COPD Year in Review 2023
Risk, pathogenesis, and diagnosis of COPD

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Contents

1) New definition & etiotypes of COPD
2) Risk factors and pathogenesis of COPD
3) Advances in diagnosis of COPD

EUROPEAN RESPIRATORY JOURNAL
TASK FORCE REPORT
A. AGUSTÍ ET AL.

Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary

Alvar Agustí[1,22], Bartolome R. Celli[2,22], Gerard J. Criner[3], David Halpin[4], Antonio Anzueto[5], Peter Barnes[6], Jean Bourbeau[7], MeiLan K. Han[8], Fernando J. Martinez[9], Maria Montes de Oca[10], Kevin Mortimer[6,11,12], Alberto Papi[13], Ian Pavord[14], Nicolas Roche[15], Sundeep Salvi[16], Don D. Sin[17], Dave Singh[18], Robert Stockley[19], M. Victorina López Varela[20], Jadwiga A. Wedzicha[6] and Claus F. Vogelmeier[21]

New definition of COPD and taxonomy

- Previous definition fails to identify the disorder at its early stages, before airflow limitation becomes evident
- Integrating different causes of COPD leading to its heterogeneous presentation

Agustí A et al. Eur Respir J 2023 Apr

GOLD 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.

GOLD 2023 defines COPD as a *heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, expectoration and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction.*

Agustí A et al. Eur Respir J 2023

WHAT IS COPD?

Global Initiative for Chronic Obstructive Lung Disease

2024 REPORT

Definition

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction.[6]

Proposed taxonomy (etiotypes) for COPD

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

Adapted from Celli *et al*. [2] and Stolz *et al*. [72].

Risk factors associated with COPD

- Preterm birth
- Indoor air pollution
- Childhood cigarette smoking

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
A. PULAKKA ET AL.

Preterm birth and asthma and COPD in adulthood: a nationwide register study from two Nordic countries

Anna Pulakka [1,2], Kari Risnes [3,4], Johanna Metsälä [1], Suvi Alenius [1,5], Katriina Heikkilä [1], Sara Marie Nilsen [3,6], Pieta Näsänen-Gilmore [1,7,8], Peija Haaramo[9], Mika Gissler [10,11,12], Signe Opdahl [13] and Eero Kajantie [1,8,13]

Nationwide medical birth registry data

- 706,717 people born 1987–1998 in Finland (4.8% preterm)
- 1,669,528 people born 1967–1999 in Norway (5.0% preterm)

Risk associated with preterm birth

- follow-up was started at the earliest when the individuals turned 18 years
- Outcome: care episodes of asthma and COPD later in life
  (inpatient or outpatient hospital or specialist care episode with corresponding ICD codes)

Pulakka A et al. Eur Respir J 2023 Jun

TABLE 1 Characteristics of the study population

	Finland, born 1987–1998	Norway, born 1967–1999
Individuals, n	**706 717**	**1 669 528**
Male	360 028 (50.9)	852 867 (51.1)
GA at birth, completed weeks		
Extremely preterm (23–27)	850 (0.1)	1359 (0.1)
Very preterm (28–31)	2793 (0.4)	6931 (0.4)
Moderately preterm (32–33)	4048 (0.6)	10 880 (0.7)
Late preterm (34–36)	26 557 (3.8)	65 057 (3.9)
Early term (37–38)	125 648 (17.8)	218 145 (13.1)
Full term (39–41)	515 608 (73.0)	1 153 153 (69.1)
Post-term (⩾42)	31 213 (4.4)	214 003 (12.8)
Birth weight Z-score	0.00±1.06	0.00±1.11
Small for gestational age	17 958 (2.5)	77 405 (4.6)
Large for gestational age	23 612 (3.3)	47 144 (2.8)
First born	281 020 (39.8)	687 968 (41.2)
Singleton	689 038 (97.5)	1 634 803 (97.9)
Caesarean section	105 846 (15.0)	135 827 (8.1)
Bronchopulmonary dysplasia[#]	616 (0.1)	N/A
Follow-up time, years	6.0 (3.2–8.9)	10.0 (7.5–10.0)
Attained age		
18–29 years	706 717 (100.0)	623 024 (37.3)
30–50 years	– (0.0)	1 046 504 (62.7)

