GOLD Update 2023

-Definition and Classification-

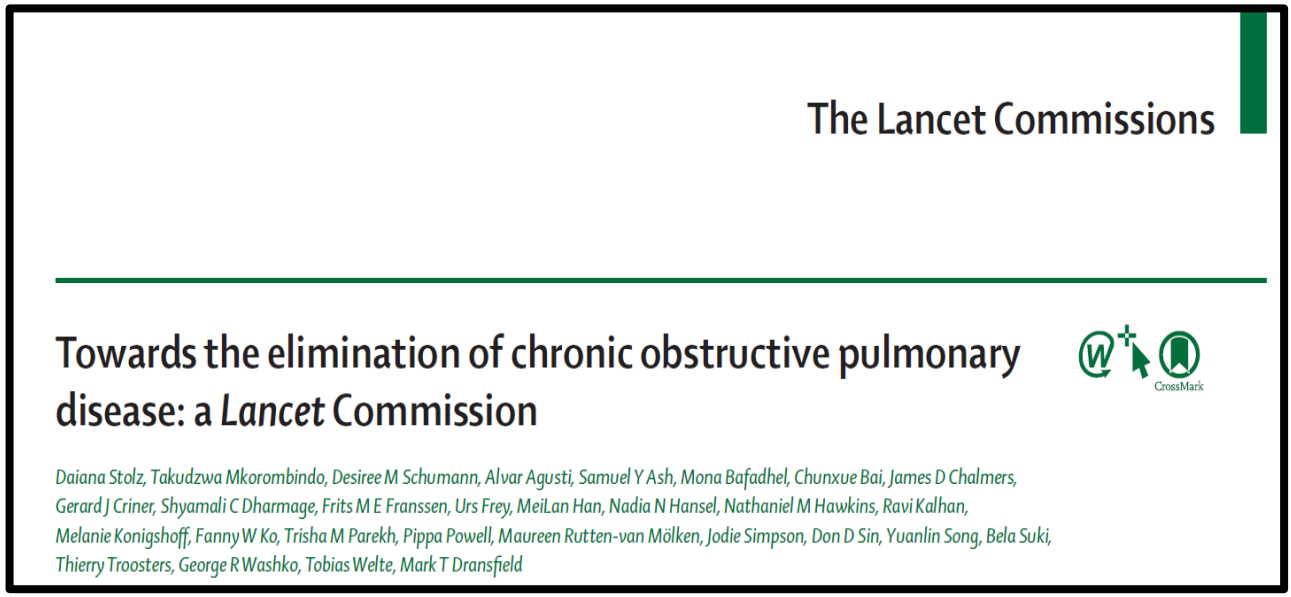
경상의대 이승준

June, 2023, COPD school

GNUH
경상국립대학교병원
Gyeongsang National University Hospital

참고 문헌

5th major revision since 2001 first publication



Lancet 2022; 400: 921–72

References

In total **387 new references** have been added to the GOLD 2023 report

Contents

Definition

GOLD 2020~2022

COPD is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases and influenced by host factors including abnormal lung development. Significant comorbidities may have an impact on morbidity and mortality

GOLD 2023

COPD is a heterogenous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum, and/or exacerbations) due to abnormalities of the airway (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airway obstruction

이전 정의와 차이점 정리

	이전	GOLD 2023
원인	Noxious particle Abnormal lung development	Heterogenous
병태생리	Abnormality of airway and alveoli	동일
증상	Persistent symptom	Chronic symptom (증상을 명시함: dyspnea, cough, sputum, exacerbation)
기류제한	-Characterized by airflow limitation (COPD의 특성으로 설명) -Persistent	-Cause airway obstruction (airway and alveolar abnormality의 결과로 설명) -Persistent, often progressive

Common, preventable and treatable disease 빠짐.

Not Common, preventable, and treatable any more?

- Defined since GOLD 2011

New opportunities

COPD is a common, preventable, and treatable disease, but extensive under and misdiagnosis leads to patients receiving no treatment or incorrect treatment. The realizatio environmental factors other than tobacco smoking can contribute to COPD, that it can early in life and affect young individuals, and that there are precursor conditions (Pre-COPD, PRISm), opens new windows of opportunity for its prevention, early diagnosis, and prompt and appropriate therapeutic intervention.

1

2

3

예방, 조기 진단, 적절한 조기치료의 중요성!!!

높은 유병률, 낮은 인지율

표 4. 주요 만성질환과 만성폐쇄성폐질환의 관리수준 비교

단위: %

주요 만성질환	유병률			인지율			치료율		
	2009	2015	2019	2007~2009	2013~2015	2019	2007~2009	2013~2015	2019
고혈압	26.3	27.8	27.2	66.3	67.3	71.4	60.3	63.6	67.1
당뇨병	11.6*	10.2	11.8	-	61.0	65.2	-	54.8	60.8
고콜레스테롤혈증	11.4	17.9	22.3	38.8	57.7	61.7	26.9	45.5	53.1
만성폐쇄성폐질환	**10.5**	**12.3**	**10.8**	-	-	**2.5†**	-	**85.5†**	**84.5§**

주: 만 30세 이상 통계[(만성폐쇄성폐질환은 만40세 이상): 인지율(유병자 중 의사진단을 받은 경우), 치료율(유병자 중 치료자)]
* 2011년 통계, † 2016–2018년 통합자료(40세이상), † 2014년 심평원 적정성 평가결과의 지속방문 환자비율, § 2018년 심평원 적정성 평가결과의 지속방문 환자비율 [11]

조절율 개념 無

Reference 1. 질병관리청 2019 국민건강통계 2. 건강보험심사평가원 만성폐쇄성폐질환 제5차 적정성 평가결과, 2020.5.28

***

Start early life and precursor condition

New opportunities

COPD is a common, preventable, and treatable disease, but extensive under and misdiagnosis leads to patients receiving no treatment or incorrect treatment. The realization that environmental factors other than tobacco smoking can contribute to COPD, that it can start early in life and affect young individuals, and that there are precursor conditions (Pre-COPD, PRISm), opens new windows of opportunity for its prevention, early diagnosis, and prompt and appropriate therapeutic intervention.

2

Precursor conditions

- **PRISm** (Preserved Ratio Impaired Spirometry): FEV1/FVC ≥ 0.7 & FEV1 < 80%

- **Mild COPD (functional term)**
  - **Mild severity of airway limitation (FEV1** ≥80%)

- **<u>Early COPD ★ (biological term)</u>**
  - Near beginning of a COPD process, not clinical early (biological early, in an experimental setting)
  - Identifying early COPD is difficult

New definition

- **Pre-COPD ★ ★ ★**
  - FEV1/FVC ≥ 0.7 and Respiratory sx.
  - and/or Structural lesions (emphysema)
  - and/or Functional abnormalities
    - low-normal FEV1, gas trapping, hyperinflation, reduced DLCO and/or rapid FEV1 decline

- **Young COPD ★** (COPD in young people, formerly)
  - COPD in the 20-50 year age

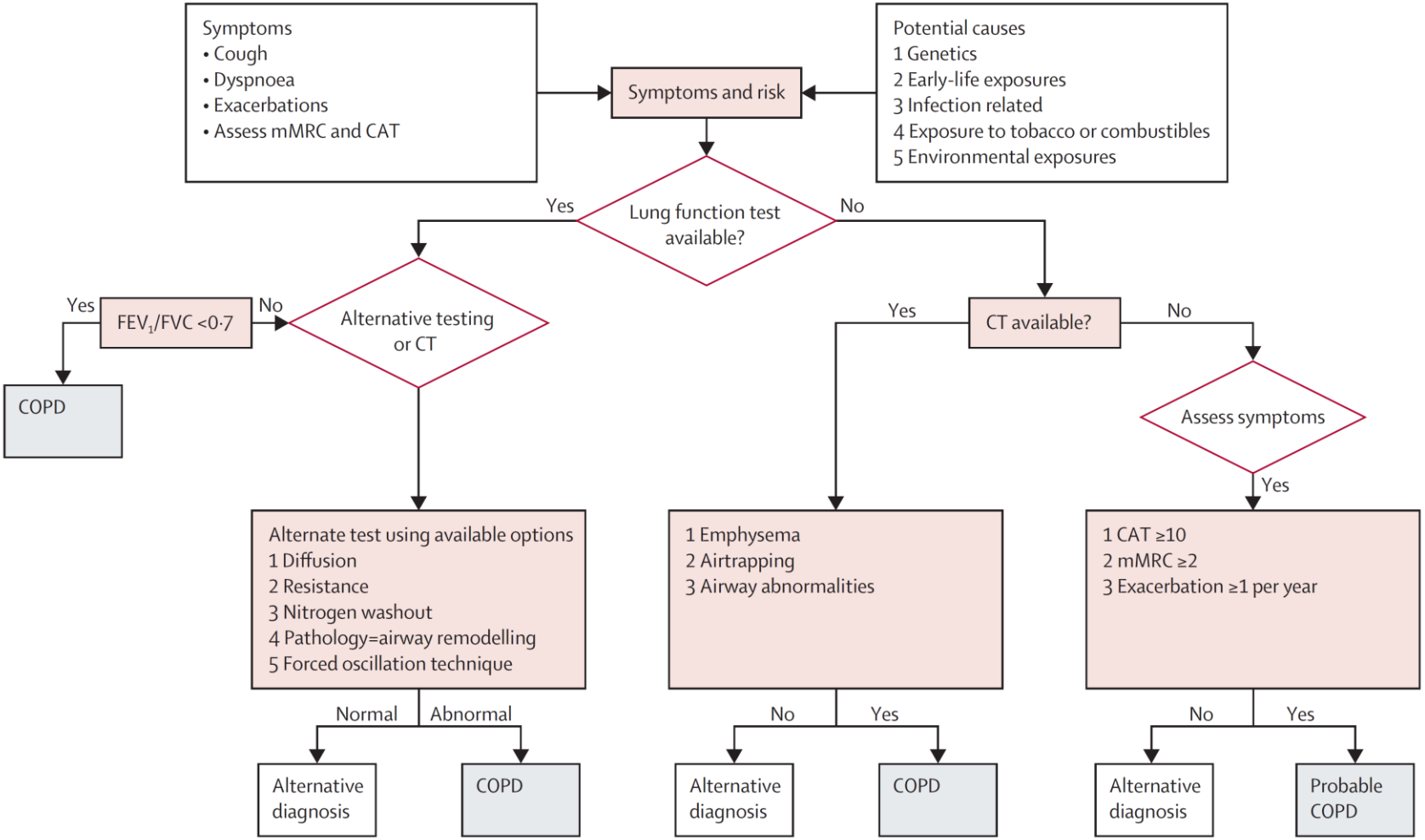
GOLD 2023

Revisiting Diagnosis of COPD

- **FEV1/FVC <0.7** capture none of this complexity nor the variation in underlying pathophysiology
  - misses early pathological changes
  - detectable only at later pathophysiological stages, largely irreversible lung damage.
- **Expansion of diagnostic criteria** to encompass COPD heterogeneity will increase sensitivity for early disease and could lead to the discovery of new preventive measures and therapeutic approaches.

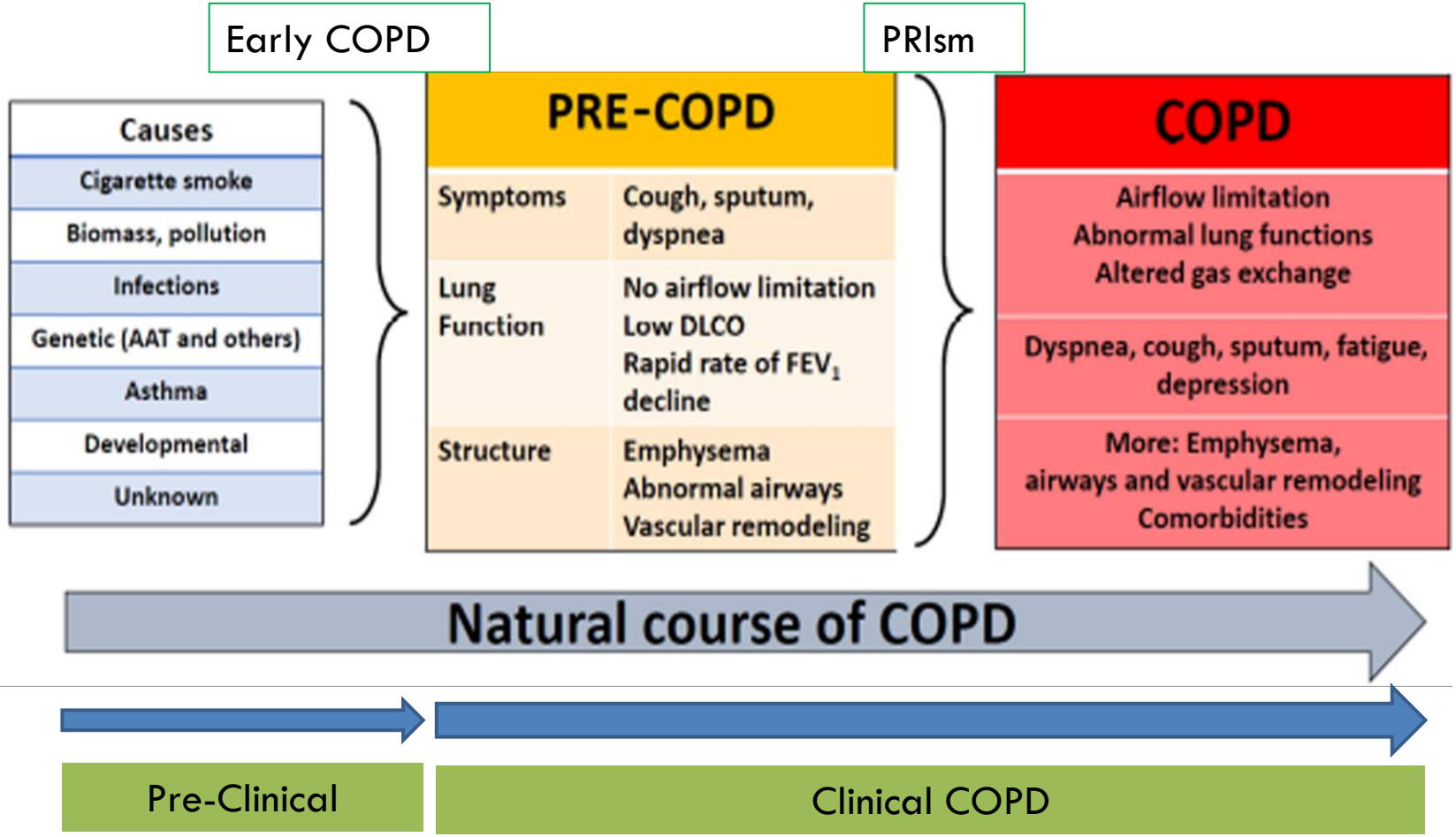
Lancet Respir Med. 2022 May;10(5):497-511.

