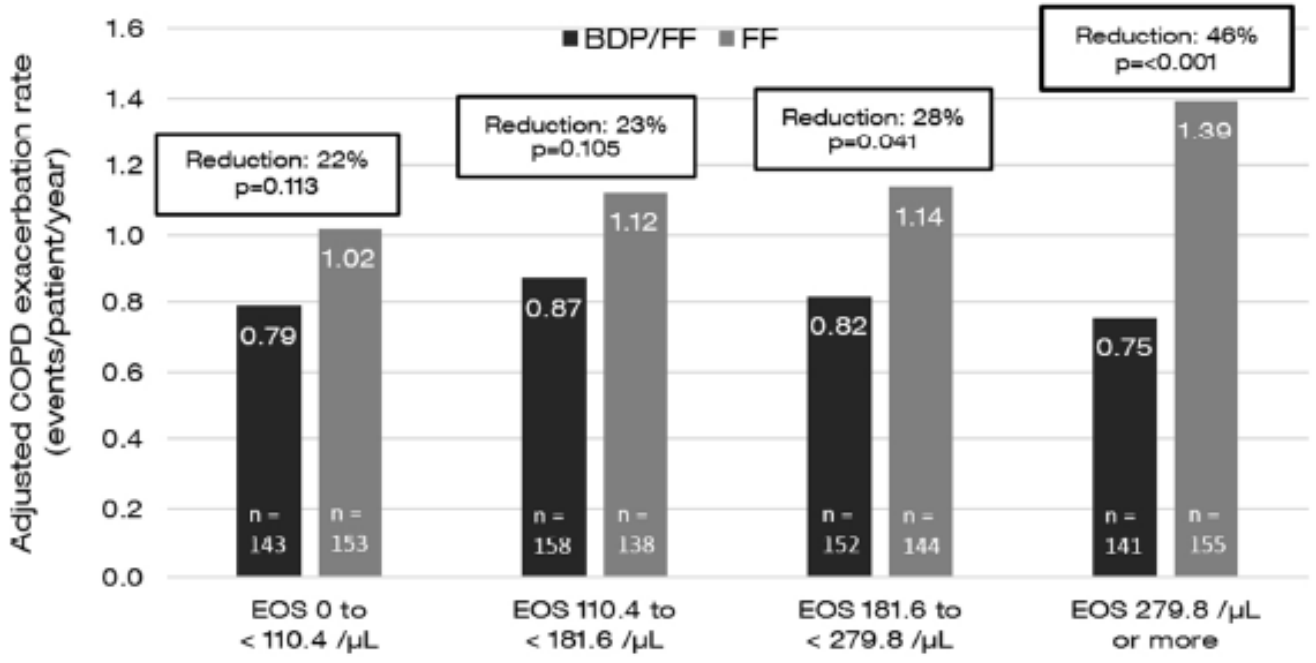
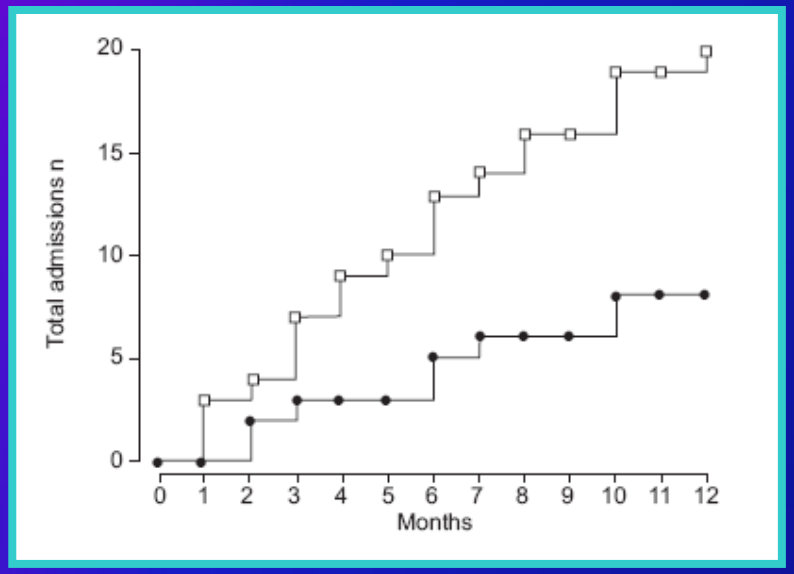
