



“호흡기내과의를사를 위한 **Respiratory
Review of 2026**”
COPD

2026.4.18
양산부산대학교병원
손은정

Contents



양산부산대학교병원
Pusan National University Yangsan Hospital

1. Case Finding and Diagnosis
2. New Goals of Management
3. Changing COPD Classification
4. Pharmacological Treatment
5. Clinical Implications: SAO, Mucus, and Frailty



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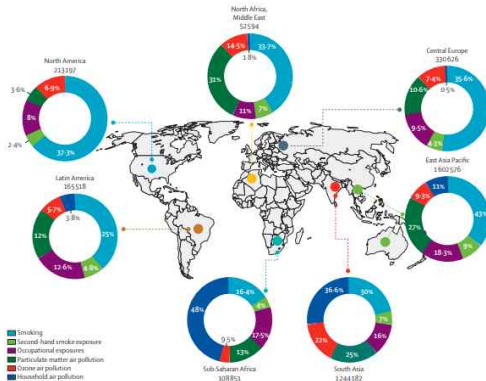


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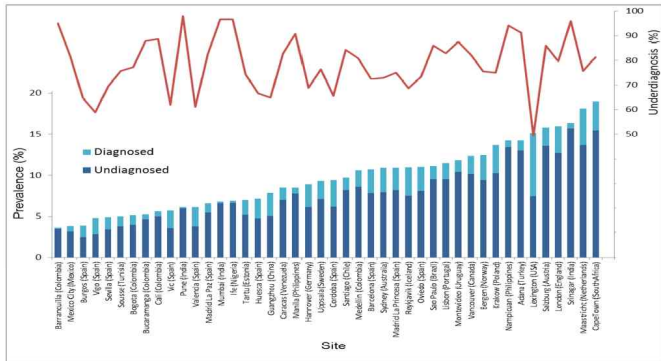
COPD Prevalence



- COPD affects >400 million people and is **the third leading cause of death worldwide**.
- Prevalence in adults ≥ 40 years was **10.6% (480 million cases)** in 2020, and is projected to rise to **~592 million** by 2050.

COPD Prevalence

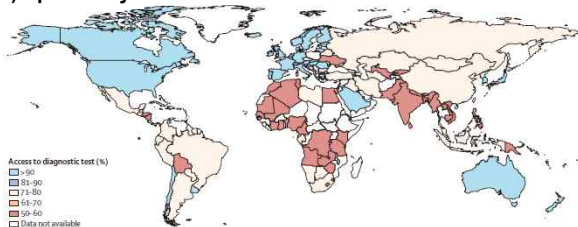
Figure 2. Prevalence of diagnosed and undiagnosed COPD (post-BD FEV1/FVC<LLN) and relative underdiagnosis by study site



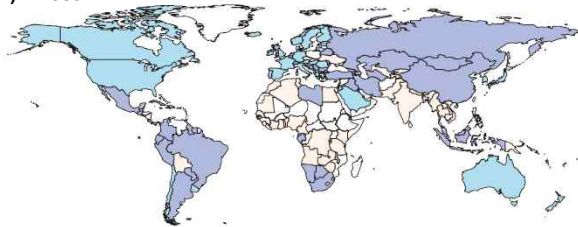
- A 27-country collaborative study found a prevalence of COPD, of 9.7%, with 81% of COPD cases being undiagnosed.
- The problem of COPD underdiagnosis (90–95% of COPD cases) was worse in LMICs.

Proportion of global population with access for diagnosis of COPD

(A) Spirometry



(B) Chest CT



	Primary and specialist care	Primary care only	Specialist care only	Limited* availability in primary or specialist care, or both	Not available
Lower-middle-income countries (n=11)					
Spirometry	2 (18%)	0	4 (36%)	5 (45%)	0
Reversibility testing	1 (9%)	0	6 (55%)	4 (36%)	0
Whole body plethysmography	0	0	3 (27%)	5 (45%)	3 (27%)
Diffusion capacity measurement	0	0	3 (27%)	5 (45%)	3 (27%)
Arterial blood gas analysis	0	0	6 (55%)	5 (45%)	0
Chest radiography	6 (55%)	3 (27%)	0	2 (18%)	0
Chest CT	1 (9%)	0	7 (64%)	3 (27%)	0
Upper-middle-income countries (n=15)					
Spirometry	3 (20%)	2 (13%)	6 (40%)	4 (27%)	0
Reversibility testing	2 (13%)	1 (7%)	8 (53%)	4 (27%)	0
Whole body plethysmography	0	0	5 (33%)	9 (60%)	1 (7%)
Diffusion capacity measurement	0	0	6 (40%)	8 (53%)	1 (7%)
Arterial blood gas analysis	1 (7%)	2 (13%)	8 (53%)	4 (27%)	0
Chest radiography	8 (53%)	4 (27%)	3 (20%)	0	0
Chest CT	3 (20%)	0	10 (67%)	2 (13%)	0
High-income countries (n=17)					
Spirometry	12 (71%)	1 (6%)	3 (18%)	1 (6%)	0
Reversibility testing	8 (47%)	0	9 (53%)	0	0
Whole body plethysmography	0	0	16 (94%)	1 (6%)	0
Diffusion capacity measurement	1 (6%)	0	14 (82%)	2 (12%)	0
Arterial blood gas analysis	1 (6%)	0	15 (88%)	1 (6%)	0
Chest radiography	12 (71%)	0	4 (24%)	1 (6%)	0
Chest CT	4 (24%)	0	12 (71%)	1 (6%)	0

Table 1: Availability of tests considered relevant in the diagnosis of chronic obstructive pulmonary disease, by country income group

Proposed diagnostic algorithm for COPD

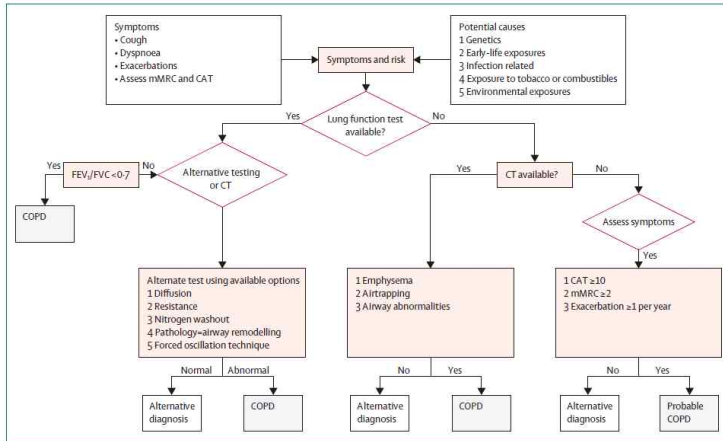


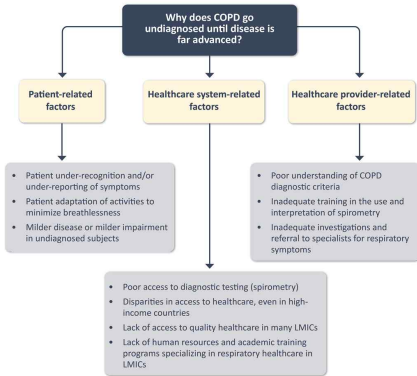
Figure 11: Proposed diagnostic algorithm for COPD

COPD=chronic obstructive pulmonary disease. mMRC=modified medical research council scale. CAT=COPD assessment test. FEV₁=forced expiratory volume in 1 s. FVC=forced vital capacity.

Screening and Case-Finding

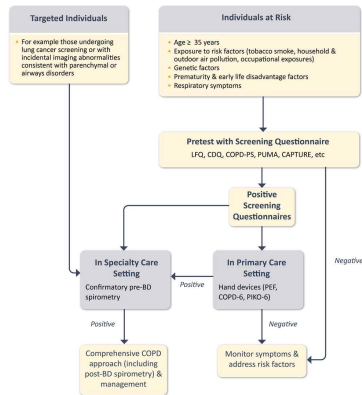
Factors that May Be Associated with COPD Underdiagnosis

Figure 2.8



An Algorithm for COPD Case-finding

Figure 2.9



Adapted from: Aaron et al. Am J Respir Crit Care Med. 2024 Apr 15;209(8):928-937.

