# Current status of ACO in Korea

2021.3.6 천식-COPD 공동 연구회 심포지엄

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# Context

- Introduction
- Prevalence
- Clinical features
- Comoridities
- Diagnosis : biomarker & imaging
- Treatment
- Outcome

# Difficulties of ACO research

- In 2014, GINA and GOLD published a joint document on ACOS

- ***Current definition***
- "Asthma-COPD overlap" are terms used to collectively describe patients who have **persistent airflow limitation** together with **clinical features that are consistent with both asthma and COPD**.

GINA 2020

# GINA & GOLD : stepwise approach

| Features: if present suggest - | ASTHMA | COPD |
|---|---|---|
| Age of onset | ❑ Before age 20 years | ❑ After age 40 years |
| Pattern of symptoms | ❑ Variation over minutes, hours or days<br>❑ Worse during the night or early morning<br>❑ Triggered by exercise, emotions including laughter, dust or exposure to allergens | ❑ Persistent despite treatment<br>❑ Good and bad days but always daily symptoms and exertional dyspnea<br>❑ 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 betwe symptoms | | |
| Past history or famil | | |
| Time course | an immediate response to bronchodilators or to ICS over weeks | |
| Chest X-ray | ❑ Normal | ❑ Severe hyperinflation |

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

*Shaded columns list features that, when present, 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.*

GINA 2019

# Prevalence

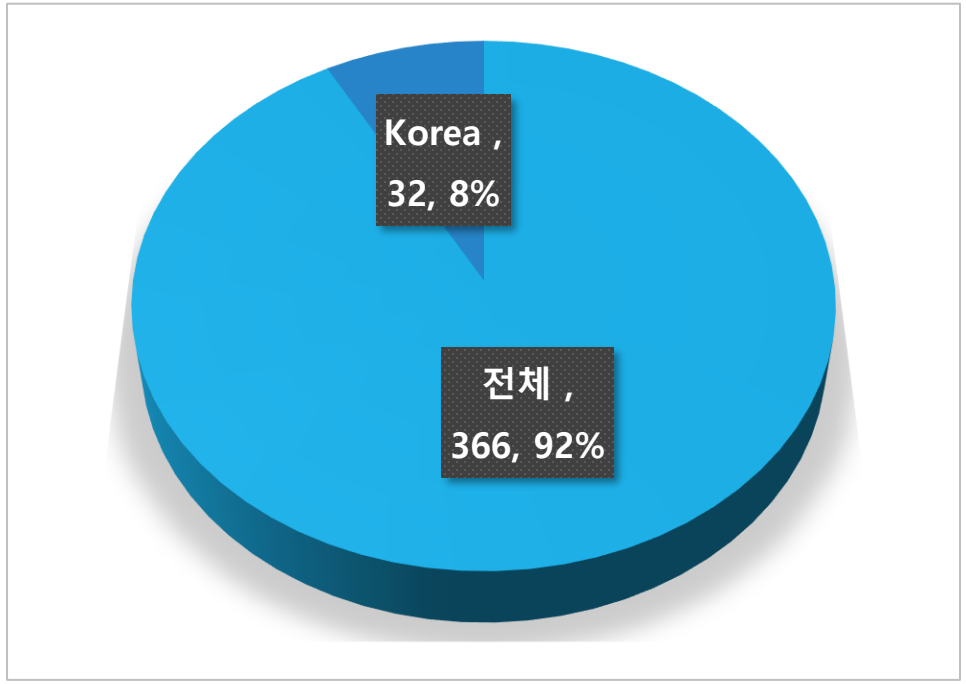
- ranged between 9% and 55%, with variation by gender and age (GINA 2020)

- No unified definition
- Excluded from either asthma or COPD study

- *Exact prevalence is unknown*
- *It varies according to diagnostic criteria*

# 국내 ACO 논문

- Pubmed ACO 논문 전체 : 366 results
- 국내 ACO 논문 : 32 results




# ACO in asthma cohort

**ACOS : (1) & (2)**

1) BDR (+) or AHR (+)

2) post-BD $FEV_1/FVC$ <0.70 for 3mo

- Asthma cohort, ≥40 years & 1) BDR (+) or AHR (+) (N=256)
- Asthma only (N=159, 62%) vs. Overlap group (N=97, 38%)

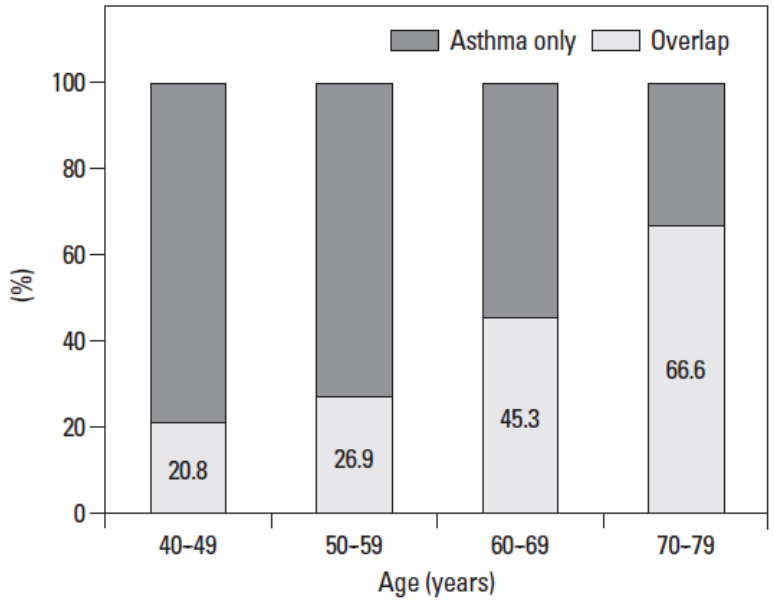
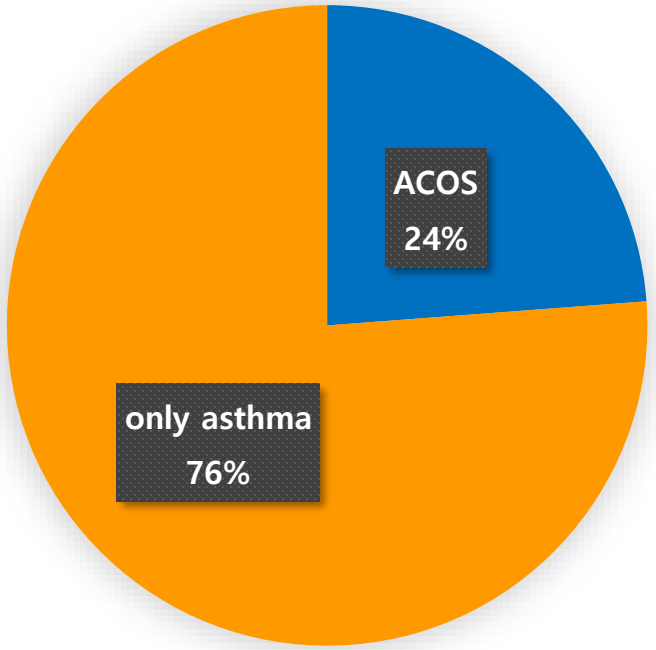



**Fig. 1.** The percentage of patients diagnosed with overlap in different age groups. The values above each bar represent the percentage of patients diagnosed with overlap in each age groups.

HY Lee et al. Yonsei Med J 55(4):980-986, 2014

- Asthma in COREA cohort (N=959) : positive BDR or AHR
- ACOS (N=228, 23.8%) vs. "only" asthma (N=731, 76.2%)

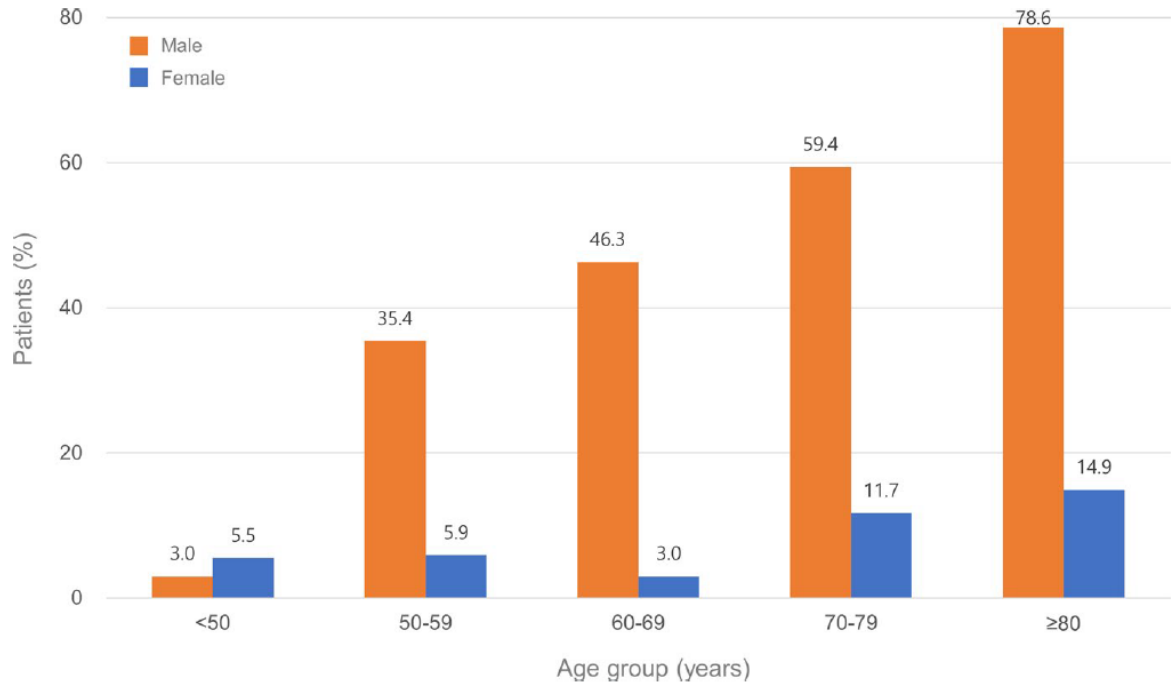



SY Park et al. Clin Exp Allergy. 2019;49:603–614.

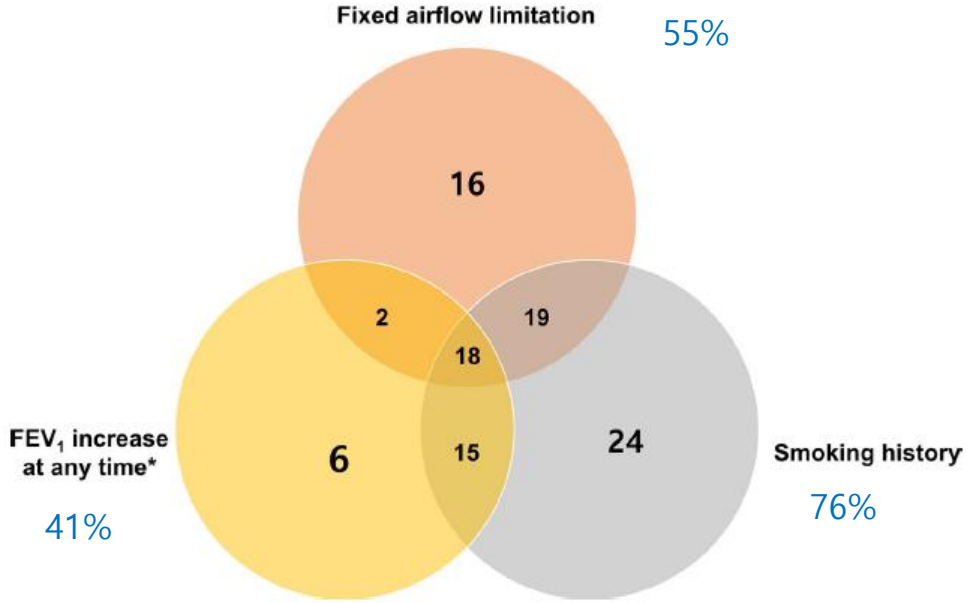
# ACO in asthma cohort

**ACOS : Specialists judgement**

- Specialist-diagnosed asthma-COPD overlap in Severe Asthma
- KoSAR cohort with severe asthma (N=482)
- 23.7% (N=114) were ACO




**The proportion of ACO by age group and sex**




**Reasons for diagnosis of ACO by specialists**

H Lee et al. Allergy. 2021;76:223-232.

# ACO in COPD cohort

**ACO** : >45years, FEV1/FVC <0.7 &

Asthma was diagnosed based on GINA definition

- Single center cohort : ASAN medical center
- Of the 2933 COPD patients, 767 (26.2%) were overlap syndrome

MA Kim et al. INT J TUBERC LUNG DIS 19(7):864–869

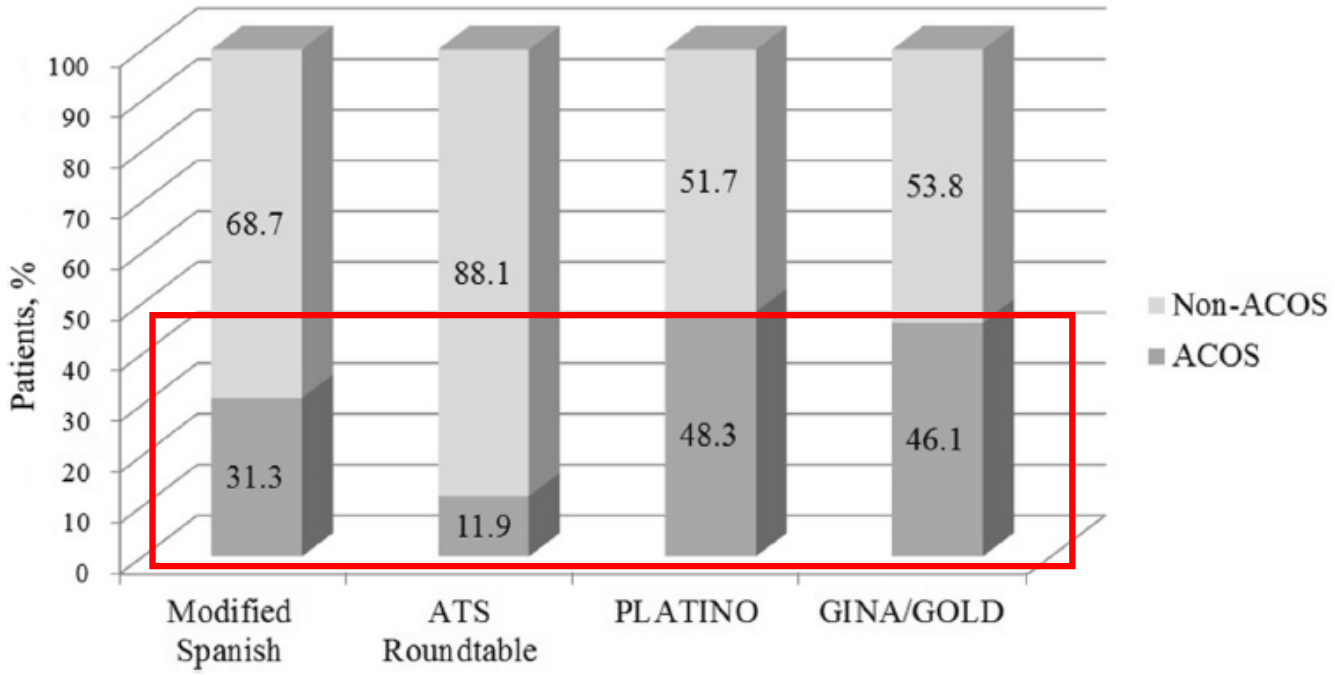
**ACO** : FEV1/FVC <0.7 & BDR (+)

- KOCOSS cohort (n=1504)
- Of the 1504 COPD patients, 223 (14.8%) were ACO

HJ Park et al. Allergy Asthma Immunol Res. 2017 September;9(5):431-437.