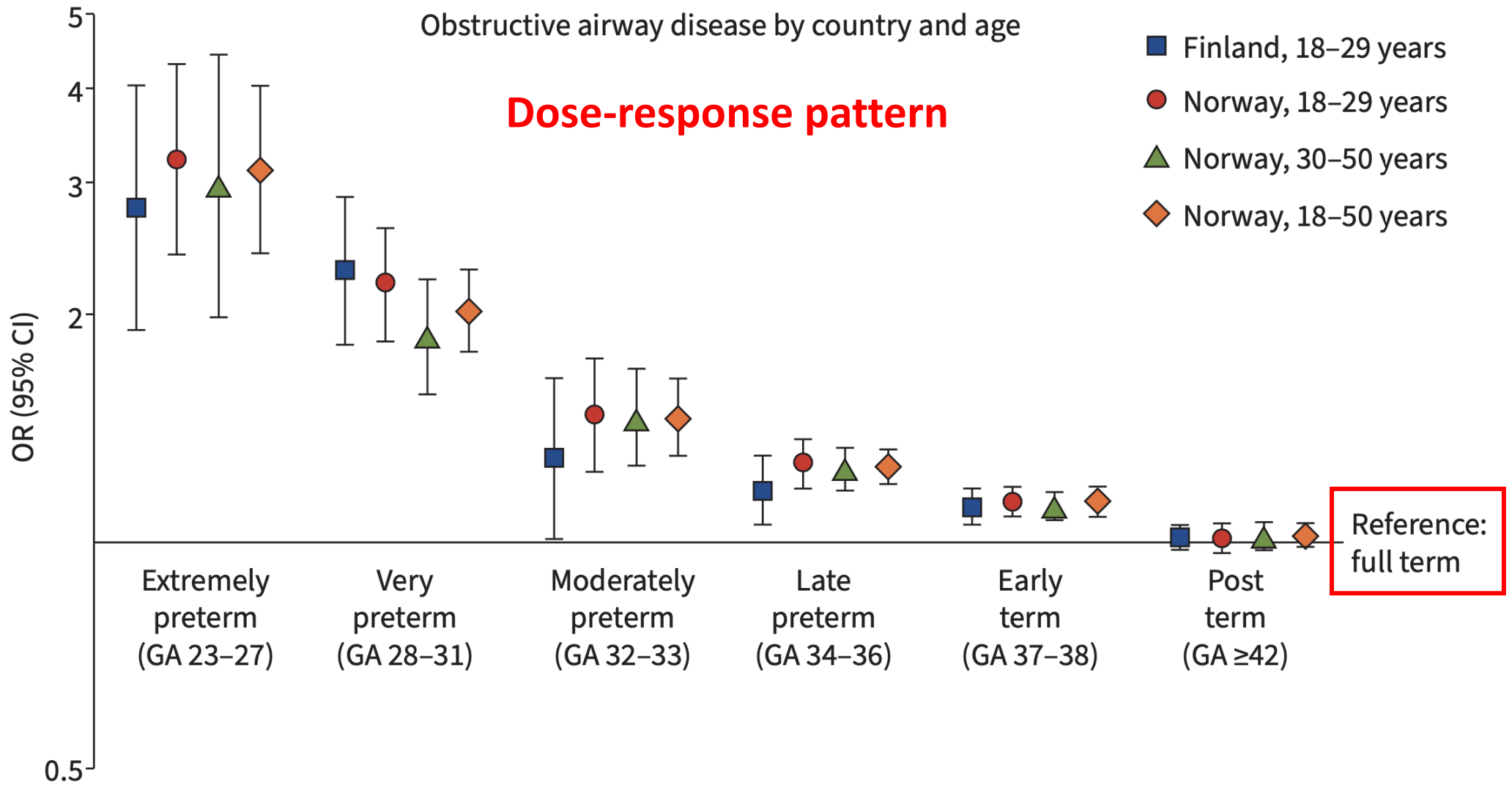
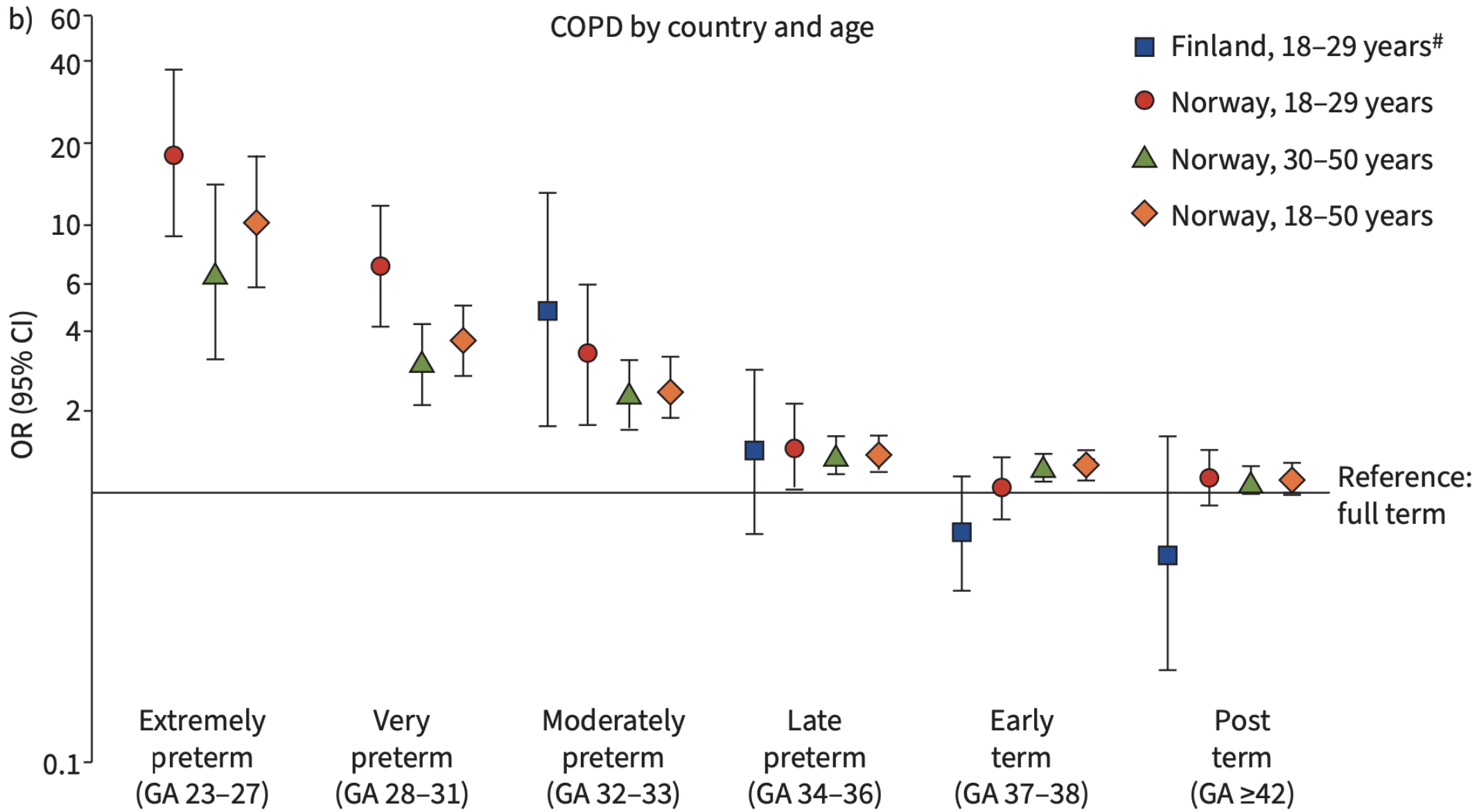


