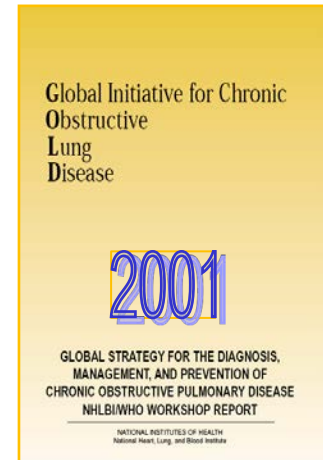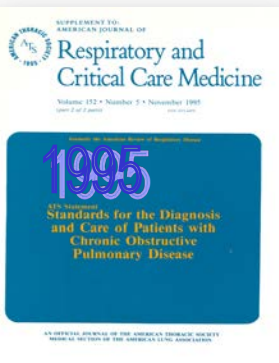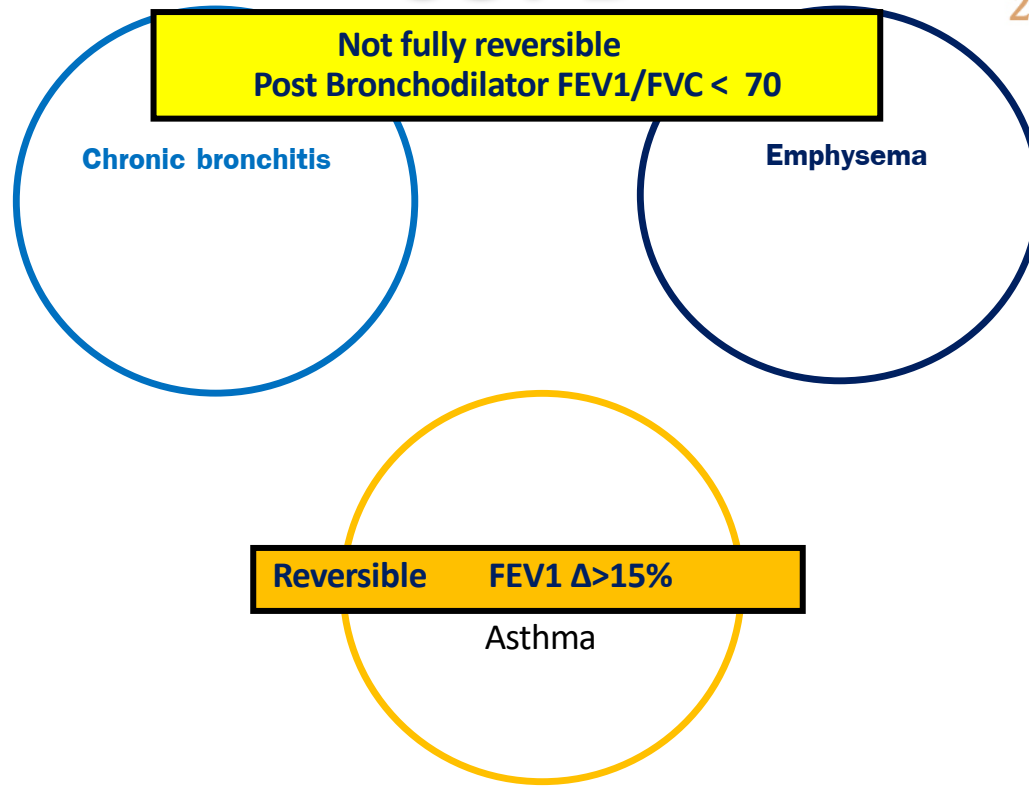# Clinical Characteristics to Differentiate Asthma, COPD, ACO

Watchara Boonsawat, MD., Ph.D.