Proposed diagnostic algorithm



Lancet Respir Med. 2022 May;10(5):497-511.

Pre-COPD is clinical COPD



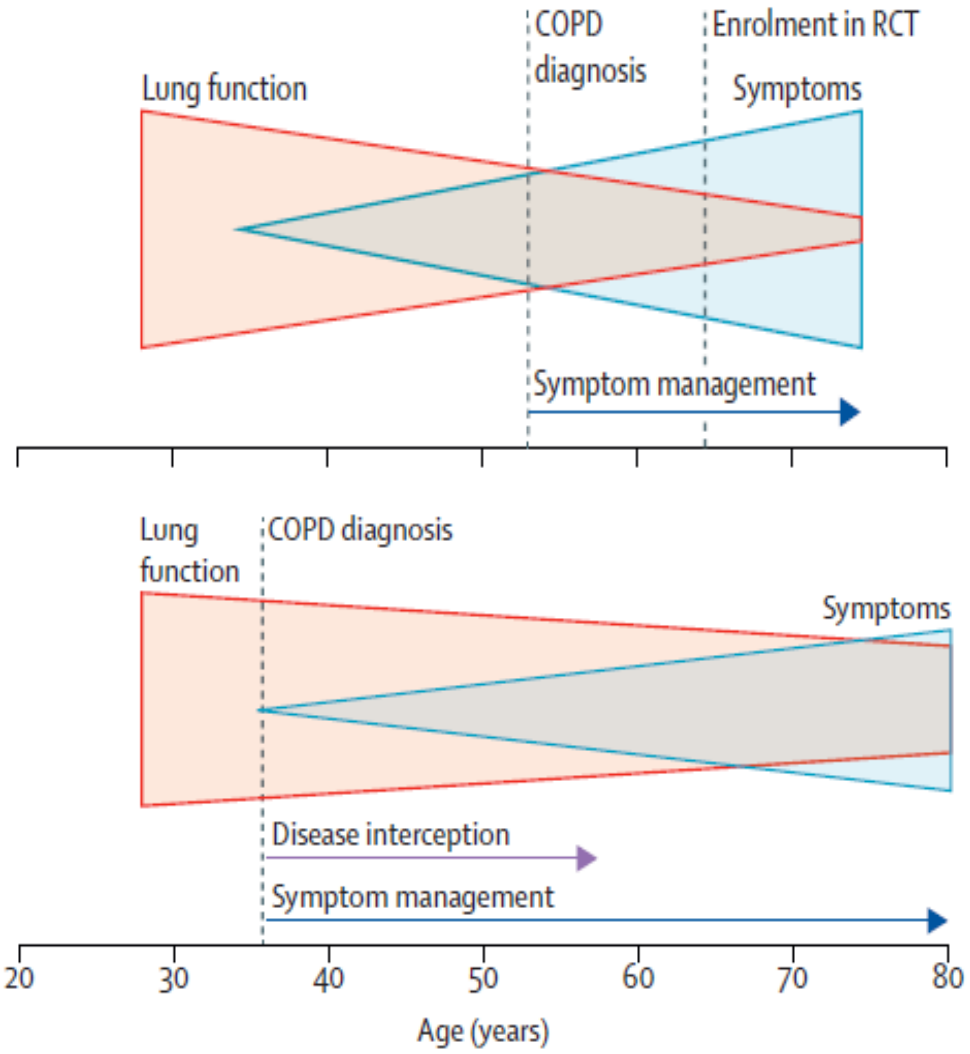
Clinics in Chest Medicine 2020 41xv-xviiDOI: (10.1016/j.ccm.2020.06.015)

Treatment of Pre-COPD and PRISm

- They should be considered "*patients*" (because they already suffer symptoms and/or have functional and/or structural abnormalities)

- They deserve care and treatment

Early diagnosis and treatment



Currently

Future implementation

-The challenge is that there is no evidence on what the best treatment is for these patients yet

Lancet 2022; 400: 921–72

Dual-BD was not effective

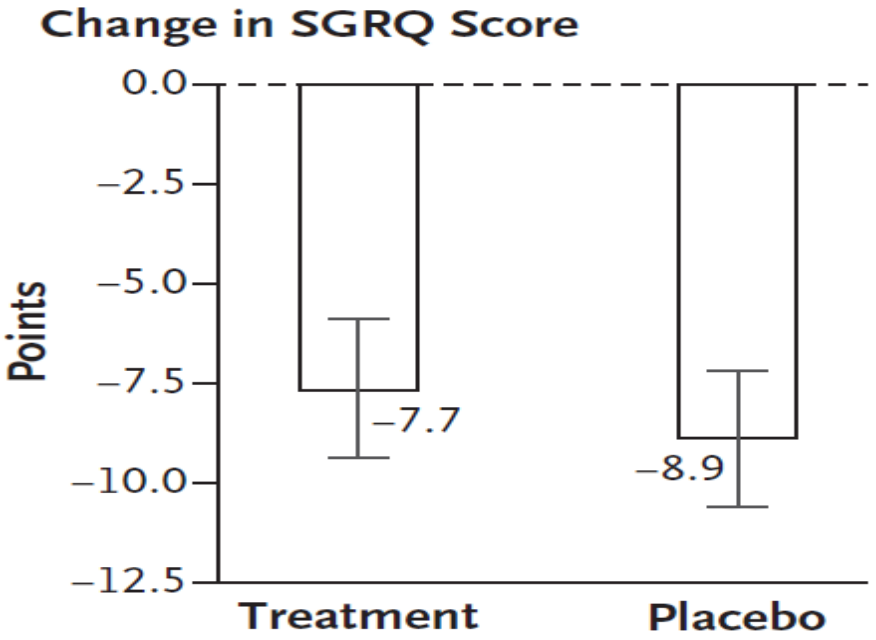
- CAT ≥ 10, ≥ 10 PYS smoking
- FEV1/FVC >0.7 and FVC > 70%
- 1st outcome: 4 points decrease in SGRQ
- Indacaterol + glycopyrrolate for 12 weeks

Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.*

Characteristic	Treatment (N=261)	Placebo (N=274)	Overall (N=535)
Age — yr	58.6±9.6	59.1±9.8	58.8±9.7
Male sex — no. (%)	127 (48.7)	133 (48.5)	260 (48.6)
Race — no. (%)†			
Black	92 (35.2)	99 (36.1)	191 (35.7)
White	148 (56.7)	154 (56.2)	302 (56.4)
Other	3 (1.1)	4 (1.5)	7 (1.3)
Postbronchodilator FEV_1 — % of predicted value	93.8±14.0	94.9±12.6	94.4±13.3
Postbronchodilator FVC — % of predicted value	92.9±12.8	94.2±13.3	93.6±13.0
Postbronchodilator FEV_1:FVC	0.78±0.05	0.78±0.05	0.78±0.05

N Engl J Med 2022;387:1173-84.

Primary outcome



Outcome	Placebo (N=244)	Treatment (N=227)	Odds Ratio (95% CI)
	no. of participants/total no. (%)		
Primary outcome			
Overall			
Modified intention-to-treat analysis	144/244 (59.0)	128/227 (56.4)	0.91 (0.60–1.37)
Sensitivity analysis 1	143/242 (59.1)	129/230 (56.1)	0.89 (0.59–1.34)
Sensitivity analysis 2	144/240 (60.0)	124/220 (56.4)	0.87 (0.57–1.33)
Sensitivity analysis 3	115/196 (58.7)	109/192 (56.8)	0.98 (0.61–1.58)
Sensitivity analysis 4	146/249 (58.6)	131/232 (56.5)	0.93 (0.65–1.35)
Per-protocol analysis	110/176 (62.5)	101/170 (59.4)	0.88 (0.65–1.20)

Responder analysis

Outcomes	Event rates		At 12 wk
	Dual bronchodilator (indacaterol-glycopyrrolate)	Placebo	RBR (95% CI)
SGRQ improvement without treatment failure†	56.4%	59.0%	4% (-12 to 21)
SGRQ and TDI‡ improvement without treatment failure	25.0%	25.6%	2% (-37 to 33)
			RBI (CI)
TDI improvement without treatment failure	36.4%	34.2%	9% (-13 to 32)
CAT improvement§ without treatment failure	74.4%	68.0%	11% (-1 to 21)

Adherence, 88%

***

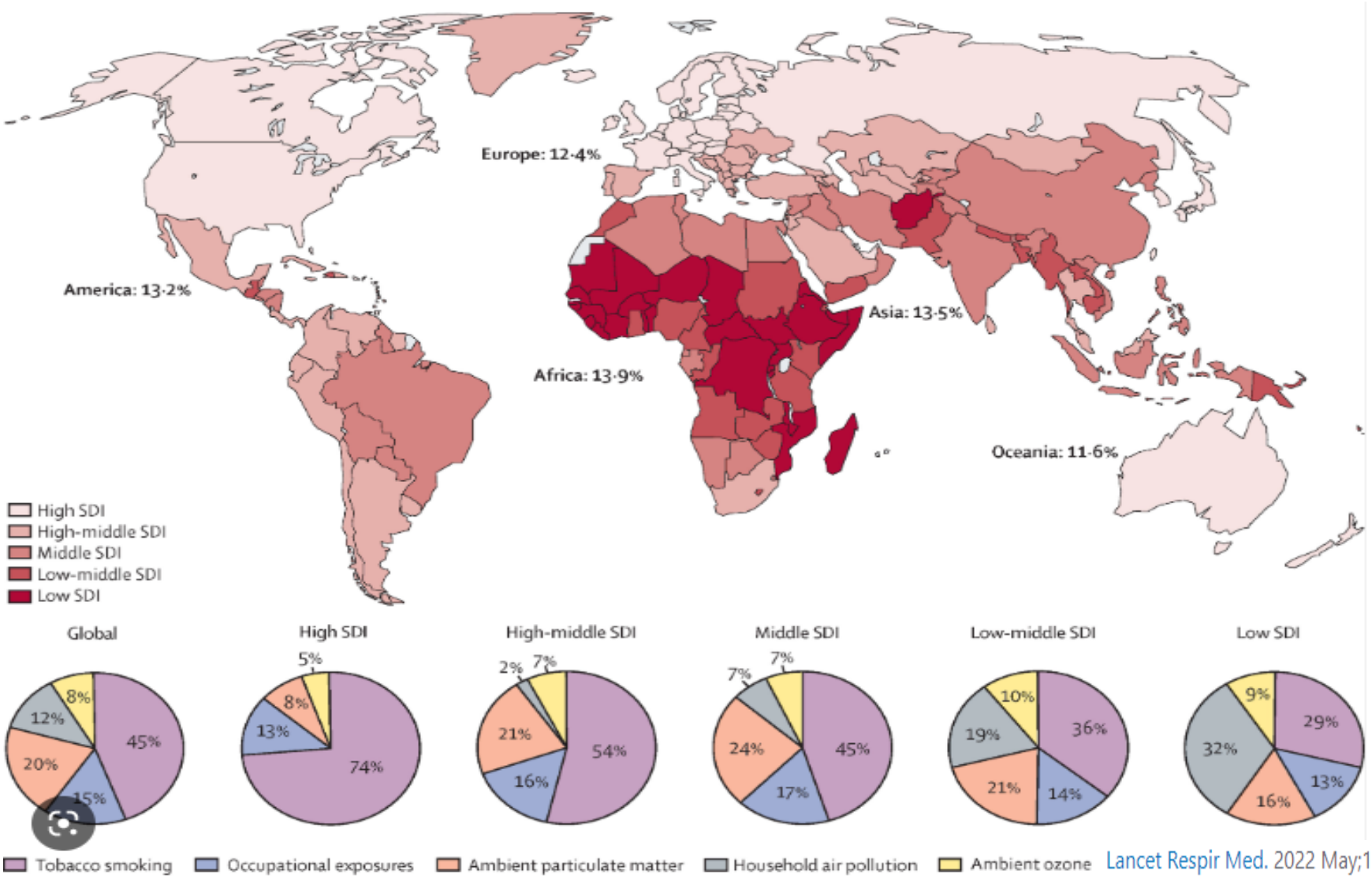
Factors other than tobacco smoking

New opportunities

COPD is a common, preventable, and treatable disease, but extensive under 3 misdiagnosis leads to patients receiving no treatment or incorrect treatment. The realization that environmental factors other than tobacco smoking can contribute to COPD, that it can start early in life and affect young individuals, and that there are precursor conditions (Pre-COPD, PRISm), opens new windows of opportunity for its prevention, early diagnosis, and prompt and appropriate therapeutic intervention.