FIGURE 1 Associations between gestational age (GA) in weeks and any obstructive airway disease (asthma or chronic obstructive pulmonary disease), adjusted for sex and birth year.


b)
COPD by country and age
Finland, 18–29 years#
Norway, 18–29 years
Norway, 30–50 years
Norway, 18–50 years
OR (95% CI)
60
40
20
10
6
4
2
0.1
Reference: full term
Extremely preterm (GA 23–27)
Very preterm (GA 28–31)
Moderately preterm (GA 32–33)
Late preterm (GA 34–36)
Early term (GA 37–38)
Post term (GA ≥42)

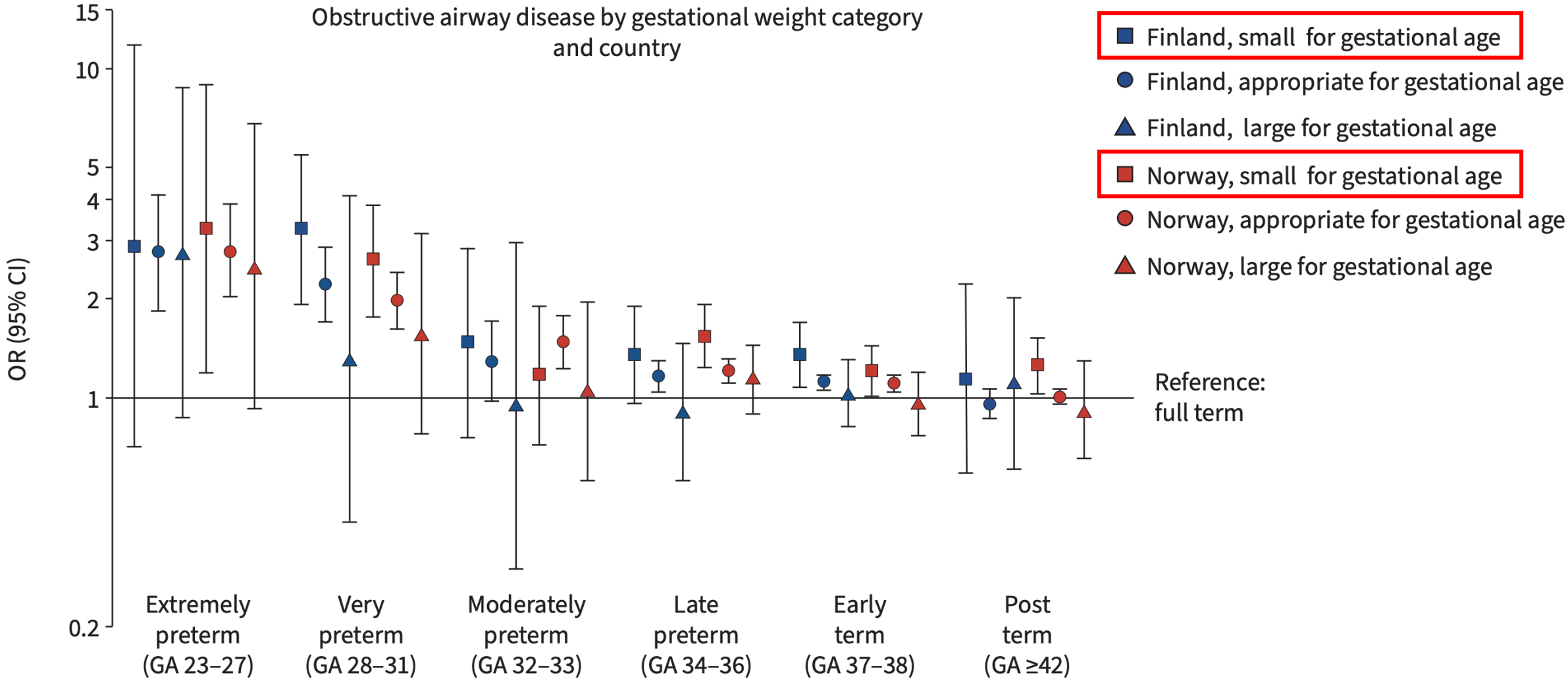


FIGURE 4 Associations between gestational age (GA) in weeks and obstructive airway disease (asthma or chronic obstructive pulmonary disease) at age 18–29 years in different birth weight groups. Models adjusted for sex and birth year.

- A large number of subjects from two Nordic countries with individual-level data
- Follow-up from birth to the **age of 50 years**

- **Earlier gestational age at birth** has **lifelong adverse implications** for respiratory health
  - Higher risk of obstructive airway disease in a dose-dependent manner
  - Similar findings for individuals born small for gestational age

- Supports the concept of **early-life origins** of chronic respiratory diseases in later life

ORIGINAL ARTICLE

Indoor Pollution and Lung Function Decline in Current and Former Smokers

SPIROMICS AIR

Nadia N. Hansel[1,2], Han Woo[1], Kirsten Koehler[2], Amanda Gassett[3], Laura M. Paulin[5], Neil E. Alexis[6], Nirupama Putcha[1], Wendy Lorizio[1], Ashraf Fawzy[1], Daniel Belz[1], Coralynn Sack[4], R. Graham Barr[7], Fernando J. Martinez[8], MeiLan K. Han[9], Prescott Woodruff[10], Cheryl Pirozzi[11], Robert Paine III[11], Igor Barjaktarevic[12], Christopher B. Cooper[12], Victor Ortega[13], Marina Zusman[3], and Joel D. Kaufman[3]

