**Supplementary Table S1. Criteria for diagnosis of ACO**

| ACO definition | Diagnostic criteria |
|----------------|---------------------|
| Definition of ACO from ATS roundtable discussion<sup>1</sup> | To fulfill ACO, the patient must have **all three major criteria** and **at least one minor criterion**.  
**Major criteria**  
Persistent airflow limitation (post-bronchodilator \( \text{FEV}_1 \)) in individuals 40 years of age or older  
At least 10 pack-years of tobacco smoking or equivalent indoor or outdoor air pollution exposure (e.g., biomass)  
Documented history of asthma before 40 years of age or BDR of >400 mL in \( \text{FEV}_1 \)  
**Minor criteria**  
Documented history of atopy or allergic rhinitis  
BDR of \( \text{FEV}_1 \) ≥200 mL and 12% from baseline values on 2 or more visits  
Peripheral blood eosinophil count of ≥300 cells/μL. |
| Modified SEPAR definition of ACO<sup>2</sup> | **Persistent airflow limitation and ≥1 of the following major criteria:**  
Bronchodilator response ≥15% and 400 mL. Previous history of asthma  
**OR ≥2 of the following minor criteria:**  
High total IgE level or history of atopy  
At least 2 separated bronchodilator responses ≥12% and ≥200 mL or blood eosinophilia >5% |
| GINA/GOLD consensus<sup>3</sup> | **More likely asthma if**  
1. Onset < age 20 years  
2. Variation in symptoms within short periods  
3. Worsening of symptoms at night/early morning  
4. Symptoms triggered by exercise, emotions/laughter, dust, or exposure to allergens  
5. Documented airflow limitation variability (peak flow, spirometry)  
6. Lung function normal between symptoms  
7. Previous doctor diagnosis of asthma  
8. Family history of asthma or atopy/eczema  
9. No worsening of symptoms over time. Symptoms vary either seasonally or from year to year  
10. May improve spontaneously or have an immediate response to bronchodilators or to inhaled steroids over weeks  
11. Chest X-ray normal  

**More likely COPD if**  
1. Onset > age 40 years  
2. Persistence of symptoms  
3. Daily symptoms with and exertional dyspnea with good/bad days  
4. Chronic cough and sputum preceded onset of dyspnea, unrelated to triggers  
5. Documented persistent airflow limitation (postbronchodilator \( \text{FEV}_1 \)/\( \text{FVC} \) <70%)  
6. Lung function abnormal between symptoms  
7. Previous doctor diagnosis of COPD, chronic bronchitis, or emphysema  
8. Heavy exposure to a risk factor (tobacco smoke, biomass fuel)  
9. Symptoms slowly worsening over time (progressive course over years)  
10. Rapid-acting bronchodilator treatment provides only limited relief  
11. Chest X-ray with features of severe hyperinflation  

If ≥3 items are present for either asthma or COPD, the patient is likely to have that disease. A similar number of items for asthma and COPD is suggestive for ACO |
| Specialist diagnosis | Diagnosis of ACO based on physician’s own knowledge and experience |

ACO: asthma-COPD overlap; ATS: American Thoracic Society; \( \text{FEV}_1 \): forced expiratory volume in 1 second; BDR: bronchodilator response; SEPAR: Spanish Society of Pneumonology and Thoracic Surgery; OR: odds ratio; GINA: Global Initiative for Asthma; GOLD: Global Initiative for Chronic Obstructive Lung Disease; COPD: chronic obstructive pulmonary disease; FVC: forced vital capacity.
Supplementary Table S2. Change in lung function in 3 years

| Parameter | ATS roundtable | Modified SEPAR definition | GINA/GOLD criteria | Specialist diagnosis |
|-----------|----------------|---------------------------|--------------------|---------------------|
|           | ACO | Non-ACO p-value | ACO | Non-ACO p-value | ACO | Non-ACO p-value | ACO | Non-ACO p-value |
| No. of patients evaluated | 5 | 293 | 45 | 253 | 56 | 239 | 72 | 170 |
| \( \Delta \text{FEV}_1 (\%) \Delta \) | -9.6±6.8 | -0.4±0.7 | 0.093 | -4.3±2.3 | 0.2±0.7 | 0.024 | -24±2.2 | -0.0±0.7 | 0.300 | -5.4±1.7 | -0.3±0.9 | 0.003 |
| p-value | 0.233 | 0.609 | 0.068 | 0.836 | 0.273 | 0.990 | 0.002 | 0.781 |
| \( \Delta \text{FEV}_1 (\text{mL}) \Delta \) | -186±116 | 2±16 | 0.127 | -47±45 | 6±17 | 0.228 | -27±36 | 5±18 | 0.435 | -35±32 | -1±21 | 0.378 |
| p-value | 0.185 | 0.922 | 0.036 | 0.705 | 0.457 | 0.788 | 0.273 | 0.967 |
| \( \Delta \text{FVC} (\%) \Delta \) | -18.9±5.7 | -2.2±0.8 | 0.007 | -43±24 | -1.9±0.9 | 0.286 | -24±2.5 | -2.0±12.9 | 0.858 | -6.1±1.9 | -2.7±1.0 | 0.055 |
| p-value | 0.03 | 0.011 | 0.039 | 0.034 | 0.010 | 0.332 | 0.002 | 0.014 |
| \( \Delta \text{FVC (ml)} \Delta \) | -412±297 | -17±24 | 0.036 | -48±72 | -19±26 | 0.677 | -33±55 | -22±28 | 0.867 | -44±43 | -27±33 | 0.779 |
| p-value | 0.237 | 0.485 | 0.510 | 0.453 | 0.550 | 0.420 | 0.314 | 0.410 |

Values are presented as means±standard error of the means. Independent T test was used to compare ACO and non-ACO COPD groups, and paired T test was used to evaluate within group change. ATS: American Thoracic Society; SEPAR: Spanish Society of Pneumonology and Thoracic Surgery; GINA: Global Initiative for Asthma; GOLD: Global Initiative for Chronic Obstructive Lung Disease; ACO: asthma–chronic obstructive pulmonary disease overlap; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity.
References

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