Population-Based Screening for Chronic Obstructive Pulmonary Disease Using the St. George's Respiratory Questionnaire in Resource-Limited Settings

© William Checkley^{1,2}, Mingling Yang^{1,2}, Nicole M. Robertson^{1,2}, Arun K. Sharma³, Ram K. Chandyo⁵, Laxman Shrestha³, Santa K. Das⁴, Bruce Kirenga⁶, Patricia Alupo⁶, Gonzalo Gianella⁷, Trishul Siddharthan^{2,8}, Suzanne L. Pollard^{1,2}, Shumonta Quaderi⁹, Natalie Rykiel^{1,2}, Oscar Flores-Flores^{2,10}, John R. Hurst⁹, and Robert A. Wise¹; the Global Excellence in COPD outcomes (GECO) Study Investigators

¹Division of Pulmonary and Critical Care and ²Center for Global Non-Communicable Disease Research and Training, School of Medicine, Johns Hopkins University, Baltimore, Maryland; ³Department of Pediatrics and the Child Health Research Project and ⁴Department of Pulmonology and Critical Care, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal; ⁵Department of Community Medicine, Kathmandu Medical College, Bhaktapur, Nepal; ⁶Makerere Lung Institute, Makerere University, Kampala, Uganda; ⁷Facultad de Medicina, Universidad Peruana Cayetano Heredia, Lima, Peru; ⁸Division of Pulmonary and Critical Care, Miller School of Medicine, University of Miami, Miami, Florida; ⁹UCL Respiratory Medicine, University College London, London, United Kingdom; and ¹⁰Facultad de Medicina Humana, Centro de Investigación del Envejecimiento, Universidad de San Martín de Porres, Lima, Peru

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Study Design: Population-based COPD screening study

Participants: Adults aged ≥ 40 years

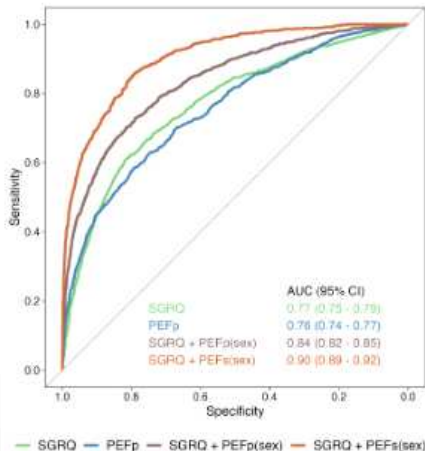
Screening Tools:

St. George's Respiratory Questionnaire (SGRQ)

Pre-bronchodilator Peak Expiratory Flow (PEF)

COPD Definition: Post BD FEV₁/FVC Z-score < -1.645

ROC curves for combination of SGRQ and PEF



Research

JAMA | **Original Investigation**

A Multidimensional Diagnostic Approach for Chronic Obstructive Pulmonary Disease

COPDGene 2025 Diagnosis Working Group and CanCOLD Investigators

New Diagnostic Criteria for COPD

Figure 1. Diagnostic Schema for Chronic Obstructive Pulmonary Disease (COPD) Using Major and Minor Criteria

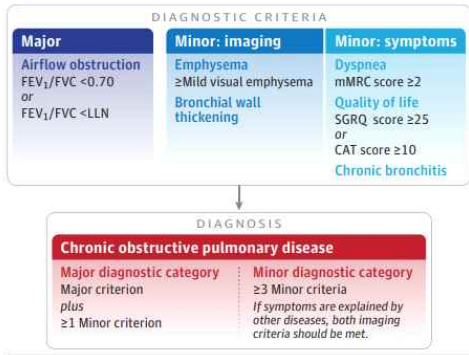
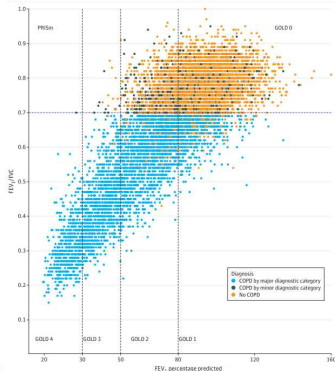


Figure 2. Reclassification of Participants by New Diagnostic Schema by Global Initiative for Chronic Obstructive Lung Disease (GOLD) Stage



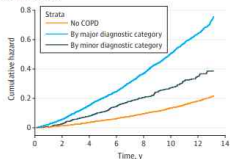
- **15.4% (811/5,250)** without airflow obstruction were newly classified as COPD (minor criteria).
- **6.8% (282/4,166)** with airflow obstruction were classified as non-COPD.

Table 1. Clinical and Imaging Characteristics of Participants in COPDGene by Reclassification Status

	Reclassification overall (N = 9416)			
	COPD by both old and new diagnostic schemas (n = 3884)	No airflow obstruction but COPD present according to new diagnostic schema (n = 811)	Airflow obstruction but no COPD according to new diagnostic schema (n = 282)	No COPD by both old and new diagnostic schemas (n = 4439)
Lung function, mean (SD)				
FEV ₁ % predicted	56.1 (22.2)	85.2 (16.4)	81.3 (14.9)	92.8 (15.0)
Questionnaires				
Chronic bronchitis, No. (%)	1073 (27.6)	410 (50.6)	0	306 (6.9)
mMRC dyspnea score, mean (SD) ^b	2.0 (1.4)	2.5 (1.1)	0.2 (0.4)	0.6 (1.1)
mMRC dyspnea score ≥ 2 , No. (%) ^b	2412 (62.1)	690 (85.1)	0	772 (17.4)
SGRQ total score, mean (SD)	38.4 (22.3)	46.7 (17.1)	8.6 (7.1)	14.5 (15.7)
SGRQ score ≥ 25 , No. (%)	2705 (69.6)	765 (94.3)	0	863 (19.4)
Frequent exacerbations, No. (%)	640 (16.5)	87 (10.7)	5 (1.8)	110 (2.5)
Imaging visual estimates, No. (%)				
Emphysema (\geq mild) ^c	3150 (81.1)	449 (55.4)	0	946 (21.3)
Bronchial wall thickening ^c	2757 (71.0)	416 (51.3)	0	572 (12.9)
Imaging quantitative estimates, mean (SD)				
Emphysema, % <-950 HU	12.5 (12.5)	1.6 (2.6)	3.8 (4.2)	1.9 (2.7)
P110, mm	2.68 (0.59)	2.48 (0.63)	2.12 (0.41)	2.06 (0.47)

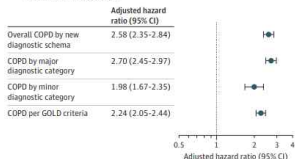
Figure 3. Associations Between Clinical Outcomes and Chronic Obstructive Pulmonary Disease (COPD) Status by New Diagnostic Schema in Genetic Epidemiology of COPD

A Multivariable cumulative hazard plot of all-cause mortality by COPD category

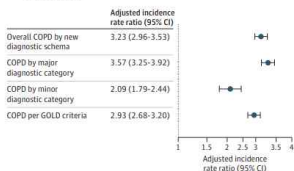


No. at risk	4721	4183	3986	3612	3276	2932	1820
No COPD	4721	4183	3986	3612	3276	2932	1820
By major diagnostic category	3884	3495	3100	2626	2160	1763	1015
By minor diagnostic category	811	670	598	517	423	354	201

B Adjusted hazard ratio for all-cause mortality by COPD category



C Adjusted incidence rate ratio for exacerbations



D Adjusted annualized change in FEV₁

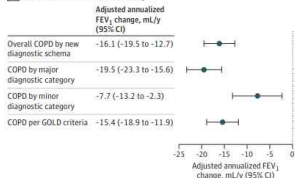
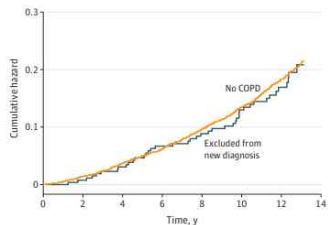


Figure 4. Associations Between the Category Excluded From Chronic Obstructive Pulmonary Disease (COPD) Diagnosis and Clinical Outcomes in the Genetic Epidemiology of COPD Study^a



No. at risk	4439	3920	3731	3370	3048	2721	1682
No COPD	4439	3920	3731	3370	3048	2721	1682
Excluded from new diagnosis	282	263	255	242	228	211	138



Original article

Identifying high-risk smokers without airflow limitation using new COPD criteria: pooled analysis of two Japanese cohorts

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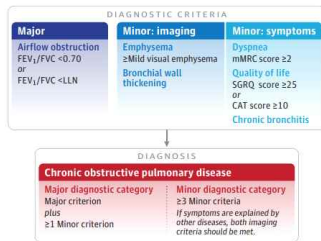
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^d Department of Respiratory Medicine, Saitama Medical University, 1397-1 Yamane, Hidaka-City, Saitama, 350-1296, Japan

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Figure 1. Diagnostic Schema for Chronic Obstructive Pulmonary Disease (COPD) Using Major and Minor Criteria



Methods

- Pooled analysis of two Japanese smoker cohorts (≥40 years).
- COPD was defined by airflow limitation plus ≥1 minor criterion or by ≥3 minor criteria.
- 3-year exacerbation risk was compared across groups.