Khon Kaen University, Khon Kaen, Thailand

Disclosure

- **Lecture honorarium: Astra Zeneca, Boehringer Ingelheim**

- **Advisory Board Member: Astra Zeneca, Boehringer Ingelheim, GSK**

Connecting a Global Community
in Clinical Chest Medicine

ometry	(BTPS)	PRED	PRE-RX BEST	%PRED	POST-RX BEST	%PRED	% CHG
FVL Time			11:00		11:30		
FVC	Liters	4.03	3.51	87	3.77	94	7
FEV1	Liters	2.99	1.46	49	1.88	63	29
FEV1/FVC	%	74	41		50		
FEF25-75%	L/min	188	33	18	42	22	26
FEF25%	L/min		80		100		25
FEF50%	L/min	226	41	18	51	23	26
FEF75%	L/min	83	14	17	19	22	30
PEF	L/min	458	213	47	229	50	7
FIVC	Liters	4.03	0.12	3	0.39	10	222
FEV1	Liters	2.99	1.46	49	1.88	63	29
IC	Liters	2.70					
FEF/FIF50		<1.00	32.43		0.29		-99
Vol Extrap	Liters		0.04		0.04		11
FVL ECode			111000		100010		
MVV	L/min	131					
f	BPM						

Prevalence of Chronic Obstructive Pulmonary Disease in China

A Large, Population-based Survey

Nanshan Zhong[1], Chen Wang[2], Wanzhen Yao[3], Ping Chen[4], Jian Kang[5], Shaoguang Huang[6], Baoyuan Chen[7], Changzheng Wang[8], Diantao Ni[9], Yumin Zhou[1], Shengming Liu[1,10], Xiaoping Wang[11], Dali Wang[12], Jiachun Lu[13], Jingping Zheng[1], and Pixin Ran[1]

[1]Guangzhou Institute of Respiratory Diseases, The First Affiliated Hospital, Guangzhou Medical College, Guangzhou, Guangdong, China; [2]Beijing Institute of Respiratory Medicine, Beijing Chaoyang Hospital, Capital University of Medical Sciences, Beijing, China; [3]The Third Hospital, Peking University, Beijing, China; [4]The Shenyang Military General Hospital, Shenyang, Liaoning, China; [5]The First Affiliated Hospital, China Medical University, Shenyang, Liaoning, China; [6]Ruijin Hospital, Shanghai Jiaotong University, Shanghai, China; [7]The General Hospital, Tianjin Medical University, Tianjin, China; [8]Xinqiao ... University, Xi'an, Shanxi, China; ... ital of Shaoguan, Shaoguan, Gua... partment of Epidemiology, ...

Rationale: The ... (COPD) in Chi...
Objectives: To o... population, spi...
Methods: Urba... randomly selec... of age or older in the selected clusters were interviewed with a standardized questionnaire revised from the international BOLD (Burden of Obstructive Lung Diseases) study. Spirometry was performed on all eligible participants. Patients with airflow limitation (FEV$_1$/FVC < 0.70) were further examined by post-bronchodilator spirometry, chest radiograph, and electrocardiogram. Post-bronchodilator FEV$_1$/FVC of less than 70% was defined as the diagnostic criterion of COPD.
Measurements and Main Results: Among 25,627 sampling subjects 20,245 participants completed the questionnaire and spirometry (response rate, 79.0%). The overall prevalence of COPD was 8.2% (men, 12.4%; women, 5.1%). The prevalence of COPD was signifi-

What This Study Adds to the Field

COPD is prevalent and underrecognized in individuals 40 years of age or older in China.

... fourth lead... nited States, but its prevalence in China is largely unknown.