***

Smoking is not the only risk factor



Lancet Respir Med. 2022 May;10(5):497-511.

Smoking, Marlboro advertisement

Smoking, Marlboro story

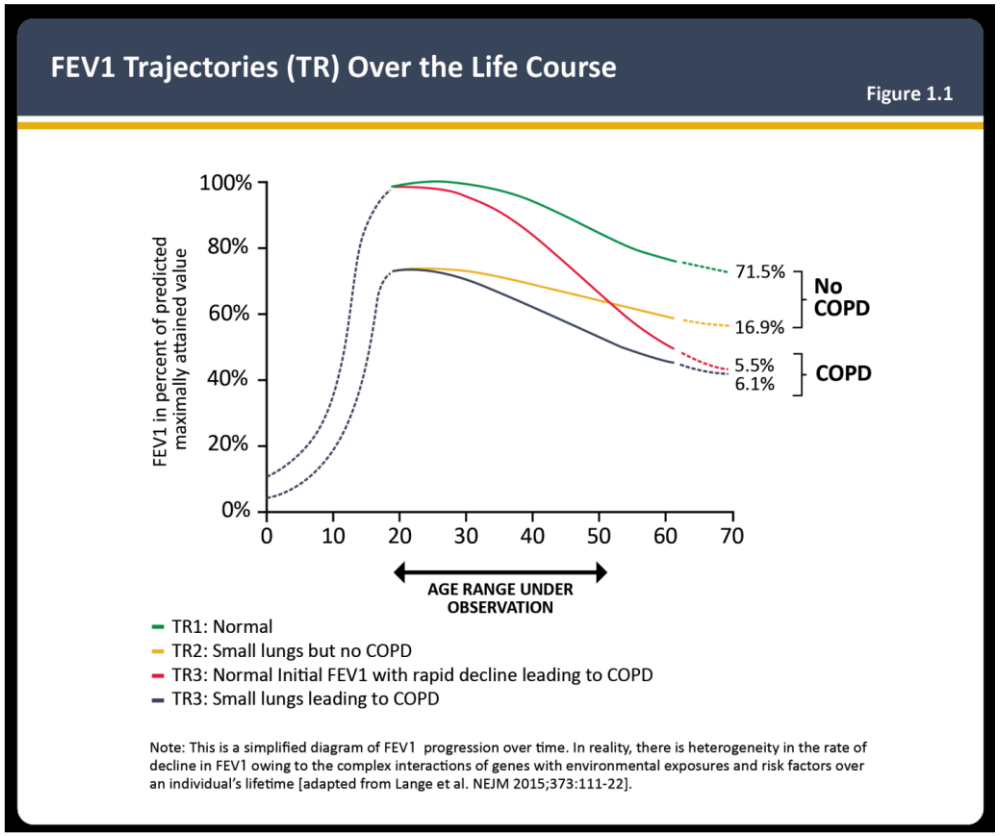
"사실 '말보로 레드'는 여성을 위한 담배였다"

Other risk factors

- Biomass exposure and Air pollution

Other risk factors

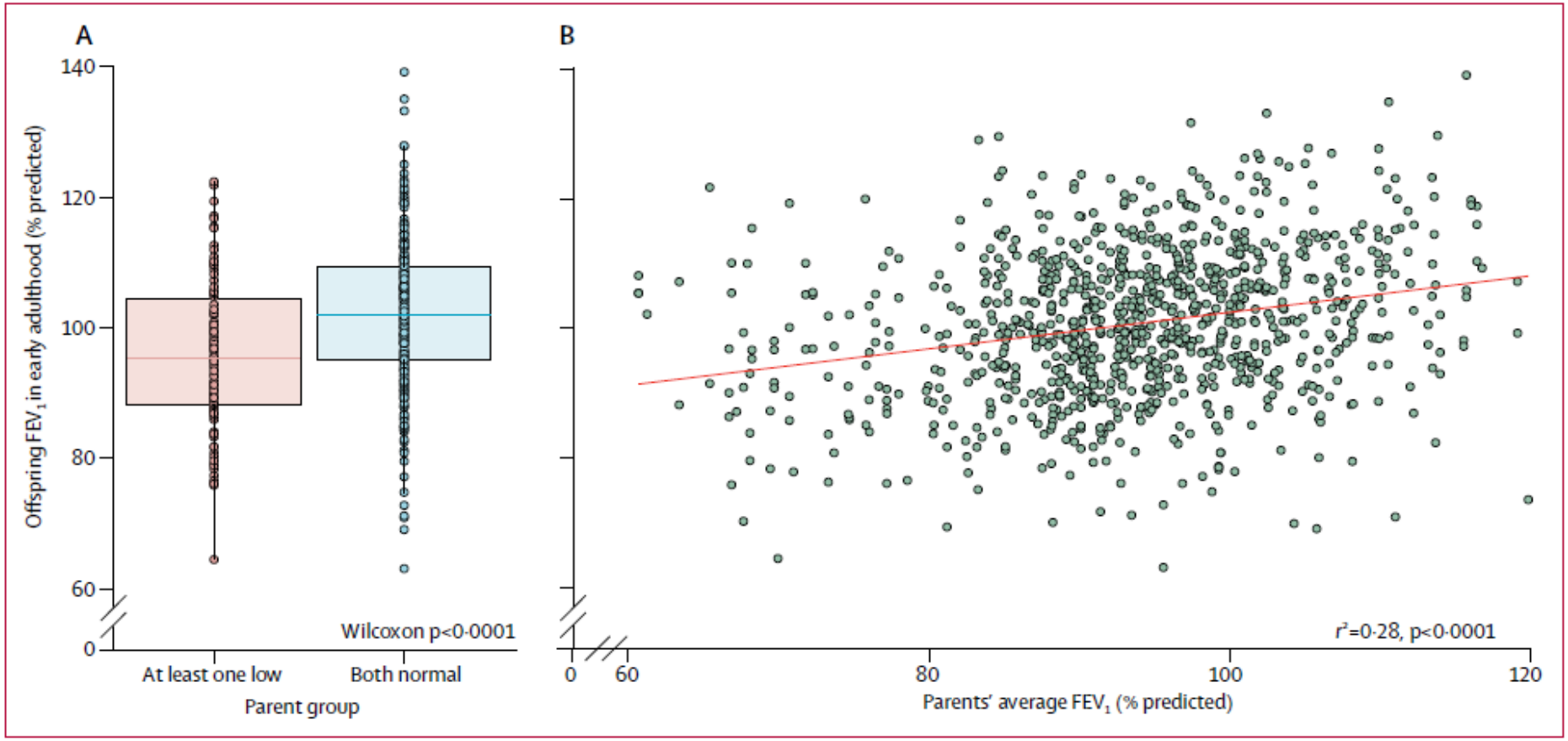
- Abnormal lung development (prematurity, dysanapsis)



- Genetics, Asthma, Infection (HIV, TB)

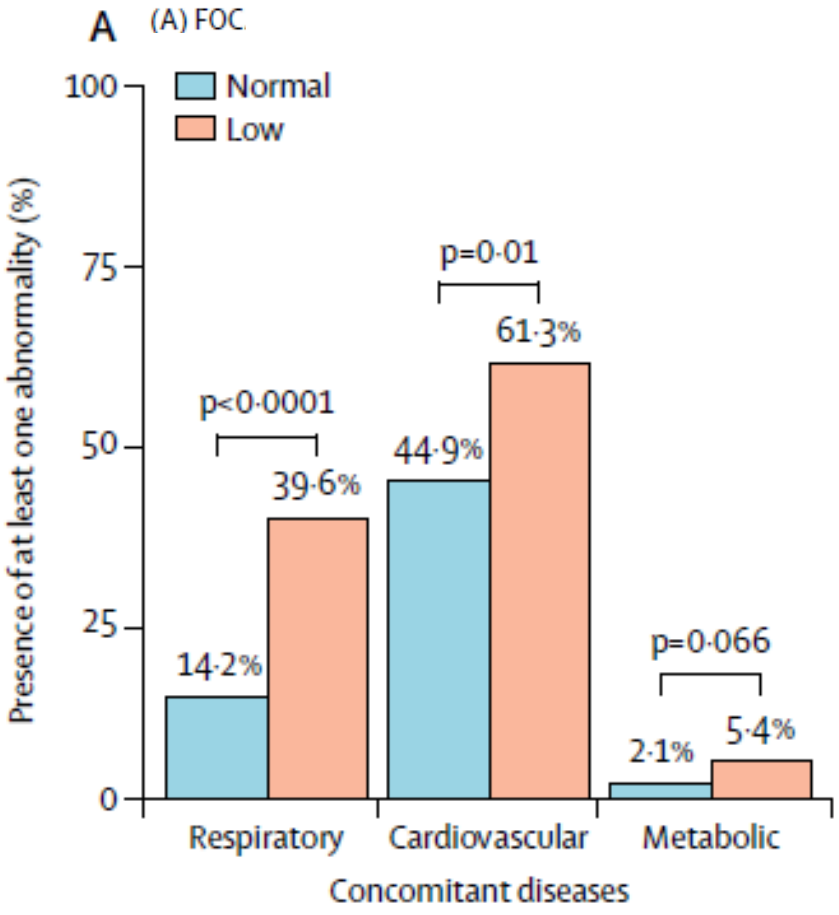
Abnormal lung development and Genetics

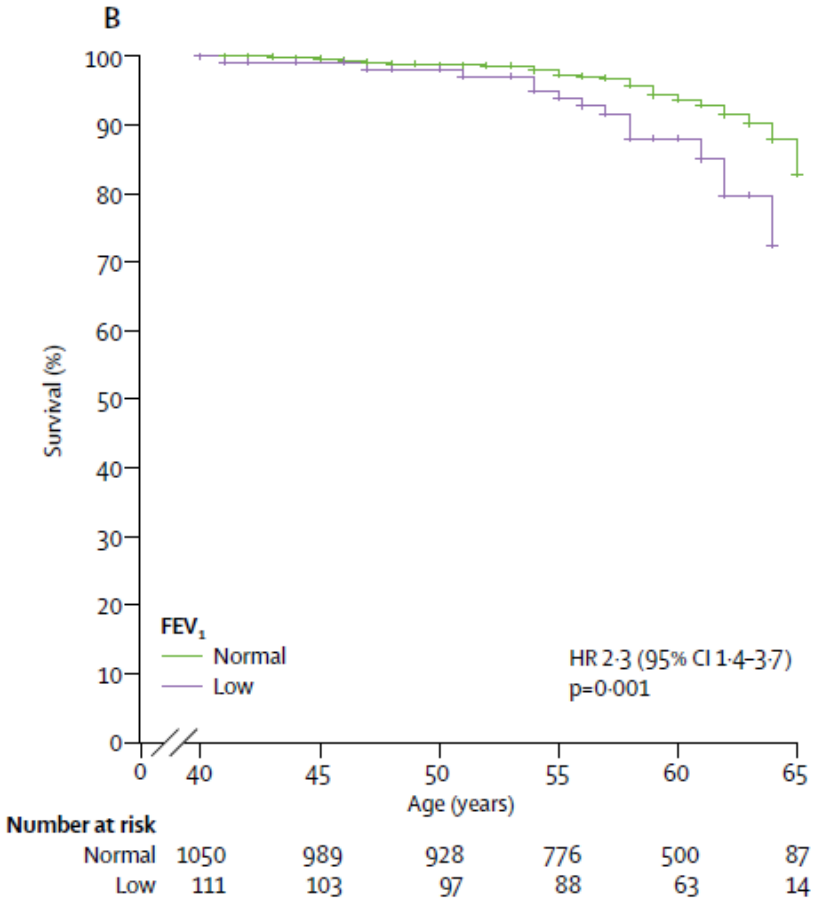
- **Framingham Offspring, CARDIA, GenIII cohort**
- **520 / 5721 (9.1%) was FEV1 < 80% at age of 25-40 years**



Lancet Respir Med 2017; **5:** 935–45

More comorbidities and poor survival





Lancet Respir Med 2017; **5:** 935–45

Proposed Taxonomy (Etiotypes) for COPD

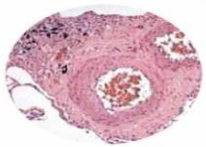
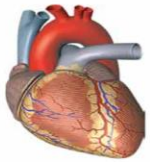
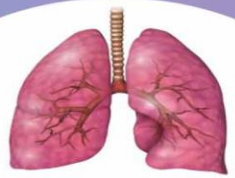
Table 1.1

Classification	Description	
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination	COPD-G (Gene)
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others	COPD-D (Development)
Environmental COPD		
Cigarette smoking COPD (COPD-C)	• Exposure to tobacco smoke, including *in utero* or via passive smoking • Vaping or e-cigarette use • Cannabis	COPD-C (cigarettes, cannabis)
Biomass and pollution exposure COPD (COPD-P)	Exposure to household pollution, ambient air pollution, wildfire smoke, occupational hazards	COPD-P (pollution)
COPD due to infections (COPD-I)	Childhood infections, tuberculosis-associated COPD, HIV-associated COPD	COPD-I (infections)
COPD & asthma (COPD-A)	Particularly childhood asthma	COPD-A (asthma)
COPD of unknown cause (COPD-U)		COPD-U (unknown)

COPD 'etiotypes' in GOLD & Lancet Commission

GOLD 2023	Lancet Commission
COPD-G: Genetically Determined	TYPE1: Genetically Determined
COPD-D: Abnormal Lung Development	TYPE 2: Early Life Events
COPD-I: Infections	TYPE 3: Infection Related
COPD-C: Cigarette Smoking (and vaping)	TYPE 4: Smoking or Vaping
COPD-P: Biomass and Pollution Exposure	TYPE 5: Environmental Exposure
COPD-A: COPD and Asthma	
COPD U: Unknown cause.	