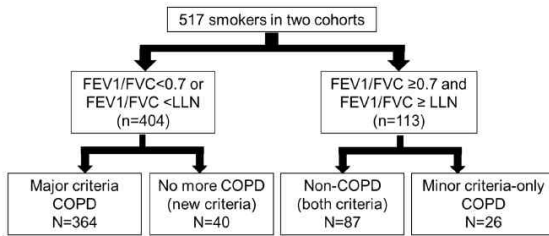
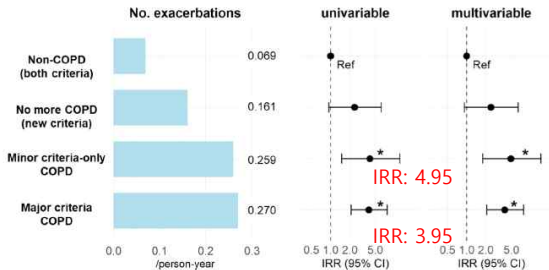


Fig. 1. Subject flow FEV1/FVC = forced expiratory volume in 1 s/forced vital capacity. LLN = lower limit of normal.



Predictors of Exacerbation

Table 2

Negative binomial models for a risk of exacerbation in patients with COPD based on new diagnostic criteria (n = 390).

Variable	IRR (95 % CI)	P value
CAT	1.04 (1.04, 1.07))	0.002
WA%	0.99 (0.99, 1.01)	0.42
LAA%	1.02 (1.01, 1.04)	0.0097
BMI	0.97 (0.90, 1.04)	0.29
age	1.01 (0.98, 1.04)	0.39
Male	1.88 (0.77, 4.57)	0.16
packyear	1.00 (0.99, 1.00)	0.55
Former smokers	0.67 (0.40, 1.11)	0.12

BMI = body mass index. CAT = COPD assessment test. FEV1 = forced expiratory volume in 1 s. FVC = forced vital capacity. LAA% = low attenuation area percentage. WA% = wall area percentage in segmental airway.

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Goals for Treatment of COPD

Goals for Treatment of Stable COPD

Figure 3.1

- Relieve Symptoms
- Improve Exercise Tolerance
- Improve Health Status



REDUCE SYMPTOMS

AND

- Prevent Disease Progression
- Prevent and Treat Exacerbations
- Reduce Mortality



REDUCE RISK

Disease Activity

- **Disease activity** refers to biological pathways that
 - ① cause the **pathological outcomes** of disease, and
 - ② are **potentially reversible or controllable** with treatment
 - If untreated or treatment is ineffective, disease activity leads to
 - disease progression
 - permanent organ damage and dysfunction
- **A key objective of COPD management** is to **reduce disease activity**, with the aim that patients have:
 - ✓ no exacerbations
 - ✓ no worsening of symptoms
 - ✓ no accelerated loss of lung function

CONCISE CLINICAL REVIEW

Is Disease Stability an Attainable Chronic Obstructive Pulmonary Disease Treatment Goal?

③ Dave Singh¹, MeiLan K. Han², Surya P. Bhatt³, Marc Miravittles⁴, Chris Compton⁵, Stefanie Kolterer⁶, Tharishini Mohan⁵, Suneal K. Sreedharan⁵, Lee Tombs⁷, and David M. G. Halpin⁸

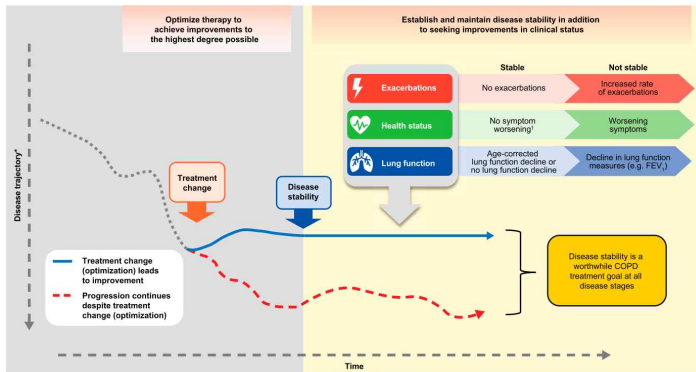


Table 2. Preliminary Definition for Disease Stability

Components	Exacerbations: Frequency	Health Status: SGRQ or CAT	Lung Function: FEV ₁
Thresholds*	No exacerbations	No worsening in SGRQ or CAT score; alternatively, no clinically significant worsening	No decrease; consideration of correction for age-related decline
Timeline	<ul style="list-style-type: none"> 6–12 months, comprising one or multiple visits in that time Benchmark current measurements against previous 6–12 months at each visit 		
Individual vs. composite assessments	<ul style="list-style-type: none"> Stability can be achieved in one or multiple components Dependent on patient factors, availability of spirometry, and setting 		
Context and setting	<ul style="list-style-type: none"> Primary care or in-clinic and research settings All disease severities, phenotypes/etiologies, and interventions 		
Other considerations	<ul style="list-style-type: none"> "Clinically significant" worsening will require definition Biomarkers may be implemented in future components once validated An expert consensus on the definition of disease stability should be reached among key experts 		

Definition of abbreviations: CAT= COPD Assessment Test; COPD = chronic obstructive pulmonary disease; SGRQ = St. George's Respiratory Questionnaire.

*Some patients may experience improvements with treatment optimization and other holistic interventions (e.g., smoking cessation, vaccination); this is also considered to be achieving disease stability.

Clinical Outcomes in Patients With COPD With Disease Stability

Data from the Korea COPD Subgroup Study Cohort

Eunjeong Son, MD, PhD; Hyewon Seo, MD, PhD; Seung Won Ra, MD, PhD; Seoung Ju Park, MD, PhD;
Soo-Jung Um, MD, PhD; Seong Yong Lim, MD, PhD; Hyoung Kyu Yoon, MD, PhD; Kwang Ha Yoo, MD, PhD;
Joon Young Choi, MD, PhD; and Chin Kook Rhee, MD, PhD

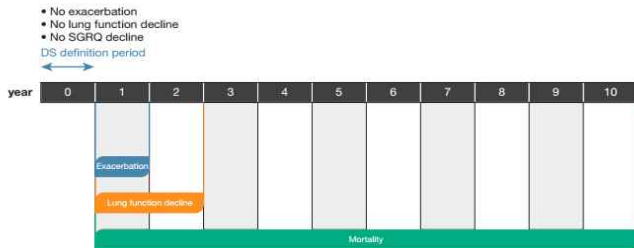


Figure 1 – Study time frame. This study defined a 1-y DS period, subsequently followed by a 1-y period of acute exacerbation occurrence, 2 y of lung function changes, and mortality rates investigated using national mortality data for up to 10 y. DS = disease stability; SGRQ = St. George's Respiratory questionnaire.

TABLE 3] Cox Proportional Hazards Regression of All-Cause Mortality According to Disease Stability

	Crude			Multivariate		
	HR	95% CI	P Value	HR	95% CI	P Value
Disease stability	0.56	0.37-1.09	.096	0.56	0.32-0.96	.036
Age	1.07	1.07-1.11	< .001	1.07	1.05-1.09	< .001
Female sex	0.71	0.34-0.90	.018	0.73	0.32-1.66	.457
BMI	0.87	0.87-0.93	< .001	0.87	0.83-0.91	< .001
Smoking status						
Never	(Reference)			(Reference)		
Prior	1.74	1.12-2.70	.014	1.51	0.73-3.10	.267
Current	1.98	1.25-3.15	.004	2.16	1.02-4.57	.045
HTN	1.27	1.02-1.58	.036	1.49	1.12-2.00	.007
HF	1.78	1.08-2.94	.025	0.70	0.26-1.90	.481
DM	1.00	0.75-1.33	.986			
MI	1.31	0.81-2.10	.269			
CVA	1.27	0.56-2.87	.572			

CVA = cerebrovascular accident; DM = diabetes mellitus; HF = heart failure; HR = hazard ratio; HTN = hypertension; MI = myocardial infarction.

TABLE 2] Comparison of Exacerbation Frequency According to the Presence of Disease Stability

Exacerbations	IRR	95% CI	P Value
Moderate-to-severe	0.30	0.20-0.43	.033
Severe	0.26	0.10-0.58	.002

Adjusted variables include age, sex, BMI, smoking status, and post-bronchodilator FEV₁ (L). IRR = incident rate ratio.