SPIROMICS AIR

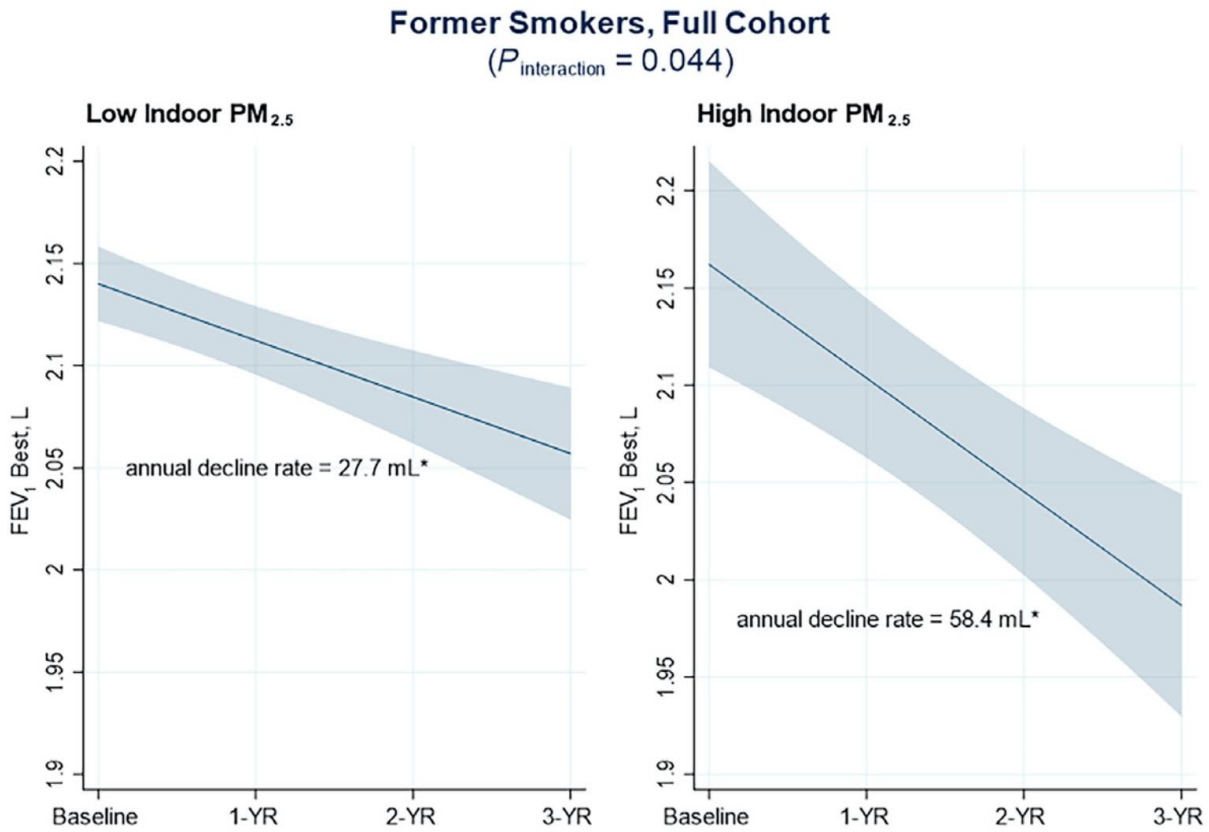
- 1,208 participants with a history of smoking with or without COPD and complete data of indoor PM and NO_2
- Mean age of 65 years, mean 50 pack-years of smoking, and 34% currently smoking

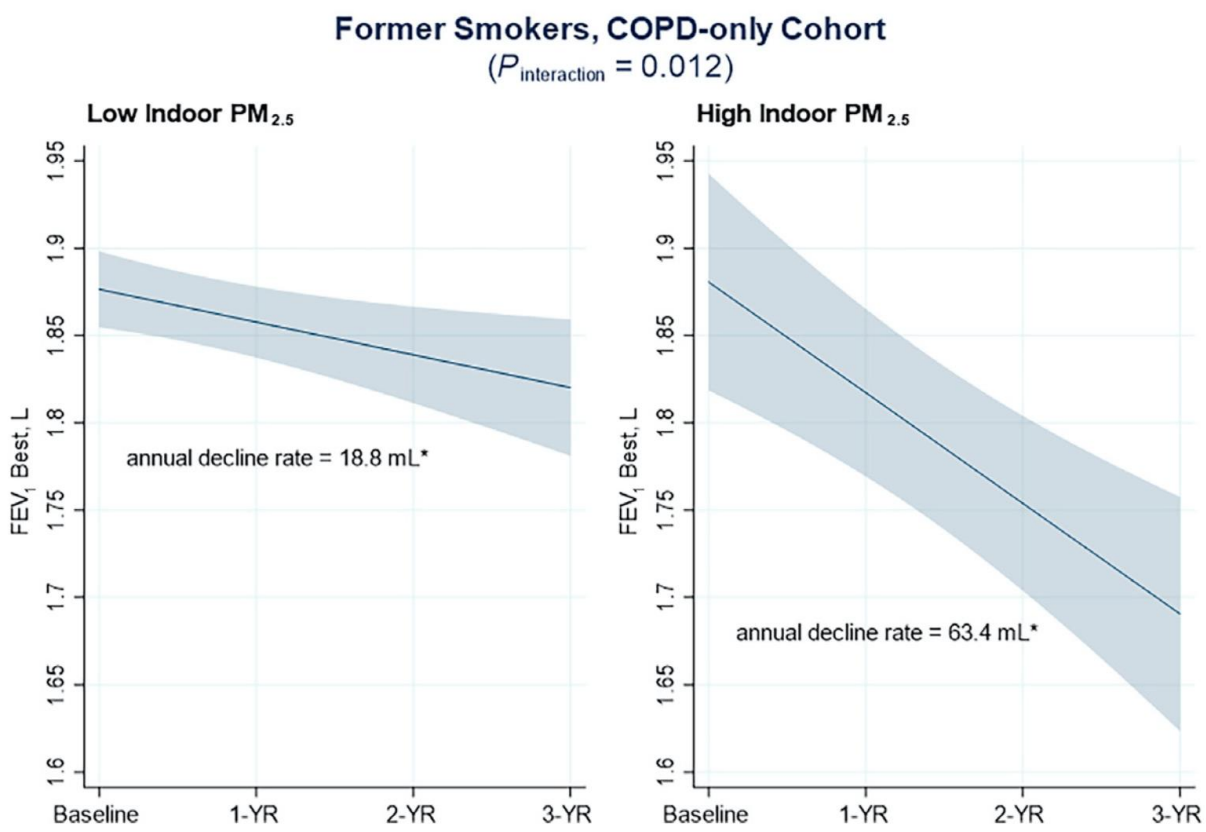
- To determine whether estimated indoor $PM_{2.5}$ and NO_2 concentrations were associated with annual lung function decline among current and former smokers with COPD from SPIROMICS (followed up to **3 years**)