Types of pulmonary hypertension

Pulmonary arterial hypertension (PAH)	PH associated with left heart disease	PH associated with lung disease	PH associated with pulmonary artery obstructions	PH with unclear and/or multifactorial mechanisms
				?
• Idiopathic/heritable • Associated conditions	• IpcPH • CpcPH	• Non-severe PH • Severe PH	• CTEPH • Other pulmonary obstructions	• Haematologic disorders • Systemic disorders
PREVALENCE				
Rare	Very common	Common	Rare	Rare
THERAPEUTIC STRATEGIES				
Medical therapy • PAH drugs • CCB in responders **Lung transplantation**	**IpcPH:** • Treatment of LHD[a] **CpcPH:** • Treatment of LHD[a] • Potentially: PAH drugs (trials)	**PH-lung disease:** • Optimized care of underlying lung disease **Severe PH:** • Potentially: PAH drugs (trials)	**Surgical therapy:** • PEA **Interventional:** • BPA **Medical therapy:** • PH drugs	**Optimized treatment of underlying disease** • Potentially: PAH drugs (trials)

ESC ERS

2022 ESC/ERS

Reason for new Etiotypes

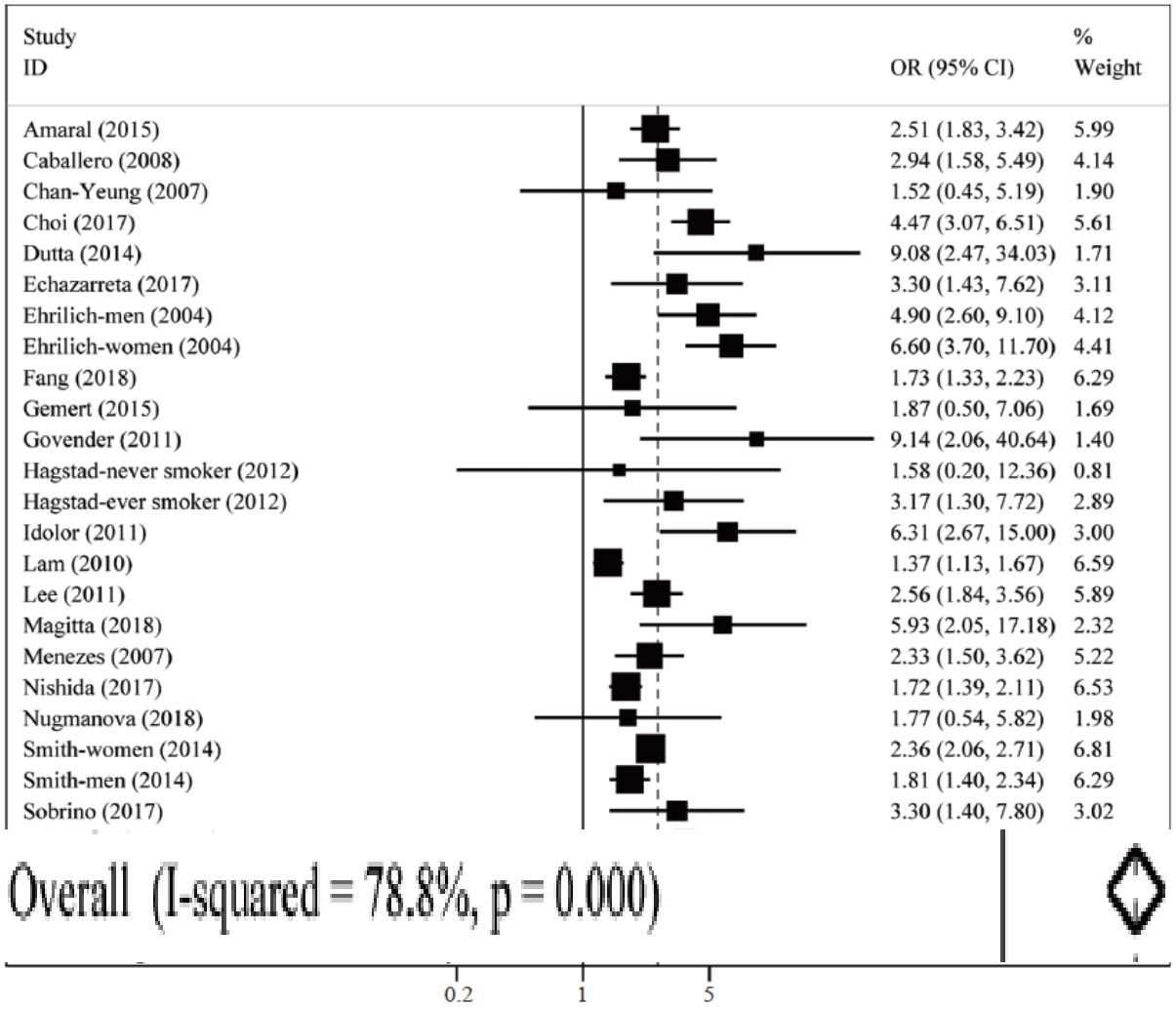
2023 REPORT

TAXONOMY

COPD has been traditionally understood as a single "disease" caused by tobacco smoking.[114] Accordingly, most efforts have been devoted to the study of the pathogenetic mechanisms of only one major cause of COPD (cigarette smoking), failing to expand the horizon about the heterogeneity of processes that we know can contribute to its final clinical presentation.[2] It is therefore important to expand the taxonomy (classification) of COPD to include non-smoking related COPD types, so specific studies can be designed and conducted for these different types of COPD or *etiotypes*.[256] **Table 1.1** combines two recent taxonomic proposals developed independently.[1,257] This proposal has relatively little impact on current clinical practice, other than illuminating this so-far ignored aspect of COPD, but it is of the outmost importance to highlight the need to explore current and future therapies in these other *etiotypes* of COPD.

GOLD report 2023 accessed to https:/goldcopd.org/2022-gold-reports.

Pulmonary tuberculosis as a risk factor for chronic obstructive pulmonary disease: a systematic review and meta-analysis

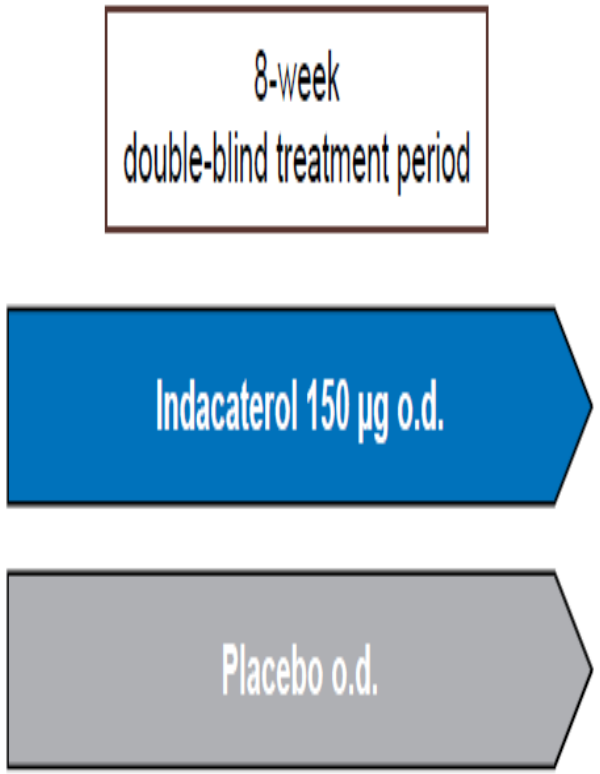


-The pooled prevalence of COPD in patients with prior pulmonary TB was 21%

Inhaled indacaterol for the treatment of COPD patients with destroyed lung by tuberculosis and moderate-to-severe airflow limitation: results from the randomized INFINITY study

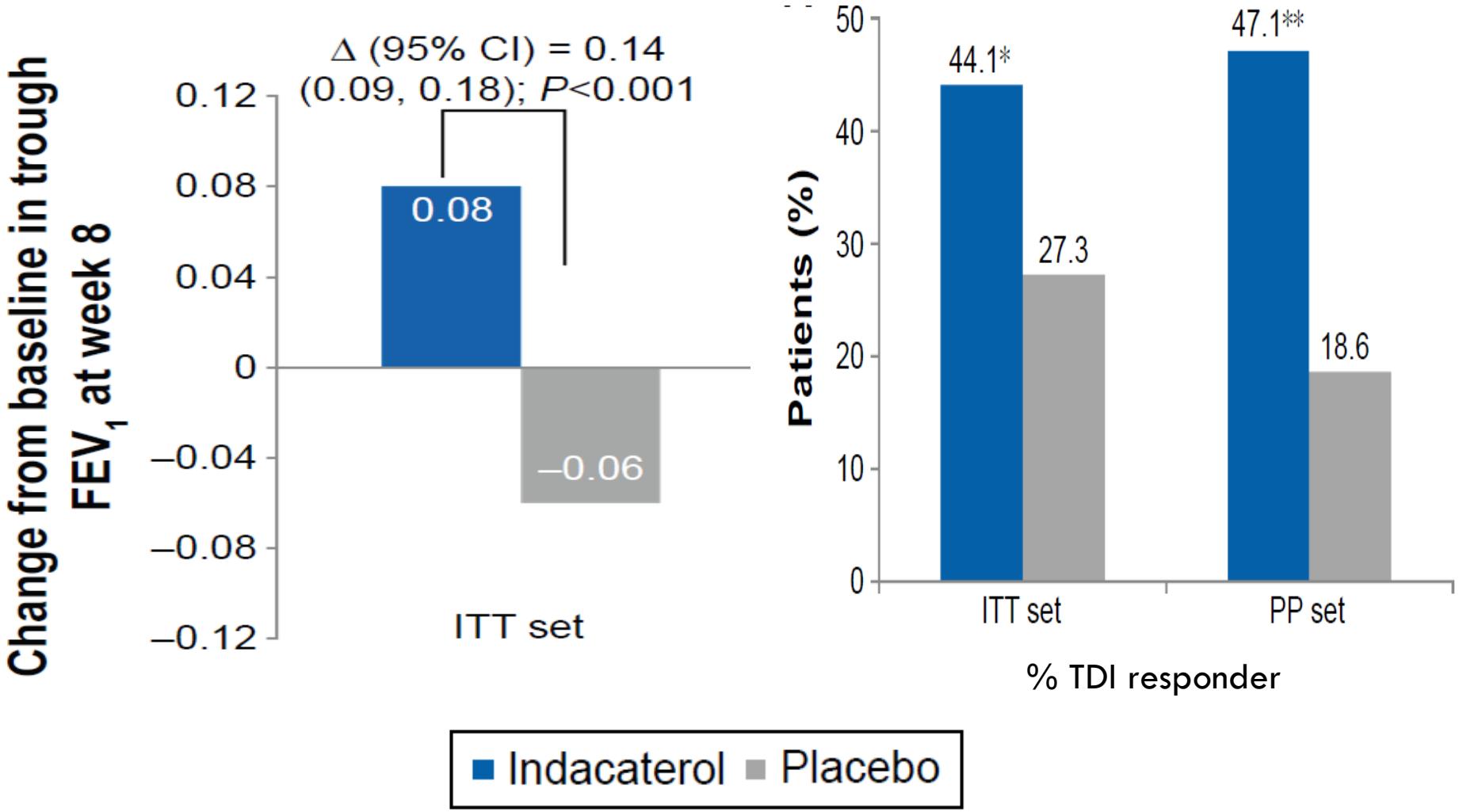
Table 1 Baseline demographic and clinical characteristics

Parameter	Indacaterol 150 µg o.d. (n=68)	Placebo (n=68)
Age, years, mean (SD)	63.9 (10.9)	64.6 (9.2)
Males	45 (66.2)	40 (58.8)
COPD duration, years, mean (SD)	4.2 (4.0)	4.3 (3.7)
Previous COPD-related medication	55 (80.9)	58 (85.3)
COPD exacerbation in previous year		
Yes	4 (5.9)	6 (8.8)
No	64 (94.1)	62 (91.2)
Smoking history		
Yes	34 (50.0)	36 (52.9)
No	34 (50.0)	32 (47.1)