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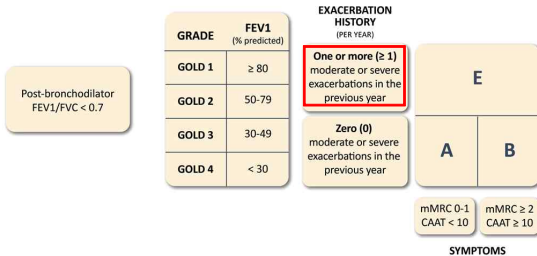
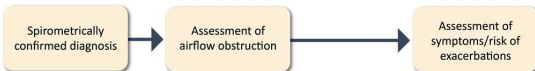
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Assessment of COPD

GOLD ABE Assessment Tool **2026 GOLD**

Figure 2.13



ORIGINAL ARTICLE

Exacerbation Risk and Mortality in Global Initiative for Chronic Obstructive Lung Disease Group A and B Patients with and without Exacerbation History

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¹COPD Center, Department of Respiratory Medicine and Allergology, Sahlgrenska University Hospital, Gothenburg, Sweden; ²Department of Internal Medicine and Clinical Nutrition and ³School of Public Health and Community Medicine, Institute of N Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; ⁴Division of Medicine/The OLIN Unit, Department of Health and Clinical Medicine, Umeå University, Umeå, Sweden; and ⁵Center of Registers Västra Götaland, Gothenburg, Sw

ORCID IDs: 0000-0002-4387-4096 (L.E.G.W.V.); 0000-0002-3292-7471 (A.L.); 0000-0001-6622-3838 (C.S.).

Study Design

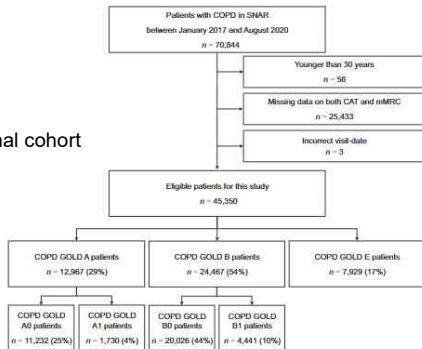
- Nationwide retrospective cohort study using the Swedish National cohort

Population

- Included 45,350 COPD patients aged ≥ 30 years (2017–2020)

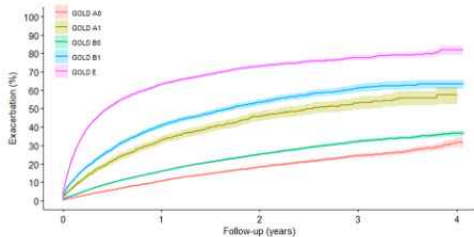
Classification

- A0: GOLD A, no exacerbation in previous year
- A1: GOLD A, one moderate exacerbation
- B0: GOLD B, no exacerbation
- B1: GOLD B, one moderate exacerbation
- E: ≥ 2 moderate or ≥ 1 severe exacerbation



Risk of Exacerbations and Hospitalization

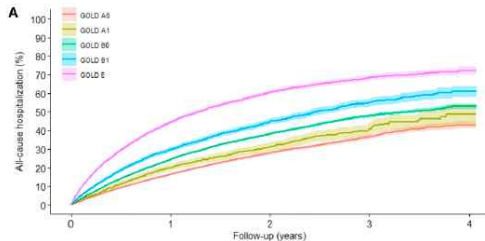
Time to First Exacerbation



Number at risk

	0	1	2	3	4
GOLD A0	11232	9607	3787	1292	63
GOLD A1	1730	989	378	113	3
GOLD B0	20017	14185	5875	2037	101
GOLD B1	4442	2170	761	228	7
GOLD E	7929	2268	733	207	4

Time to Hospitalization

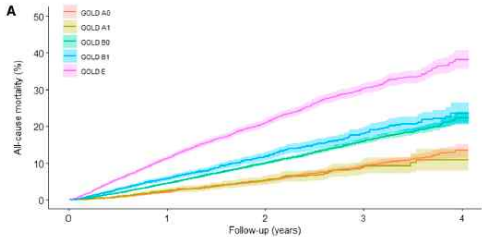


Number at risk

	0	1	2	3	4
GOLD A0	11232	8124	3410	1142	61
GOLD A1	1730	1194	504	182	5
GOLD B0	20017	13035	5030	1699	74
GOLD B1	4442	2674	985	321	6
GOLD E	7929	3649	1128	363	21

Risk of Mortality

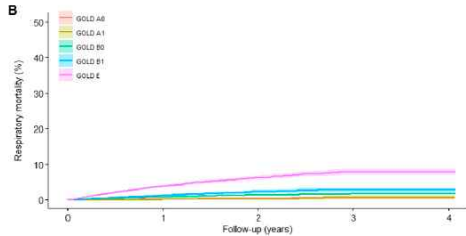
Time to death for any cause



Number at risk

	0	1	2	3	4
GOLD A0	11232	9627	4665	1723	98
GOLD A1	1730	1477	734	265	9
GOLD B0	20017	16800	7895	3068	165
GOLD B1	4442	3659	1693	654	27
GOLD E	7929	6059	2689	1033	54

Time to death for respiratory cause



Number at risk

	0	1	2	3	4
GOLD A0	11232	9627	4665	1723	98
GOLD A1	1730	1477	734	265	9
GOLD B0	20017	16800	7895	3068	165
GOLD B1	4442	3659	1693	654	27
GOLD E	7929	6059	2689	1033	54

Comparison of Clinical Outcomes

Table 5. Crude and Adjusted Hazard Ratios for Moderate Exacerbation and for All-Cause, Respiratory, and Cardiovascular Hospitalization and Mortality for Group B1 versus Group B0

		Moderate Exacerbation							
Group	Crude HR (95% CI)	Adj. HR (95% CI)	Crude HR (95% CI)	Adj. HR (95% CI)	Crude HR (95% CI)	Adj. HR (95% CI)	Crude HR (95% CI)	Adj. HR (95% CI)	Crude HR (95% CI)
B0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
B1	2.72 (2.59–2.87)	<u>2.56 (2.40–2.74)</u>	1.24 (1.18–1.31)	<u>1.28 (1.21–1.35)</u>	1.69 (1.55–1.85)	<u>1.44 (1.27–1.62)</u>	1.10 (0.98–1.23)	1.12 (0.96–1.30)	1.19 (1.08–1.31)
		All-Cause Hospitalization		Respiratory Hospitalization*		Cardiovascular Hospitalization*			
B0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
B1	1.24 (1.18–1.31)	<u>1.28 (1.21–1.35)</u>	1.69 (1.55–1.85)	<u>1.44 (1.27–1.62)</u>	1.10 (0.98–1.23)	1.12 (0.96–1.30)	1.19 (1.08–1.31)	1.04 (0.91–1.18)	1.62 (1.26–2.07)
		All-Cause Mortality		Respiratory Mortality*		Cardiovascular Mortality*			
B0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
B1	1.19 (1.08–1.31)	1.04 (0.91–1.18)	1.62 (1.26–2.07)	1.13 (0.79–1.64)	1.18 (0.82–1.69)	0.90 (0.53–1.53)	1.19 (1.08–1.31)	1.04 (0.91–1.18)	1.62 (1.26–2.07)

Definition of abbreviations: Adj. = adjustment for age, sex, smoking status, and lung function (FEV₁% predicted); CI = confidence interval; HR = hazard ratio; Ref = reference group.

B0 and B1 groups are Global Initiative for Chronic Obstructive Lung Disease classification B patients without and with an exacerbation in the past year, respectively.

*Death from other cause considered as competing risk.

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Management of COPD

Initial Pharmacological Treatment

Figure 3.8

Initiate Treatment

INITIAL treatment - for patients with COPD who are naive to maintenance pharmacological treatment

EXACERBATION HISTORY
(PER YEAR)

One or more (≥ 1)
moderate or severe
exacerbations in the
previous year

GROUP E

LABA + LAMA*

consider LABA+LAMA+ICS* if blood eos ≥ 300

Zero (0)
moderate or severe
exacerbations in
the previous year

GROUP A

A bronchodilator

mMRC 0-1, CAAT < 10

GROUP B

LABA + LAMA*

mMRC ≥ 2 , CAAT ≥ 10

SYMPTOMS

*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAAT™: Chronic Airways Assessment Test™.