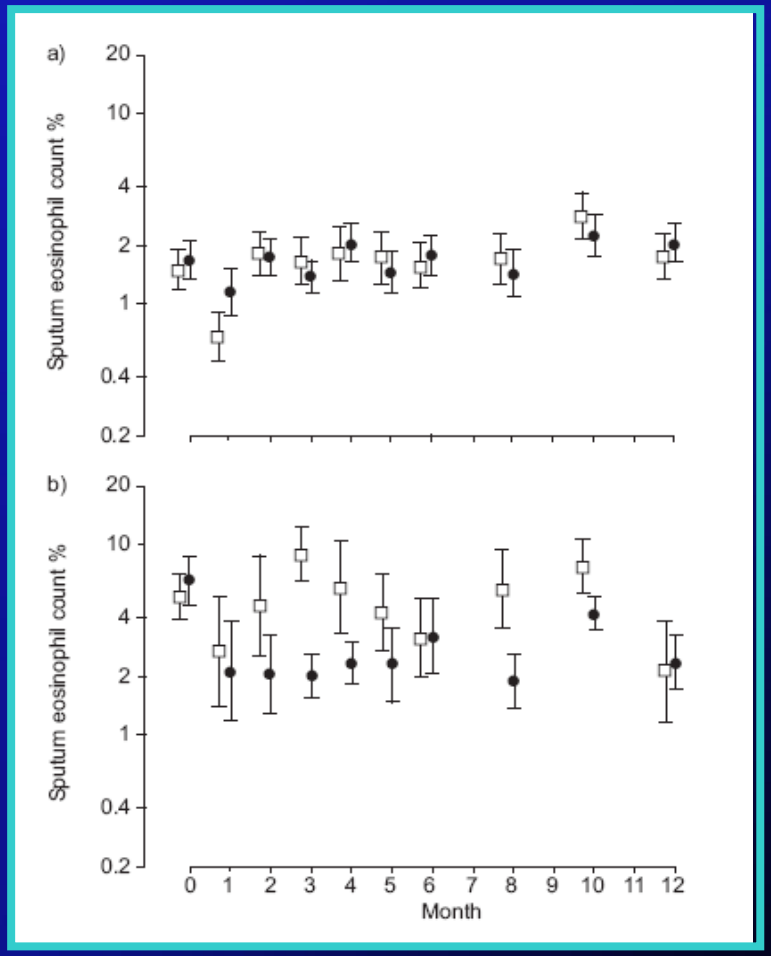