Int J COPD 2017;12:1589-1596

FEV1(1st), Symptom(2nd) improve



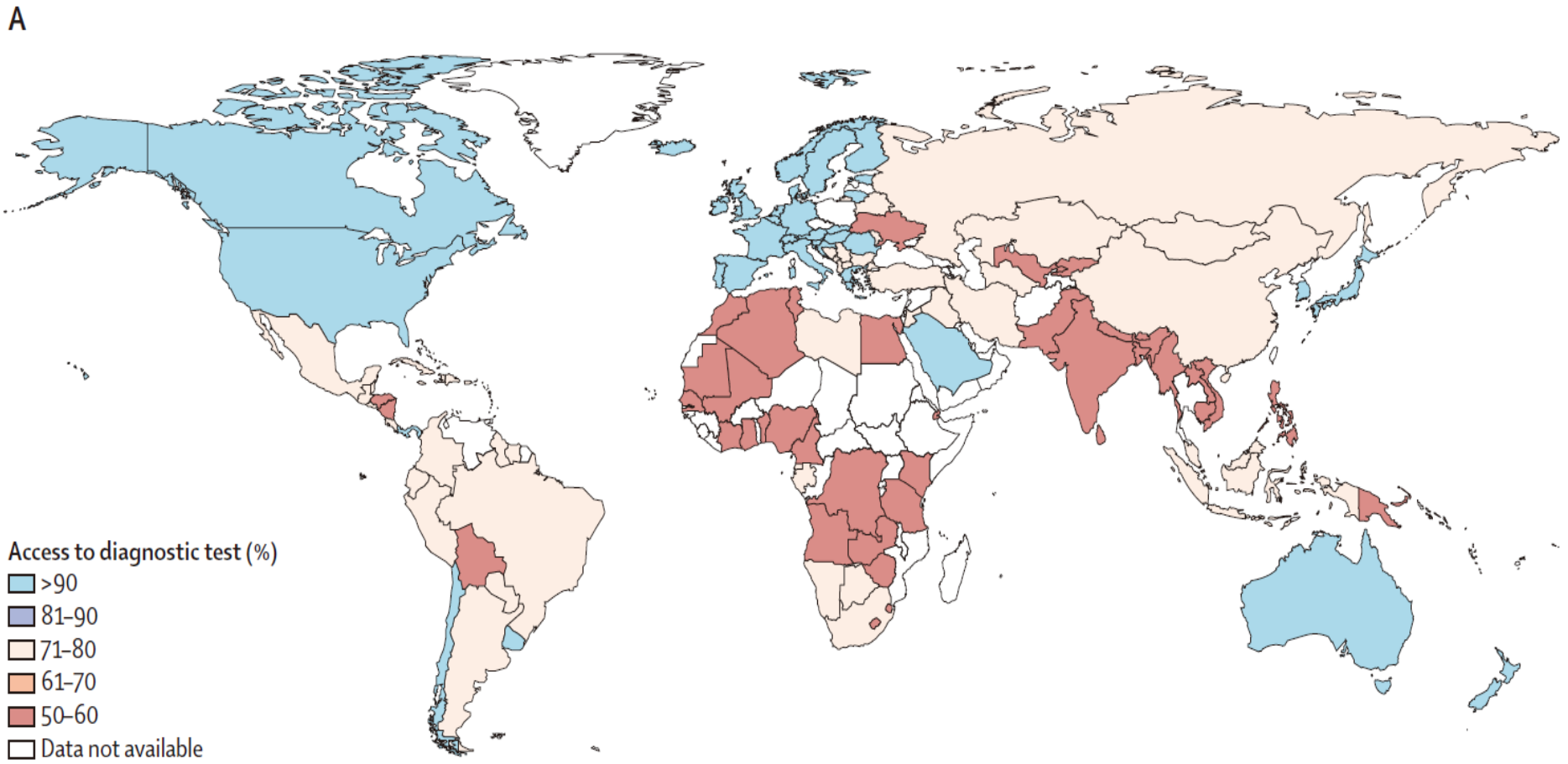
Int J COPD 2017;12:1589-1596

Screening and Case-finding

- The role of **screeing spirometry** for diagnosis of COPD in general population is controversial
- Sx.(-) & Risk factor (-): screening spirometry is not indicated
- Sx. (+) or Risk factor (+): screening spirometry should be considered
- GOLD advocates active case finding (screening tool) , but not screening spirometry

GOLD 2023

Proportion of global population with access to spirometry



Lancet Respir Med. 2022 May;10(5):497-511.

JAMA | Original Investigation

Discriminative Accuracy of the CAPTURE Tool for Identifying Chronic Obstructive Pulmonary Disease in US Primary Care Settings

1) Have you ever lived or worked in a place with dirty or polluted air, smoke, second-hand smoke, or dust?
- ☐ No0
- ☐ Yes1

위험인자

2) Does your breathing change with the seasons, weather, or air quality?
- ☐ No0
- ☐ Yes1

증상, 계절/공기질에 따라 변화

3) Does your breathing make it difficult to do such things as carry heavy loads, shovel dirt or snow, jog, play tennis, or swim?
- ☐ No0
- ☐ Yes1

증상, 활동시호흡곤란

4) Compared to others your age, do you tire easily?
- ☐ No0
- ☐ Yes1

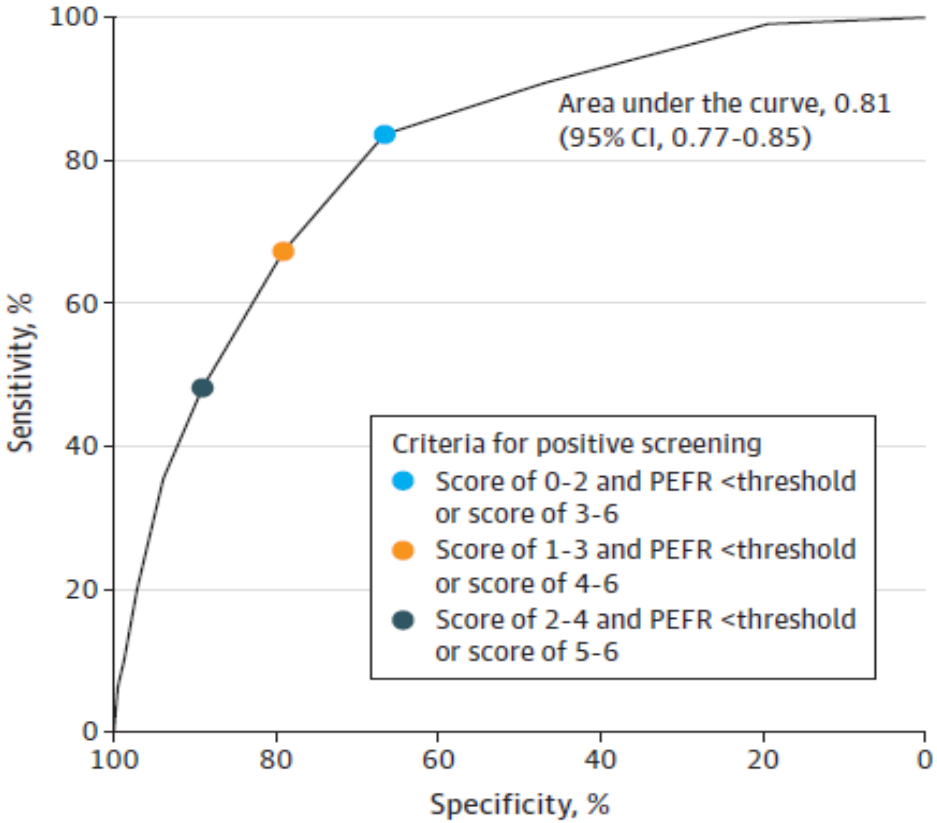
증상, 피곤함

5) In the past 12 months, how many times did you miss work, school, or other activities due to a cold, bronchitis, or pneumonia?
- ☐ None0
- ☐ Once1
- ☐ 2 or more2

악화

JAMA. 2023;329(6):490-501.

Results

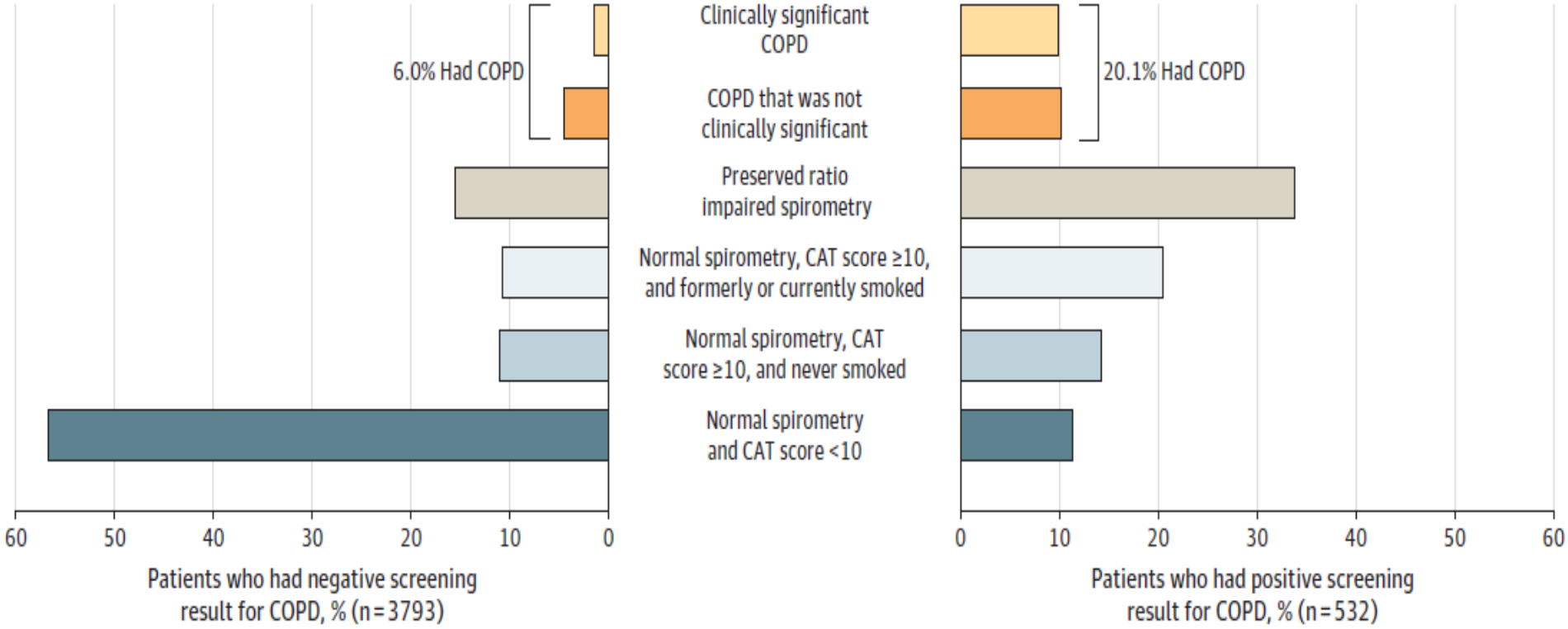


- N=4325
- (2.5%)110/4325 were undiagnosed clinically significant COPD (FEV1<60%)
- 53 had a positive screening result
- Sensitivity 48.2%, specificity 88.6%

Further research is needed to optimize performance of the screening tool and to understand whether its use affects clinical outcomes

JAMA. 2023;329(6):490-501.

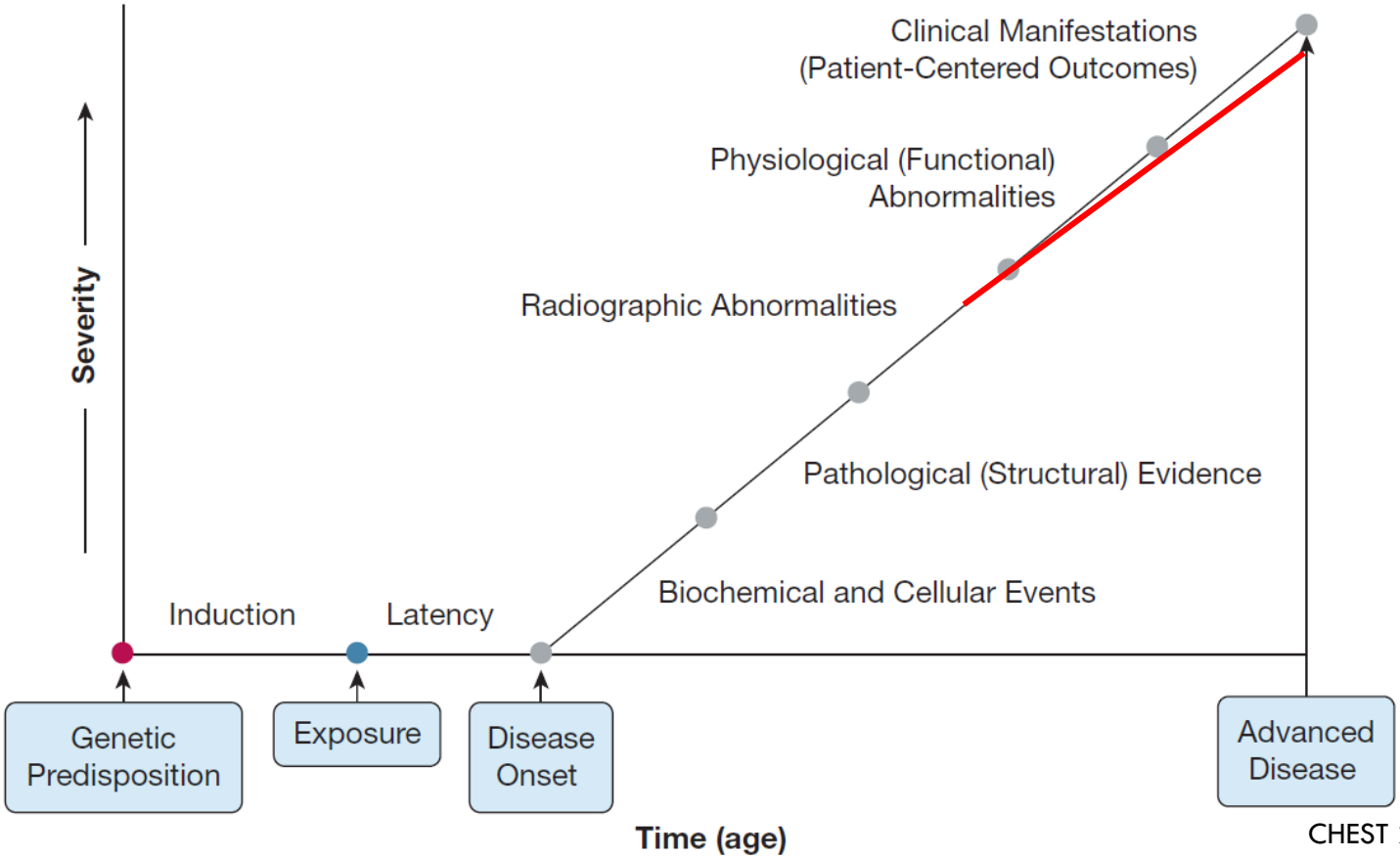
Screening may distinguish Clinically not important COPD, Pre-COPD



JAMA. 2023;329(6):490-501.