# ACO in COPD cohort

- SNUH COPD cohort (N=301)
- Exacerbation analysis in 194 patients who followed up ≥1 year




YS Jo et al. Ann Allergy Asthma Immunol 118 (2017) 696-703

- KOCOSS cohort
- ACO (47.7%, 660/1383) by modified Spanish criteria
- ACO (1.9%, 26/1383) by ATS Roundtable criteria

JH Song et al. Medicine (2018) 97:36(e12049)

# ACO in COPD cohort

- KNHANES
- $FEV_1$/FVC ratio <0.7 & FEV1 ≥60% predicted (N=2,140)
- Clustering analysis using 6 key input variables
  - age, BMI, $FEV_1$ % predicted, self-reported wheezing, smoking status, and pack-years of smoking

- Near normal (n=232, 11%)
- Asthma (n=392, 18%)
- COPD (n=37, 2%)
- Asthmatic-predominant overlap (n=893, 42%)
- COPD-predominant overlap (n=586, 27%)

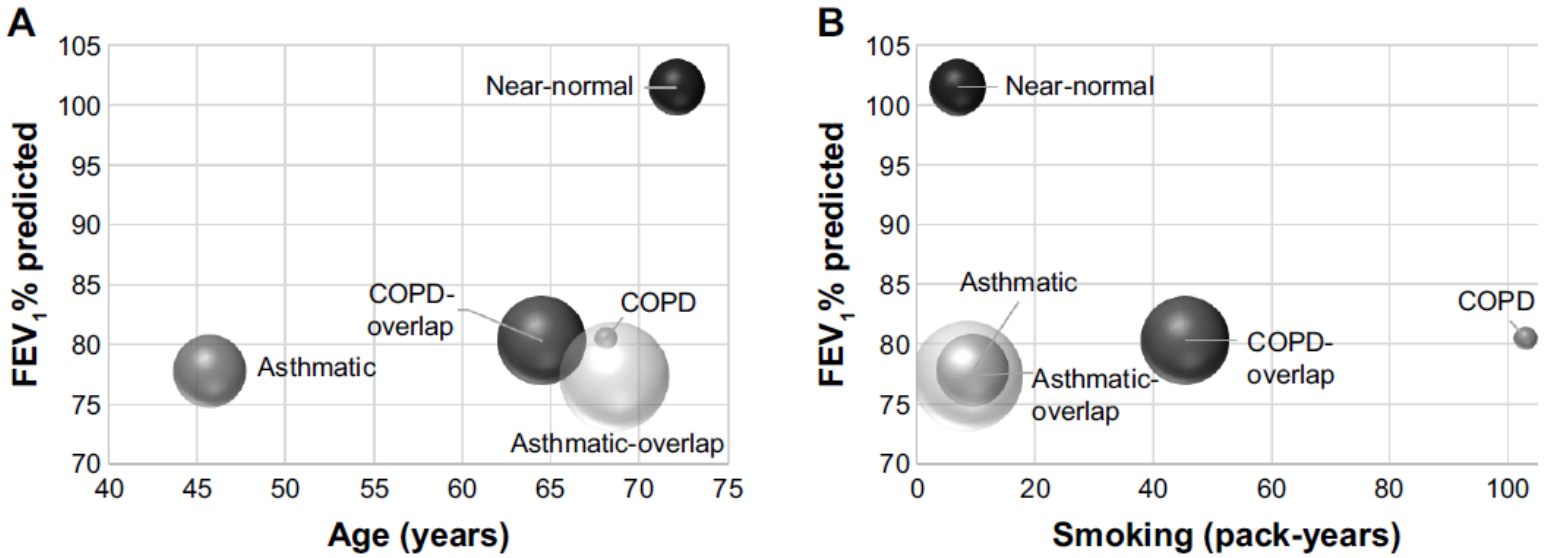



**Figure 2** Distribution of five clusters according to mean $FEV_1$% predicted and amount of smoking.

JH Lee et al. International Journal of COPD 2017:12

# ACO in COPD cohort

- KOCOSS cohort : ACO study by the Korean Asthma Research Group since 2016
- 5 diagnostic criteria

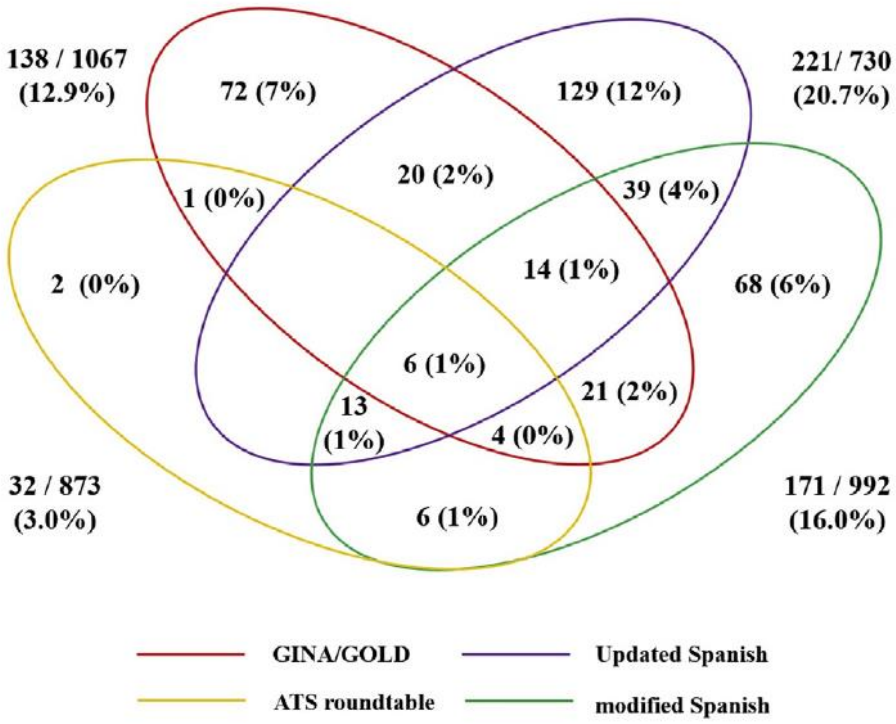



**TABLE I.** The prevalence of asthma-chronic obstructive pulmonary disease overlap based on 5 diagnostic criteria

| Criteria | No. of patients, n (%) | |
|---|---|---|
| | Meet the criteria | Do not meet the criteria |
| Specialists' diagnosis ACO | 264 (24.7) | 720 (67.5) |
| ATS roundtable criteria[10] | | |
| Major | | |
| Post-BD $FEV_1$/FVC <0.7 and age ≥40 | 1067 (100) | – |
| Smoking ≥10 pack-years or exposure to air pollution ≥10 y | 898 (89.4) | 5.3 (5.3) |
| History of asthma before 40 y or BDR >400 mL in $FEV_1$ | 75 (7.0) | 911 (85.4) |
| Minor | | |
| History of atopy or allergic rhinitis | 77 (7.2) | 893 (83.7) |
| Separate BDR ≥12% and 200 mL | 45 (4.2) | 1022 (95.8) |
| Blood eosinophil count ≥300 cells/μL | 234 (21.9) | 739 (69.3) |
| ACO (all 3 major and at least 1 minor) | 32 (3.0) | 841 (78.8) |
| GINA/GOLD document* | | |
| Component of asthmatic feature ≥3 | 152 (14.2) | 915 (85.8) |
| Component of COPD feature ≥3 | 1026 (96.2) | 41 (3.8) |
| ACO (≥3 asthma and ≥3 COPD features) | 138 (12.9) | 929 (87.1) |
| Modified Spanish COPD guidelines[11] | | |
| Major criteria | | |
| Previous history of asthma | 330 (30.9) | 722 (67.7) |
| BDR >15% and 400 mL | 13 (1.2) | 1054 (98.8) |
| Minor criteria | | |
| IgE >100 IU, or history of atopy | 396 (37.1) | 305 (28.6) |
| BDR >12% and 200 mL | 45 (4.2) | 1022 (95.8) |
| Blood eosinophil >5% | 180 (16.9) | 832 (78.0) |
| ACO (at least 1 major or 2 minor) | 171 (16.0) | 821 (76.9) |
| Updated Spanish COPD guidelines[12] | | |
| Age ≥35, smoker ≥10 pack-years, and post-BD $FEV_1$/FVC <0.7 | 898 (84.2) | 56 (5.3) |
| Current diagnosis of asthma† | 10 (0.9) | 1057 (99.1) |
| BDR ≥15% and 400 mL, and/or eosinophilia in blood ≥300 cells/μL | 243 (22.8) | 731 (68.5) |
| ACO (1 and 2 or 1 and 3) | 221 (20.7) | 509 (47.7) |

*ACO*, Asthma-COPD overlap; *ATS*, American Thoracic Society; *BDR*, bronchodilator response; *COPD*, chronic obstructive pulmonary disease; *FeNO*, fractional exhaled nitric oxide; *$FEV_1$*, forced expiratory volume in 1 s; *FVC*, forced vital capacity; *GINA*, Global Initiative for Asthma; *GOLD*, Global Initiative for Chronic Obstructive Lung Disease; *PEF*, peak expiratory flow.

*GOLD/GINA criteria–based ACO was defined if the patients met at least 3 items in both the asthma and COPD categories.[13,14]

†Current diagnosis of asthma must include (a) and (b): (a) respiratory symptoms of variable course with history and/or symptoms causing clinical suspicion; family asthma history or personal history of asthma in childhood, or personal history of atopy, or inflammation of the upper airway (eg, rhinosinusitis), (b) post-BD $FEV_1$ ≥12% and 200 mL, or diurnal variability of PEF ≥20%, or FeNO ≥50 ppb.

YS Jo et al. J Allergy Clin Immunol Pract 2020;8:1625-33

# Clinical features

There is broad agreement that patients **with features of both asthma and COPD** experience

- ***Frequent exacerbations***
- ***Have poor quality of life***
- ***More rapid decline in lung function***
- ***Higher mortality***
- ***Greater use of healthcare resource***

compared with patients with asthma or COPD alone

# Clinical features

**Clinical features of ACO in asthma study**

| Author | ACO definition | Demographics | symptoms | Lung function | Laboratory | Medication |
|---|---|---|---|---|---|---|
| HY Lee et al.<br>Yonsei Med J 55(4):980-986, 2014<br><br>- Single center | 1) BDR (+) or AHR (+)<br>2) post-BD $FEV_1$/FVC <0.70 | Older<br>More male<br>More former smoker | | Low $FEV_1$<br>Lower $FEV_1$/FVC ratio<br>High FRC & RV<br>Lower PC20/PD15 | Lower blood eosinophil count | |
| SY Park et al.<br>Clin Exp Allergy. 2019;49:603–614.<br><br>- COREA cohort | 1) BDR (+) or AHR (+)<br>2) post-BD $FEV_1$/FVC <0.70 for 3mo | Older<br>More male<br>More former smokers<br><br>More atopy test positive<br>Longer duration of asthma (47.8 vs 75.1 mo) | Longer symptom duration | Low $FEV_1$<br>Low $FEV_1$/FVC ratio<br>More $FEV_1$ change & high BDR (+)<br>Lower PC20 | | |
| H Lee et al.<br>Allergy. 2021;76:223-232.<br><br>- KoSAR cohort | Specialist-diagnosed asthma-COPD overlap in Severe Asthma cohort | Older<br>More male<br>More former smoker | * No difference in QoL | Lower $FEV_1$ & FVC<br>Lower $FEV_1$/FVC ratio<br><br>* No difference in FeNO | Lower blood eosinophil % & higher neutrophil %<br><br>* No difference in sputum eosinophil % | More LAMA<br>More xanthine<br>More sustained systemic steroid<br><br>* No difference in ICS/LABA, LTRA, omalizumab |

# Clinical features of ACO in COPD study

| Author | ACO definition | Demographics | symptoms | Lung function | Laboratory | Medication |
|---|---|---|---|---|---|---|
| CK Rhee et al.<br>COPD. 2014 Apr;11(2):163-70.<br><br>- NHI database | 1) COPD : >40years, ICD-10 codes for COPD or emphysema (J42.x-J44.x, except J430), use of COPD drug ≥2/year<br><br>2) Asthma : ICD-10 code for asthma (J45.x-J46), use of asthma drug ≥2/year | More male, younger | | | | More ICS containing inhaler |
| MA Kim et al.<br>Int J Tuberc Lung Dis. 2015 Jul;19(7):864-9.<br><br>- ASAN COPD cohort | >45years, FEV1/FVC <0.7<br><br>Asthma was diagnosed based on GINA definition | older, less male<br>Less smokers | | Low $FEV_1$/FVC ratio<br>Low $FEV_1$<br>More BDR (+) | | More ICS/LABA<br>Less Tiotropium |
| YS Jo et al.<br>Ann Allergy Asthma Immunol 118 (2017) 696-703<br><br>- SNUH cohort | Modified Spanish<br>ATS Roundtable<br>PLATINO<br>GINA/GOLD | | Low ACT, low mini-AQLQ<br><br>High CAT, high SGRQ, high CCQ | High $FEV_1$, FVC<br>High $FEV_1$/FVC ratio<br>→ only in MS<br><br>More BDR (+) | High blood eosinophil<br>High total IgE | |
| JH Lee et al.<br>International Journal of COPD 2017:12<br><br>- KNHANES | COPD predominant overlap in cluster analysis | Older & more male & more former smokers than asthmatic<br><br>More PY than asthmatics, less PY than COPD | Less self-reported wheezing than asthmatics<br><br>Lower EQ-5D index than asthmatics<br><br>More wheezing than COPD | | | Less LAMA than COPD<br><br>More SABA & theophylline than asthma<br><br>More OCS, IVCS than asthmatics |
| HJ Park et al.<br>Allergy Asthma Immunol Res. 2017 September;9(5):431-437.<br><br>- KOCOSS | $FEV_1$/FVC <0.7 & BDR (+) | More male<br>More current smoker | Low SGRQ | | | |

# Clinical features of ACO in COPD study (Cont)

| Author | ACO definition | Demographics | symptoms | Lung function | Laboratory | Medication |
|---|---|---|---|---|---|---|
| MH Kim et al.<br>International Journal of COPD 2018:13 1251-1260<br><br>- KNHANES | (1) ≥40 years & FEV1/FVC <0.7 & $FEV_1$ ≥ 50%<br>(2) Self-reported wheezing | Low SES in asthma-predominant ACO | Low EQ-5D in asthma-predominant ACO | Low $FEV_1$, FVC | | More ICS containing inhalers<br>More LAMA, more LTRA, more OCS, more SABA, more systemic bronchodilator, more theophylline |
| HY Park et al.<br>Respiratory Research (2018) 19:36<br><br>- KOLD cohort | ATS roundtable | | | Better $FEV_1$, high reversibility | Less emphysema, % (14.9 vs 14.7%) | More ICS containing inhalers (38 vs 53%, p=0.051) |
| YS Jo et al.<br>Allergy. 2019;74:186–203.<br><br>- KOCOSS cohort | Specialists' Dx<br>ATS Roundtable<br>GINA/GOLD<br>Modified Spanish<br>Updated Spanish | Less male & less former smoker in Specialists & GINA/GOLD | High mMRC<br>High CAT, SGRQ<br><br>More Sx variation (diurnal, seasonal) | High $FEV_1$, FVC<br>High $FEV_1$/FVC ratio<br>High Dlco<br>High BDR (+)<br>High IC<br>- in Specialists' & GINA/GOLD | High blood eosinophil<br><br>High total IgE, esp in modiofied Spanish & updated Spanish | More ICS containing inhaler use |
| YS Jo et al.<br>J Allergy Clin Immunol Pract 2020;8:1625-33<br><br>- KOCOSS cohort | | | | | | |