Chronic obstructive pulmonary disease (COPD) is a disease state characterized by airflow limitation that is not fully reversible (1). As a major public health problem, COPD is the fourth leading
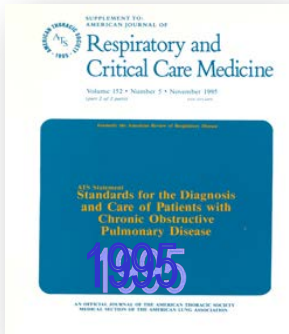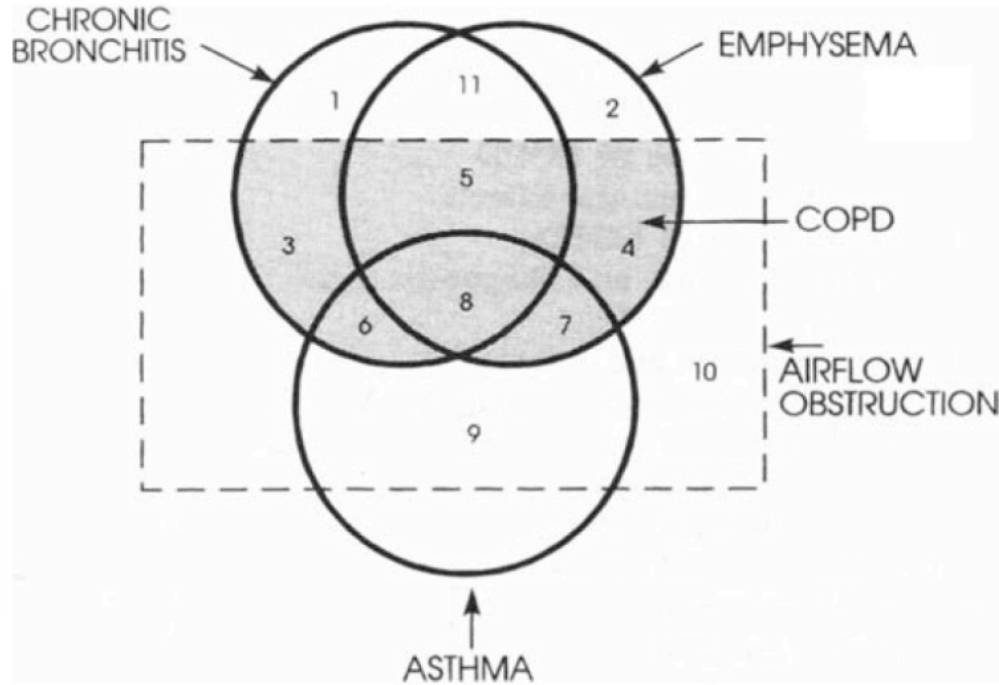

Prevalence COPD = 8.2 %

two-thirds (61.4%) of patients with COPD,
 including 81.8% of male patients with COPD
and 24.0% of female patients with COPD, were smokers;

13.2% of smokers had COPD,

THORAX

CHEST Congress 2019 | Thailand
Bangkok | 10-12 April

Asthma

Episodic respiratory symptoms
Variable airflow obstruction
occurring spontaneously, with
treatment or after provocation

COPD

Incompletely reversible
airflow obstruction

Overlap syndrome

Asthma and COPD—that is, symptoms of
increased variability of airflow and
incompletely reversible airflow obstruction

- Asthma with chronic bronchitis
- Chronic obstructive bronchitis
- Asthma with permanent obstruction
- COPD with a reversible component

Connecting a Global Community
in Clinical Chest Medicine

How important is it?