Can Screening for COPD Improve Outcomes? No

- By the time physiologic impairment is present, disease is well established and often advanced, with limited opportunity for disease modification



CHEST 2020 Jan;157(1):9-12

Screening for Chronic Obstructive Pulmonary Disease
US Preventive Services Task Force Reaffirmation Recommendation Statement

US Preventive Services Task Force

Summary of Recommendation

Population	Recommendation	Grade
Asymptomatic adults	The USPSTF recommends against screening for chronic obstructive pulmonary disease in asymptomatic adults.	D

To whom does this recommendation apply?	• This recommendation applies to adults who do not recognize or report respiratory symptoms. • It does not apply to persons with symptoms such as chronic cough, sputum production, difficulty breathing, or wheezing. • It does not apply to populations at very high risk for COPD, such as persons with α-1 antitrypsin deficiency or workers exposed to certain toxins at their job.
What's new?	This recommendation is consistent with the 2016 USPSTF recommendation.
How to implement this recommendation?	• Do not screen for COPD in patients with no symptoms. • Clinicians can help reduce patients' risk for COPD by supporting them in not starting to smoke and helping them quit if they do.

Can Screening for COPD Improve Outcomes? Yes

- Screening for unacknowledged and unaddressed respiratory symptoms is different approach

  (not truly asymptomatic)

- COPD screen tool

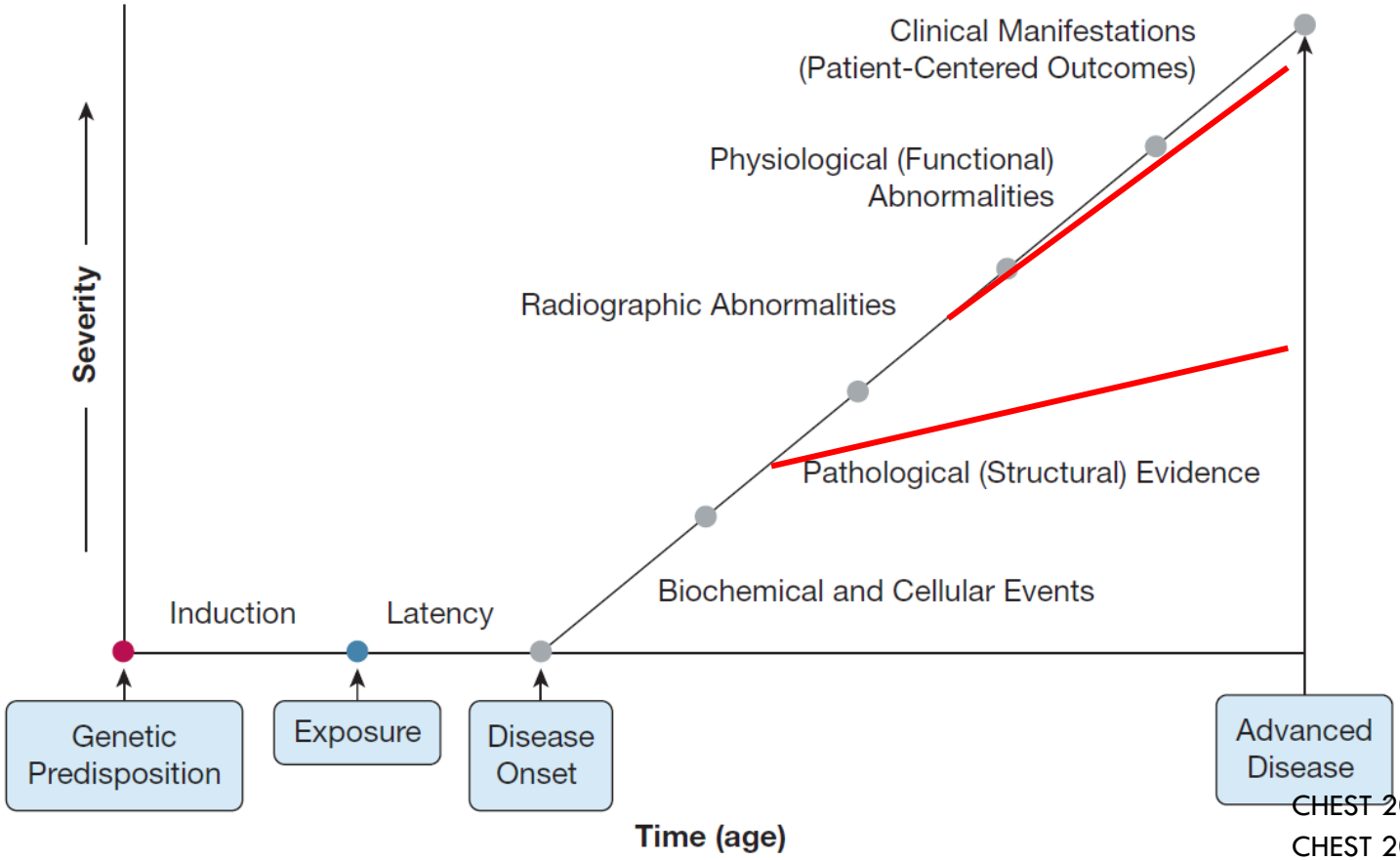
  -Focus on risk factors >> symptoms

  -Goal is diagnosis >> clinical improvement

CHEST 2020 Jan;157(1): 7-9

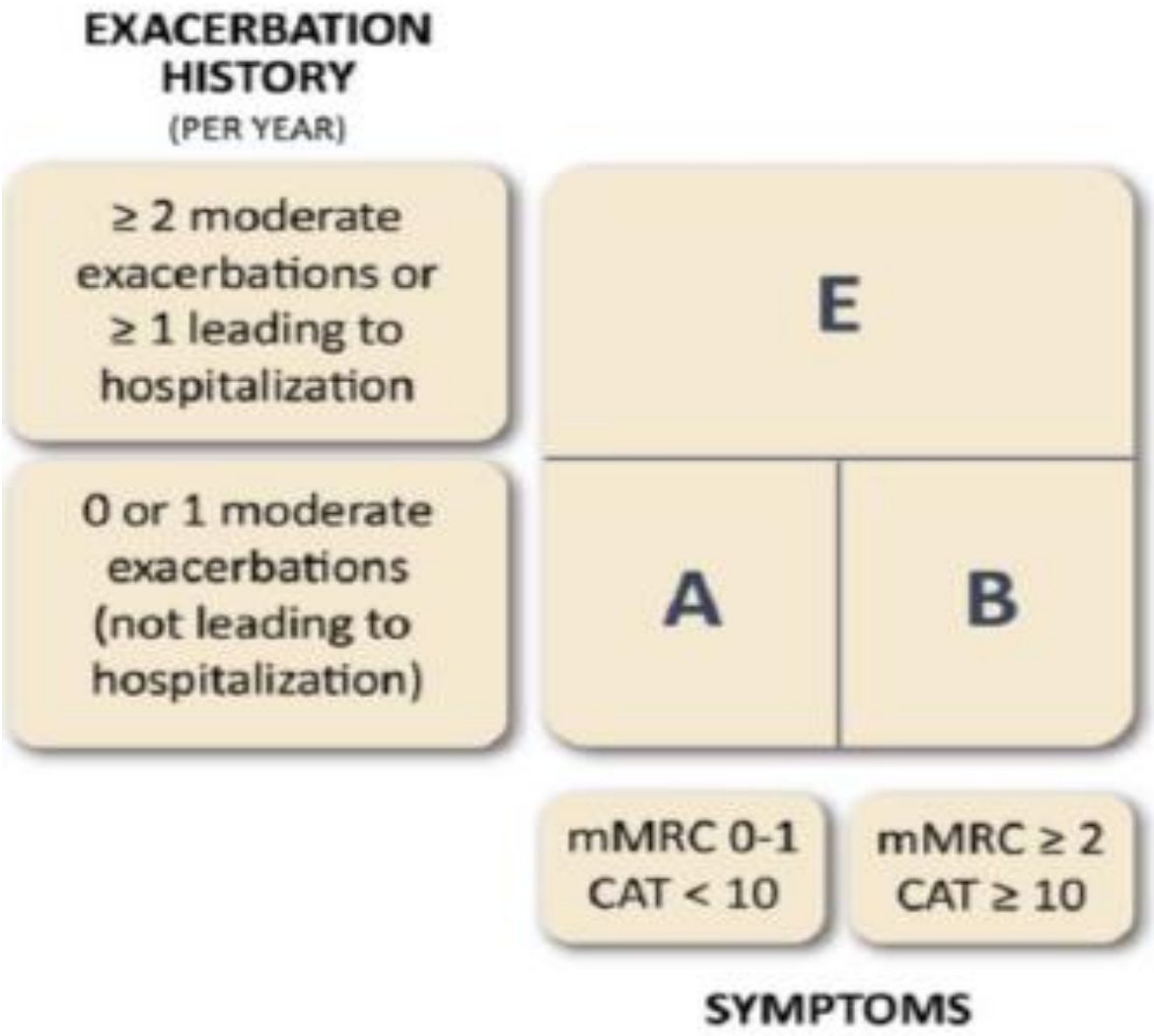
Future direction of screen

- Develop better, more symptom based tools and appropriate follow-up

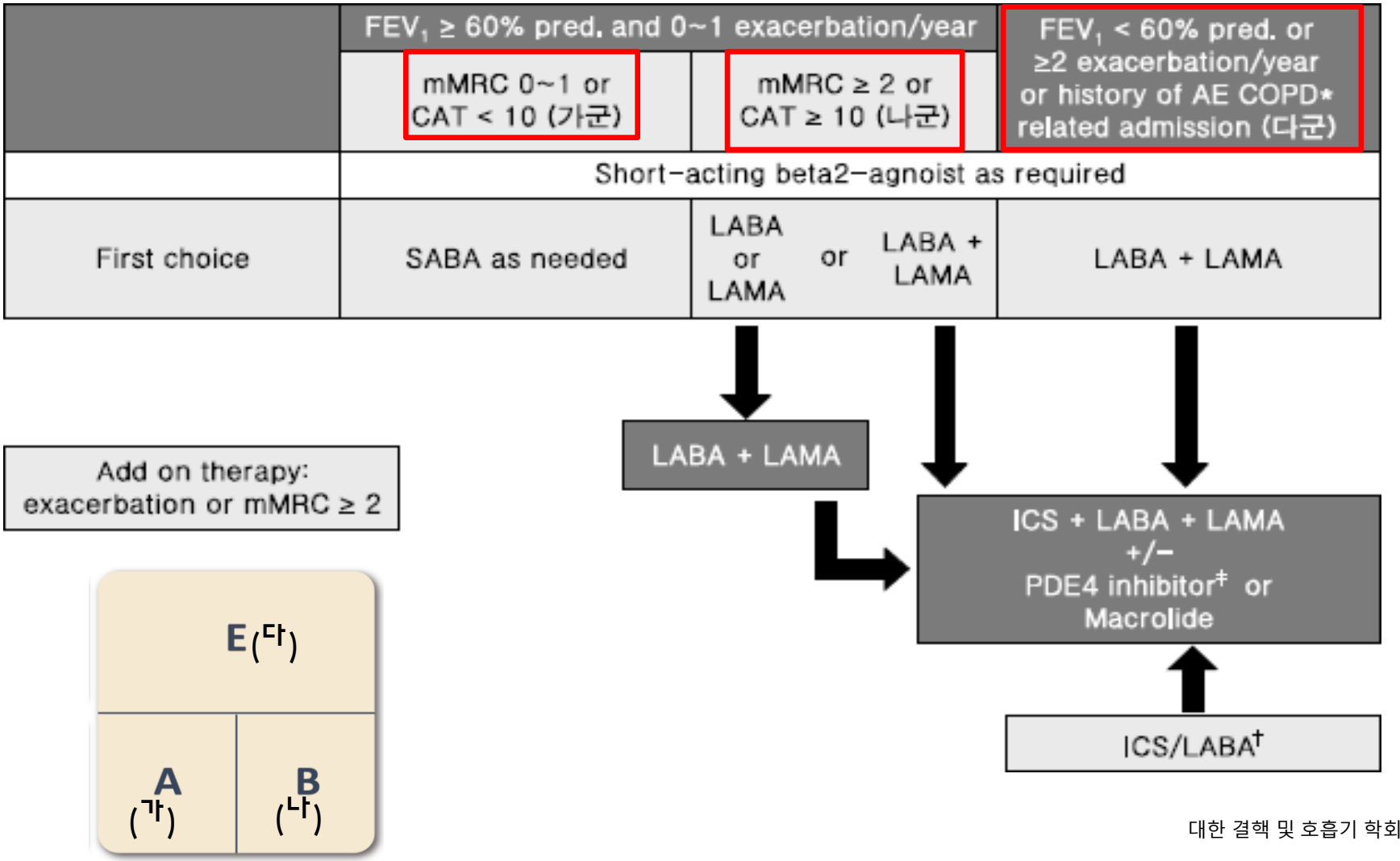


CHEST 2020 Jan;157(1):9-12
CHEST 2020 Jan;157(1): 7-9

Revised ABE Assessment Tool



국내 COPD 진료지침, 2018



대한 결핵 및 호흡기 학회

Why ???