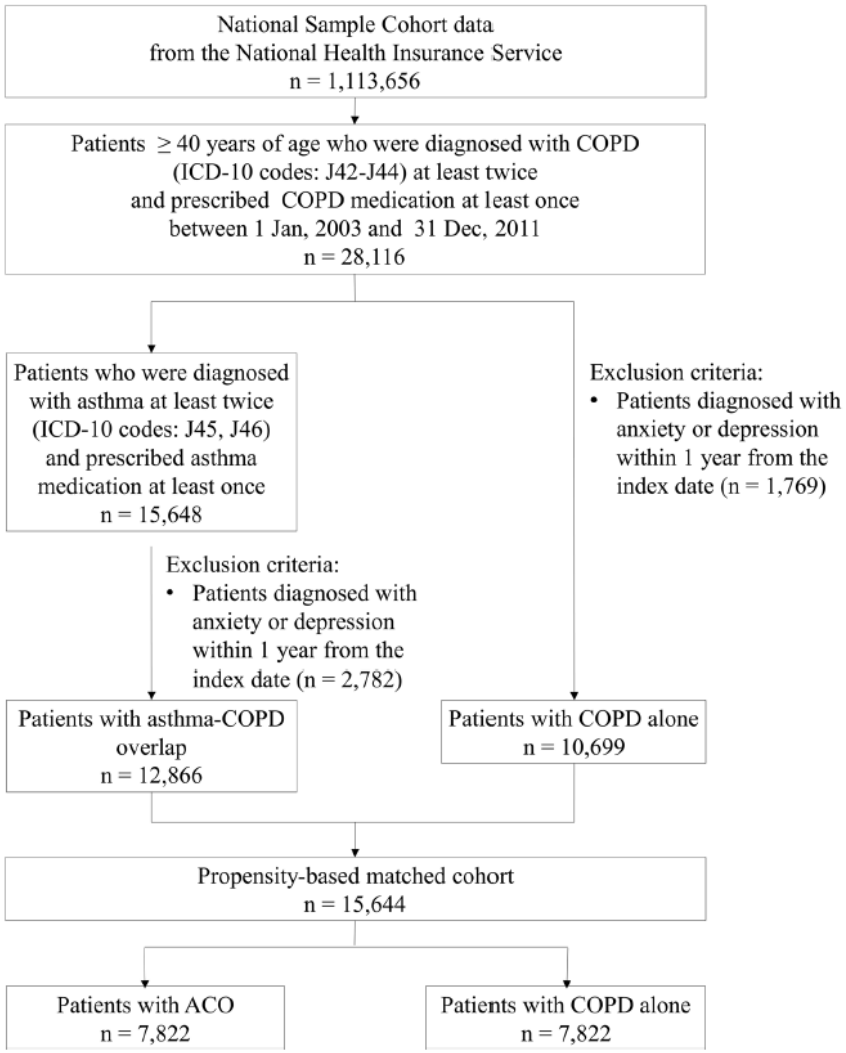
# Previous Exacerbation history

| Author | ACO definition | Definition of previous AE | Results |
|---|---|---|---|
| CK Rhee et al.<br>COPD. 2014 Apr;11(2):163-70.<br><br>- NHI database | 1) COPD : >40years, ICD-10 codes for COPD or emphysema (J42.x-J44.x, except J430), use of COPD drug ≥2/year<br>2) Asthma : ICD-10 code for asthma (J45.x-J46), use of asthma drug ≥2/year | Hospitalization | More in ACO (14.5 vs 6.1%, p<0.001) |
| H Lee et al.<br>Allergy. 2021;76:223-232.<br><br>- KoSAR cohort | Specialist-diagnosed asthma-COPD overlap in Severe Asthma cohort | Steroid burst Tx ≥3days | More in ACO group (52.7% vs 38.2%, p=0.012) |
| | | Steroid burst Tx ≥5days | More in ACO group (22.6% vs 11.5%, p=0.005) |
| | | Unscheduled ER visit<br>Hospitalization / ICS admission | More in ACO group (23% vs 10.6%, p=0.006)<br>Not different |
| HJ Park et al.<br>Allergy Asthma Immunol Res. 2017 September;9(5):431-437<br><br>- KOCOSS cohort | $FEV_1$/FVC <0.7 & BDR (+) | Any AE required systemic corticosteroid, antibiotics or both | 27.5% of pure COPD vs 20.3% of ACO (p=0.086) |
| | | Severe AE requiring hospitalization | 12.7% vs 8.3% of COPD vs ACO (p=0.150) |
| YS Jo et al. Ann Allergy Asthma Immunol 118 (2017) 696-703<br><br>- SNUH cohort | Modified Spanish, ATS Roundtable, PLATINO, GINA/GOLD | Any AE | More in ACO group<br>50.5 vs 19.5% in MS<br>40.7 vs 20% in PLATINO |
| | | Moderate to severe AE | More in ACO group<br>46.1 vs 14.0% in MS<br>34.3 vs 15.3 in PLATINO |
| HR Kang et al.<br>Respiratory Research (2019) 20:80 | ICD-10 code for COPD & asthma | ICD codes for primary Dx related to COPD (or asthma in ACO) & moderate to severe AE (hospitalization/ER visit/ outpatient clinic with either an OCS or anti within 5 days of the visit) | No difference in frequent AE (≥2)<br>No difference in Hospitalization/ED visit/outpatient visit |
| JH Song et al.<br>Medicine (2018) 97:36(e12049)<br>- KOCOSS cohort | Modified Spanish<br>ATS Roundtable | Total AE (/yr)<br>Severe AE (/yr) | N-S<br>N-S |
| YS Jo et al.<br>J Allergy Clin Immunol Pract 2020;8:1625-33<br>- KOCOSS cohort | Specialists' Dx, Modified Spanish, ATS Roundtable, PLATINO, GINA/GOLD | Moderate to severe AE | More in ACO<br>22.8 vs 13.6% in MS criteria |

# Comorbidities

| Author | ACO definition | Comorbidities |
|---|---|---|
| CK Rhee et al.<br>COPD. 2014 Apr;11(2):163-70.<br>- NHI database | 1) COPD : >40years, ICD-10 codes for COPD or emphysema (J42.x-J44.x, except J430), use of COPD drug ≥2/year<br>2) Asthma : ICD-10 code for asthma (J45.x-J46), use of asthma drug ≥2/year | More IHD, DM, HTN, less CHF<br>More osteoporosis<br>More depressive disorder |
| DW Lee et al.<br>Int J Tuberc Lung Dis. 2015 Oct;19(10):1246-51.<br>- KNHANES IV & V (2008-2011) | 1) Physician diagnosed asthma before 40 YO, or wheeze during exercise for 1yr<br><br>2) Aged ≥ 50yrs with $FEV_1/FVC$ <0.7 | Low BMD, high osteopenia |
| DW Lee et al.<br>International Journal of COPD 2017:12 2355–2362<br>- KNHANES IV & V (2008-2011) | | Sarcopenia, osteopenia, osteoporosis, low BMD<br>→ Profound risk in Sarcopenic group, esp in ACO patients |
| JH Lee et al.<br>International Journal of COPD 2017:12<br>- KNHANES | COPD predominant overlap in cluster analysis | More HTN, DM, hyperlipidemia, coronary artery disease than asthmatics |
| MH Kim et al.<br>International Journal of COPD 2018:13 1251-1260<br>- KNHANES | 1) ≥ 40 years & $FEV_1/FVC$ <0.7 & $FEV_1$ ≥ 50%<br>2) Self-reported wheezing | More osteoporosis in asthma-predominant ACO |
| H Lee et al.<br>Allergy. 2021;76:223-232<br>- KoSAR cohort | Specialist-diagnosed asthma-COPD overlap in Severe Asthma cohort | Less AR & chronic sinusitis<br>Less aspirin intolerance<br>More PTB history<br>More HTN |
| HR Kang et al.<br>Respiratory Research (2019) 20:80<br>- NHI database | ICD-10 code for COPD & asthma | More Depression & anxiety |
| YS Jo et al.<br>J Allergy Clin Immunol Pract 2020;8:1625-33<br>- KOCOSS | Specialists' Dx, ATS Roundtable, GINA/GOLD, Modified Spanish, Updated Spanish | More asthma<br>More atopy / AR |

# Mood disorders




- **The risk of depression**

- **Higher in ACO** (aHR 1.10; p=0.0039)

- aged 40-64 years & female

- **The risk of anxiety**

- **Higher in ACO** (aHR 1.06; p=0.0272)

- aged 40-64 years

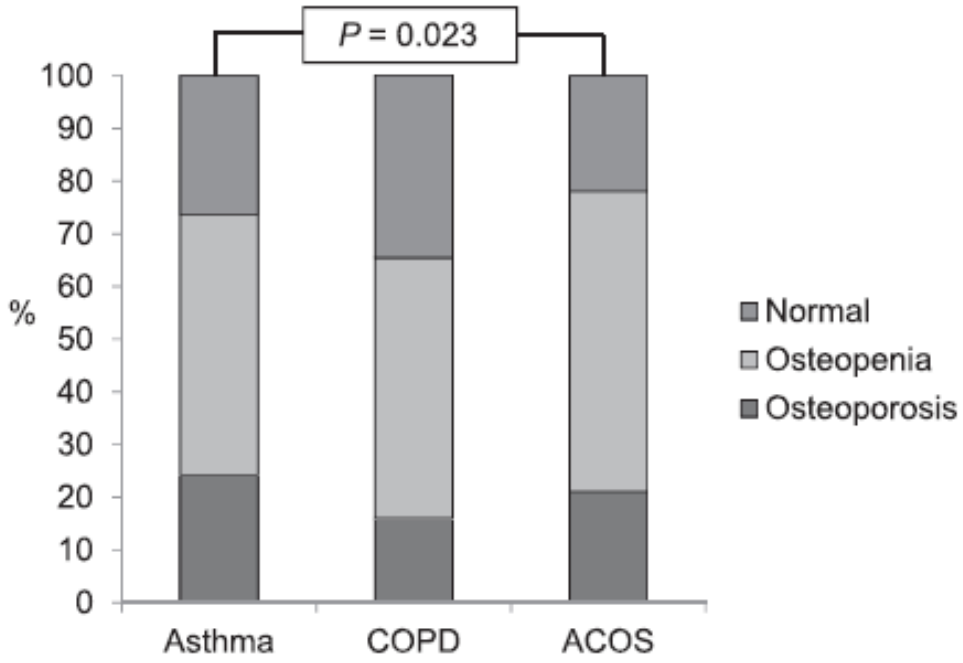
HR Kang et al. Respiratory Research (2019) 20:80

# Osteopenia / Osteoporosis & Sarcopenia

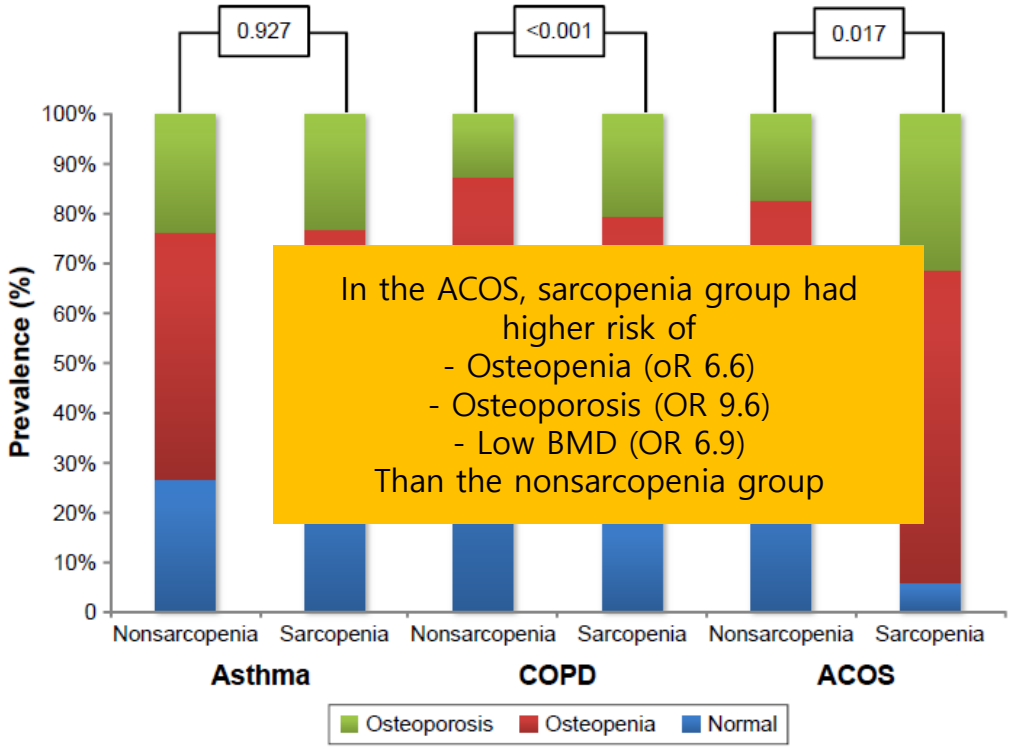
**ACOS : (1) & (2)**

1) Aged ≥ 50yrs with $FEV_1/FVC$ <0.7
2) Physician diagnosed asthma before 40 YO, or wheeze during exercise for 1yr

- KNHANES IV & V (2008-2011)
- Obstructive Lung disease (OLD) (N=979)




DW Lee et al. INT J TUBERC LUNG DIS 19(10):1246-1251.

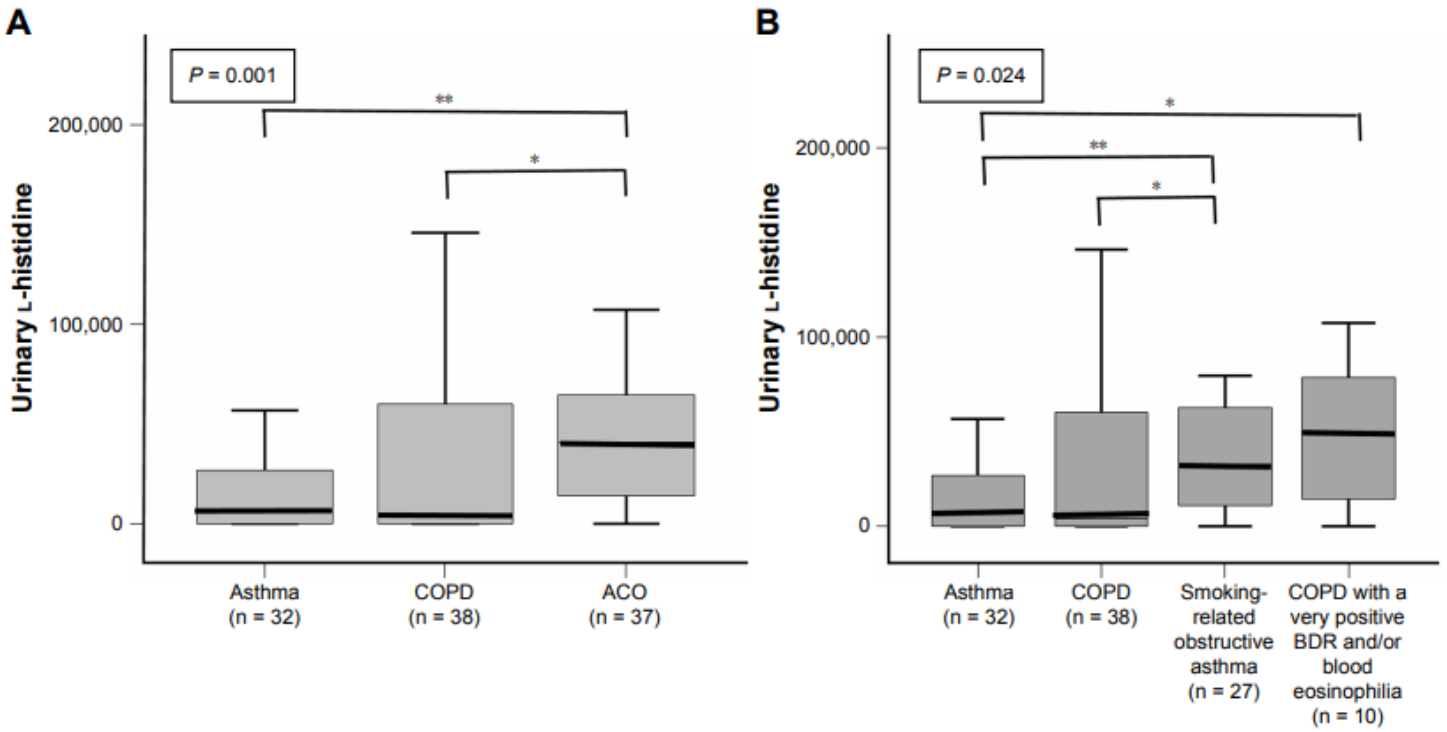



DW Lee et al. International Journal of COPD 2017:12 2355–2362

# Biomarker

## Urinary L-histidine

- Prospective cohort : Asthma (N=32), COPD (N=38), ACO (N=37) by Spanish recommendation
- Urinary  L-histidine levels using liquid chromatography-mass spectrometry & metabolomic analysis




JY Oh et al. International Journal of COPD 2018:13 1809–1818

# Serum club cell secretory protein

- Prospective cohort : Asthma (N=32), COPD (N=38), ACO (N=37) by Spanish recommendation
- Serum CC-16 level by ELISA kits

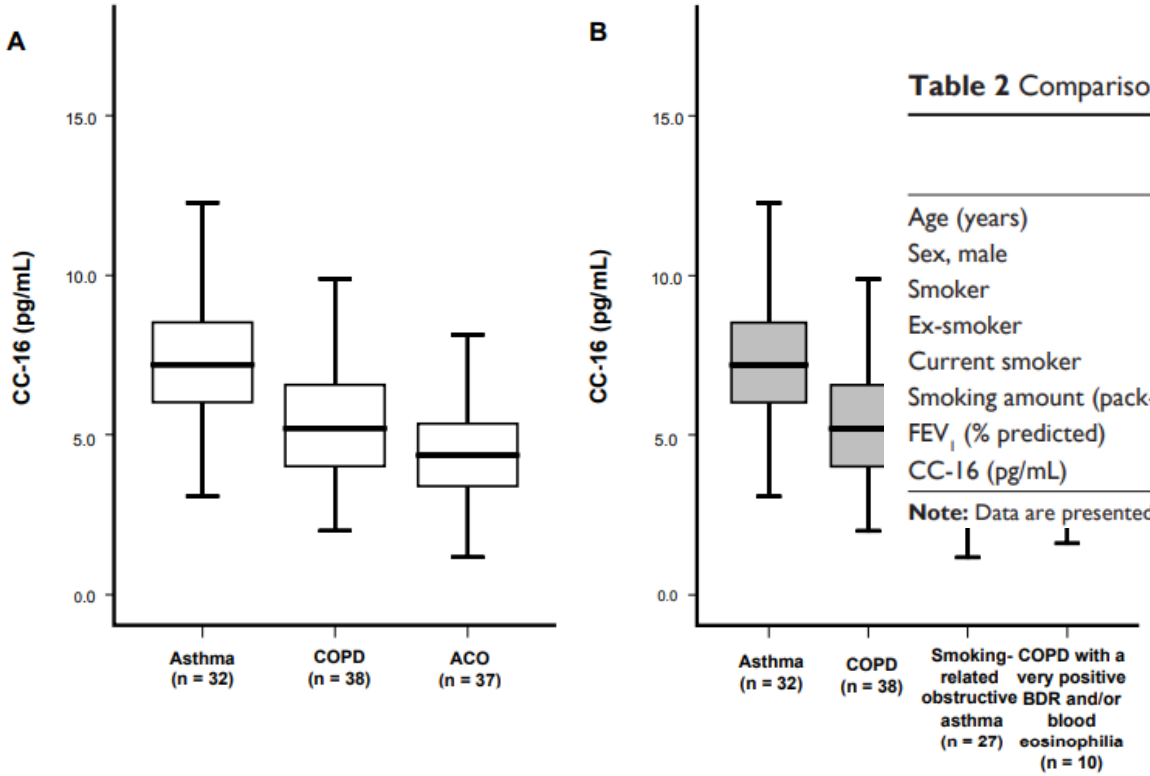



**Table 2** Comparison of frequent and nonfrequent exacerbators

| | Frequent exacerbators n=12 | Non-frequent exacerbators n=95 | P-value |
|---|---|---|---|
| Age (years) | 61.5 (54.3–72.3) | 64.0 (57.0–70.0) | 0.657 |
| Sex, male | 10 (83.3%) | 72 (75.8%) | 0.547 |
| Smoker | 10 (83.3%) | 64 (67.3%) | 0.010 |
| Ex-smoker | 9 (75.0%) | 35 (36.8%) | |
| Current smoker | 1 (8.3%) | 29 (30.5%) | |
| Smoking amount (pack-years) | 37.5 (12.5–48.8) | 40.0 (33.8–54.8) | 0.301 |
| $FEV_1$ (% predicted) | 44.0 (28.3–75.8) | 71.0 (55.0–85.0) | 0.021 |
| CC-16 (pg/mL) | 4.09 (2.31–5.57) | 5.49 (3.92–7.53) | 0.023 |

**Note:** Data are presented as the median (IQR) for continuous variables and percentage (number) for categorical variables.