Figure 1a: Adjusted COPD exacerbation rate (events/patient/year) with BDP/FF (black) and FF (grey) stratified by baseline blood eosinophil quartile.

Siddiqui, Paggiaro et al, Am J Respir Crit Care Med. 2015

A strategy aiming to minimize sputum eosinophilia reduces the number of severe exacerbations of COPD



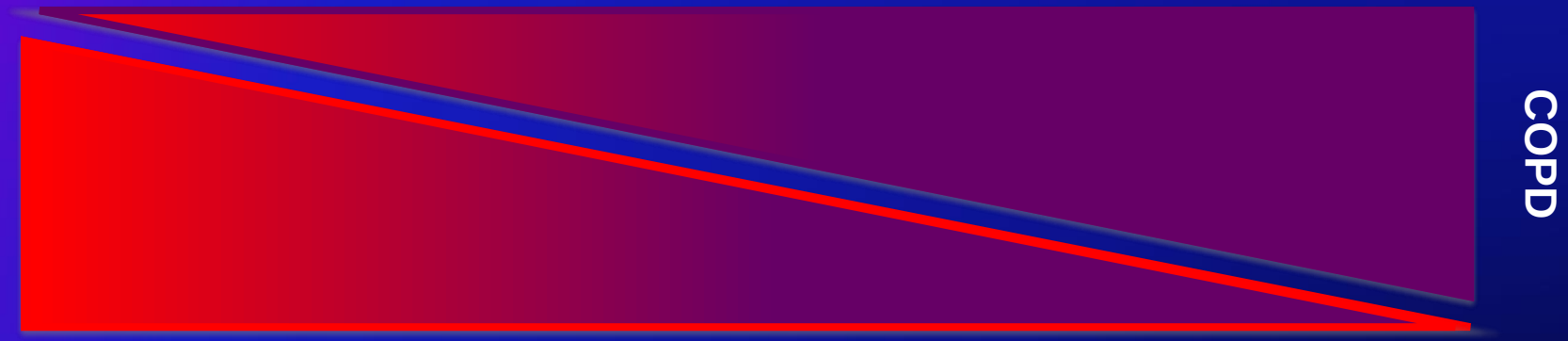


Siva et al, ERJ 2007

Asthma and COPD

COPD

- **Partial reversibility**
- **Eosinophilic inflammation**



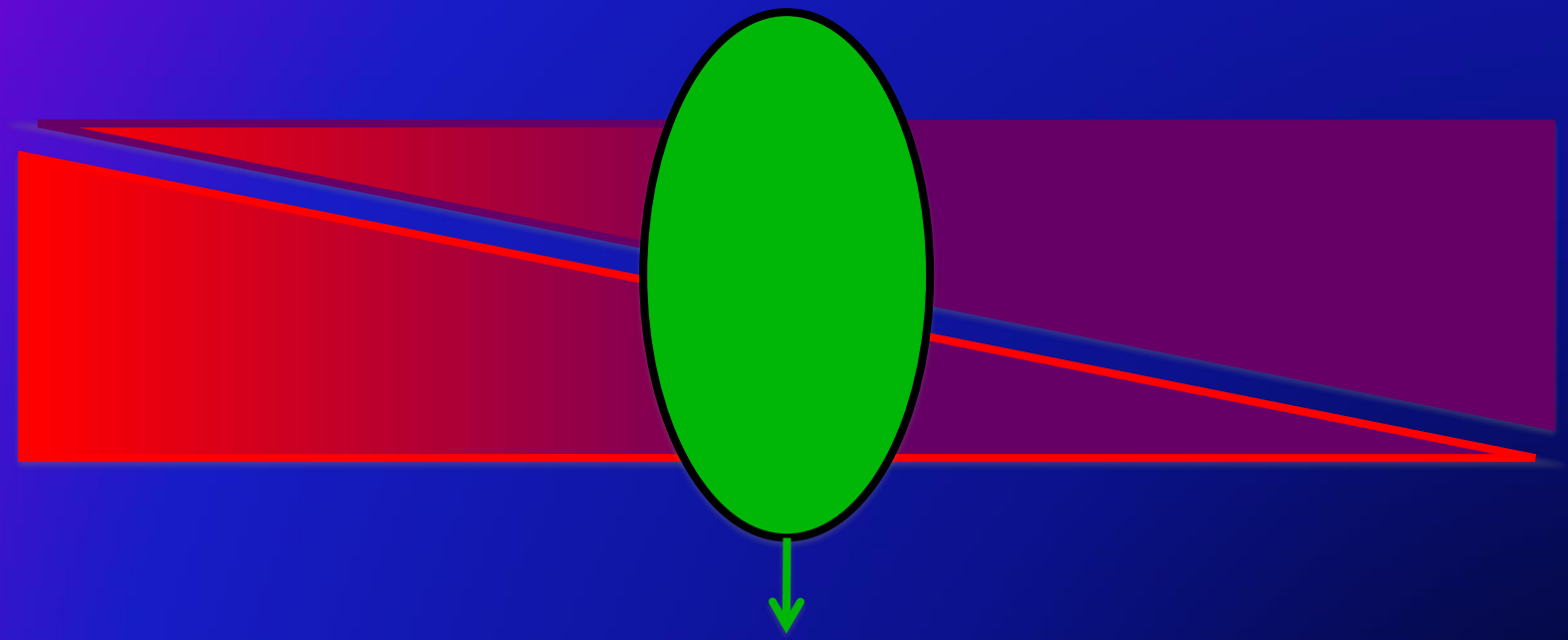
Asthma

- **Aging**
- **Adult onset**
- **Smoking**
- **Not fully reversible**

From Papi

Asthma and COPD

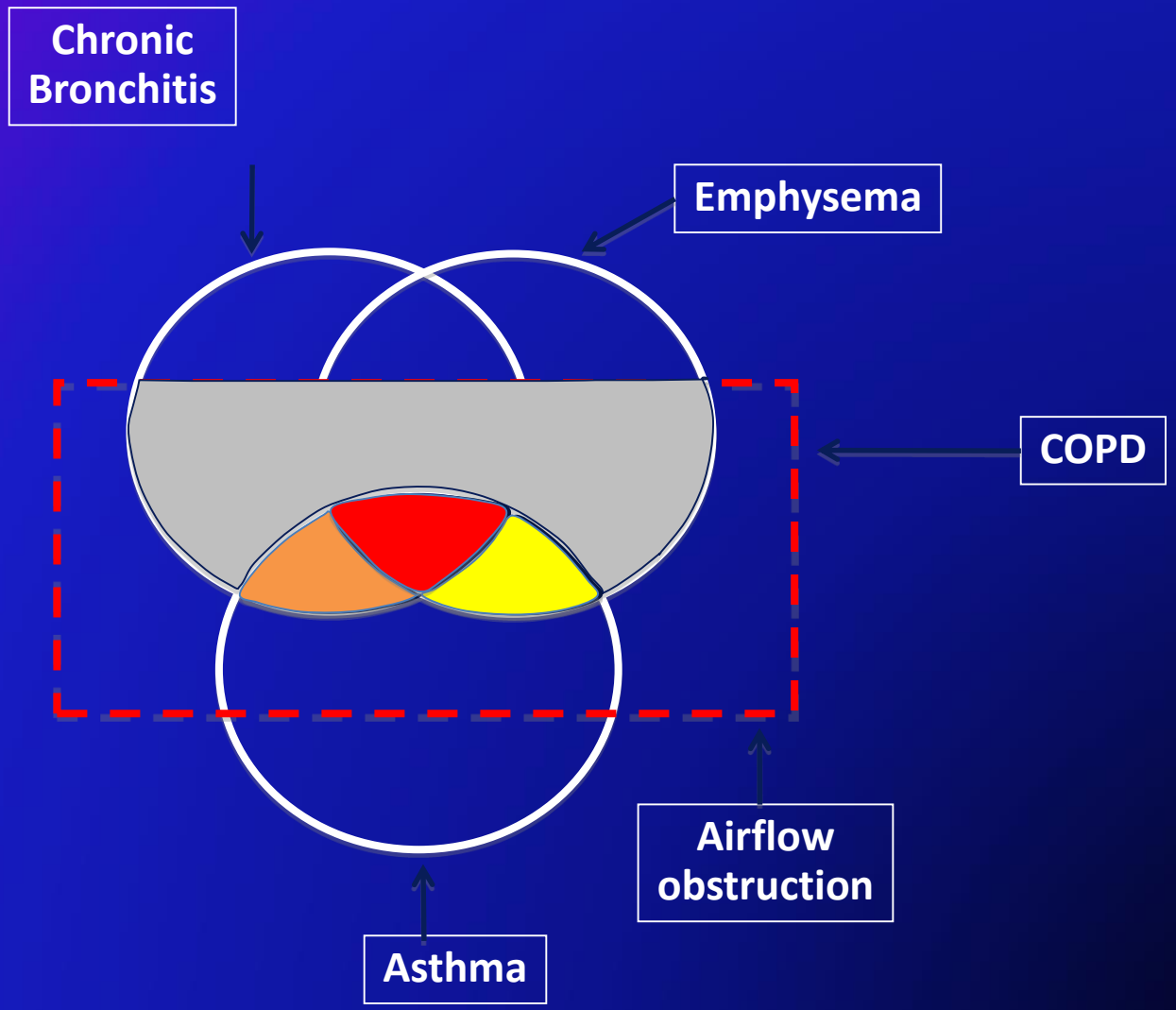
Overlap syndrome



- **Excluded from clinical trials of treatment**
- **Uncertainties in the diagnosis**
- **Model for identify mechanistic pathways leading to the development of COPD**

From Papi

The non proportional Venn Diagram



AJRCCM ATS-COPD 1995

Diagnosis of Diseases of Chronic Airflow Limitation:

Asthma COPD and Asthma - COPD Overlap Syndrome (ACOS)

Based on the Global Strategy for Asthma Management and Prevention and the Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease.

STEP 1 DIAGNOSE CHRONIC AIRWAYS DISEASE

STEP 2 SYNDROMIC DIAGNOSIS IN ADULTS

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

Feature if present suggests	ASTHMA	COPD
Age of onset	☐ Before age 20 years	☐ After the 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 (FEV1/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 SPECIALIZED INVESTIGATIONS or REFER IF

- 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 or either asthma or COPD
- Comorbidities present
- Reasons for referral for other diagnosis as outlined in the GINA and GOLD strategy reports.