Hansel NN et al. Am J Respir Crit Care Med 2023 Nov

Table 2. Estimated Change in FEV_1 (in milliliters) per Year, by Estimated Indoor $PM_{2.5}$ Concentration

	Former Smokers			Current Smokers		
	Low Indoor $PM_{2.5}$ (95% CI)	High Indoor $PM_{2.5}$ (95% CI)	Interaction* *P* Value	Low Indoor $PM_{2.5}$ (95% CI)	High Indoor $PM_{2.5}$ (95% CI)	Interaction* *P* Value
	<8.4μg/m³	≥8.4μg/m³				
Full cohort						
Main model†	−27.7 (−39.8, −15.7)	−58.4 (−83.7, −33.2)	**0.044**	−62.6 (−78.6, −46.7)	−64.5 (−78.6, −50.5)	0.871
Main model additionally adjusted for SHS‡	−27.9 (−40.0, −15.9)	−59.0 (−84.2, −33.8)	**0.042**	−62.4 (−78.3, −46.5)	−65.9 (−80.2, −51.6)	0.769
COPD-only cohort						
Main model†	−18.8 (−33.1, −4.4)	−63.4 (−93.1, −33.6)	**0.012**	−55.1 (−73.8, −36.3)	−57.4 (−73.4, −41.5)	0.855
Main model additionally adjusted for SHS‡	−18.4 (−32.8, −3.9)	−63.2 (−93.0, −33.5)	**0.012**	−54.9 (−73.7, −36.2)	−58.6 (−75.5, −41.7)	0.786