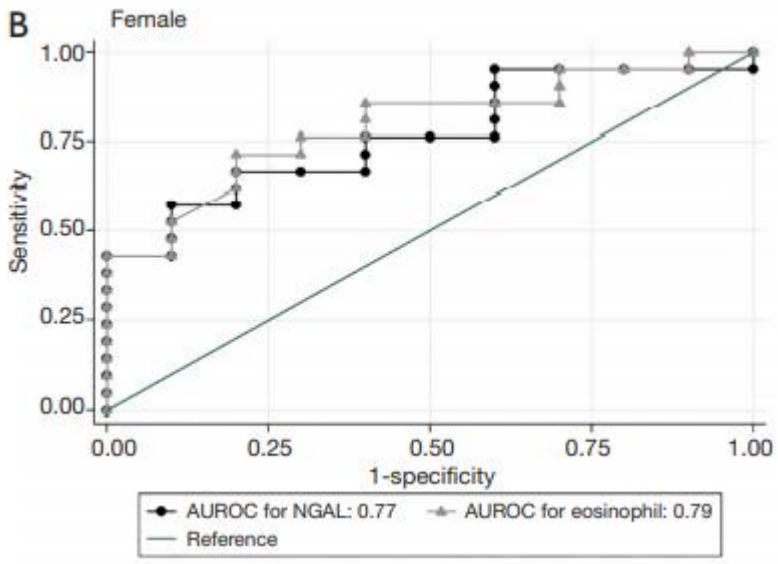
JY Oh et al. International Journal of COPD 2018:13 3411–3417

# NGAL

- 137 COPD patients from CODA cohort : COPD (N=60) vs. ACO (N=77) by BDR positivity or history of asthma
- ELISA kits

**Table 2** Radiologic feature and inflammatory markers in patients with non-ACO and ACO

| Variable | Non-ACO (n=60) | ACO (n=77) | P value |
|---|---|---|---|
| Radiologic finding | | | |
| Emphysema index | 9.7±8.3 | 7.2±7.1 | 0.06 |
| Mean wall area (%) | 69.2±4.7 | 69.5±5.2 | 0.78 |
| Inflammatory markers | | | |
| IL-6 (pg/mL) | 2.7±3.5 | 3.0±4.4 | 0.77 |
| IL-8 (pg/mL) | 16.6±20.8 | 21.2±23.5 | 0.20 |
| NGAL (ng/mL) | 15.9±7.9 | 15.6±6.6 | 0.92 |
| Blood eosinophil, % | 2.7±3.6 | 3.3±4.0 | 0.11 |
| Blood eosinophil, cell/μL | 188.7±286.2 | 230.9±361.8 | 0.04 |
| hs-CRP, mg/dL | 0.22±0.28 | 0.42±0.88 | 0.91 |

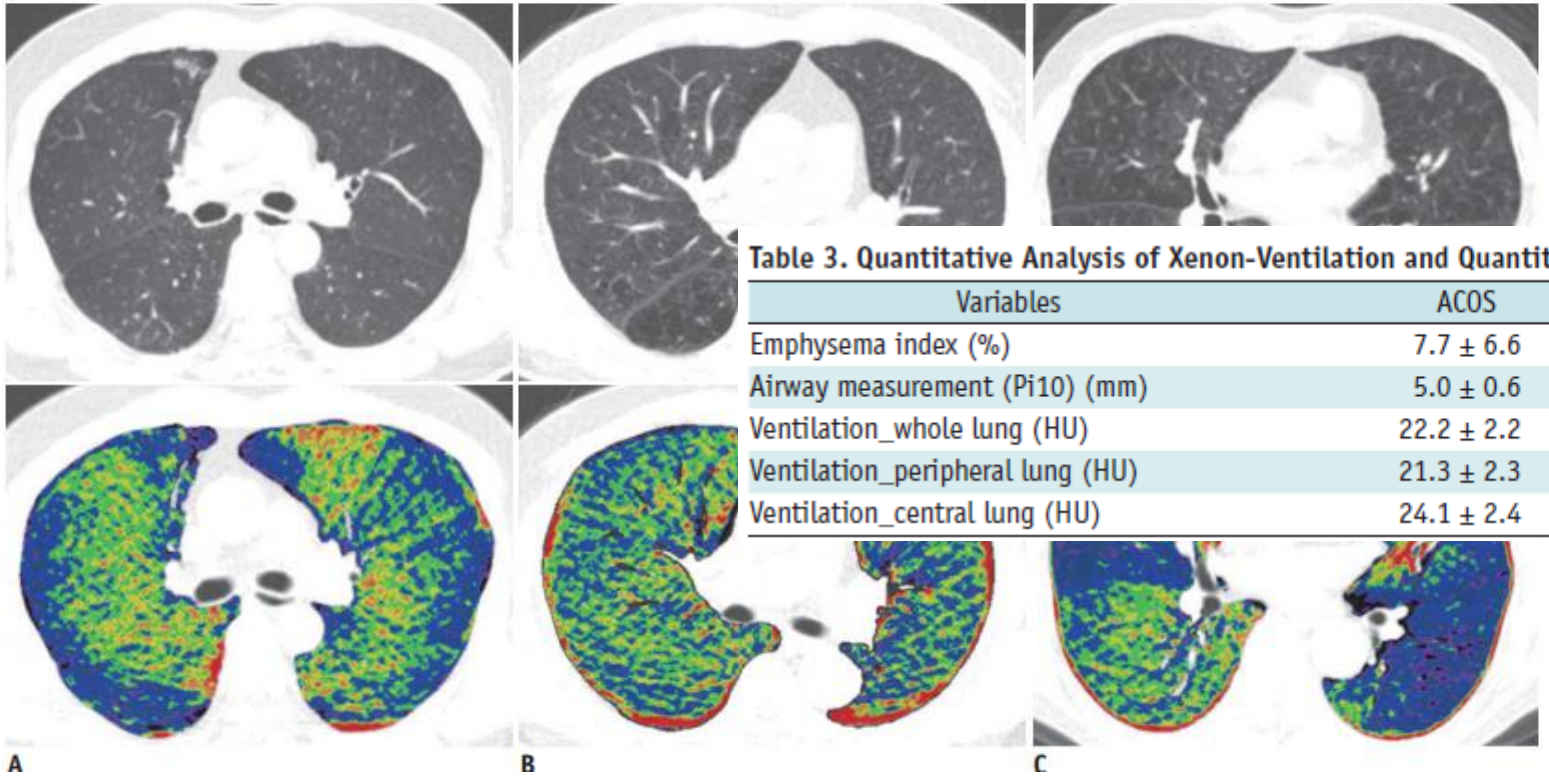



YS Jo et al. J Thorac Dis 2018;10(8):5047-5056

# Diagnostic approach for better ACO classification

- Regional ventilation abnormalities in ACO (N=21) & COPD (N=46)
- Xenon-ventilation dual-energy CT (DECT)

  1) peripheral wedge/diffuse defect, 2) diffuse heterogeneous defect, 3) lobar/segmental/subsegmental defect, and 4) no defect on ventilation maps




| Disease | Pattern (1) | Pattern (2) | Pattern (3) | *P** |
|---|---|---|---|---|
| ACOS (n = 21) | 14 (66.7) | 2 (9.5) | 5 (23.8) | < 0.001† |
| COPD (n = 46) | 5 (10.9) | 21 (45.7) | 20 (43.5) | |

**Table 3. Quantitative Analysis of Xenon-Ventilation and Quantitative CT Densitometry in Patients with ACOS and COPD**

| Variables | ACOS | COPD | *P** |
|---|---|---|---|
| Emphysema index (%) | 7.7 ± 6.6 | 12.0 ± 12.4 | 0.070 |
| Airway measurement (Pi10) (mm) | 5.0 ± 0.6 | 4.7 ± 0.7 | 0.041† |
| Ventilation_whole lung (HU) | 22.2 ± 2.2 | 23.3 ± 3.7 | 0.130 |
| Ventilation_peripheral lung (HU) | 21.3 ± 2.3 | 22.8 ± 3.7 | 0.045† |
| Ventilation_central lung (HU) | 24.1 ± 2.4 | 24.4 ± 4.1 | 0.710 |

HJ Hwang et al. Korean J Radiol 2020;21(9):1104-1113

# Genome-wide association study (GWAS)

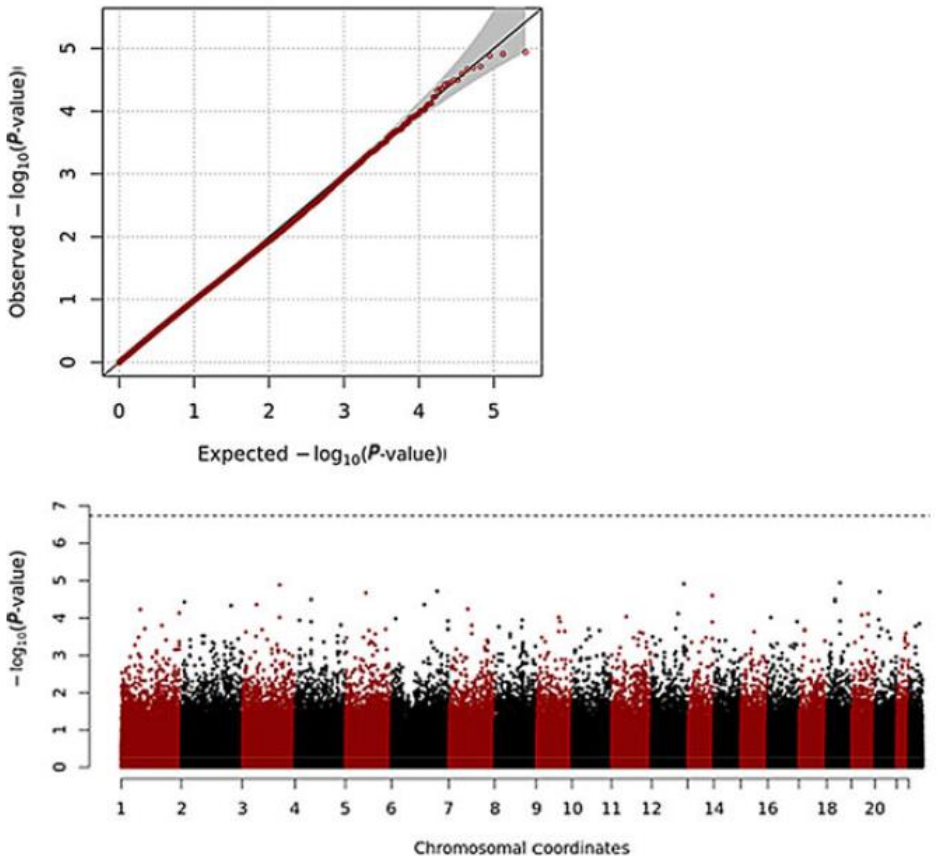
**ACOS : (1) & (2)**

1) BDR (+) or AHR (+)

2) post-BD $FEV_1/FVC$ <0.70 for 3mo

- Asthma in COREA cohort (N=959) : positive BDR or AHR
- ACOS (N=228, 23.8%) vs. "only" asthma (N=731, 76.2%)

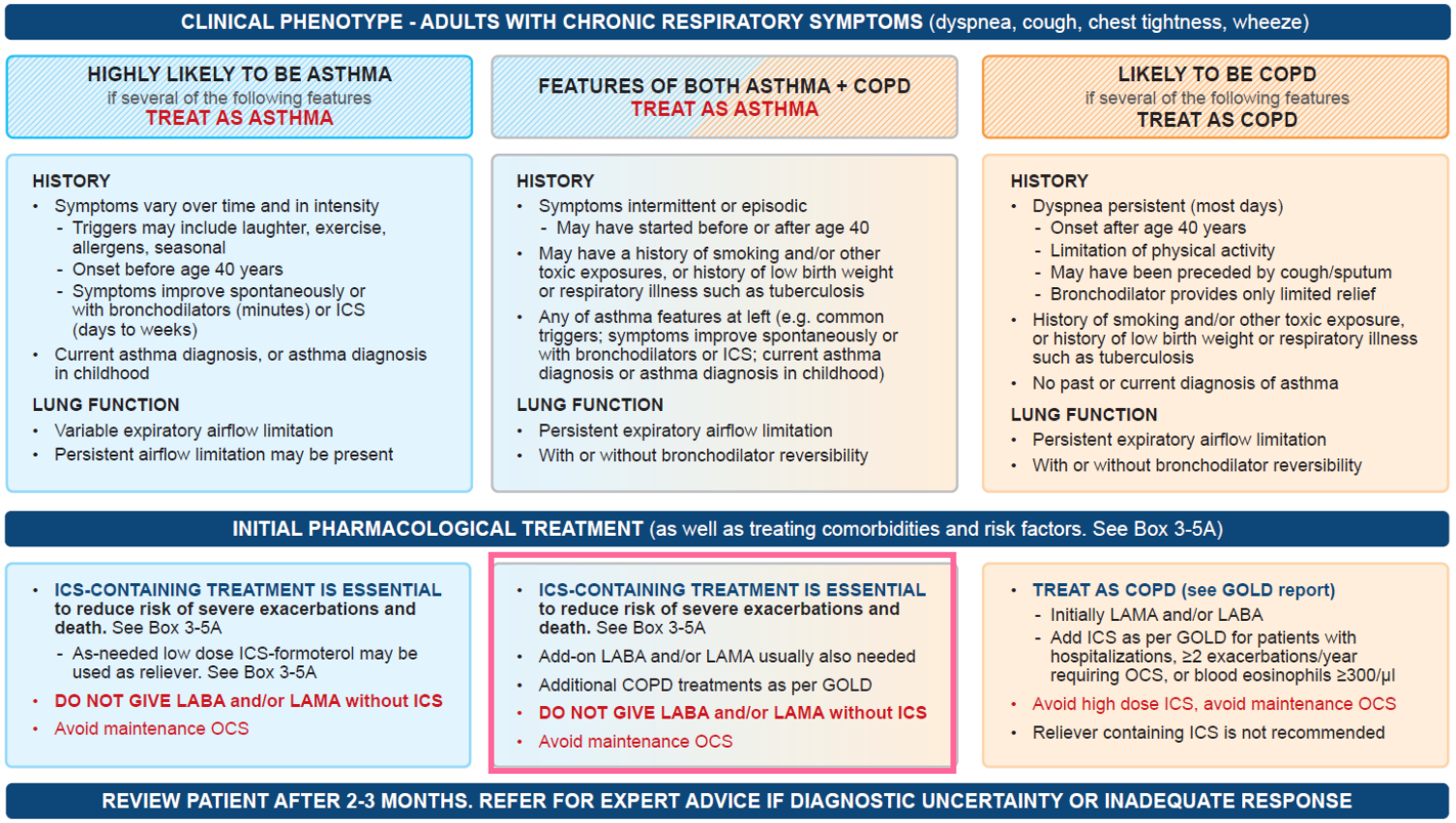
- GWAS : 1433 patients with genetic information in the COREA cohort,
  : ACOS (N=77) vs "only" asthma (N=1356)




*No significant SNPs* were found b/w ACOS and "only" asthma group

SY Park et al. Clin Exp Allergy. 2019;49:603–614.