The effect of exacerbation history on outcomes in the IMPACT trial

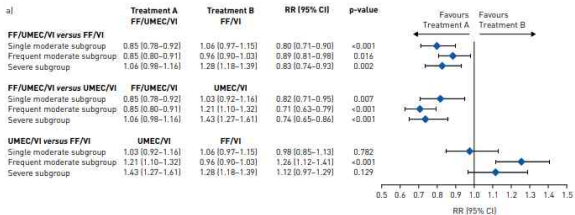
David M.G. Halpin¹, Mark T. Dransfield², MeiLan K. Han³, C. Elaine Jones⁴, Sally Kilbride⁵, Peter Lange^{6,7}, David A. Lipson^{8,9}, David A. Lomas¹⁰, Fernando J. Martinez¹¹, Steve Pascoe^{8,12}, Dave Singh¹³, Robert Wise¹⁴ and Gerard J. Criner¹⁵

Study design

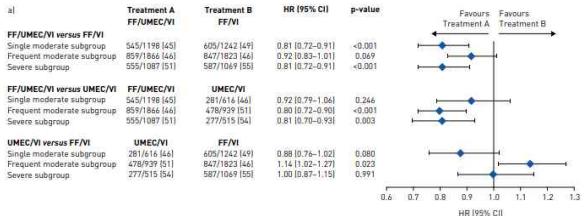
- Post-hoc subgroup analysis of the 52-week IMPACT trial(N=10,355).
- Included 10,355 symptomatic COPD patients with prior exacerbation history
- Divided by prior 12-month exacerbation history:
 - Single Moderate group: 1 moderate, 0 severe
 - Frequent Moderate group: ≥ 2 moderate, 0 severe
 - Severe group: ≥ 1 severe, any moderate
- Randomized (2:2:1) to Once-daily FF/UMEC/VI vs. FF/VI or UMEC/VI

Annual Exacerbation Rates During Treatment

Annual rate of moderate to severe exacerbations

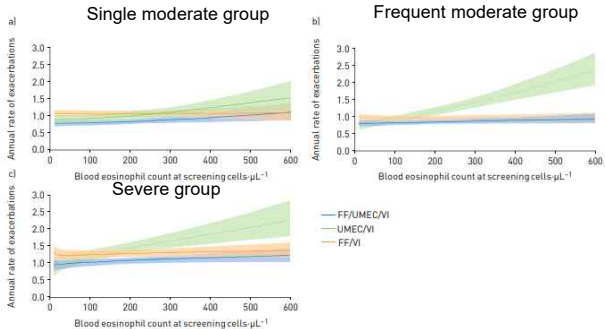


Time-to-first moderate to severe exacerbation

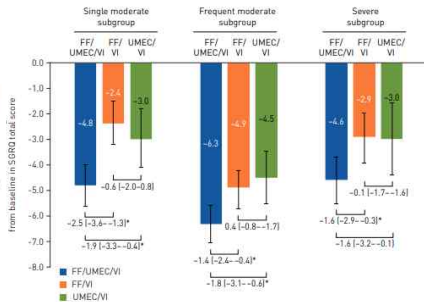


Exacerbation Rates According to BEC

Annual rate of moderate or severe exacerbations



SGRQ Improvement by Inhaled Therapy

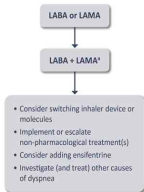


2 Adjust Treatment

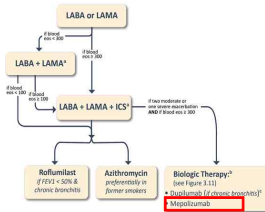
CONTINUE CURRENT TREATMENT

unless dyspnea or exacerbation(s) require optimization

IF PERSISTENT DYSPNEA



IF ONE OR MORE MODERATE OR SEVERE EXACERBATION



*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment.

*Listed in order of approval in the US.

*Patient-reported history of chronic bronchitis (chronic productive cough) for 3 months in the year up to screening, absent other known causes. Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood eosinophils ≥ 300 cells/ μ l de-escalation is more likely to be associated with the development of exacerbations.

ORIGINAL ARTICLE

Mepolizumab to Prevent Exacerbations of COPD with an Eosinophilic Phenotype

F.C. Sciruba,¹ G.J. Criner,² S.A. Christenson,³ F.J. Martinez,⁴ A. Papi,⁵ N. Roche,⁶ J. Bourbeau,⁷ S. Korn,⁸ M. Bafadhel,⁹ M.L.K. Han,¹⁰ S. Kolterer,¹¹ K. Miller,¹² D. Mouneimne,¹³ J. Fletcher,¹³ B. Mayer,¹⁴ J. Min,¹⁵ and I.D. Pavord,¹⁶ for the MATINEE Study Investigators*

Study Design

- Phase 3, randomized, double-blind, placebo-controlled trial

Study Population

- Patients with COPD
 - History of exacerbations
 - Blood eosinophil count ≥ 300 cells/ μ L
 - Receiving triple therapy

Intervention

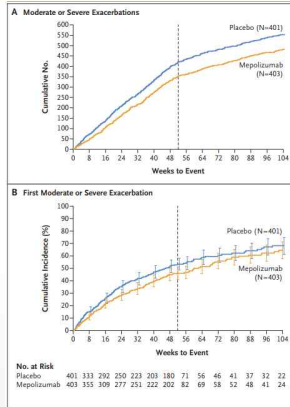
- 1:1 ratio, to receive mepolizumab (100 mg, SC) or placebo every 4 weeks for 52 to 104 weeks.

Primary Endpoint

- Annualized rate of moderate or severe COPD exacerbations

Table 2. Primary and Secondary Efficacy End Points.*

End Point	Mepolizumab (N=403)	Placebo (N=401)
Primary end point		
Annualized rate of moderate or severe exacerbations (95% CI) — events/yr	0.80 (0.70–0.91)	1.01 (0.89–1.15)
Rate ratio vs. placebo (95% CI)	0.79 (0.66–0.94)	—
P value	0.01	—



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ORIGINAL ARTICLE

Distinct Morphological Types of Small Airway Obstructions in Smokers with Emphysema and End-Stage Chronic Obstructive Pulmonary Disease

Vincent Geudens¹, Charlotte De Fays^{1,2}, Lynn Willems¹, Astrid Vermaut¹, Gitte Aerts¹, Pieterjan Kerckhof¹, Janne Kaes¹, Charlotte Hooft¹, Xin Jin¹, Hanne Beeckmans¹, Yousry Mohamady¹, Lucia Aversa¹, Tinne Goos¹, Marie Vermant¹, Iwein Gyselincx¹, Janne Verhaegen¹, Jan Van Slambrouck¹, Celine Aelbrecht¹, Andrew Higham³, Walter Coudyzer⁴, Emanuela E. Cortesi¹, Arno Vanstapel¹, John E. McDonough⁶, Marianne S. Carton¹, Rozenn Quarck¹, Matthieu N. Boone⁷, Lieven J. Dupont¹, Birgit Weynand⁵, Charles Pilette², Stephanie Everaerts¹, Dirk E. Van Raemdonck¹, Laurens J. Ceulemans¹, James C. Hogg⁸, Tillie-Louise Hackett⁹, Robin Vos¹, Wim A. Wuyts¹, Wim Janssens¹, Joseph Jacob^{9,10}, Bart M. Vanaudenaerde¹, and Ghislaine Gayan-Ramirez¹

Study design

- Cross-sectional analysis using explanted lungs and donor controls

Population

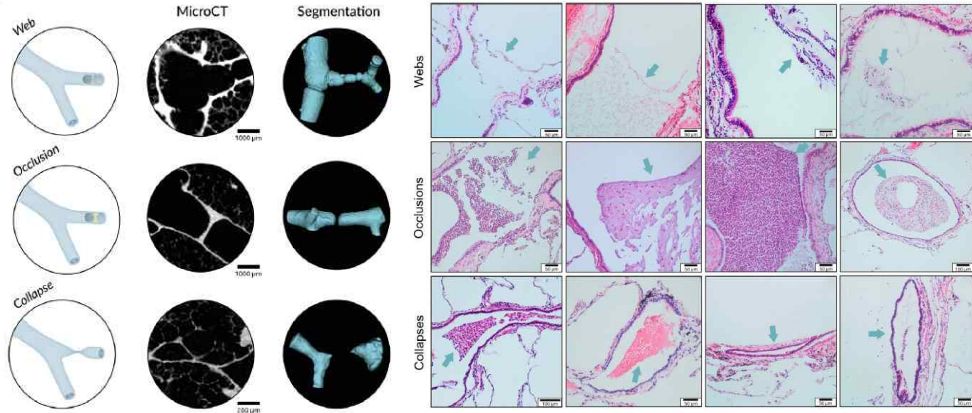
- Non-smokers (control)
- Smokers without emphysema
- Smokers with emphysema
- End-stage COPD