Overlap syndrome are excluded from clinical trials of asthma or COPD treatment

For clinicians to select appropriate therapy

Studying overlap syndrome may identify mechanistic pathways leading to the development of COPD
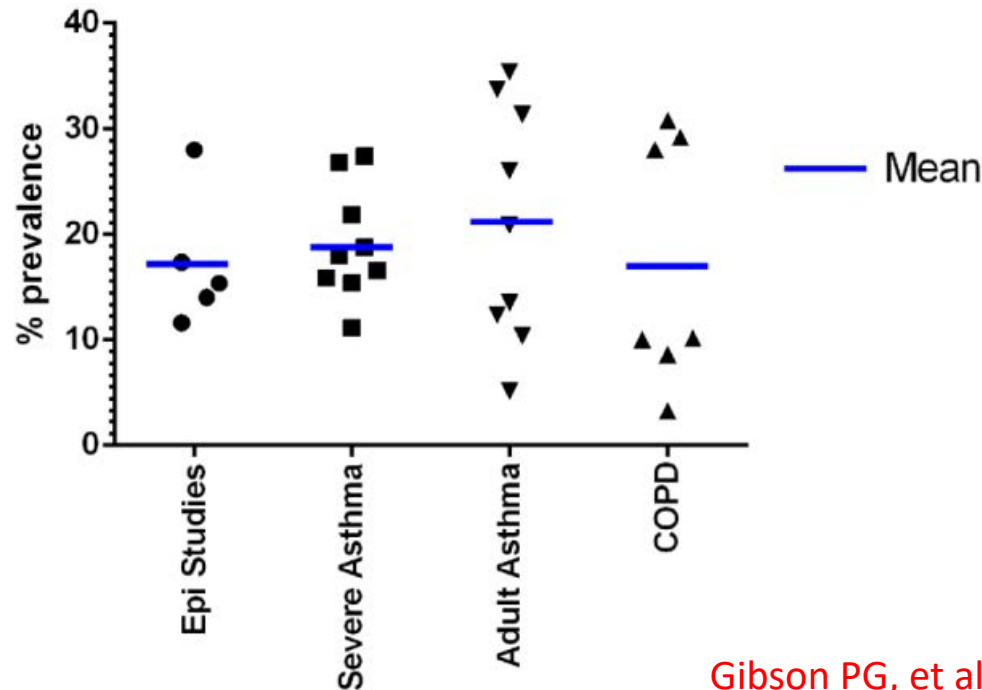
Connecting a Global Community
in Clinical Chest Medicine

What is the prevalence of asthma-COPD overlap?

A. 10

B. 20

C. 40

D. 50

What is the prevalence of asthma-COPD overlap?

A. 10

B. 20

C. 40

D. 50

Prevalence of asthma-COPD overlap

Gibson PG, et al. Thorax 2015;70:683–691.

most guidelines and publications largely agree on the following components or traits of ACO

- presence of persistent airflow limitation in adults $\geq$ 40 years of age

- a significant smoking or biomass exposure history

- a history of atopy or asthma

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.

Sin DD. Tuberculosis and respiratory diseases 2017;80:11-20.

ARCHIVOS DE BRONCONEUMOLOGIA

www.archbronconeumol.org

Recommendations of SEPAR

Spanish COPD Guidelines (GesEPOC): Pharmacological Treatment of Stable COPD[☆,☆☆,★]

Table 1

Major and Minor Criteria for Establishing the Diagnosis of Mixed COPD Asthma Phenotype in COPD.[20]

Major criteria
Very positive bronchodilator test (increase in FEV_1 >15% and >400 mL)
Eosinophilia in sputum
Personal history of asthma

Minor criteria
High levels of total IgE
Personal history of atopy
Positive bronchodilator test on at least two occasions (increase of FEV_1 >12% and >200 mL)

2major criteria or
1major and 2minor criteria should be met.

Definitions

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]
Asthma-COPD overlap syndrome (ACOS) [a description]
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.

Stepwise approach to diagnosis and initial treatment

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)

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	☐ Persistent despite treatment
	☐ Worse during the night or early morning	☐ Good and bad days but always daily symptoms and exertional dyspnea
	☐ Triggered by exercise, emotions including laughter, dust or exposure to allergens	☐ Chronic cough & sputum preceded on-set 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	☐ Previous doctor diagnosis of COPD, chronic bronchitis or emphysema
	☐ Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)	☐ 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	☐ Symptoms slowly worsening over time (progressive course over years)
	☐ May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks	☐ 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 - 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 3 - Spirometry

- Essential if chronic airways disease is suspected
  - Confirms chronic airflow limitation
  - More limited value in distinguishing between asthma with fixed airflow limitation, COPD and ACOS
- Measure at the initial visit or subsequent visit
  - If possible measure before and after a trial of treatment
  - Medications taken before testing may influence results
- Peak expiratory flow (PEF)
  - Not a substitute for spirometry
  - Normal PEF does not rule out asthma or COPD
  - Repeated measurement may confirm excessive variability, found in asthma or in some patients with ACOS