To highlight clinical relevance of exacerbations

Myocardial infarction[1-5]	COPD exacerbation[6-8]
7% - 10% Hospital mortality	**5% - 10%** Hospital mortality
7% - 15% CCU mortality	**20% - 24%** ICU mortality

1 year mortality 22-23%[9-10]

1 in 4

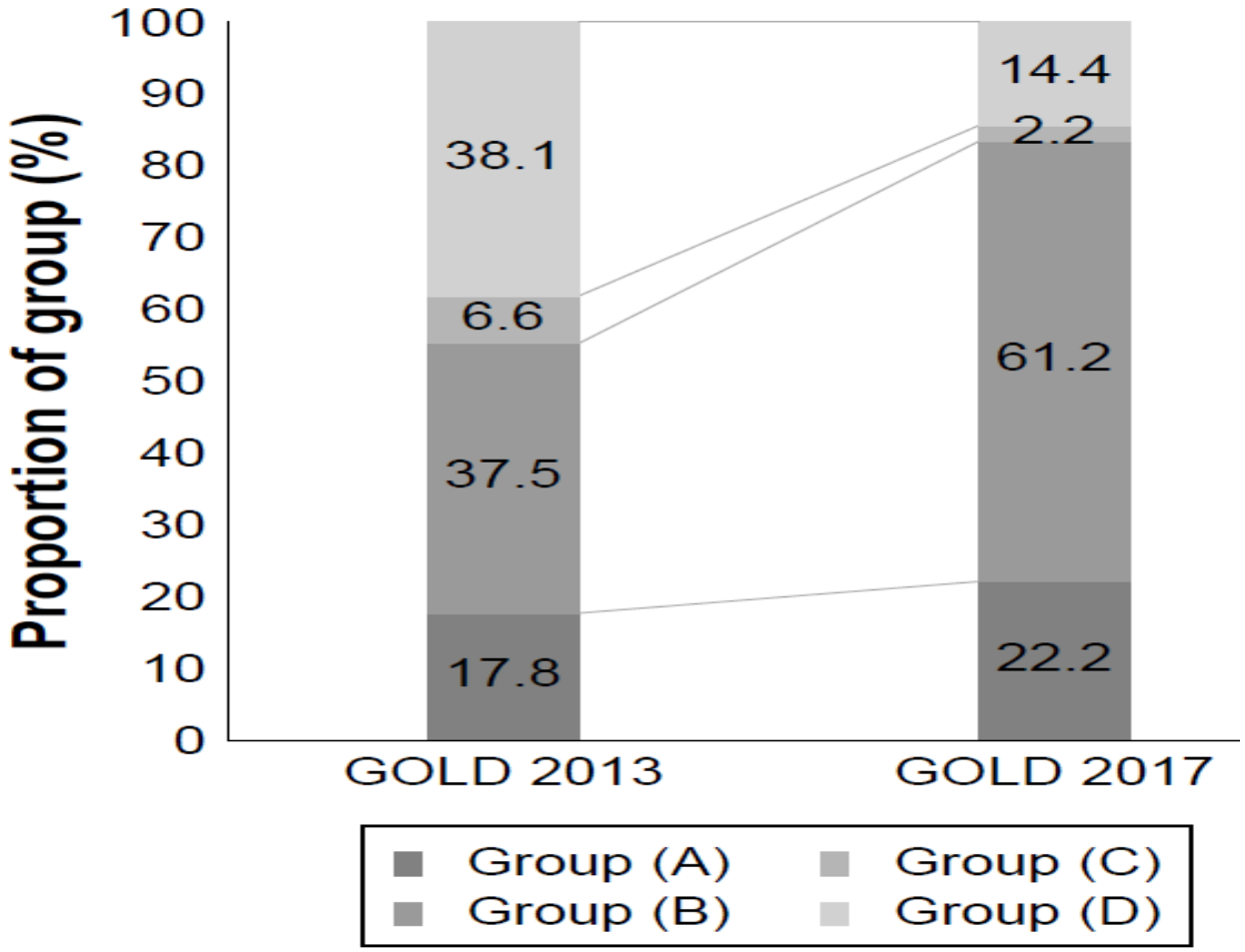
COPD patients die within 1 year* of their first severe exacerbation[10]

(Compared with MI: 8–19%)[11†]

*1-year mortality data from 102,274 patients after a first severe COPD exacerbation requiring hospitalisation between 1990 and 2005 in Quebec, Canada.
†1-year mortality data from 5383 patients after a myocardial infarction requiring hospitalisation between 1997 and 2005 in Worcester, MA, USA.

1. Jakhadar et al. Am J Epi 2004; 2. McGovern et al. Circulation 2001; 3. Ting et al. Ann Acad Med 2007; 4. Rotstein et al. Eur Heart J 1999; 5. Krumholz et al. JAMA 2009; 6. Seneff et al. JAMA 2009; 7. Murata et al. Ann Emerg Med 1991; 8. Adams et al. Clust 2000. 9. Ho TW et al. PLoS One. 2014. 10. Suissa S, et al. Thorax 2012;67:957–963. 11. McManus DD, et al. Am J Med 2011;124:40–47.

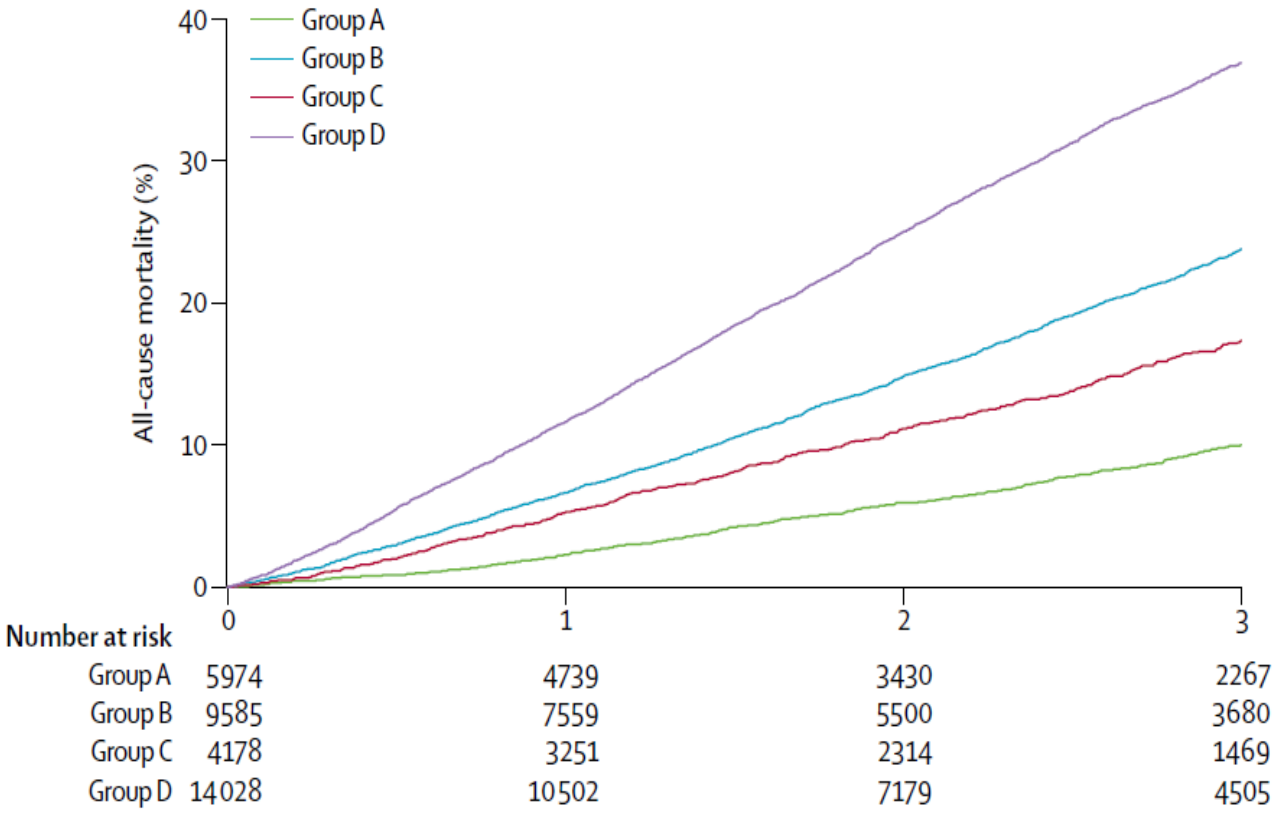
Why ???



2.2% in Korean COPD cohort

Int J Chron Obstruct Pulmon Dis. 2018 Oct 23;13:3473-3484.

Why ???



Failed to predict mortality, Danish cohort

Lancet Respir Med 2018; 6: 204–12

Why ???

- We acknowledge, that this proposal will have to be validated by appropriate clinical research

International Journal of Chronic Obstructive Pulmonary Disease Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Prognostic Properties of the GOLD 2023 Classification System

Kristian Brat[1–3], Michal Svoboda[4], Jaromir Zatloukal[5,6], Marek Plutinsky[1,2], Eva Volakova[5,6], Patrice Popelkova[7,8], Barbora Novotna[9], Tomas Dvorak[10], Vladimir Koblizek[11,12]

[1]Department of Respiratory Diseases, University Hospital Brno, Brno, Czech Republic; [2]Faculty of Medicine, Masaryk University, Brno, Czech

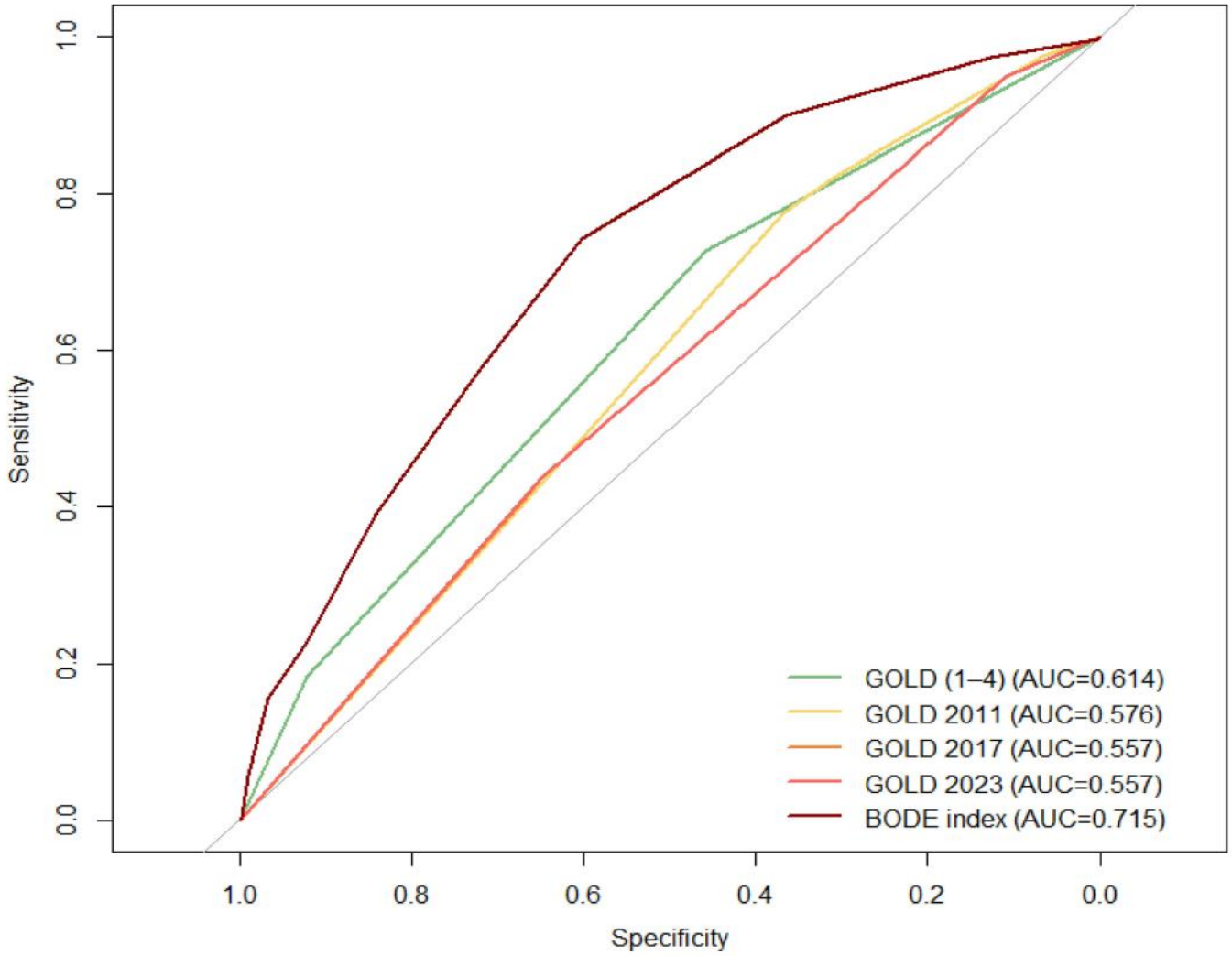
- 782, Czech COPD cohort
- Risk of death compared with GOLD A

-GOLD B (HR 1.82; 95% CI, 1.14-2.92)

-GOLD E (HR 2.48; 95% CI, 1.54-3.99)