Techniques

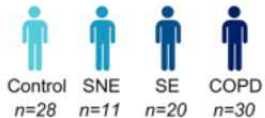
- Micro-computed tomography (micro-CT)
- Histological analysis

Multiple types of obstructions in terminal bronchioles

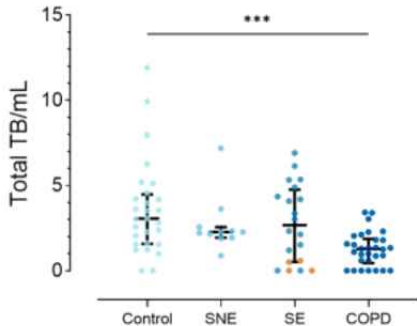
A



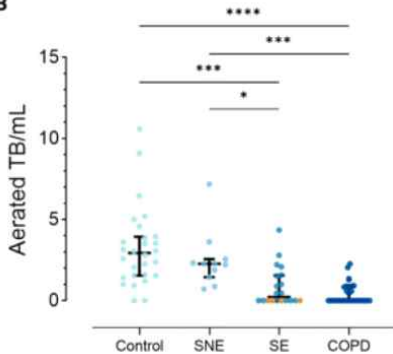
Total and Aerated number of terminal bronchioles



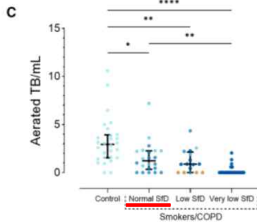
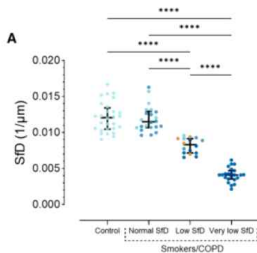
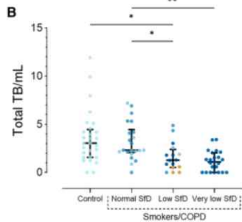
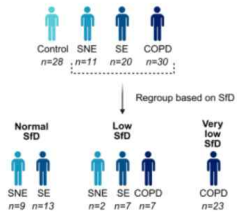
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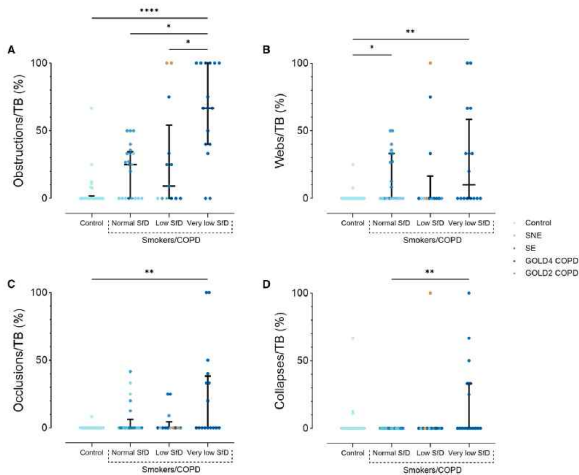
B



Stratification Based on Alveolar Surface Density(SfD)



Airway Changes with Disease Progression



Oscillometry-defined Small Airway Dysfunction in Tobacco-exposed Adults with Impaired or Preserved Airflow

Mustafa Abdo^{1,2,3}, Henrik Watz^{3,4}, Frederik Trinkmann^{2,3}, Sabine Bohnet⁵, Miriam Annabelle Marcella Guess⁵, Johannes Roeben⁵, Katharina May⁶, Martin Reck^{1,3}, Benjamin-Alexander Bollmann^{3,7,9}, Susanne Stiebeler^{1,10}, Sabine Dettmer^{8,9}, Benjamin Waschki^{3,11}, Klaus F. Rabe^{1,3,12}, Klaas Frederik Franzen^{3,5*}, and Jens Vogel-Claussen^{3,6,9*}; on behalf of the HANSE Trial Group

¹LungenClinic Grosshansdorf, Airway Research Center North, Grosshansdorf, Germany; ²Department of Pneumology and Critical Care Medicine, Thoraxklinik at Heidelberg University Hospital, Translational Lung Research Center Heidelberg, Heidelberg, Germany; ³German Center for Lung Research, Gießen, Germany; ⁴Velocity Clinical Research Germany GmbH, Ahrensburg, Germany; ⁵Department of Respiratory Medicine and ⁶Department of Radiology, University Medical Center Schleswig-Holstein, Lübeck, Germany; ⁷Department of Respiratory Medicine and Infectious Diseases and ⁸Department of Diagnostic and Interventional Radiology, Hannover Medical School, Hannover, Germany; ⁹Biomedical Research in End Stage and Obstructive Lung Disease Hannover, Hannover, Germany; ¹⁰Radiologische Allianz, Hamburg, Germany; ¹¹Itzehoe Hospital, Itzehoe, Germany; and ¹²Christian-Albrechts University of Kiel, Kiel, Germany

ORCID IDs: 0000-0002-3300-1398 (M.A.); 0000-0002-1070-3661 (B.W.).

Study design

- Subcohort analysis of the HANSE lung cancer screening trial in Germany

Population

- 1,628 tobacco-exposed adults (55–79 yrs) with ≥ 10 pack-years

Assessments

- Spirometry, oscillometry, AI-based CT, EQ-5D-5L questionnaires

Groups

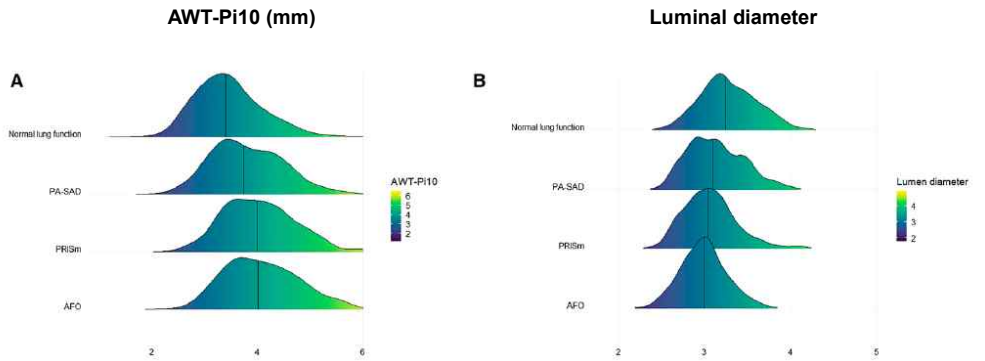
- AFO
- PRISm
- PA-SAD (FDR or AX > ULN)
- Normal

Clinical and Functional Differences Across Groups

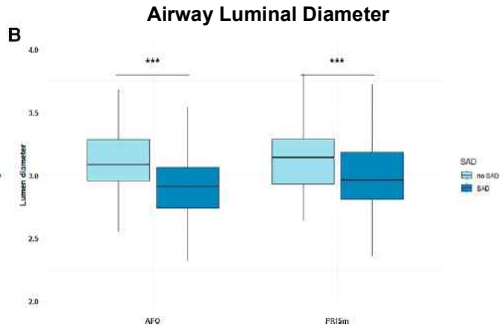
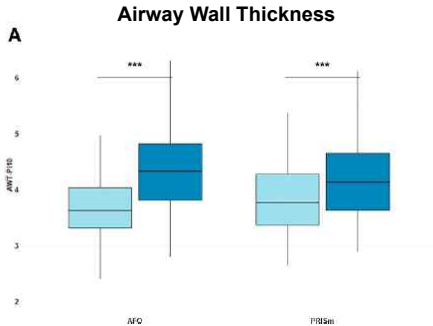
Table 1. Baseline Clinical and Imaging Characteristics According to Study Group