# Approach to initial treatment with ACO




- *ACO is a single phenotype?*
- *Pivotal role of ICS in ACO?*
- *ICS beneficial on outcome of ACO?*

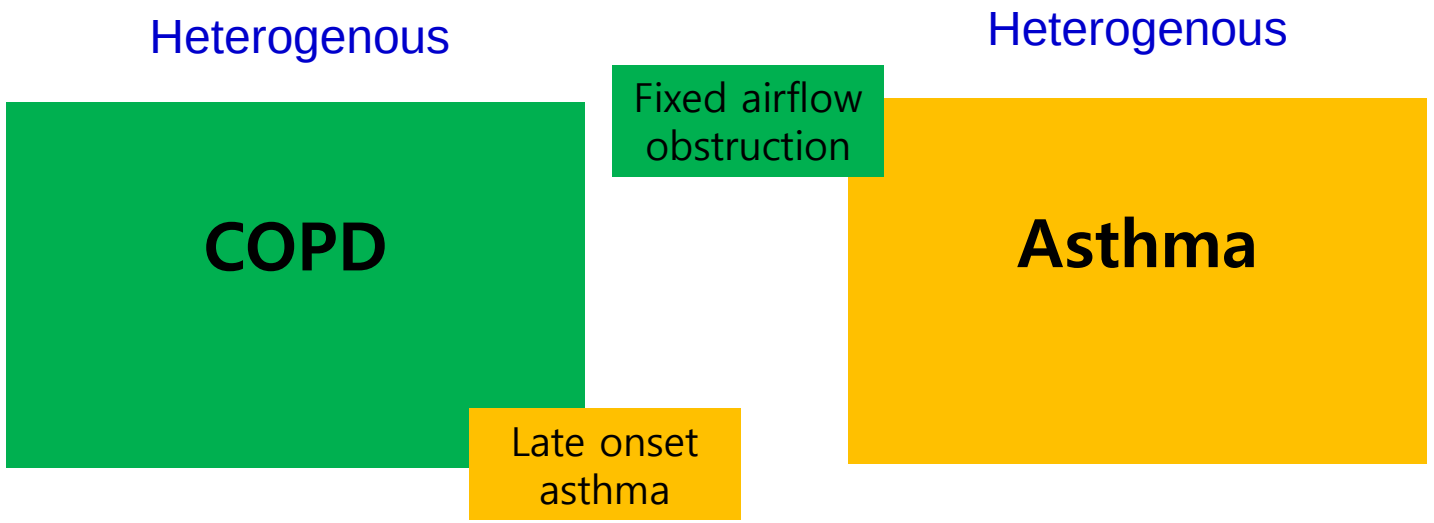
*Lack of Evidence.*

GINA 2020. Box 5-2

# Heterogeneity of chronic airway disease

- "Asthma" and "COPD" are umbrella labels for *heterogeneous conditions*. Each include several different clinical phenotypes, and are likely to have several different underlying mechanisms, some of which may be common to both asthma and COPD.

GINA 2020



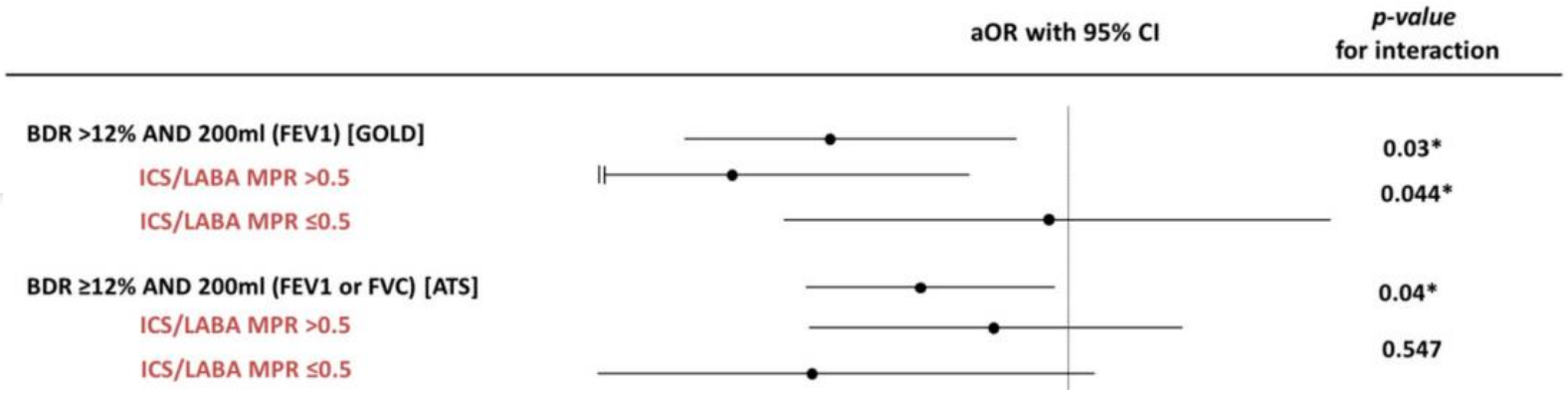

- BDR (+)
- Eosinophil ↑ in Sputum/Blood

- Smoker
- Eosinophil ↓ in Sputum/Blood

# COPD with BDR (+) : ICS/LABA 치료시 AE risk 감소

Korean 4 prospective COPD cohort (N=854)

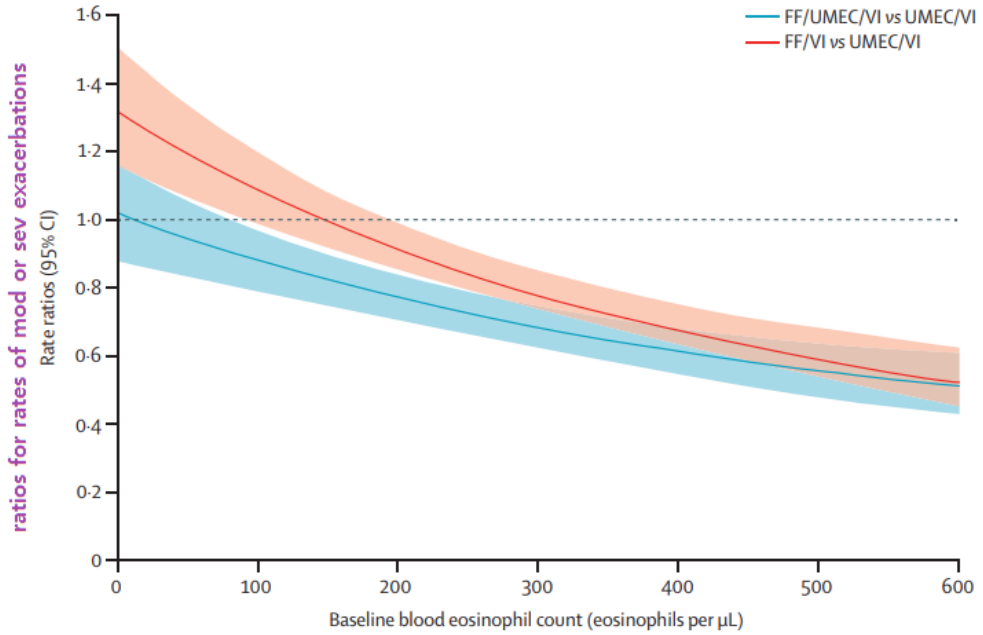
**Primary outcome**: severe exacerbation




JH Kim. Respir Res 2017;18:107.

IMPACT trial

## COPD with high Blood Eo → ICS/LABA or ICS/LABA/LAMA치료시 AE risk 감소




- **Inclusion** : age≥40, CAT ≥10 and either
  - $FEV_1$<50% pred & ≥ 1 AE
  - $FEV_1$ 50-80% pred & ≥2 moderate or ≥1 severe AE
- Single Ellipta inhaler, DPI, 52wks, N=10,355
- **Triple** (fluticasone/umeclidinium/vilanterol) vs **ICS/LABA** vs **LABA/LAMA**
- **Primary endpoint**: moderate-to-severe AE

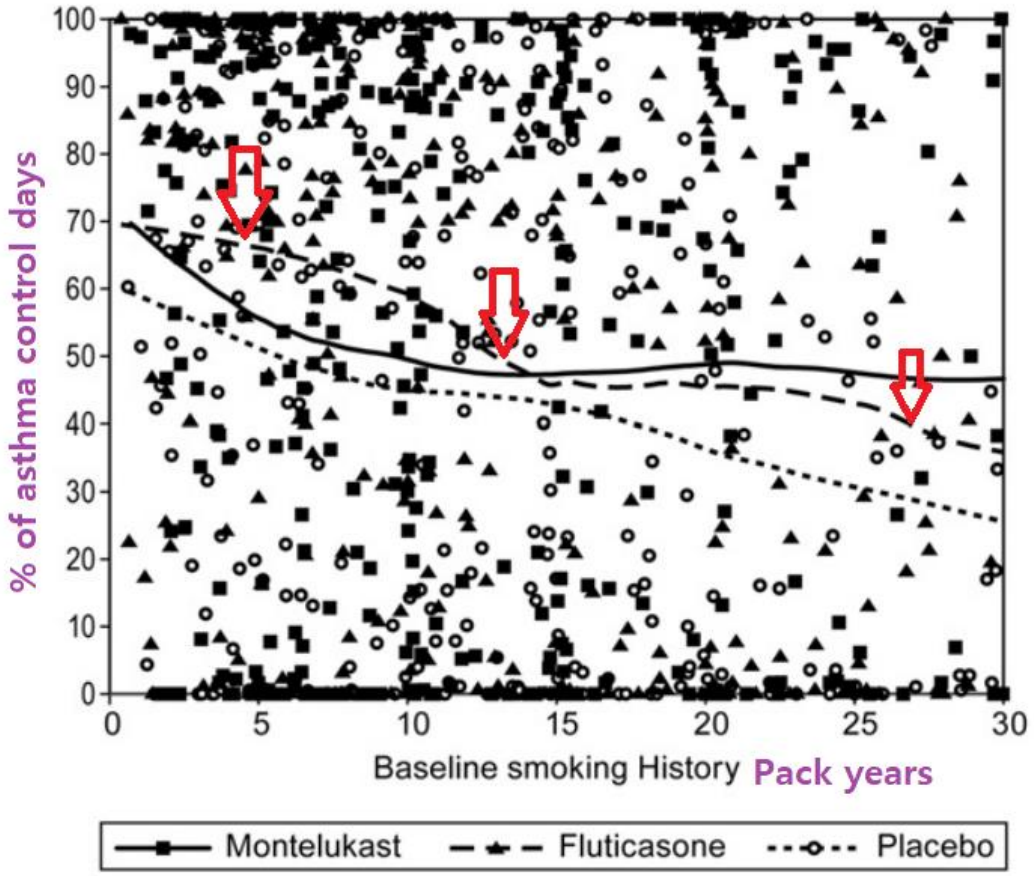
Pascoe S. Lancet Respir Med 2019;7:745-56.

## Asthma + Smoker ➔ ICS 효과 ↓

RCT of BA with self-reported active smoking 0.5-2 ppd (N=1,019)

**Montelukast** vs **FP** 250 μg BID vs **Placebo** for 6 months

**Primary endpoint**: % of asthma control days



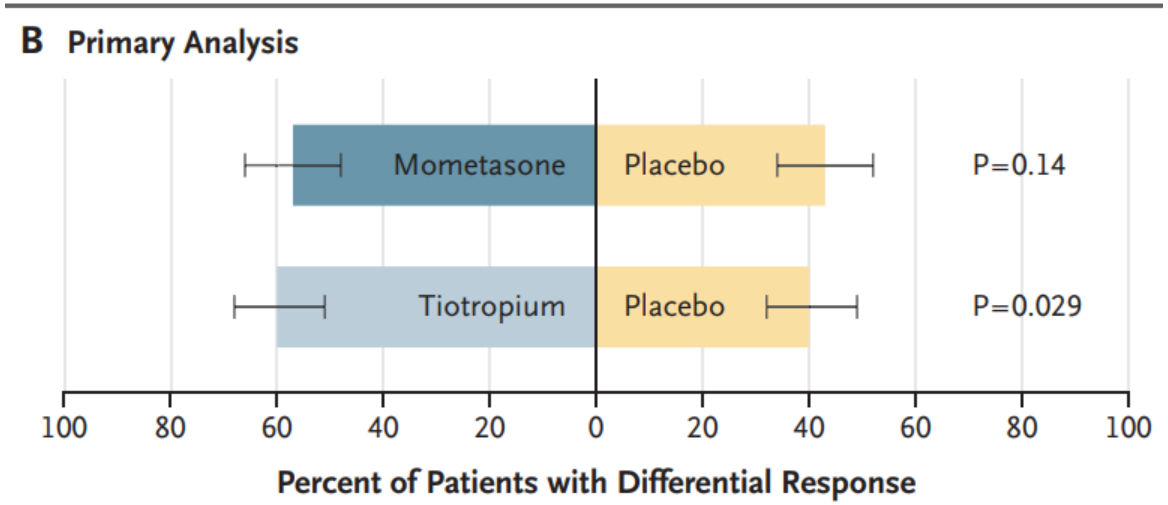

Price D. J Allergy Clin Immunol 2013;131:763.

Mild asthma with **low Sputum Eo** ➔ no difference in response to ICS or Tio than placebo

RCT of low sputum eosinophil (<2%) (**SIENA trial**) (N=295)

**Momethasone 200μg bid (ICS)** *vs* **TIO SMI 5 μg qd (LAMA)** *vs* **Placebo** for 12 weeks

**Primary outcome**: Response (composite outcome of asthma control : treatment failure, annualized asthma control days, FEV1)




Lazarus S. N Engl J Med 2019;380:2009.

# Asthma-COPD overlap, also called asthma + COPD

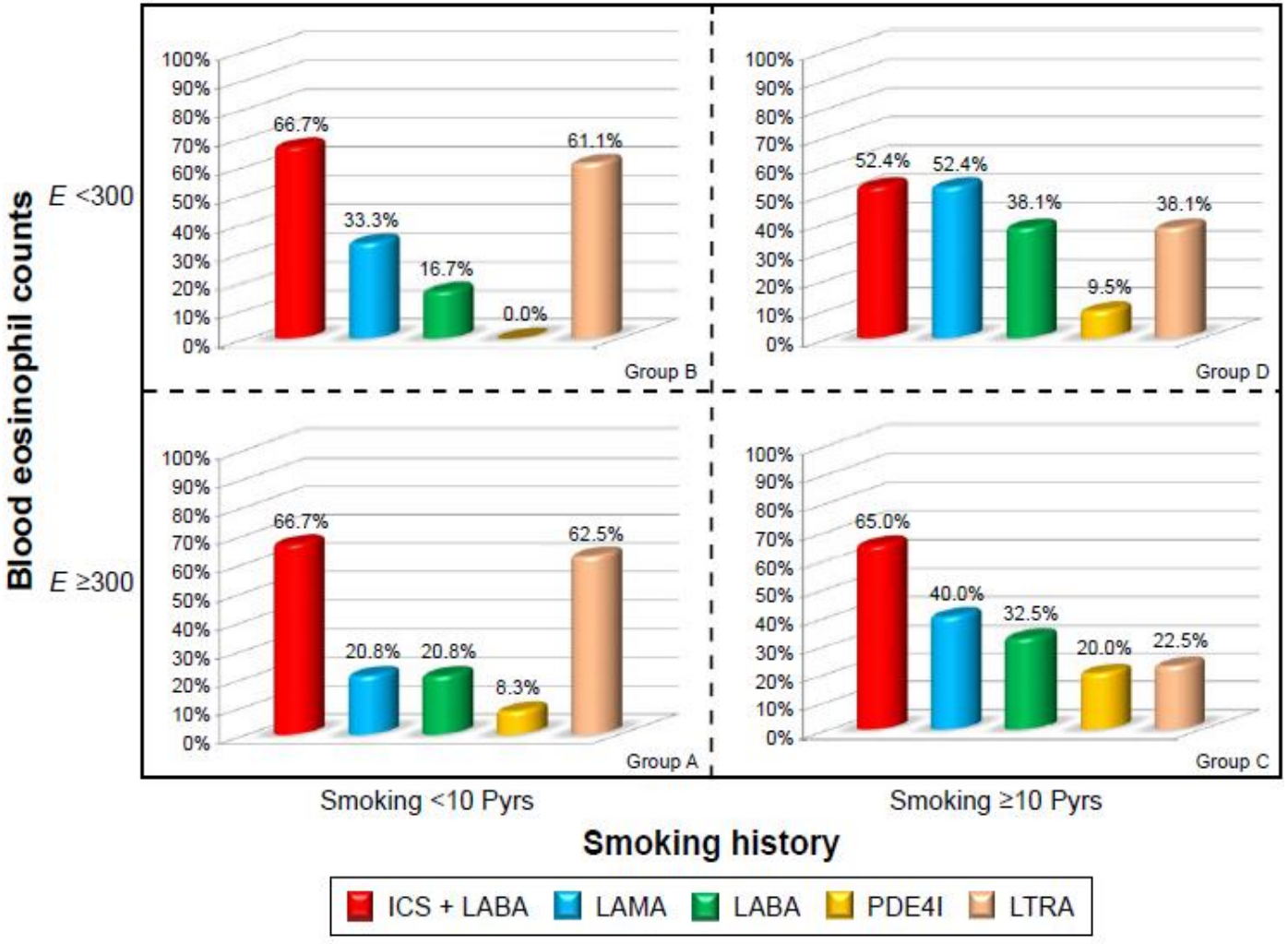
- This is not a definition of a single disease entity, but a descriptive term for clinical use that includes several different clinical phenotypes reflecting different underlying mechanisms.