Int J COPD 2023;18:661-667

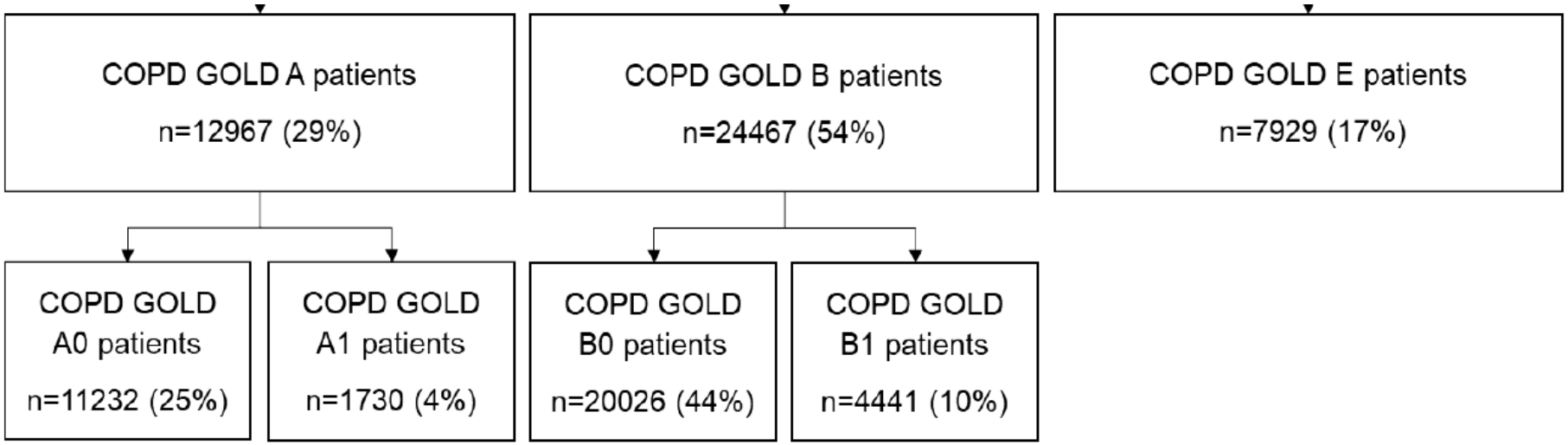
Poor prognostic properties



Int J COPD 2023;18:661-667

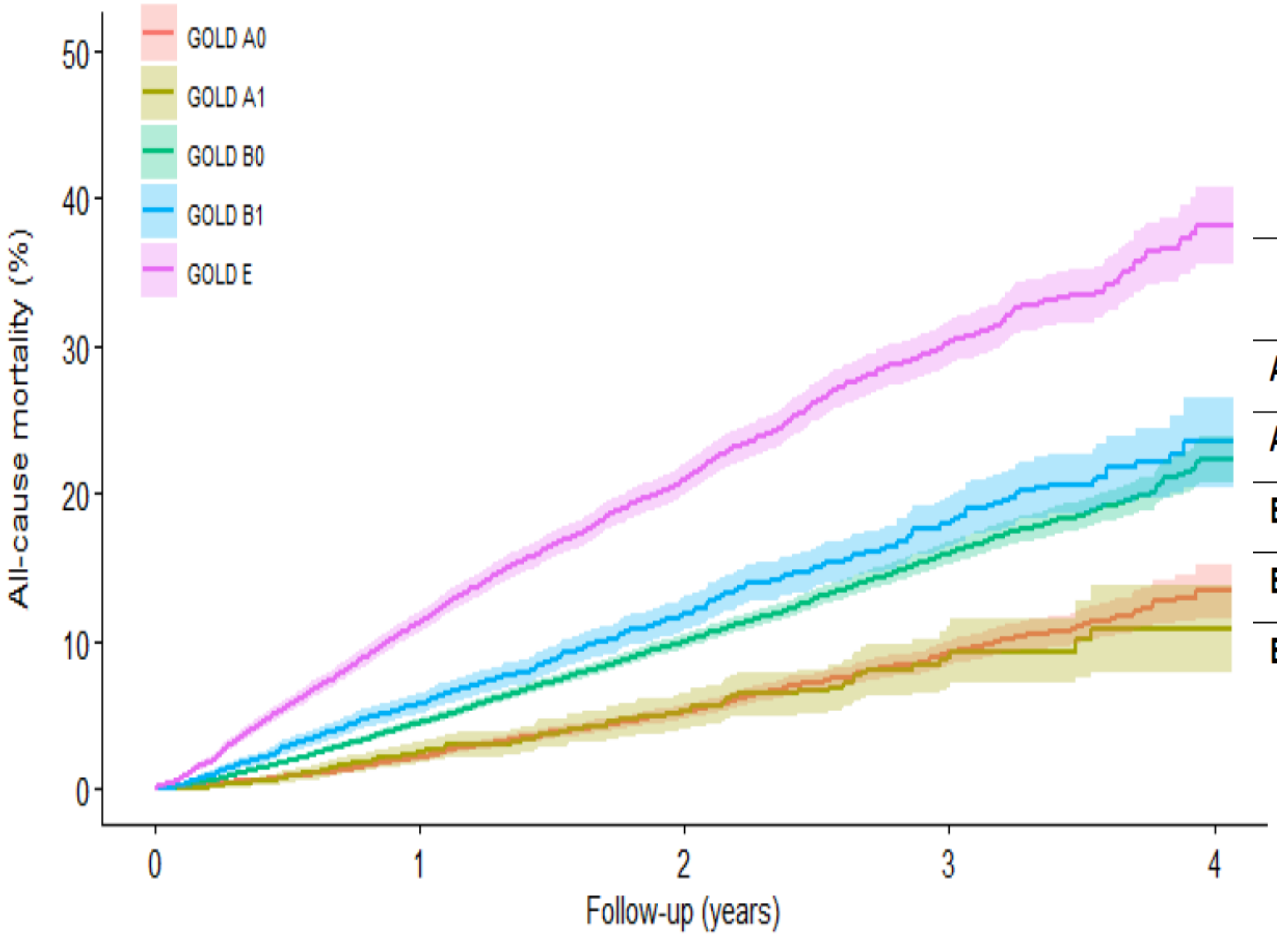
Exacerbation risk and mortality in COPD GOLD group A and B patients with and without exacerbation history

- N=45,350, Swedish cohort
- A1, B1: previous exacerbation (+)
- A0, B0: previous exacerbation (-)
- A0 vs A1 vs B0 vs B1 vs E



Am J Respir Crit Care Med. 2023 Apr 11. doi: 10.1164/rccm.202209-1774OC. Online ahead of print.

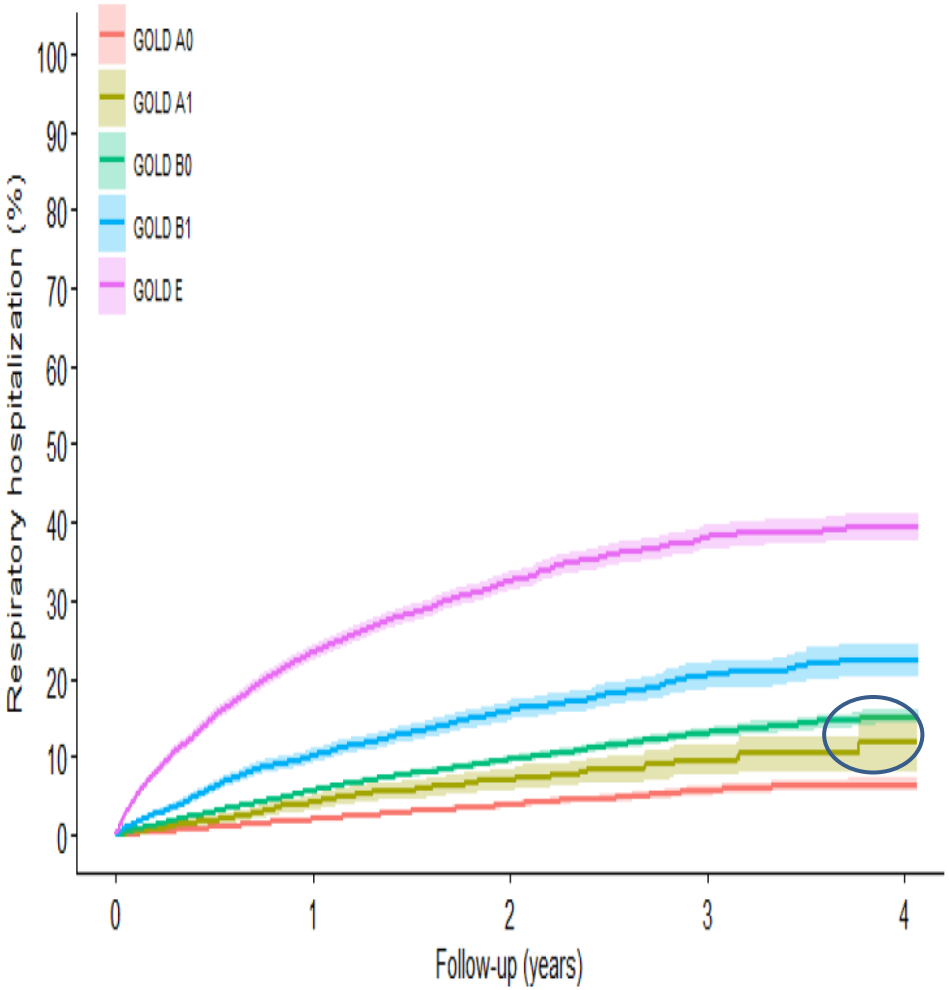
Mortality

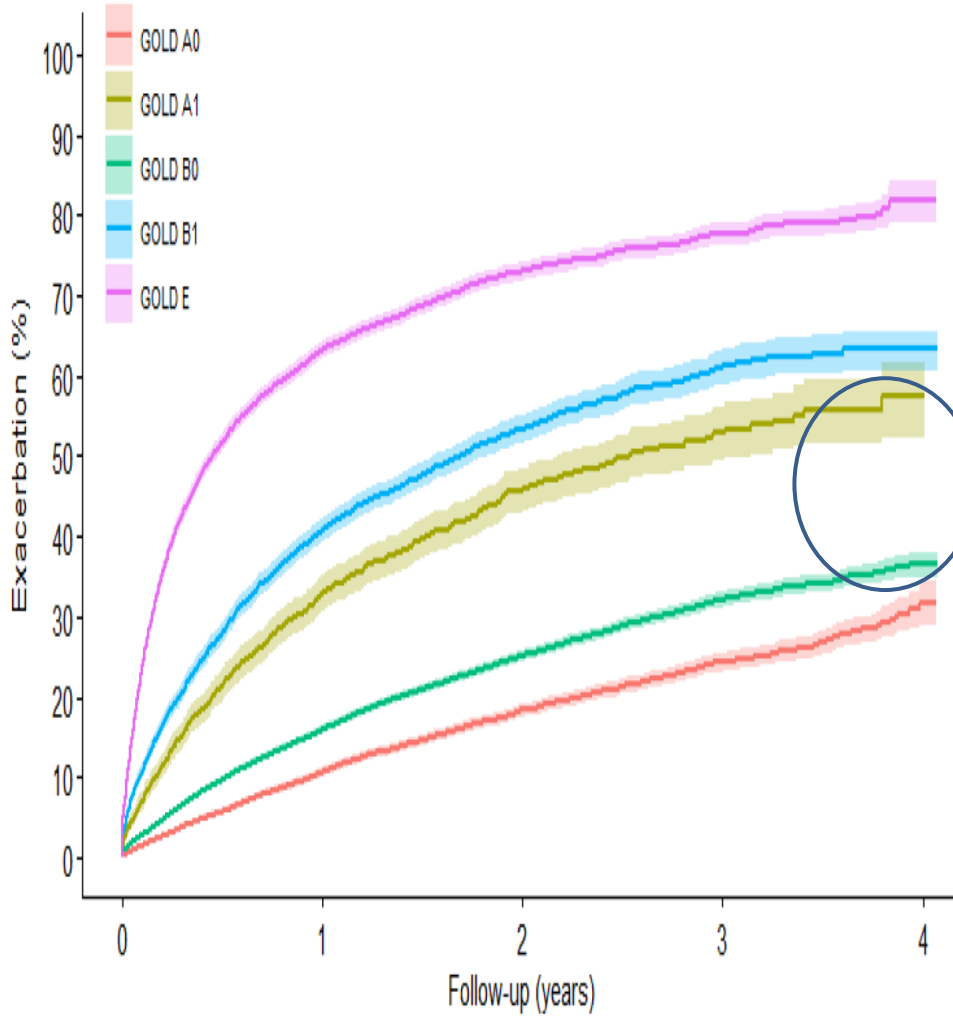


	All-cause mortality	
	Crude HR (95%CI)	Adj HR (95%CI)
A0	Ref	Ref
A1	0.97 (0.78-1.20)	1.01 (0.76-1.35)
B0	1.88 (1.72-2.05)	1.57 (1.39-1.77)
B1	2.23 (1.98-2.50)	1.64 (1.40-1.91)
E	4.19 (3.82-4.59)	2.38 (2.09-2.71)

Am J Respir Crit Care Med. 2023 Apr 11. doi: 10.1164/rccm.202209-1774OC. Online ahead of print.

Respiratory hospitalization, Moderate exacerbation





Am J Respir Crit Care Med. 2023 Apr 11. doi: 10.1164/rccm.202209-1774OC. Online ahead of print.

요 약

- 새로운 정의를 통해 낮은 진단율과 치료율을 개선하고자 함
- 조기진단 (Pre-COPD, COPD전증)과 조기치료로 질병의 진행예방이 필요함
- COPD의 원인에 따른 개별 접근과 치료에 대한 연구가 필요함
- COPD 진단뿐만 아니라 결과를 호전시킬 수 있는 COPD 선별검사 도구 개발이 필요함
- COPD 환자 분류는 ABE 분류로 변경되었으며 survival 차이는 입증되고 있고 추가적인 타당성 확인이 필요함

감사합니다

GNUH
Gyeongsang National University Hospital
경상국립대학교병원