Variable	AFO (n = 353)	PRISm (n = 245)	PA-SAD (n = 266)	Normal Lung Function (n = 758)	P Value	Post Hoc
Demographics						
Age, yr	64 ± 6	63 ± 6	65 ± 6	64 ± 6	0.021	*
Sex, male	56	57	53	58	0.62	—
BMI, kg/m ²	26.4 ± 4.5	28.8 ± 5.2	29.3 ± 4.9	26.1 ± 3.7	<0.001	††§§
Smoking status, active smokers	60	59	49	51	0.003	†§§
Smoking quantity, PY	47 ± 19	47 ± 25	41 ± 17	40 ± 17	<0.001	†§§
Smoking abstinence, yr	3.8 ± 6.9	4.1 ± 7.4	6.3 ± 9.0	5.5 ± 8.6	<0.001	†§§
Regular physical activity	78	76	81	87	0.003	§§
Symptoms and QoL						
EQ-5D-5L score	0.91 ± 0.14	0.88 ± 0.19	0.89 ± 0.16	0.93 ± 0.12	<0.001	††§
EQ-5D-5L VAS	77.6 ± 16.0	77.1 ± 17.0	78.7 ± 16.0	81.1 ± 15.0	<0.001	††§
mMRC score ≥ 1	24.3	14.7	8.5	4.7	<0.001	††§§
Respiratory disease and cardiometabolic comorbidities						
Respiratory disease	50	26	20	13	<0.001	†§§§
Asthma	15	11	10	6.0	<0.001	†§
COPD	40	18	7	6	<0.001	††§§
Metabolic disease	50	61	61	44	<0.001	††
CVD	54	65	65	50	<0.001	†§§
Spirometry						
FEV ₁ % predicted	63 ± 14	68 ± 5	85 ± 8	91 ± 11	<0.001	††§§§
FEV ₁ z-score	-2.27 ± 0.83	-2.05 ± 0.29	-0.90 ± 0.53	-0.54 ± 0.69	<0.001	††§§§
FVC% predicted	86 ± 14	73 ± 5	88 ± 9	94 ± 11	<0.001	††§§
FVC z-score	-0.9 ± 0.94	-1.75 ± 0.38	-0.77 ± 0.6	-0.4 ± 0.72	<0.001	††§§
FEV ₁ :FVC	0.57 ± 0.08	0.71 ± 0.05	0.75 ± 0.05	0.75 ± 0.05	<0.001	†§§§
FEV ₁ :FVC z-score	-2.54 ± 0.72	-0.83 ± 0.6	-0.30 ± 0.66	-0.29 ± 0.7	<0.001	†§§§
MEF75% z-score	2.4 ± 0.90	3.2 ± 0.50	3.8 ± 0.50	3.9 ± 0.50	<0.001	†§§§
FEF25-75%:FVC	0.27 ± 0.09	0.51 ± 0.14	0.63 ± 0.18	0.63 ± 0.19	<0.001	†§§§
FEF25-75% z-score	-2.18 ± 0.58	-1.32 ± 0.47	-0.41 ± 0.59	-0.26 ± 0.69	<0.001	†§§§
Airway oscillometry						
R5, kPa · L ⁻¹ · s ⁻¹	0.41 ± 0.15	0.40 ± 0.14	0.45 ± 0.12	0.27 ± 0.08	<0.001	††§§
R5 z-score	0.67 ± 1.58	0.76 ± 1.62	0.80 ± 1.85	0.03 ± 0.67	<0.001	††§
FDR, kPa · L ⁻¹ · s ⁻¹	0.12 ± 0.08	0.11 ± 0.08	0.13 ± 0.06	0.03 ± 0.03	<0.001	††§§§
FDR z-score	1.24 ± 1.80	0.80 ± 1.80	1.33 ± 1.43	-0.77 ± 0.79	<0.001	††§§§
AX, kPa · L ⁻¹	1.94 ± 1.85	1.76 ± 1.72	2.0 ± 1.23	0.43 ± 0.27	<0.001	††§§
AX z-score	3.9 ± 4.0	3.6 ± 4.0	3.9 ± 2.7	0.31 ± 0.6	<0.001	††§§
F _{res}	21.2 ± 6.8	20.5 ± 6.3	22.7 ± 4.0	13.4 ± 3.5	<0.001	††§§
X5, kPa · L ⁻¹ · s ⁻¹	-0.23 ± 0.17	-0.24 ± 0.16	-0.25 ± 0.12	-0.11 ± 0.04	<0.001	††§§

Airway Structural Changes Across Study Groups



SAD Aggravates Airway Remodeling in AFO and PRISm



Predictors of Small Airway Dysfunction

Table 2. Linear Mixed-Effects Model Demonstrates Predictors of Small Airway Disease

Predictor	Standard Estimate	SE	P Value
Predictors of AX			
Age	0.250	0.026	<0.001
Sex, male	-0.410	0.047	<0.001
BMI	0.380	0.023	<0.001
Smoking status, former	-0.056	0.061	0.35
Smoking quantity	0.001	0.023	0.97
Duration of abstinence	-0.120	0.033	<0.001
Physical activity	-0.170	0.061	<0.01
History of respiratory disease	0.440	0.054	<0.001
Intercept	1.35	0.100	0.24
Predictors of FDR			
Age	0.150	0.027	<0.001
Sex, male	-0.230	0.049	<0.001
BMI	0.350	0.025	<0.001
Smoking status, former	-0.010	0.060	0.90
Smoking quantity	0.036	0.024	0.13
Duration of abstinence	-0.065	0.034	0.058
Physical activity	-0.160	0.063	0.011
History of respiratory disease	0.346	0.056	<0.001
Intercept	-2.70	0.99	<0.001

AX = area under the reactance curve; BMI = body mass index; FDR = frequency dependence of resistance.

Association of Physical Frailty With Incidence and Life Expectancy of COPD

A Population-Based Cohort Study



Chao Liu, MD; Hui Xiong, MD; Xia Han, MD; Yanling Lv, MD; Decai Wang, MD; Jiannan Hu, MD; Ziling Li, MD; Xinyue Ma, MD; Yunfei Zhu, MD; Shuyun Xu, PhD; and Liangkai Chen, PhD

Study Design

- Population-based cohort study using the UK Biobank

Population

- 412,351 adults without COPD at baseline
- 60,584 adults with COPD

Mean follow-up

- 13.5 years

Physical frailty assessed

- using five components; weight loss, exhaustion, low physical activity, slow gait speed, and low grip strength

Classification

- Nonfrailty; 0 components, Prefrailty; 1~2 components, Frailty; ≥ 3 components.

TABLE 1 | Basic Characteristics of Frailty Phenotypes Among Participants With and Without COPD

Variables	Participants Without COPD (n = 412,351; 100.0%)	Frailty Phenotype			Participants With COPD (n = 56,584; 100.0%)	Frailty Phenotype		
		Nonfrailty (n = 243,777; 59.1%)	Prefrailty (n = 155,114; 37.6%)	Frailty (n = 13,460; 3.3%)		Nonfrailty (n = 34,297; 56.6%)	Prefrailty (n = 23,128; 38.2%)	Frailty (n = 3,159; 5.2%)
Age, y	56.1 [8.1]	55.9 [8.1]	56.3 [8.2]	57.4 [7.8]	59.2 [7.4]	58.9 [7.5]	59.5 [7.4]	<u>60.0 [6.7]</u>
BMI, kg/m ²	27.5 [4.8]	26.7 [4.2]	28.4 [5.1]	31.5 [6.6]	26.9 [4.7]	26.0 [3.9]	27.7 [5.1]	<u>30.1 [6.7]</u>
Male	182,641 (44.3)	113,461 (46.5)	64,471 (41.6)	4,709 (35.0)	33,406 (55.1)	19,743 (57.6)	12,196 (52.7)	1,467 (46.4)
White ethnicity	388,601 (94.2)	234,246 (96.1)	142,792 (92.1)	11,563 (85.9)	60,333 (99.6)	34,245 (99.9)	22,980 (99.4)	3,108 (98.4)
Townsend Deprivation Index	-2.2 (-3.7 to 0.4)	-2.5 (-3.8 to -0.2)	-1.9 (-3.5 to 1.0)	0.1 (-2.6 to 3.2)	-1.9 (-3.5 to 1.0)	-2.3 (-3.8 to 0.1)	-1.5 (-3.3 to 1.7)	1.1 (-2.0 to 4.0)
Smoking status								
Does not smoke	235,303 (57.1)	142,418 (58.4)	85,980 (55.4)	6,905 (51.3)	24,228 (40.0)	15,142 (44.2)	8,323 (36.0)	763 (24.2)
Previously smoked	139,543 (33.8)	82,176 (33.7)	52,918 (34.1)	4,449 (33.1)	24,667 (40.7)	13,749 (40.1)	9,656 (41.8)	1,262 (40.0)
Currently smokes	37,505 (9.1)	19,183 (7.9)	16,216 (10.5)	2,106 (15.7)	11,689 (19.3)	5,406 (15.8)	5,149 (22.3)	<u>1,134 (35.9)</u>
Alcohol consumption frequency								
Daily or most days	82,037 (19.9)	54,430 (22.3)	26,301 (17.0)	1,306 (9.7)	14,937 (24.7)	9,377 (27.3)	5,132 (22.2)	428 (13.6)
3-4 times a week	96,425 (23.4)	63,985 (26.3)	31,028 (20.0)	1,412 (10.5)	13,847 (22.9)	8,835 (25.8)	4,617 (20.0)	395 (12.5)
1-2 times a week	107,904 (26.2)	64,456 (26.4)	40,691 (26.2)	2,757 (20.5)	14,622 (24.1)	8,293 (24.2)	5,673 (24.5)	656 (20.8)
1-3 times a month	46,899 (11.4)	25,729 (10.6)	19,477 (12.6)	1,693 (12.6)	5,909 (9.8)	3,092 (9.0)	2,477 (10.7)	340 (10.8)
Never or special occasions only	79,086 (19.2)	35,177 (14.4)	37,617 (24.3)	6,292 (46.8)	11,269 (18.6)	4,700 (13.7)	5,229 (22.6)	1,340 (42.4)
Sedentary behavior, h/d	4.5 [2.6]	4.3 [2.4]	4.7 [2.7]	5.5 [3.3]	4.7 [2.6]	4.3 [2.4]	5.0 [2.7]	<u>5.8 [3.5]</u>
No. of long-term morbidity								
0	146,632 (35.6)	100,993 (41.4)	44,336 (28.6)	1,303 (9.7)	14,192 (23.4)	10,018 (29.2)	4,048 (17.5)	126 (4.0)
1	137,442 (33.3)	83,654 (34.3)	51,016 (32.9)	2,772 (20.6)	18,860 (31.1)	11,895 (34.7)	6,588 (28.5)	377 (11.9)
2	77,233 (18.7)	39,945 (16.4)	33,897 (21.9)	3,391 (25.2)	13,857 (22.9)	7,474 (21.8)	5,723 (24.7)	660 (20.9)
3	33,219 (8.1)	14,004 (5.7)	16,379 (10.6)	2,836 (21.1)	7,624 (12.6)	3,297 (9.6)	3,635 (15.7)	692 (21.9)
4	12,036 (2.9)	3,892 (1.6)	6,407 (4.1)	1,737 (12.9)	3,532 (5.8)	1,132 (3.3)	1,849 (8.0)	551 (17.4)
≥ 5	5,789 (1.4)	1,289 (0.5)	3,079 (2.0)	1,421 (10.6)	2,519 (4.2)	481 (1.4)	1,285 (5.6)	<u>753 (23.8)</u>