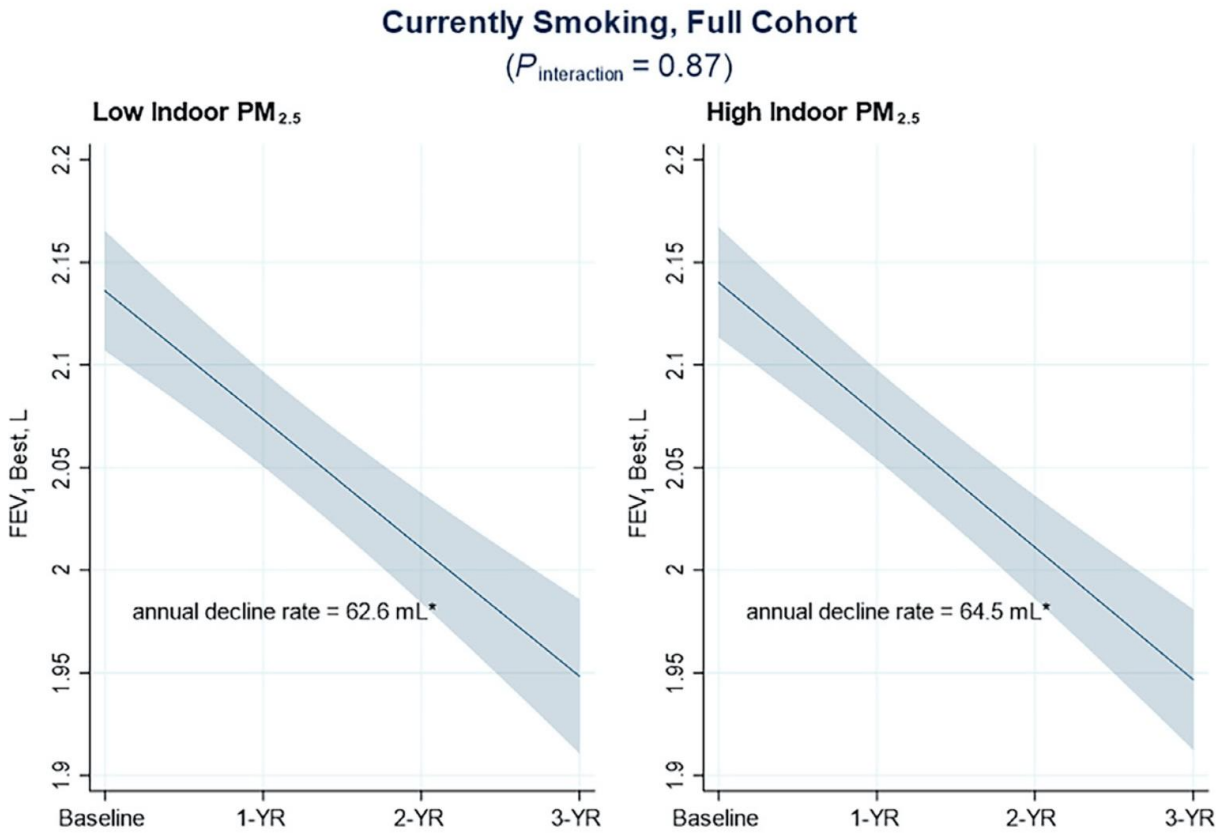


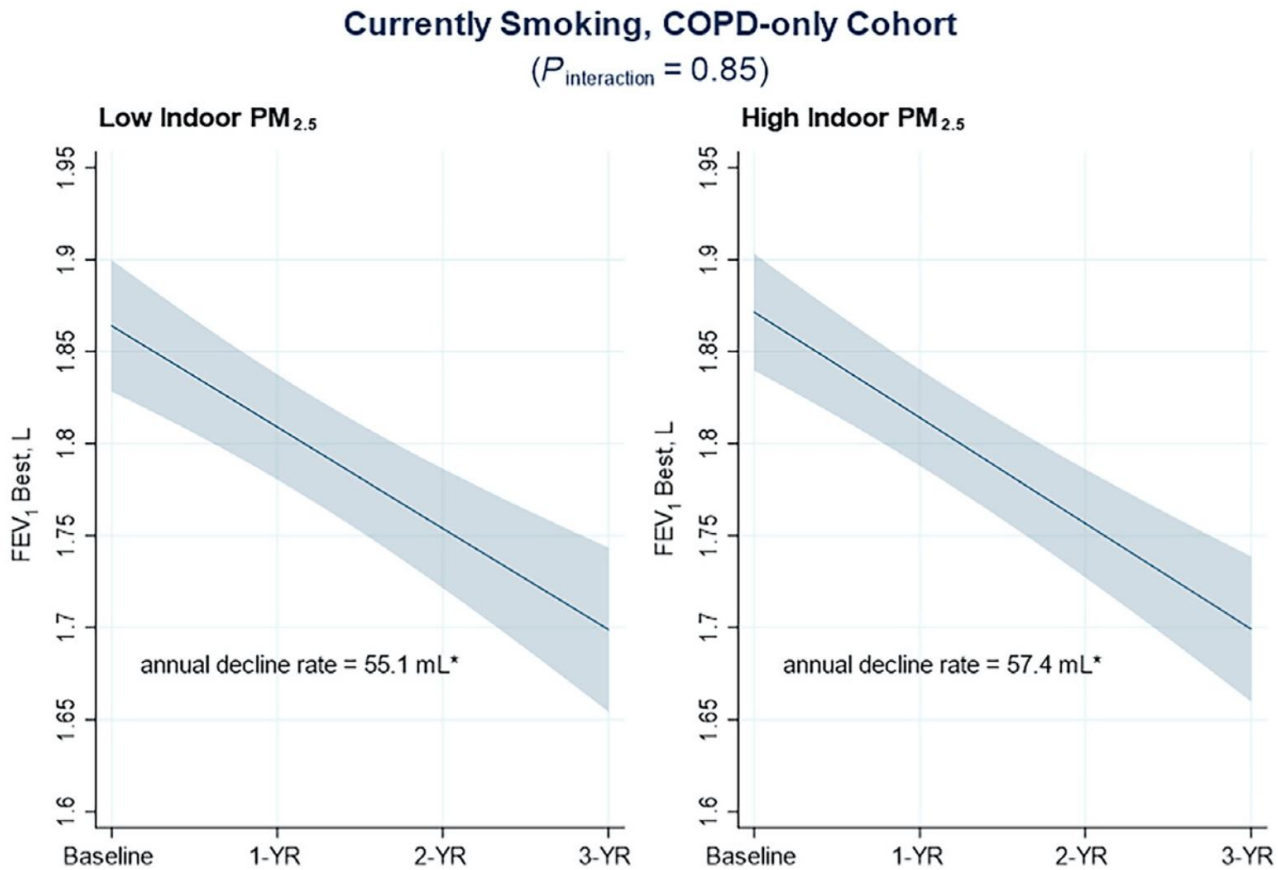
Annual decline rate = 27.7 mL

Annual decline rate = 58.4 mL

Annual decline rate = 18.8 mL

Annual decline rate = 63.4 mL





Annual decline rate = 62.6 mL

Annual decline rate = 64.5 mL

Annual decline rate = 55.1 mL

Annual decline rate = 57.4 mL

- Each **10 µg/m³** estimated increment of indoor $PM_{2.5}$ concentration was associated with a **15 ml per year** additional loss of lung function

- Impact of indoor air pollution on lung function in smokers
  - **Rapid FEV_1 decline in former smokers**
  - **No significant influence in current smokers**

- A significant and rapid FEV_1 decline was observed despite the relatively low absolute level of $PM_{2.5}$ in the SPIROMICS cohort

ORIGINAL ARTICLE

Childhood Cigarette Smoking and Risk of Chronic Obstructive Pulmonary Disease in Older U.S. Adults

James D. Sargent[1,2], Michael Halenar[3], Alexander W. Steinberg[4], Jenny Ozga[3], Zhiqun Tang[3], Cassandra A. Stanton[3], and Laura M. Paulin[4]

[1]Department of Pediatrics and [2]Department of Biomedical Data Sciences, Geisel School of Medicine, Hanover, New Hampshire; [3]Westat, Rockville, Maryland; and [4]Section of Pulmonary and Critical Care, Department of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire

2020 National Health Interview Survey (NHIS) in US

- 22,374 adults aged >40 years
- 13,024 never smokers (60%) 9,350 ever smokers

- 1,490 (**16% of ever smokers**) started smoking regularly **before age 15 years**
- 7,860 started smoking regularly after age ≥ 15 years