Step 4 – Commence initial therapy

- Initial choices based on syndromic assessment and spirometry
  - If features are consistent with asthma, treat as asthma
  - If features are consistent with COPD, treat as COPD
  - If syndromic assessment suggests ACOS, or there is significant uncertainty about the diagnosis of COPD, start treatment as for asthma pending further investigation
- Consider both efficacy and safety
  - If any features of asthma, do not prescribe LABA without ICS
  - If any features of COPD, give symptomatic treatment with bronchodilators or combination therapy, but not ICS alone
  - If ACOS, give ICS and consider LABA and/or LAMA
- Other important strategies for ACOS and COPD
  - Non-pharmacological strategies including smoking cessation, pulmonary rehabilitation, vaccinations, treatment of comorbidities

Step 5 – Refer for specialized investigations if needed

- Refer for expert advice and extra investigations if patient has:
  - Persistent symptoms and/or exacerbations despite treatment
  - Diagnostic uncertainty, especially if alternative diagnosis (e.g. TB, cardiovascular disease) needs to be excluded
  - Suspected airways disease with atypical or additional symptoms or signs (e.g. hemoptysis, weight loss, night sweats, fever, chronic purulent sputum). Do not wait for a treatment trial before referring
  - Suspected chronic airways disease but few features of asthma, COPD or ACOS
  - Comorbidities that may interfere with their management
  - Issues arising during on-going management of asthma, COPD or ACOS

- A Thai male 54 year old. Smoking 20 pack-year

- CC: cough, wheeze and dyspnea for 6 months. He had more symptoms during the night.

- He was treated with Salbutamol MDI 2puff prn, Salbutamol tab 1x3, Bromhexine 1x3

- He had frequent Emergency room Visit for exacerbsations in the past 6 months

- PE: RR 16 /min PR 70/min BP 135/80
  - Chest expiratory wheezing

CHEEP, SURA   Id: HO1981   Room: Out-Pt
Male   Date: 22/04/10
54   Race: Asian   Temp: 29   PBar: 749
t(cm): 165   Weight(kg): 54.0   Physician: DR.WATCHARA
fo: COPD POST BD 3 HRS   Technician: KEAW/V/3/1

ometry	(BTPS)	PRED	PRE-RX BEST	%PRED	POST-RX BEST	%PRED	% CHG
FVL Time			11:00		11:30		
FVC	Liters	4.03	3.51	87	3.77	94	7
FEV1	Liters	2.99	1.46	49	1.88	63	29
FEV1/FVC	%	74	41		60		
FEF25-75%	L/min	188	33	18	42	22	25
FEF25%	L/min		80		100		25
FEF50%	L/min	226	41	18	51	23	26
FEF75%	L/min	83	14	17	19	22	30
PEF	L/min	458	213	47	229	50	7
FIVC	Liters	4.03	0.12	3	0.39	10	222
FEV1	Liters	2.99	1.46	49	1.88	63	29
IC	Liters	2.70					
FEF/FIF50		<1.00	32.43		0.29		-99
Vol Extrap	Liters		0.04		0.04		11
FVL ECode			111000		100010		
MVV	L/min	131					
f	BPM						

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	☐ Persistent despite treatment
	☐ Worse during the night or early morning	☐ Good and bad days but always daily symptoms and exertional dyspnea
	☐ Triggered by exercise, emotions including laughter, dust or exposure to allergens	☐ Chronic cough & sputum preceded on-set 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	☑ Previous doctor diagnosis of COPD, chronic bronchitis or emphysema
	☐ Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)	☑ 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	☐ Symptoms slowly worsening over time (progressive course over years)
	☐ May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks	☐ 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