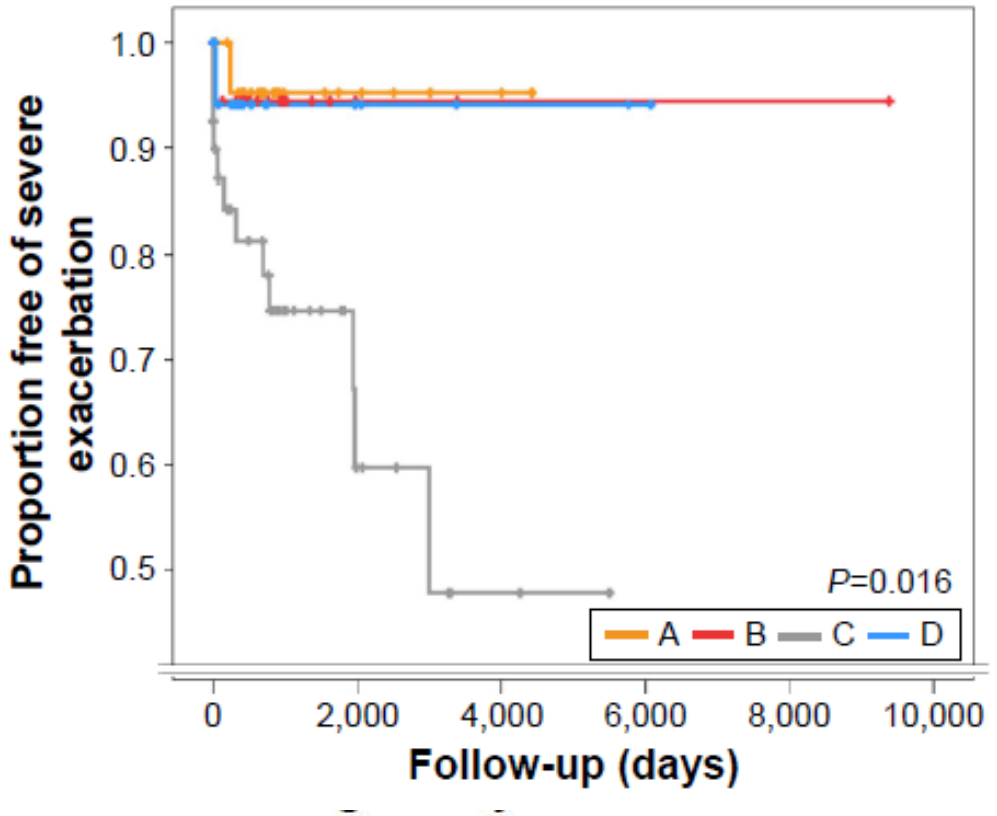
# Heterogeneity of ACO

**ACOS : (1) and/or (2)**

(1) $FEV_1/FVC$ <0.7 with BDR (+)

(2) BHR (+)




HS Joo et al. International Journal of COPD 2017:12 697–703

# Heterogeneity of ACO

**ACOS : (1) & (2)**

(1) ≥ 40 years & FEV1/FVC <0.7 & $FEV_1$ ≥ 50%

(2) Self-reported wheezing

- KNHANES 2007-2012
- 4 group by (1) Self-reported wheezing : index of airway hyper-responsiveness, & (2) Smoking : S- indicates never smoked or had smoked <100 cigarettes in lifetime

| | |
|---|---|
| **W- S-**<br>N=681 | **W- S+**<br>N=1178 |
| **W+ S-**<br>**(asthma-predominant ACO)**<br>N=154 | **W+ S+**<br>**(COPD-predominant ACO)**<br>N=256 |

- **Asthma-predominant ACO**
  - lowest SES, $FEV_1$, FVC, QoL level
- **COPD-predominant ACO**
  - highest hospitalization rate
  - medical cost & health care utilization

MH Kim et al. International Journal of COPD 2018:13 1251-1260

# ICS treatment on ACO : $FEV_1$, AE

**ACOS : (1) & (2)**

1) Age ≥40 years, smoking PY ≥10

2) post-BD $FEV_1$/FVC <0.70 **&**

BDR (+) or AHR (+)

- ACOS from SNUH cohort (N=125)
- ICS treatment group (N=90) vs. non-ICS treatment group (N=35)

**Table 2**

Annual rate of decrease in $FEV_1$ in patients with asthma–chronic obstructive pulmonary disease overlap syndrome in non-ICS and ICS treatmen

| | Total dataset (unadjusted) | | Total dataset (adjusted) | | PS-matched data |
|---|---|---|---|---|---|
| | Δ$FEV_1$ (mL/y), mean (95% CI) | *P* value | Δ$FEV_1$ (mL/y), mean (95% CI) | *P* value | Δ$FEV_1$ (mL/y), m |
| ICS | −7.25 (−34.21 to 5.07) | .521 | −9.61 (−20.51 to 1.29) | .598 | −12.88 (−34.49 |
| Non-ICS | −14.57 (−17.91 to 3.40) | | −15.68 (−35.41 to 4.06) | | −12.37 (−31.15 |

Abbreviations: CI, confidence interval; Δ, change; $FEV_1$, postbronchodilator forced expiratory volume in 1 second; ICS, inhaled corticosteroid;

**Table 3**

Incidence rates of severe exacerbation of patients with asthma–chronic obstructive pulmonary disease overlap syndrome

| | Total dataset | | | | | PS-matched dataset | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | ICS (n = 90) | | Non-ICS (n = 35) | | IRR[a] for ICS vs non-ICS (95% CI) | ICS (n = 31) | | Non-ICS (n = 31) | | IRR[a] for ICS vs non-ICS (95% CI) |
| | n (%) | Rate[b] | n (%) | Rate[b] | | n (%) | Rate[b] | n (%) | Rate[b] | |
| Severe exacerbation | 15 (16.7) | 0.06 | 3 (8.6) | 0.03 | 1.88 (0.37–9.71) | 4 (12.9) | 0.02 | 2 (6.45) | 0.01 | 1.24 (0.44–3.46) |

Abbreviations: CI, confidence interval; ICS, inhaled corticosteroid; IRR, incidence rate ratio; PS, propensity score.

[a]Adjusted by age, sex, body mass index, smoking history (pack-years), postbronchodilator forced expiratory volume in 1 second (percentage of predicted), degree of initial response to $\beta_2$ agonist (percentage of change in forced expiratory volume in 1 second), and medication possession ratio of long-acting $\beta_2$ agonist, long-acting muscarinic antagonist, short-acting $\beta_2$ agonist, short-acting muscarinic antagonist, and theophylline.

[b]Incidence rate (per patient-year).





**Figure 2.** P
matched by

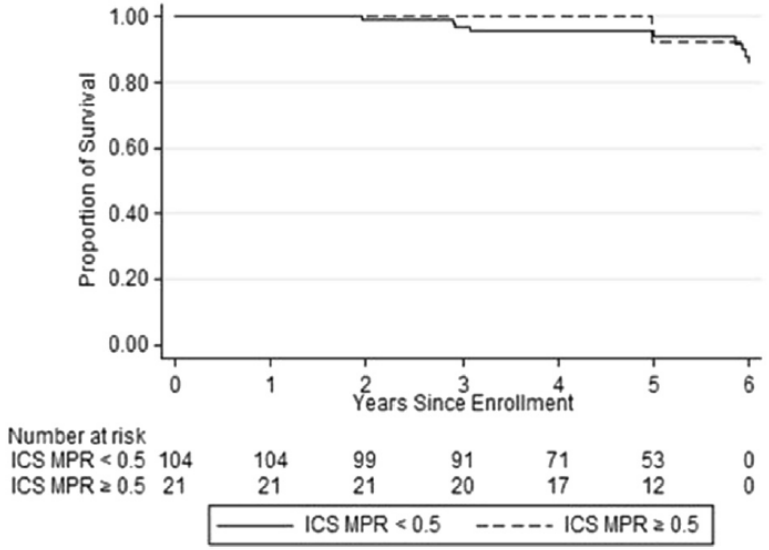



**Figure 3.** Probabilities of survival between the ICS treatment group with an MPR less than 50% and that with an MPR of at least 50% during 6 years with censoring of the data analysis at 7 years ($P = .473$, log-rank test). ICS, inhaled corticosteroid; MPR, medication possession ratio.

ICS treatment on ACO : no significant effect on $FEV_1$ decline & severe AE, mortality

HS Lim et al. Ann Allergy Asthma Immunol 113 (2014) 652e657

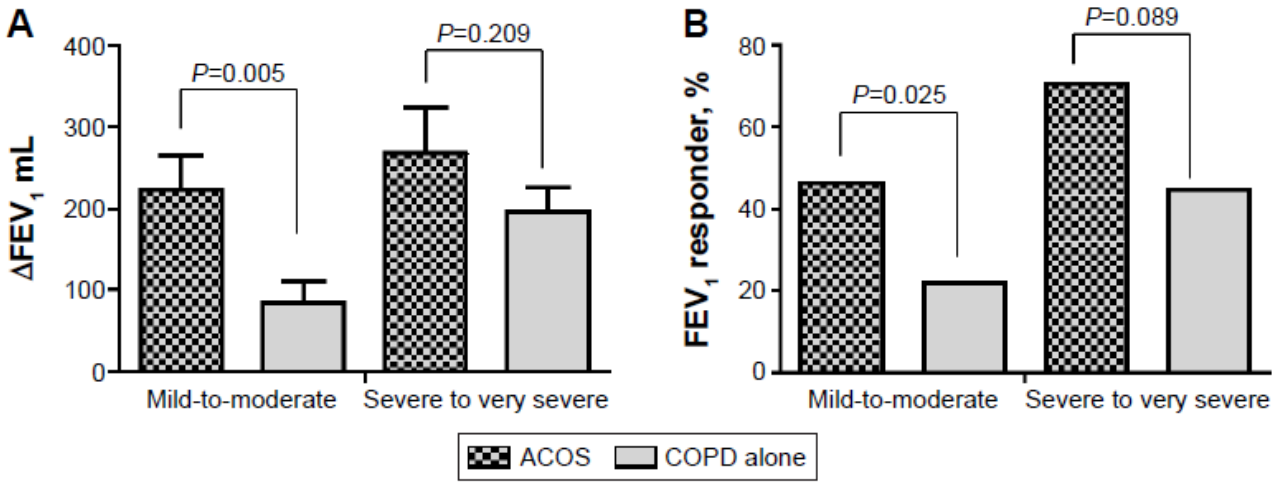
# ICS/LABA on ACO & COPD : $FEV_1$ improvement

- KOLD cohort
- ICS/LABA on ACOS (N=45) vs. COPD (N=107)

**ACOS : 1) & 2)**

1) COPD : Age ≥40 years, smoking PY >10, & post-BD $FEV_1$/FVC <0.70
2) History of asthma, and self-reported wheezing within 1 year & BDR (+)

| | ACOS (*N*=45) | COPD alone (*N*=107) | *P*-value |
|---|---|---|---|
| Changes of pulmonary function and symptom score | | | |
| Δ $FEV_1$, mL | 240.2±33.5 | 124.6±19.8 | 0.002 |
| Δ FVC, mL | 304.8±59.0 | 150.2±38.1 | 0.030 |
| Δ TLC, mL | 435.3±264.0 | 888.3±247.7 | 0.213 |
| Δ RV, mL | −93.3±156.0 | 102.8±129.5 | 0.380 |
| Δ IC, mL | 166.9±84.9 | 141.5±62.6 | 0.820 |
| Δ mMRC | −0.05±0.17 | −0.39±0.08 | 0.126 |
| Acute exacerbation, % | 15.0 | 12.2 | 0.719 |




ICS/LABA on $FEV_1$ improvement: better in ACO compared with COPD alone

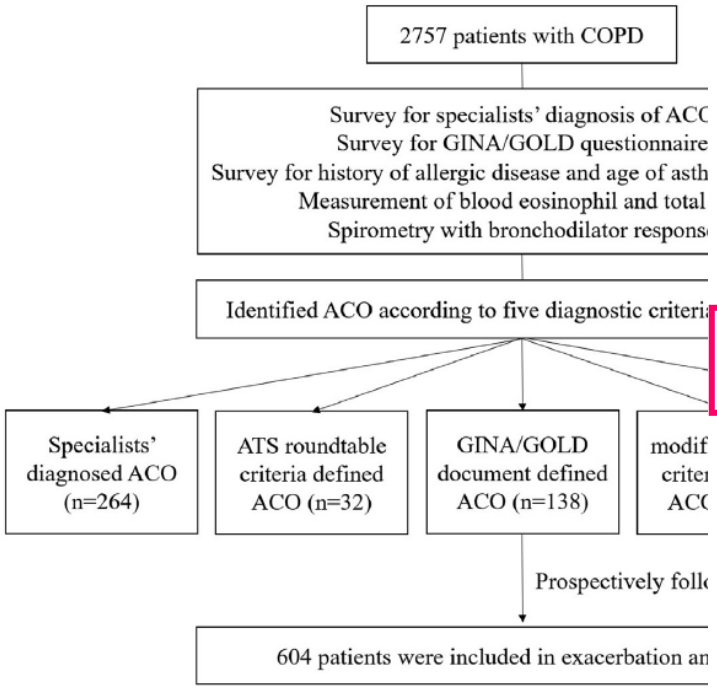
SY Lee et al. International Journal of COPD 2016:11 2797–2803

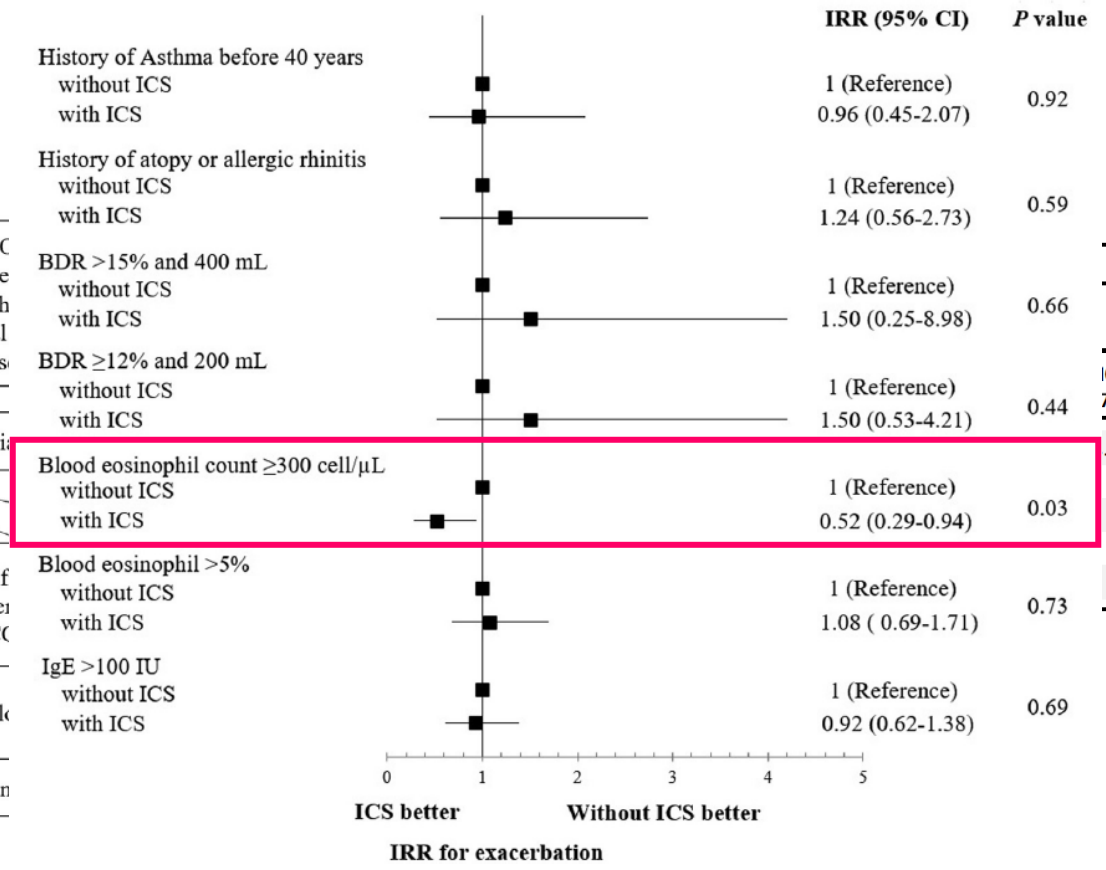
# ICS on AE risk

**ACO : 5 sets of diagnostic criteria**

- GINA/GOLD guideline
- ATS roundtable
- Modified Spanish
- Updated Spanish
- Specialist's judgement