Sargent JD et al. Am J Respir Crit Care Med 2023 Aug

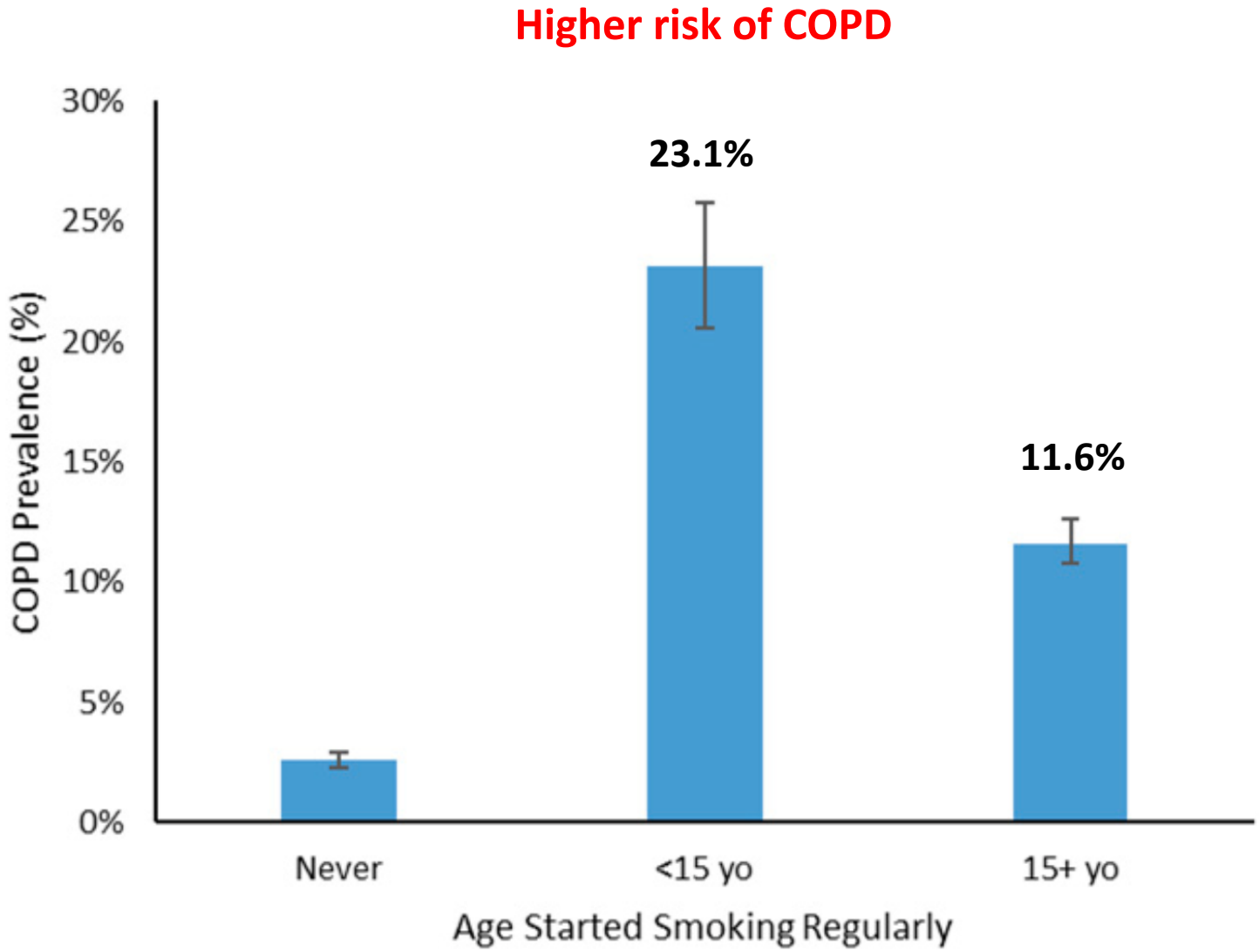


Figure 2. Prevalence of COPD by childhood smoking. COPD = chronic obstructive pulmonary disease.