GINA 2014

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 favor of each diagnosis and select a diagnosis.

Feature if present suggests	ASTHMA	COPD
Age of onset	☐ Before age 20 years	☐ After the age 40 years
Pattern of symptoms	☐ Variation over minutes, hours or days ☐ Worse during the night or early morning	☐ Persistent despite treatment ☐ Good and bad days but always daily symptoms and

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
SPECIALIZED
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 or either asthma or COPD
- Comorbidities present
- Reasons for referral for either diagnosis as outlined in the GINA and GOLD strategy reports.

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Box 6-6 Specialized investigations sometimes used in distinguishing asthma and COPD

Test	Asthma	COPD
Lung function tests		
DLCO	Normal (or slightly elevated).	Often reduced.
Airway hyperresponsiveness (AHR)	Not useful on its own in distinguishing asthma from COPD, but high levels of AHR favor asthma	
Arterial blood gases	Normal between exacerbations	May be chronically abnormal between exacerbations in more severe forms of COPD
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		
Blood eosinophilia	Supports asthma diagnosis	May be present during exacerbations
Sputum inflammatory cell analysis	Role in differential diagnosis is not established in large populations	
FENO	A high level (>50 ppb) in non-smokers supports a diagnosis of eosinophilic airway inflammation	Usually normal. Low in current smokers.
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

Suggested treatment for Asthma-COPD syndrome

STEP 4: Commence initial therapy

Faced with a differential diagnosis equally balanced between asthma and COPD (i.e. ACOS) the default position should be to start treatment accordingly for asthma (see below). This recognizes the pivotal role of ICS in preventing morbidity and even death in patients with uncontrolled asthma symptoms, for whom even seemingly 'mild' symptoms (compared to those of moderate or severe COPD) might indicate significant risk of a life-threatening attack[442].

- Where the syndromic assessment suggests asthma or ACOS, or there is significant uncertainty about the diagnosis of COPD, it is prudent to start treatment as for asthma until further investigation has been performed to confirm or refute this initial position.
  - Treatments will include an ICS (in a low or moderate dose, depending on level of symptoms).
  - A long-acting bronchodilator (LABA) must also be continued (if already prescribed), or added. However, it is important that patients should not be treated with a LABA without an ICS (often called LABA monotherapy) if there are features of asthma.
- Likewise, patients with COPD should receive appropriate symptomatic treatment with bronchodilators or combination therapy, but not ICS alone (as monotherapy).
- Treatment of ACOS should also include advice about other therapeutic strategies[447] including:
  - Smoking cessation
  - Pulmonary rehabilitation
  - Vaccinations
  - Treatment of comorbidities, as advised in the GINA and GOLD reports.

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Special Article

Consensus Document on the Overlap Phenotype COPD–Asthma in COPD☆

Juan José Soler-Cataluña,[a,*] Borja Cosío,[b] José Luis Izquierdo,[c] José Luis López-Campos,[d] José M. Marín,[e] Ramón Agüero,[f] Adolfo Baloira,[g] Santiago Carrizo,[e] Cristóbal Esteban,[h] Juan B. Galdiz,[i] M. Cruz González,[j] Marc Miravitlles,[k] Eduard Monsó,[l] Teodoro Montemayor,[m] Josep Morera,[n] Francisco Ortega,[d] Germán Peces-Barba,[o] Luis Puente,[p] José Miguel Rodríguez,[p] Ernest Sala,[b] Jaume Sauleda,[b] Joan B. Soriano,[q] José Luis Viejo[r]