- KOCOSS cohort : ACO study by the Korean Asthma Research Group since 2016




| | | GINA non-ACO (N = 929) | | |
|---|---|---|---|---|
| ICS 7) | *P* value | With ICS (N = 268) | Without ICS (N = 472) | *P* value |
| .65 | .05 | 3.0 ± 2.08 | 3.33 ± 4.57 | .64 |
| | .046 | 0.90 (0.67-1.22) | | .49 |
| | .046 | 0.90 (0.66-1.23) | | .51 |
| | .011 | 0.92 (0.67-1.28) | | .64 |
| | .031 | 0.96 (0.68-1.35) | | .81 |

ICS reduce the risk of AE in ACO

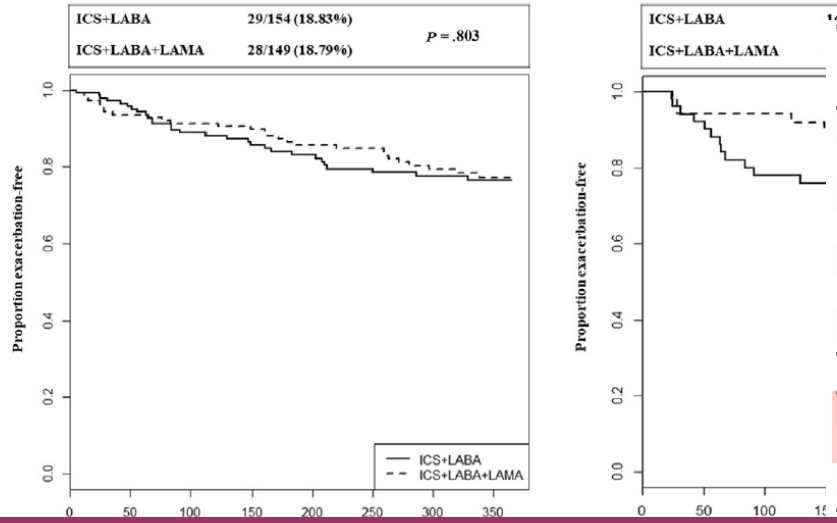
YS Jo et al. J Allergy Clin Immunol Pract 2020;8:1625-33

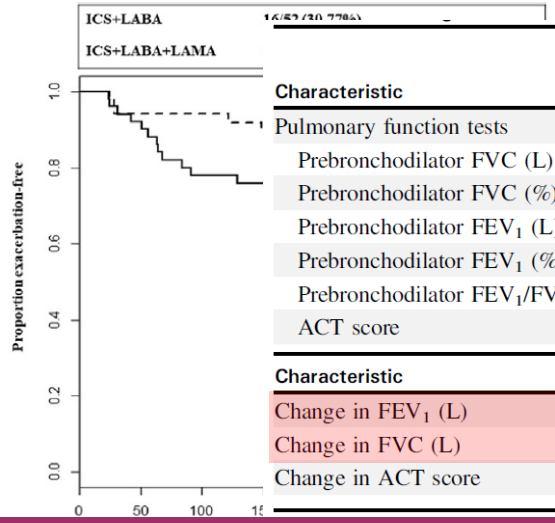
# ICS/LABA vs triple on AE & $FEV_1$

**ACO : 1) & 2)**

1) Positive BDR or provocation test
2) $FEV_1/FVC<0.7$

- The ACO Treatment with Optimal Medications (ATOMIC) Study
- ACO with $FEV_1$ >30% & moderate to high dose of ICS/LABA were enrolled
- Noninferiority trial comparing ICS/LABA (N=154) vs. ICS/LABA/LAMA (N=149)
- Primary endpoint : time to first exacerbation




| Characteristic | ICS + LABA Baseline | ICS + LABA Last visit | *P* value | ICS + LABA + LAMA Baseline | ICS + LABA + LAMA Last visit | *P* value |
|---|---|---|---|---|---|---|
| Pulmonary function tests | | | | | | |
| Prebronchodilator FVC (L) | 2.94 ± 0.90 | 2.94 ± 0.87 | .871 | 2.95 ± 0.95 | 3.07 ± 0.92 | .001 |
| Prebronchodilator FVC (%) | 78.92 ± 12.90 | 79.07 ± 12.98 | .838 | 79.43 ± 16.14 | 83.48 ± 15.29 | <.001 |
| Prebronchodilator $FEV_1$ (L) | 1.90 ± 0.65 | 1.92 ± 0.64 | .476 | 1.82 ± 0.61 | 1.93 ± 0.62 | .001 |
| Prebronchodilator $FEV_1$ (%) | 68.09 ± 13.11 | 69.59 ± 14.11 | .075 | 65.32 ± 12.96 | 70.27 ± 13.80 | <.001 |
| Prebronchodilator $FEV_1/FVC$ (%) | 64.56 ± 10.44 | 65.14 ± 10.45 | .313 | 62.39 ± 11.34 | 63.24 ± 11.24 | .245 |
| ACT score | 21.68 ± 3.27 | 21.87 ± 3.22 | .595 | 21.02 ± 3.72 | 21.34 ± 3.58 | .358 |

| Characteristic | ICS + LABA | ICS + LABA + LAMA | *P* value |
|---|---|---|---|
| Change in $FEV_1$ (L) | 0.017 ± 0.244 | 0.108 ± 0.352 | .023 |
| Change in FVC (L) | −0.004 ± 0.270 | 0.125 ± 0.386 | .004 |
| Change in ACT score | 0.183 ± 3.768 | 0.315 ± 3.902 | .786 |

LAMA add on ICS/LABA : time to first exacerbation (-), lung function improvement (+)

**FIGURE 2.** T
LABA group and the ICS + LABA+ LAMA group. Exacerbation events were not significantly different between the groups. (**B**) Comparison involving only those patients who had experienced at least 1 or more exacerbation in the previous year.

SY Park et al. J Allergy Clin Immunol Pract 2020 Nov 9 ePub

# Outcome

- Exacerbation
- Lung function
- Healthcare utilization / medical cost
- Mortality

# Exacerbation

| Author | | ACO definition | Outcome | Results | Risk of AE |
|---|---|---|---|---|---|
| MA Kim et al.<br>Int J Tuberc Lung Dis.<br>2015 Jul;19(7):864-9. | Single center cohort | >45years, FEV1/FVC <0.7<br><br>Asthma was diagnosed based on GINA definition | Hospitalization due to respiratory cause | High risk of hospitalization (31.3% vs 13.0%, p<0.001) |  |
| | | | All cause mortality | Higher death rate (54.9 vs 45.1%, p<0.001) | |
| YS Jo et al.<br>Ann Allergy Asthma Immunol 118 (2017) 696-703 | SNUH cohort | Modified Spanish, ATS Roundtable, PLATINO, GINA/GOLD | Moderate to severe | aHR 1.97*, 1.07, 1.35 and 2.01 for criteria |  |
| HJ Park et al.<br>Allergy Asthma Immunol Res. 2017 September;9(5):431-437 | KOCOSS cohort | FEV1/FVC <0.7 & BDR (+) | Any AE required systemic corticosteroid, antibiotics or both | - At 1yr FU : 20.9% vs 18.0% (p=0.461)<br>- At 2yr FU : 19.7 vs 14.3% (p=0.144) |  |
| | | | Severe AE requiring hospitalization | - At 1yr FU : 5.5 vs 1.5% (p=0.030)<br>- At 2yr FU : 5.6 vs 0.8% (p=0.015)<br>***of COPD vs ACO*** | |
| MH Kim et al.<br>International Journal of COPD 2018:13 1251-1260 | KNHANES | 1) ≥40 years & FEV1/FVC <0.7 & FEV1 ≥ 50%<br>2) Self-reported wheezing | Severe Exacerbation (hospitalization or ER visit) | aHR 1.79 and 2.11 compared to the W-S- & W-S+ group in COPD-predominant ACO |  |
| | | | Health care utilization | Greater medical costs in COPD-predominant ACO | |
| JH Song et al. Medicine (2018) 97:36(e12049) | KOCOSS cohort | Modified Spanish<br>ATS Roundtable | Moderate to severe | aHR 0.73, 0.63 for modified Spanish & ATS Roundtable criteria, p for both 0.11 & 0.449 |  |
| SY Park et al.<br>Clin Exp Allergy.<br>2019;49:603–614 | COREA cohort | 1) BDR (+) or AHR (+)<br>2) post-BD $FEV_1$/FVC <0.70 for 3mo | Acute moderate to severe AE rate over 1yr & 3yr | 1.61 vs 2.38; p<0.001 for 1yr &<br>0.73 vs 0.65; p=0.07 for 3yr |  |

# Longitudinal changes of Lung function in asthma cohort

**TABLE 2** Longitudinal analysis over 1 and 3 y

| | "Only" asthma | ACOS | *P*-value |
|---|---|---|---|
| Method 1 | | | |
| Mean ± SD ΔFEV1 over 1 y, % | 6.36 ± 4.26 (n = 345) | 7.19 ± 5.07 (n = 135) | 0.09 |
| Mean ± SD ΔFEV1 over 3 y, % | 4.82 ± 2.64 (n = 149) | 5.76 ± 3.46 (n = 70) | 0.045 |
| Mean ± SD ΔFVC over 1 y, % | 6.08 ± 4.90 (n = 345) | 7.97 ± 6.46 (n = 135) | 0.002 |
| Mean ± SD ΔFVC over 3 y, % | 4.69 ± 3.29 (n = 149) | 6.13 ± 3.90 (n = 70) | 0.005 |
| Mean ± SD ΔFEV1 over 1 y, mL | 175.82 ± 129.27 (n = 349) | 208.55 ± 165.91 (n = 136) | 0.040 |
| Mean ± SD ΔFEV1 over 3 y, mL | 133.36 ± 91.88 (n = 151) | 158.10 ± 105.9 (n = 70) | 0.095 |
| Mean ± SD ΔFVC over 1 y, mL | 172.89 ± 133.31 (n = 349) | 261.53 ± 181.53 (n = 135) | <0.001 |
| Mean ± SD ΔFVC over 3 y, mL | 128.65 ± 84.12 (n = 151) | 195.33 ± 100.61 (n = 70) | <0.001 |
| Mean ± SD Δ(FEV1/FVC) over 1 y | 0.04 ± 0.02 (n = 349) | 0.04 ± 0.03 (n = 136) | 0.004 |
| Mean ± SD Δ(FEV1/FVC) over 3 y | 0.03 ± 0.01 (n = 151) | 0.03 ± 0.02 (n = 70) | 0.005 |
| Method 2 | | | |
| Mean ± SD {(MAX)-(MIN)}FEV1 over 1 y, % | 15.92 ± 11.29 (n = 345) | 18.17 ± 12.57 (n = 135) | 0.058 |
| Mean ± SD {(MAX)-(MIN)}FEV1 over 3 y, % | 22.25 ± 11.58 (n = 149) | 23.85 ± 11.29 (n = 70) | 0.336 |
| Mean ± SD {(MAX)-(MIN)}FVC over 1 y, % | 15.98 ± 11.64 (n = 345) | 19.19 ± 13.91 (n = 135) | 0.018 |
| Mean ± SD {(MAX)-(MIN)}FVC over 3 y, % | 22.60 ± 13.64 (n = 149) | 26.19 ± 15.81 (n = 70) | 0.086 |
| Mean ± SD {(MAX)-(MIN)}FEV1 over 1 y, mL | 449.48 ± 364.64 (n = 349) | 518.90 ± 419.99 (n = 136) | 0.092 |
| Mean ± SD {(MAX)-(MIN)}FEV1 over 3 y, mL | 616.69 ± 415.65 (n = 151) | 649.86 ± 372.18 (n = 70) | 0.569 |
| Mean ± SD {(MAX)-(MIN)}FVC over 1 y, mL | 441.95 ± 357.38 (n = 349) | 636.18 ± 434.69 (n = 136) | <0.001 |
| Mean ± SD {(MAX)-(MIN)}FVC over 3 y, mL | 605.36 ± 412.98 (n = 151) | 817.29 ± 410.45 (n = 70) | <0.001 |
| **Method 3** | **β** | **Standard error** | ***P*-value** |
| Lung function decline FEV1 over 1 y, % | 0.44 | 0.26 | 0.080 |
| Lung function decline FEV1 over 3 y, % | 0.17 | 0.10 | 0.082 |
| Lung function decline FVC over 1 y, % | 0.83 | 0.27 | ≤0.001 |
| Lung function decline FVC over 3 y, % | 0.17 | 0.10 | 0.100 |
| Lung function decline FEV1/FVC over 1 y, % | −0.001 | 0.01 | 0.840 |
| Lung function decline FEV1/FVC over 3 y, % | 0.001 | 0.0 | 0.190 |
| ACT score | | | |
| Change in ACT score over 1 y | −0.029 | 0.08 | 0.730 |
| Change in ACT score over 3 y | 0.004 | 0.03 | 0.88 |

COREA cohort : ACOS vs " Only asthma"

**Greater $\triangle FEV_1$ & FVC decline in ACOS**

SY Park et al. Clin Exp Allergy. 2019;49:603–614.

# Changes of Lung function in COPD cohort

- KOLD cohort
- ACO (n=47, 19.7%) vs non-ACO COPD (n=192, 80.3%)

**ACO : 3 major & at least 1 minor ("ATS roundtable criteria")**

**Major :** 1) post-BD $FEV_1$/FVC <0.7
2) at least 10 PY of smoking history
3) history of asthma or BDR >400 mL

**Minor** : 1) history of atopy or allergic rhinitis
2) 2 separate BDR (+)
3) blood eosinophil ≥300 cells/uL

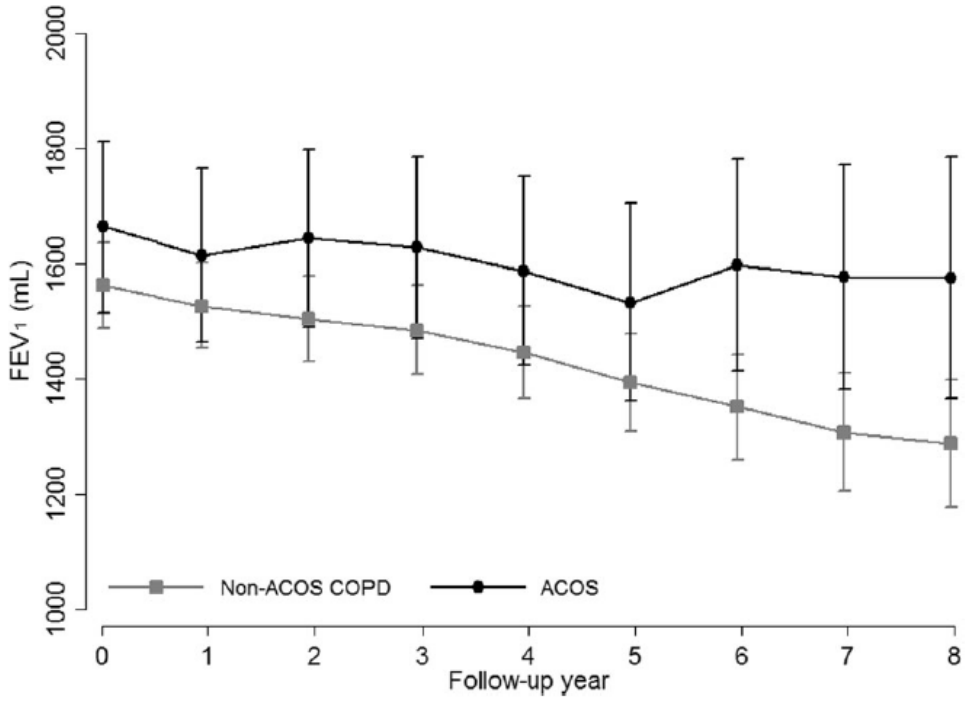



**Table 4** Longitudinal changes in annual pre-bronchodilator forced expiratory volume in 1 s (mL) between non-ACO COPD and ACO

| | Non-ACO COPD ($n = 192$) | ACO ($n = 47$) | $P$ for interaction* |
|---|---|---|---|
| Crude, *mL* | −29.26 (−35.78, −22.75) | −13.87 (− 27.22, − 0.52) | 0.042 |
| Model 1, *mL* | − 29.17 (− 35.73, − 22.61) | −13.58 (− 27.01, − 0.14) | 0.041 |
| Model 2, *mL* | −29.19 (− 35.74–22.64) | −13.64 (− 27.07, − 0.22) | 0.041 |
| Model 3, *mL* | −29.16 (− 35.73, − 22.60) | −13.61 (− 27.06, − 0.17) | 0.042 |