What is the diagnosis

A. COPD

B. Asthma

C. ACO

What is the diagnosis

A. COPD

B. Asthma

C. **ACO**

Sura, Torchip
Male
Race: Asian
55

ID: HO1981
Date: 11/03/11
Temp: 26

11 months after treatment with ICS/LABA

ometry	(BTPS)	PRED	PRE-RX BEST	%PRED	POS BEST
FVL Time			20:06		
FVC	Liters	4.00	4.17	104	
FEV1	Liters	2.96	2.77	94	
FEV1/FVC	%	74	66		
FEF25-75%	L/min	186	95	51	
FEF25%	L/min		254		
FEF50%	L/min	224	134	60	
FEF75%	L/min	82	34	41	
PEF	L/min	456	430	94	
FIVC	Liters	4.00	0.30	7	
FEV1	Liters	2.96	2.77	94	
IC	Liters		3.29		
FEF/FIF50		<1.00	0.09		
Vol Extrap	Liters		000000		
FVL ECode					
MVV	L/min	130			
f	BPM				

Name: T...
Gender: Male
Age: 56   Race: Asian
Height(cm): 165   Weight(kg): 55.0
...ny Info: ASTHMA

ID: HO1981
Date: 21/10/11
Temp: 26
Physician: Dr V...
Technician: Ke...

Spirometry

	(BTPS)	PRED	PRE-RX BEST	%PRED	POST BEST
FVL Time			18:42		
FVC	Liters	3.98	4.12	103	
FEV1	Liters	2.93	3.13	107	
FEV1/FVC	%	73	76		
FEF25-75%	L/min	183	144	79	
FEF25%	L/min		378		
FEF50%	L/min	222	198	89	
FEF75%	L/min	81	49	61	
PEF	L/min	454	475	105	
FIVC	Liters	3.98	0.00		
FEV1	Liters	2.93	3.13	107	
IC	Liters				
FEF/FIF50		<1.00			
Vol Extrap	Liters		0.10		
FVL ECode			000011		
MVV	L/min	128			
f	BPM				

Treatable traits: toward precision medicine of chronic airway diseases

Alvar Agusti[1], Elisabeth Bel[2], Mike Thomas[3], Claus Vogelmeier[4],
Guy Brusselle[5,6], Stephen Holgate[7], Marc Humbert[8], Paul Jones[9],
Peter G. Gibson[10], Jørgen Vestbo[11], Richard Beasley[12] and Ian D. Pavord[13]

Should the terms "asthma" and "COPD" be abandoned?

The proposal outlined in this Perspective, *i.e.* to manage patients with airway disease based on those treatable traits present in each individual and to abandon the traditional diagnostic labels, is a paradigm change. We are firmly convinced that it better reflects the clinical and biological complexity of airway diseases, and may eventually result in better patient management than the current "label-based" approach. However, we also
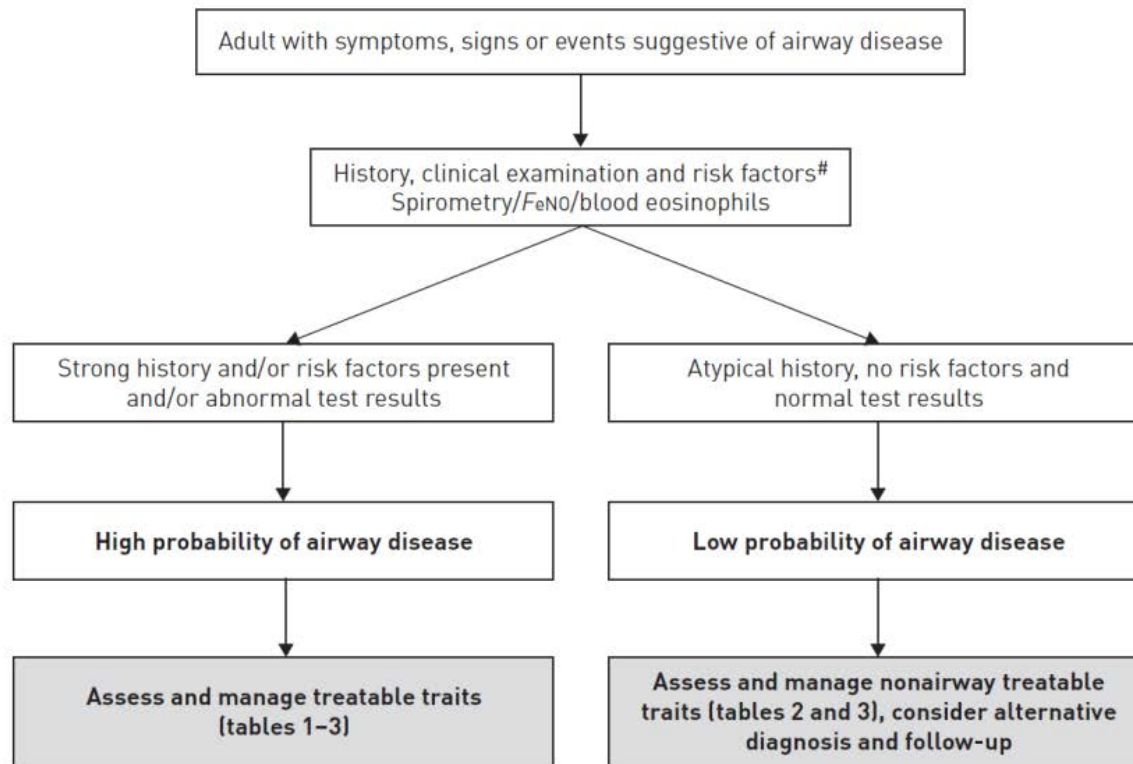
FIGURE 1 Proposed diagnostic strategy for an adult with symptoms, signs or events suggestive of airway disease. For further explanations, see text. F_{eNO}: exhaled nitric oxide fraction. [#]: smoking, allergies, sputum production, occupation, lung development and growth.