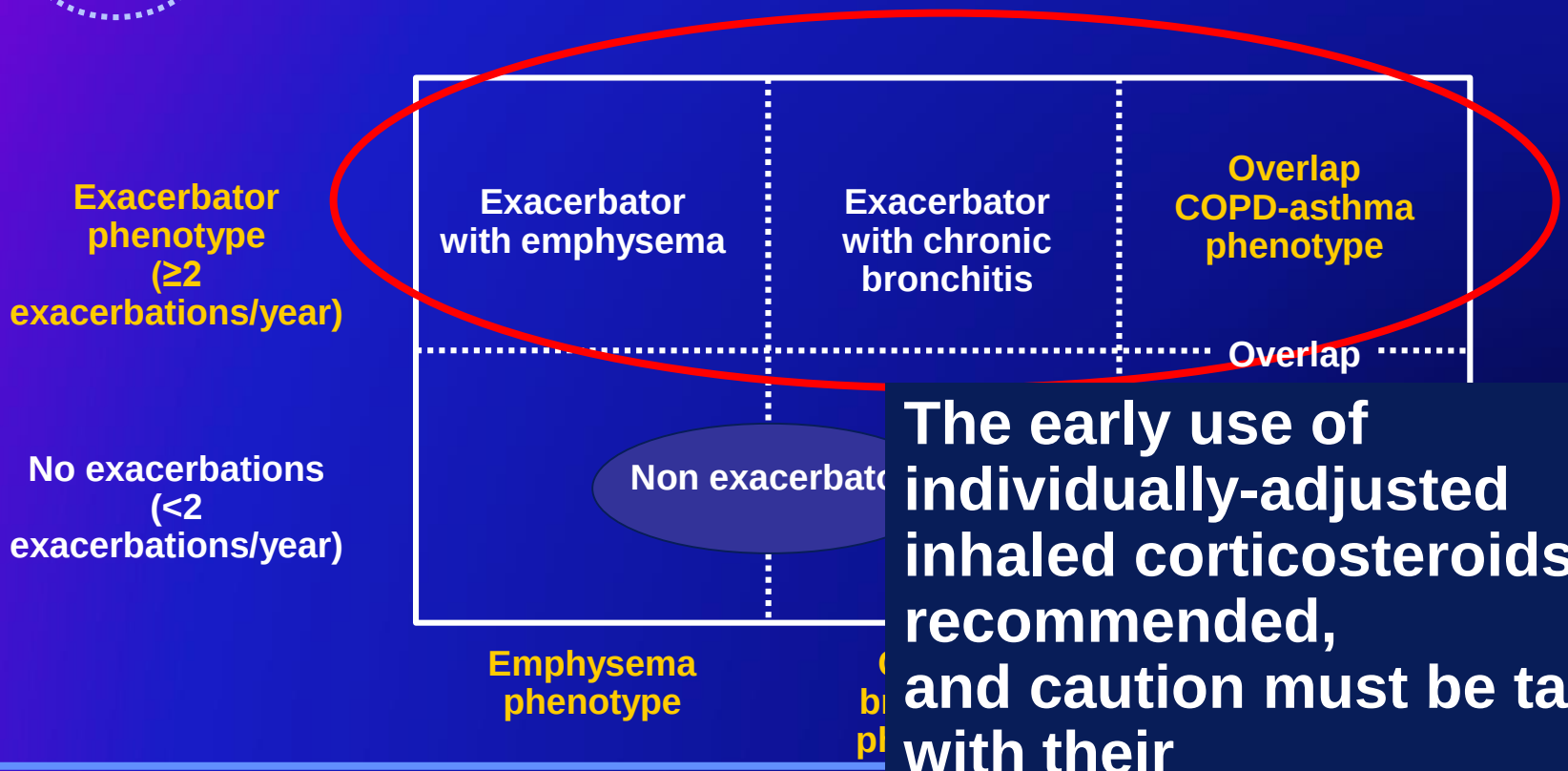
Arch Bronconeumol. 2012;48:331–7.

Table 4
Major and Minor Criteria for the Identification of the Mixed COPD/Asthma Phenotype.

Diagnostic Criteria of the Mixed COPD/Asthma Phenotype That Were Agreed Upon[a]	% of Agreement in Order to Be Considered a Major Criterion[b]	Type of Criterion
Very positive bronchodilator test (increase of FEV_1 ≥15% and ≥400 ml over baseline)	83	Major
Eosinophilia in sputum	78	Major
Personal history of asthma (history before the age of 40)	78	Major
High total IgE	50	Minor
Personal history of atopy	50	Minor
Positive bronchodilator test (increase in FEV_1 ≥12% and ≥200 ml over baseline) on 2 or more occasions	39	Minor

Phenotype diagnosis

Step 2 → Phenotype characterization



The early use of individually-adjusted inhaled corticosteroids is recommended, and caution must be taken with their abrupt withdrawal.