Data are presented as No. (%), mean [SD], or median (interquartile range).

TABLE 2] Association Between Physical Frailty and Incident COPD

Characteristic	No.	Cases/Person-Years	Model 1	Model 2	Model 3
Physical frailty phenotype					
Nonfrailty	24,3777	4,084/3,222,704	1.00 (reference)	1.00 (reference)	1.00 (reference)
Prefrailty	155,114	5,301/2,010,021	1.92 (1.85-2.01)	1.45 (1.39-1.51)	<u>1.45 (1.39-1.51)</u>
Frailty	13,460	1,310/164,261	4.96 (4.65-5.28)	2.23 (2.08-2.39)	<u>2.21 (2.06-2.37)</u>
Components of frailty					
Weight loss	61,999	1,858/806,275	1.22 (1.16-1.29)	1.03 (0.98-1.08)	1.04 (0.98-1.09)
Exhaustion	49,476	2,232/637,701	2.16 (2.06-2.27)	1.39 (1.33-1.46)	<u>1.24 (1.18-1.31)</u>
Low physical activity	35,685	2,125/45,4460	2.44 (2.33-2.57)	1.54 (1.47-1.62)	<u>1.32 (1.25-1.39)</u>
Slow gait speed	29,457	2,559/363,388	3.32 (3.17-3.48)	1.86 (1.77-1.95)	<u>1.63 (1.54-1.71)</u>
Low grip strength	57,372	2,751/727,324	1.66 (1.59-1.74)	1.31 (1.25-1.38)	<u>1.19 (1.14-1.25)</u>

Analysis of incident COPD risk according to frailty

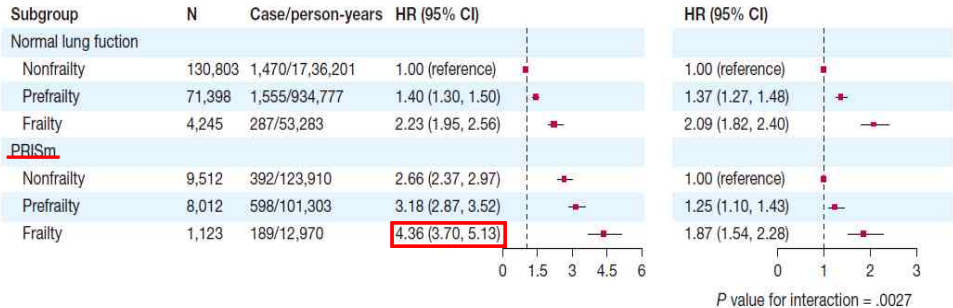
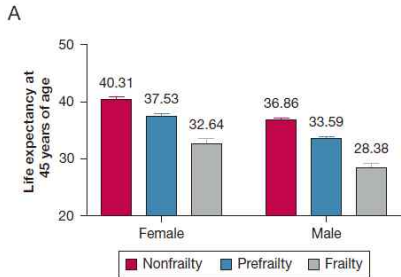
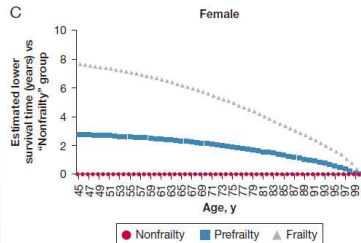
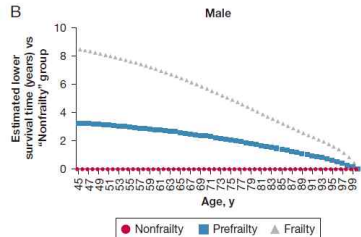


Figure 2 – Joint and stratified analysis of incident COPD risk according to frailty phenotype in PRISm and normal lung function. Model adjusted for age, sex, race, Townsend Deprivation Index, and assessment centers, sedentary behavior, smoking status, alcohol consumption, BMI, number of long-

Life Expectancy by Frailty



- COPD at 45 years of age, frailty was associated with a reduction in life expectancy of 8.49 years for male individuals and 7.67 years for female individuals compared with their nonfrail counterparts.



ORIGINAL ARTICLE

Airway Mucus Plugs on Chest Computed Tomography Are Associated with Exacerbations in Chronic Obstructive Pulmonary Disease

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Study design

- Multicenter prospective cohort study

Population

- GOLD 2–4 COPD from two cohorts
- COPDGene (n=3,250), ECLIPSE (n=1,716)

Assessment

- Baseline chest CT → mucus plug score (0, 1–2, ≥3)

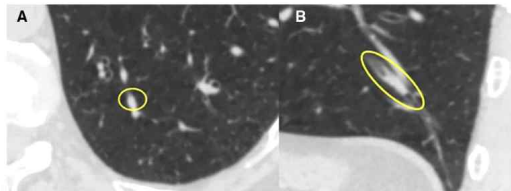


Figure 1. Example of a mucus plug on chest computed tomography imaging. Computed tomography axial (A) and sagittal (B) sections showing a mucus plug (encircled) occluding the lumen of an airway in the left lower lobe of a COPDGene (Genetic Epidemiology of COPD) participant with COPD. COPD = chronic obstructive pulmonary disease.

Association Between Mucus Plug Score and Exacerbation

Table 2. Association between Ordinal Mucus Plug Score Groups and AEs

	COPDGene			ECLIPSE		
	0	1-2	≥3	0	1-2	≥3
No. of patients	1,808	753	689	926	373	417
Moderate to severe AEs	Ref.	1.070 (1.048–1.093)	1.145 (1.098–1.195)	Ref.	1.056 (1.019–1.094)	1.115 (1.039–1.197)
Severe AEs	Ref.	1.045 (1.008–1.084)	1.092 (1.016–1.175)	Ref.	1.169 (1.072–1.273)	1.365 (1.15–1.622)

Summary

1. 2026 GOLD에서는 **COPD 선별을 위한 screening 및 case-finding**에 대한 보다 구체적인 접근 전략이 제시되었습니다.
2. 또한 **중등도 급성 악화가 1회 이상인 경우부터 E 그룹으로 분류**되며, 치료 옵션으로 **biologics인 mepolizumab**이 새롭게 포함되었습니다.
3. COPD의 새로운 치료 목표로 악화, 증상 악화, 폐기능 저하가 없는 상태인 **Disease stability** 개념이 제시되었습니다.
4. **Small airway dysfunction**는 spirometry가 정상이어도 이미 존재할 수 있는 임상적으로 중요한 병변이다.
5. **Frailty와 mucus plug**는 COPD 예후와 관련된 중요한 인자입니다.

경청해 주셔서 감사합니다.

Thank you for your attention