Data are presented as mean (95% confidence interval)
Model 1: Adjusted for baseline age, baseline body mass index and smoking status during the study period; Model 2: Further adjusted for at least 2 exacerbations per a year during study period; Model 3: Further adjusted for use of ICS/LABA or ICS during the study period

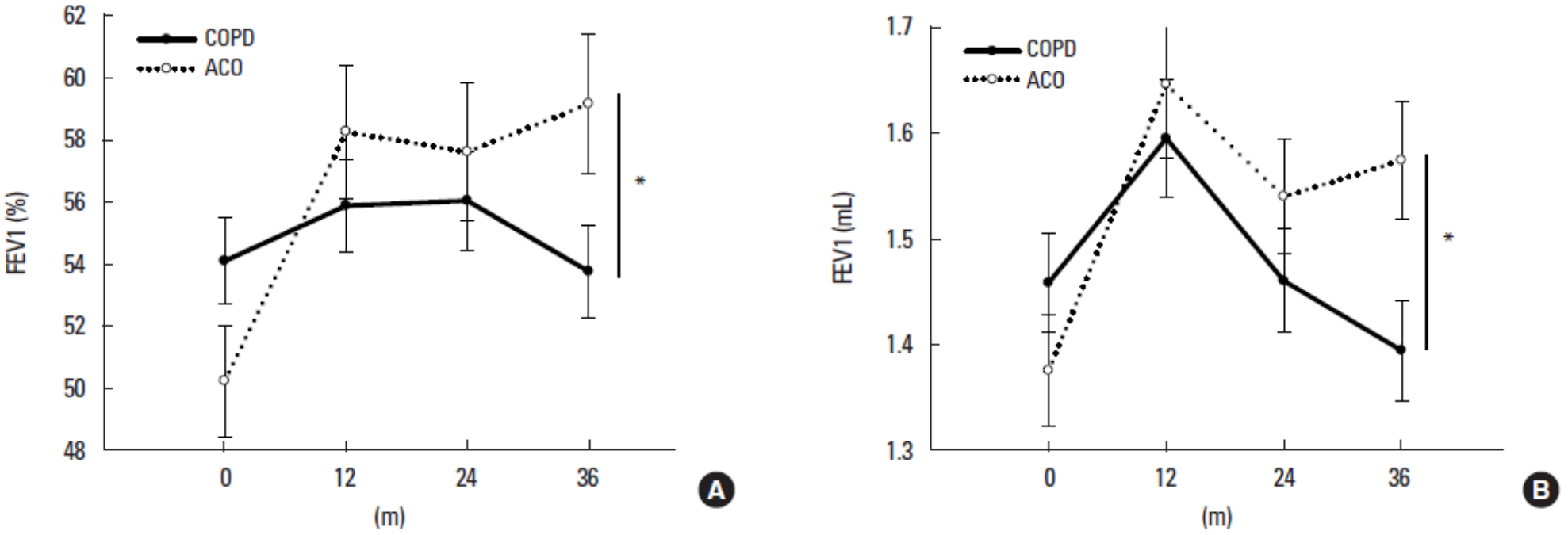
ACO has *favorable longitudinal changes in lung function* than COPD alone

HY Park et al. Respiratory Research (2018) 19:36

# Changes of Lung function in COPD cohort

- KOCOSS cohort : COPD (n=1281, 85.2%) vs ACO (n=223, 14.8%)

**ACO** : $FEV_1/FVC$ <0.7 & BDR (+)




ACO showed a *higher likelihood of $FEV_1$ recovery* than those with pure COPD

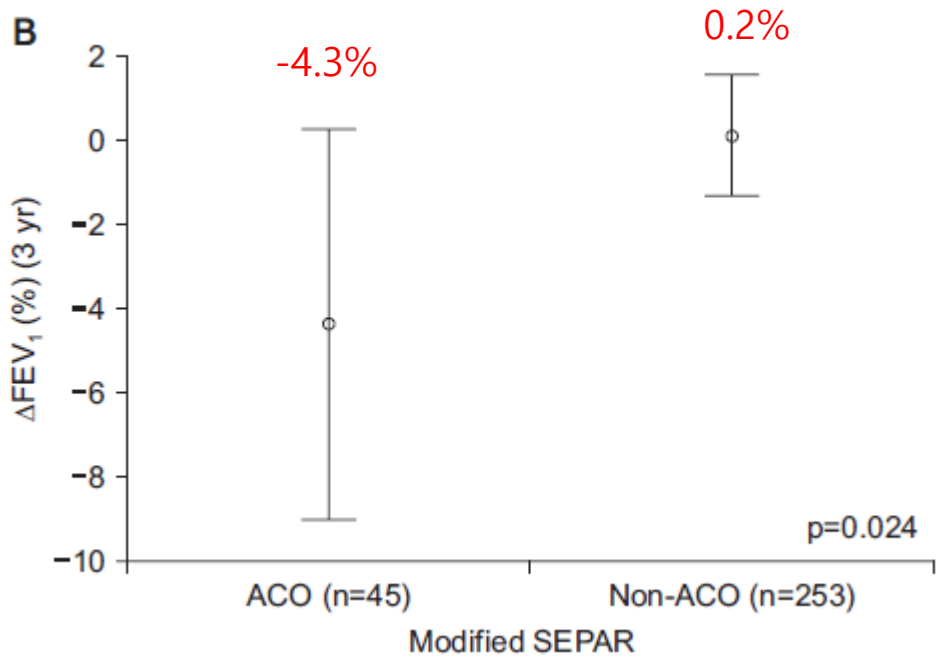
HJ Park et al. Allergy Asthma Immunol Res. 2017 September;9(5):431-437

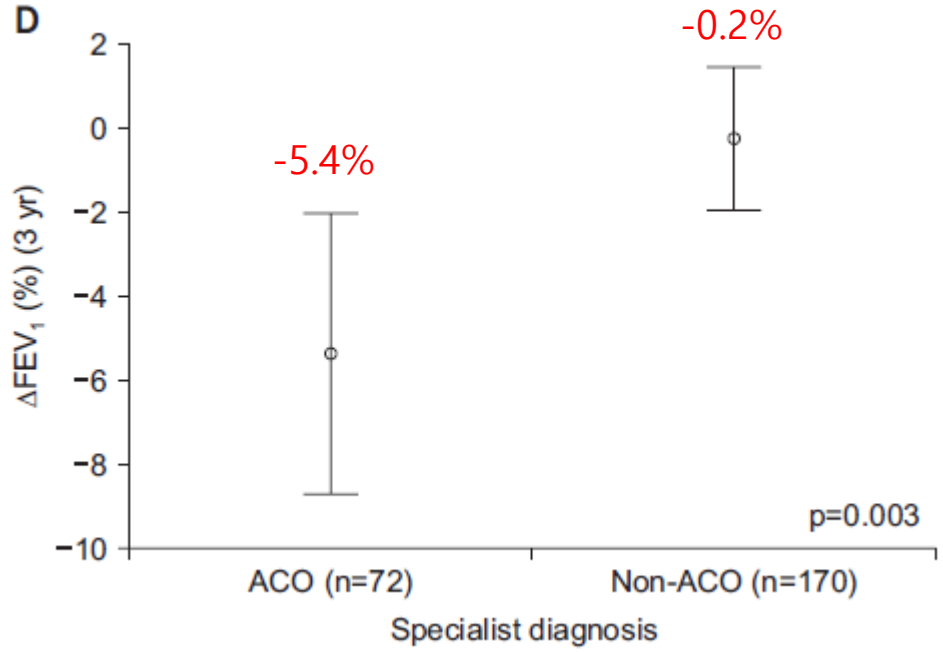
# Changes of Lung function in COPD cohort

**ACO : 5 sets of diagnostic criteria**

- GINA/GOLD guideline
- ATS roundtable
- Modified Spanish (SEPAR)
- Specialist's judgement

- KOCOSS cohort




ACO by modified SEPAR definition & specialists diagnosis,

*$FEV_1$ decreased more than COPD alone*

JU Lim et al. Tuberc Respir Dis 2020;83 Supple 1:S34-S45

# Socioeconomic impact : Healthcare utilization & Cost

**ACO : (1) & (2)**

(1) COPD : >40years, ICD-10 codes for COPD or emphysema (J42.x-J44.x, except J430), use of COPD drug ≥2/year

(2) Asthma : ICD-10 code for asthma (J45.x-J46), use of asthma drug ≥2/year

**Table 2.** Healthcare utilization of COPD patients[†]

| | Overlap syndrome | COPD without asthma | *p*-value |
|---|---|---|---|
| Cost of all medical utilization (USD) | | | |
| Cost of outpatient services | 790 ± 71 | 413 ± 512 | <0.001 |
| Cost of inpatient services | 3,373 ± 4,628 | 3,010 ± 5,013 | <0.001 |
| Total cost | 1,807 ± 3,096 | 829 ± 2,215 | <0.001 |
| Used days | | | |
| Outpatient services | 9.2 ± 9.76 | 7.4 ± 8.11 | <0.001 |
| Inpatient services | 25.44 ± 34.74 | 23.19 ± 36.41 | <0.001 |
| Total used days | 16.81 ± 24.56 | 10.5 ± 17.46 | <0.001 |

Data are expressed as the mean ± SD.
[†]Costs or used days per person. Costs and used days are restricted to COPD-related ones.

CK Rhee et al. COPD. 2014 Apr;11(2):163-70.

**ACO :** self-reported wheezing history & $FEV_1/FVC$ <0.7

| | ACOS | COPD | Asthma | P value |
|---|---|---|---|---|
| Total length of healthcare utilization, days | 60 | 45 | 33 | <0.001 |
| Outpatients, days | 57 | 43 | 41 | <0.001 |
| Inpatients, days | 15 | 13 | 14 | 0.165 |
| Total Medical cost, US dollar | 1629 | 1303 | 1287 | <0.001 |
| Outpatients | 1221 | 953 | 951 | <0.001 |
| Inpatients | 1909 | 2154 | 1834 | <0.001 |

*Higher healthcare utilization & medical cost* in ACO

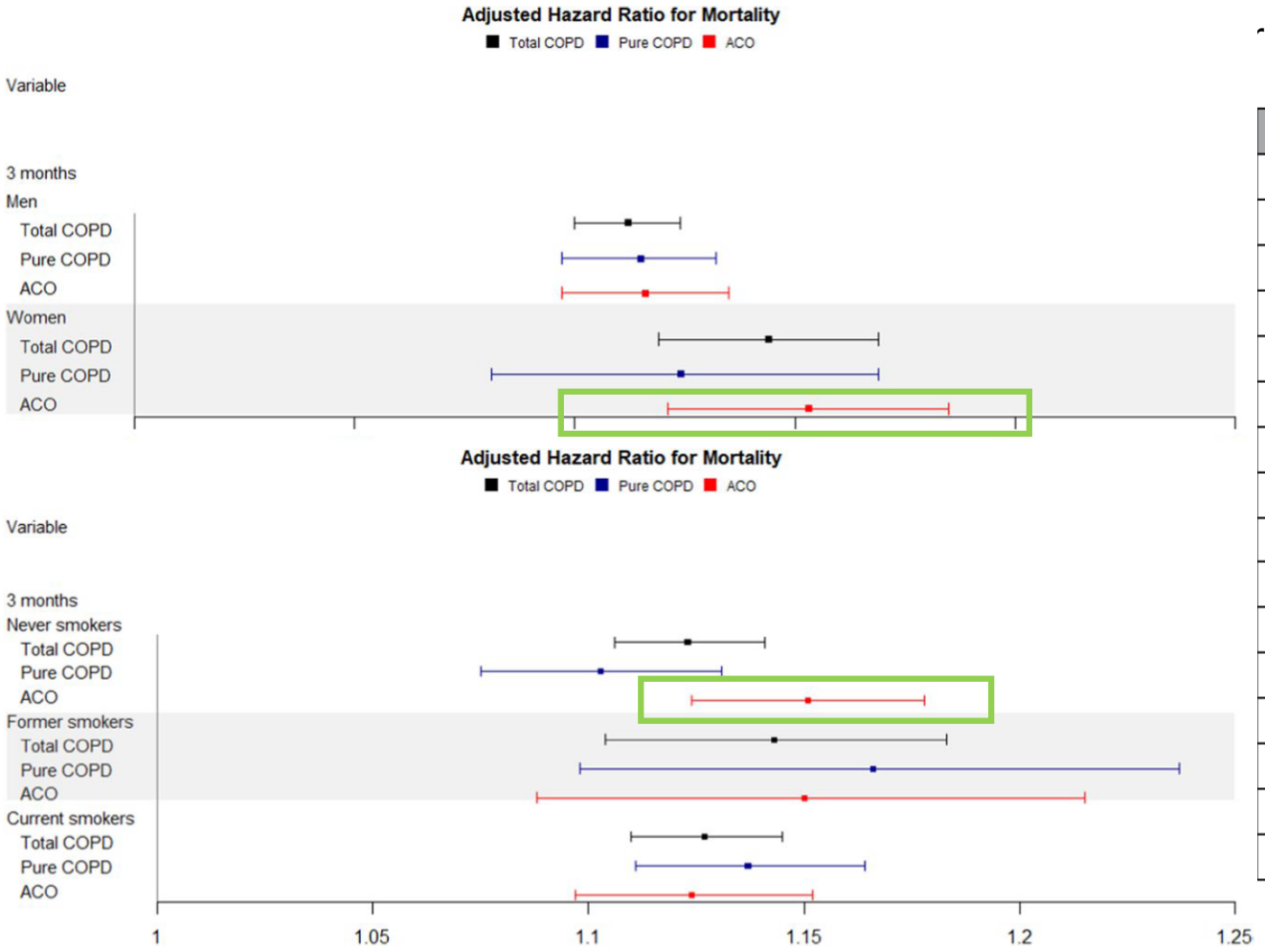
JH Kim et al. J Thorac Dis 2017;9(6):1547-1556

# Mortality associated with $PM_{10}$ exposure

**ACO : (1) & (2)**

(1) COPD : >40years, ICD-10 codes for COPD or emphysema (J42.x-J44.x, except J430), use of COPD drug ≥2/year

(2) Asthma : ICD-10 code for asthma (J45.x-J46), use of asthma drug ≥2/year




t (NHIS-NSC) database, a population-based cohort

| | N (%) | HR | 95% CI | | aHR | 95% CI | |
|---|---|---|---|---|---|---|---|
| **12 months** | | | | | | | |
| Total COPD | 6,313 | 1.018 | 1.001 | 1.035 | 1.011 | 0.994 | 1.027 |
| Pure COPD | 3,186 (50.47) | 1.015 | 0.992 | 1.040 | 1.004 | 0.981 | 1.028 |
| ACO | 3,127 (49.53) | 1.020 | 0.997 | 1.044 | 1.015 | 0.993 | 1.039 |
| **6 months** | | | | | | | |
| Total COPD | 6,313 | 1.179 | 1.167 | 1.190 | 1.123 | 1.111 | 1.135 |
| Pure COPD | 3,186 (50.47) | 1.186 | 1.170 | 1.202 | 1.124 | 1.106 | 1.142 |
| ACO | 3,127 (49.53) | 1.171 | 1.155 | 1.188 | 1.125 | 1.108 | 1.143 |
| **3 months** | | | | | | | |
| Total COPD | 6,313 | 1.166 | 1.156 | 1.176 | 1.117 | 1.107 | 1.128 |
| Pure COPD | 3,186 (50.47) | 1.169 | 1.155 | 1.183 | 1.116 | 1.100 | 1.131 |
| ACO | 3,127 (49.53) | 1.163 | 1.149 | 1.177 | 1.124 | 1.109 | 1.140 |
| **1 month** | | | | | | | |
| Total COPD | 6,313 | 1.035 | 1.019 | 1.051 | 1.022 | 1.009 | 1.036 |
| Pure COPD | 3,186 (50.47) | 1.035 | 1.012 | 1.059 | 1.017 | 0.998 | 1.036 |
| ACO | 3,127 (49.53) | 1.035 | 1.012 | 1.057 | 1.026 | 1.007 | 1.046 |

YM Lee et al. Sci Rep. 2020 Feb 12;10(1):2402.

# Summary

- 한국의 ACO 연구는 다양한 분야에서 이루어지고 있다.
- 대체적으로 기존에 알려진 ACO group 의 특징과 비슷한 양상을 보인다.
- Asthma, COPD 와 마찬가지로 ACO 또한 heterogeneous 하기때문에, optimal 치료에 대해서는 아직 debate 가 있고, 추가적인 연구가 필요하다.
- 일관되지 않은 ACO group 의 폐기능의 변화에 대해서는 추적 연구가 필요하다.

# Thank you
# for your attention !