Spanish Guidelines of overlap syndrome suggest the combined treatment with ICS and one or more bronchodilators

Treatment of the phenotype

In all the patients with mixed COPD–asthma phenotype, the early administration of inhaled corticosteroid treatment should be assessed

As in asthma, in patients with mixed COPD–asthma phenotype the dosage of inhaled corticosteroids should be adjusted according to the control of the symptoms, lung function and/or the presence of eosinophils in sputum

In severe cases of patients with COPD and mixed COPD–asthma phenotype, triple therapy with a long-acting anticholinergic, a long-acting beta-2 agonist and an inhaled corticosteroid may be indicated

In patients with COPD and mixed COPD–asthma phenotype, the abrupt withdrawal of maintenance treatment with inhaled corticosteroids may produce exacerbations in some patients, although there is not sufficient evidence in this type of patients

Soler Cataluna et al, Arch Bronc 2012

Asthma-COPD Overlap Syndrome: What We Know and What We Don't

Don D. Sin, M.D.

Table 3. Definition of ACOS from ATS Roundtable Discussions[13]

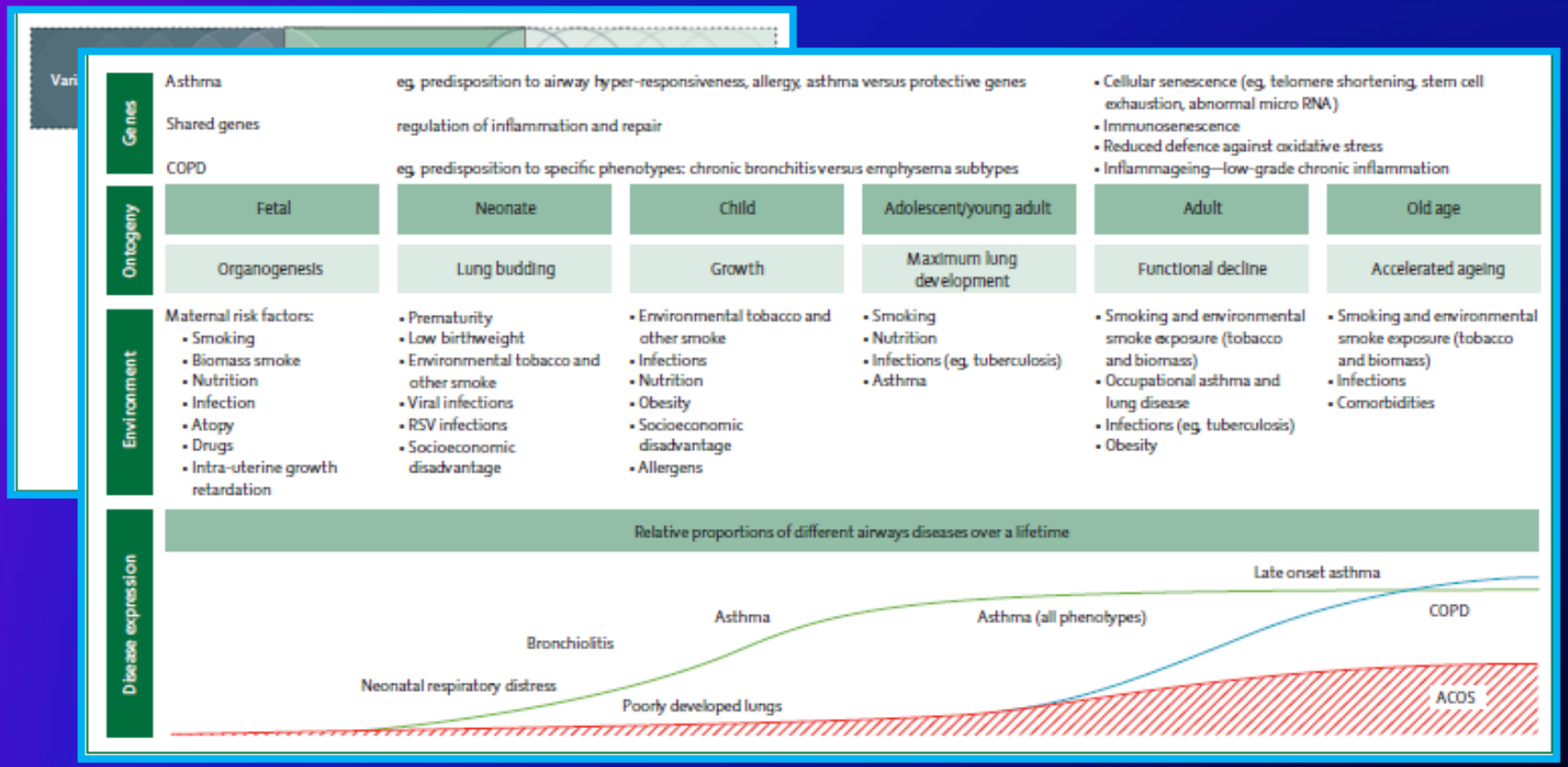
Major criteria	Minor criteria
Persistent airflow limitation (post-bronchodilator FEV_1/FVC <0.70 or LLN) in individuals 40 years of age or older; LLN is preferred	Documented history of atopy or allergic rhinitis
At least 10 pack-years of tobacco smoking or equivalent indoor or outdoor air pollution exposure (e.g., biomass)	BDR of FEV_1 ≥200 mL and 12% from baseline values on 2 or more visits
Documented history of asthma before 40 years of age or BDR of >400 mL in FEV_1	Peripheral blood eosinophil count of ≥300 cells/μL