TABLE 1 List of potential pulmonary, extrapulmonary and behavioural/lifestyle treatable traits to consider in patients with chronic airway diseases

Trait	Treatment
Pulmonary treatable traits	
Airway smooth muscle contraction	Bronchodilators
Eosinophilic airway inflammation	Corticosteroids/Type 2 biologics
Chronic sputum production	Smoking cessation, macrolides, PDE4 inhibitors
Bacterial colonisation	Macrolides, tetracyclines
Bronchiectasis	Macrolides, tetracyclines, nebulised antibiotics/aminoglycosides
Cough reflex hypersensitivity	Gabapentin, P2X3, speech pathology intervention
Chronic respiratory failure	Oxygen/NIV/lung transplant
Pulmonary hypertension	Oxygen/NIV/lung transplant
Emphysema	Lung volume reduction/transplant

Extrapulmonary treatable traits

Rhinosinusitis	Topical steroids/surgery
Deconditioning	Rehabilitation
Cachexia	Diet/physical activity
Obesity	Diet/physical activity/bariatric surgery
Cardiovascular disease	ACE inhibitors/diuretics/β-blockers
Vocal cord dysfunction	Speech pathology therapy
Depression	Cognitive and behavioural therapy
Anxiety	Anxiolytics
Systemic inflammation	Statins?

Treatable behavioural/lifestyle factors

Poor inhalation technique	Education
Nonadherence to treatment	Reassurance/education/periodic check-up
Smoking	Cessation support
Exposure to sensitising agents	Avoidance/desensitisation
Side-effects of treatments	Treatment optimisation
Polypharmacy	Medication review
Poor family and social support	Family therapy education/self-management support

---

PDE4: phosphodiesterase-4; P2X3: P2X3 receptor antagonist; NIV: noninvasive ventilation; ACE: angiotensin-converting enzyme.

- The overlap between asthma and COPD is increasingly recognized

- More research is needed to define these overlap phenotypes and to understand the best way of managing these patients

Connecting a Global Community
in Clinical Chest Medicine

Join colleagues from around the region to gain access to the CHEST learning and training experience at our regional congress. This unique program will go beyond the classroom-style setting to connect you to leading experts who will teach and develop you and your team.

Learn More: athens.chestnet.org

CHEST®
Regional Congress

ATHENS 2019
GREECE | 27-29 JUNE

ΕΛΛΗΝΙΚΗ ΠΝΕΥΜΟΝΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ
HELLENIC THORACIC SOCIETY