To fulfill ACOS, the patient must have all three major criteria and at least one minor criterion.
ACOS: asthma-COPD overlap syndrome; COPD: chronic obstructive pulmonary disease; ATS: American Thoracic Society; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; LLN: lower limit of normal; BDR: bronchodilator response.

The asthma–COPD overlap syndrome: towards a revised taxonomy of chronic airways diseases?

Eric D Bateman, Helen K Reddel, Richard N van Zyl-Smit, Alvar Agusti

Lancet Respiratory Medicine 2015



The asthma–COPD overlap syndrome: towards a revised taxonomy of chronic airways diseases?

Eric D Bateman, Helen K Reddel, Richard N van Zyl-Smit, Alvar Agusti

Lancet Respiratory Medicine 2015

Panel 1: A clinical description of the asthma–COPD overlap syndrome

- Age 40 years or older (usually)
- Airflow limitation persistent and not fully reversible, but often with existing or historical variability or airway hyper-reactivity, or both
- Respiratory symptoms, including exertional dyspnoea, are persistent but variability can be prominent
- Might have had symptoms in childhood or early adulthood
- Frequently a history of doctor-diagnosed asthma (existing or previous), allergies, a family history of asthma, or a history of noxious exposures—or any of these features
- Symptoms are partly but substantially reduced by treatment
- Exacerbations can be more common than in COPD but are reduced by treatment
- Symptoms worsen over time
- Treatment needs are high
- Comorbidities can contribute to impairment
- Chest radiograph—as for COPD (eg, hyperinflation or bullae might be seen)
- Increase in eosinophils or neutrophils, or both, in sputum

Key messages

- Asthma–COPD overlap syndrome (ACOS) is not a disease entity but a term applied to patients with clinical features of both asthma and chronic obstructive pulmonary disease (COPD)
- ACOS is associated with greater morbidity than asthma and COPD alone, and with relative treatment refractoriness, but since most clinical studies have excluded such patients, information is sparse
- The clinical usefulness of ACOS is predominantly in non-specialist practice where detailed diagnostic tests are not available
- Recommendations based on consensus suggest that patients with suspected ACOS should be given both a long-acting bronchodilator (the cornerstone of COPD treatment) and an inhaled corticosteroid (the cornerstone of asthma treatment)
- Evolving concepts of gene–environment interactions in the natural history and pathogenesis of chronic airways diseases point to the need for a revised and expanded taxonomy based on phenotyping and endotyping rather than clinical descriptions alone, in which inclusive terms like ACOS might not be needed

Asthma-COPD overlap syndrome: do we really need that ?

- **Do we really need asthma-chronic obstructive pulmonary disease overlap syndrome?**
  - **Cazzola M, Rogliani P**
  - **J Allergy Clin Immunol. 2016 Oct;138(4):977-983**

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- **Main characteristics of Asthma and COPD**
  - **Typical patient: Definite Asthma vs Definite COPD**
  - **Several intermediate situations («…. a continuum ….»**

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- Main characteristics of Asthma and COPD
  - Typical patient: Definite Asthma vs Definite COPD
  - Several intermediate situations («…. a continuum ….»
- Dutch hypothesis reconsidered
  - Asthma with some COPD features
  - COPD with some asthma features
- Phenotyping and endotyping single patient