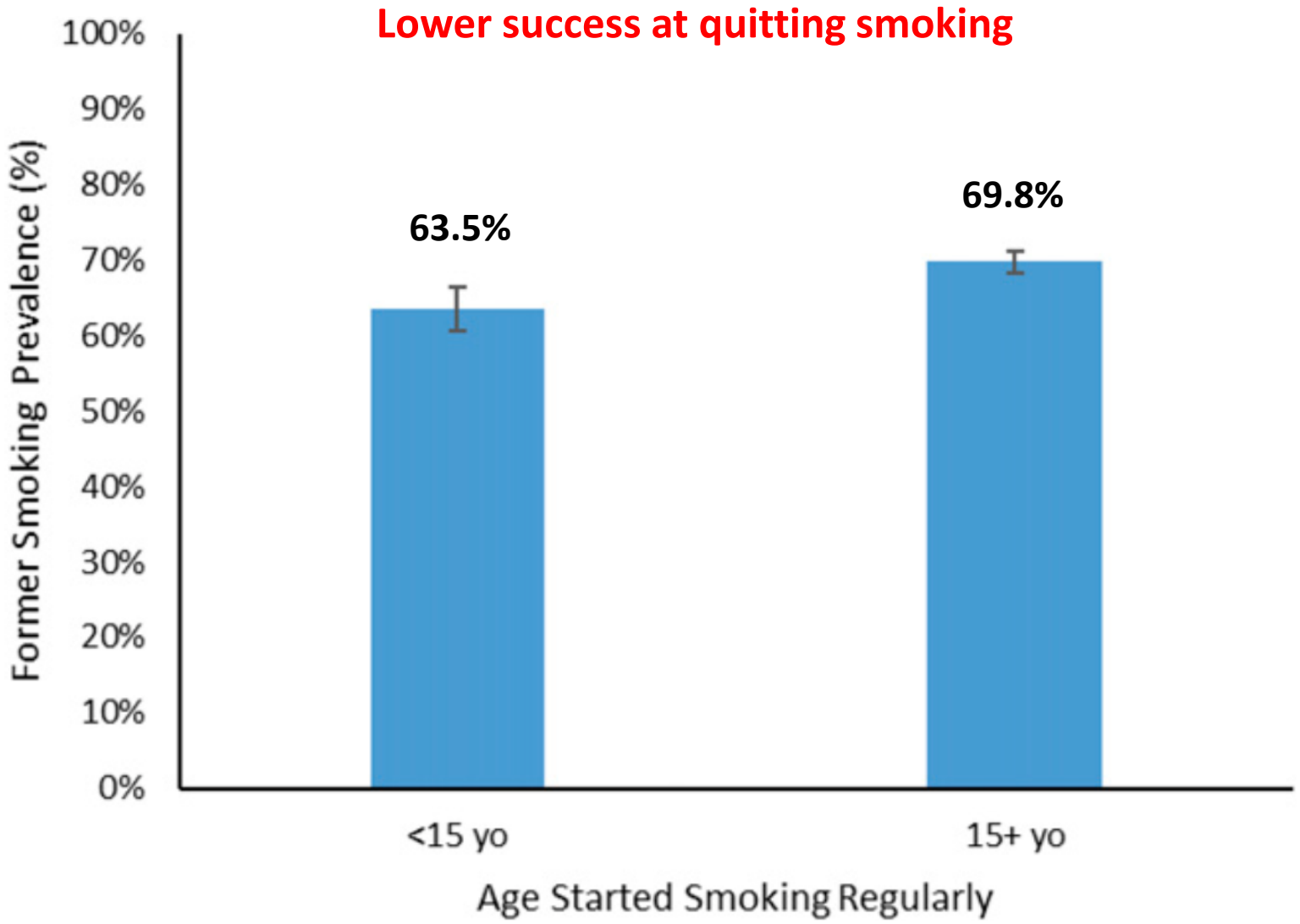


Figure 3. Percentage of former smokers by childhood smoking. Percentages significantly different at $P < 0.001$.

Table 2. Multivariable Association between Chronic Obstructive Pulmonary Disease and Childhood Smoking by Current Smoking Status, Entering Age Started Smoking Regularly Separately from Smoking Status

		Relative Risk			
	% with COPD	Unadjusted	Adjusted*	95% CI for Adjusted	*P* Value for Adjusted
Age started smoking regularly, yr					
⩾15	11.6	Ref	Ref	Ref	Ref
<15	23.1	1.99	1.41	1.22–1.63	<0.001
Smoking status					
Never-smoker	2.6	0.22	0.44	0.37–0.51	<0.001
Never + former smoker	5.5	Ref	Ref	Ref	Ref
Current smoker	18.0	3.28	1.51	1.32–1.74	<0.001
Cigarette pack-years†		1.37	1.18	1.16–1.21	<0.001

*Adjusted also for age, gender, race, poverty, and urbanicity.

Table 3. Multivariable Association between Chronic Obstructive Pulmonary Disease and Childhood Smoking by Current Smoking Status, Combining Age Started Smoking Regularly with Smoking Status and Smoking Intensity

Smoking Status/Intensity	Age Started Smoking Regularly (yr)	% with COPD	RR		95% CI for Adjusted	*P* Value[†]
			Unadjusted	Adjusted*		
Never-smoker	—	2.6	Ref	Ref	Ref	Ref
Former smoker	<15	19.5	7.55	2.83	2.24–3.57	0.010
	⩾15	10.0	3.88	2.22	1.90–2.60	
Current light smoker	<15	20.3	7.87	5.53	3.38–9.05	0.070
	⩾15	9.7	3.75	2.83	1.64–4.88	
Current medium smoker	<15	30.6	11.86	6.00	4.40–8.17	0.030
	⩾15	19.0	7.35	4.09	3.18–5.26	
Current heavy smoker	<15	35.1	13.61	4.03	2.95–5.50	0.004
	⩾15	18.7	7.24	2.59	2.00–3.36	
Cigarette pack-years[‡]	—	—	1.37	1.20	1.18–1.23	<0.001

- Smoking initiation **earlier than 15 years of age**
  - Higher risk of developing COPD
  - Higher likelihood of failure in smoking cessation

- **Regardless of current or past smoking status** and the **quantity of smoking**, initiating smoking before the age of 15 is associated with a higher risk of COPD

Advances in diagnosis of COPD

- Screening and case finding studies
- New strategy using the FEV_1/FVC ratio severity
- Prediction of COPD development and lung function decline
  - Clinical variables
  - Bronchodilator responsiveness
  - CT imaging machine learning

U.S. Preventive Services TASK FORCE

Final Recommendation Statement

Chronic Obstructive Pulmonary Disease: Screening

May 10, 2022

Recommendation Summary

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

JAMA | Original Investigation

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

Fernando J. Martinez, MD, MS; MeiLan K. Han, MD, MS; Camden Lopez, MS; Susan Murray, ScD; David Mannino, MD; Stacey Anderson, MPH; Randall Brown, MD, MPH; Rowena Dolor, MD; Nancy Elder, MD, MPH; Min Joo, MD, MPH; Irfan Khan, MD; Lyndee M. Knox, PhD; Catherine Meldrum, PhD; Elizabeth Peters, BSN, RN; Cathie Spino, ScD; Hazel Tapp, PhD; Byron Thomashow, MD; Linda Zittleman, MPH; Barry Make, MD; Barbara P. Yawn, MD, MSc, MPH; for the CAPTURE Study Group

Usefulness of CAPTURE tool for identifying undiagnosed, clinically significant COPD

- In the US primary care setting
- Clinically significant COPD
  - → Spirometry-defined COPD (post-BD $FEV_1/FVC < 0.70$ or pre-BD $FEV_1/FVC < 0.65$) combined with either an **FEV_1 less than 60%pred**. or a self-reported history of an **acute respiratory illness** within the past 12 months

Outcome: sensitivity and specificity for detecting clinically significant COPD

Martinez FJ et al. JAMA 2023 Feb

JAMA | Original Investigation

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

Fernando J. Martinez, MD, MS; MeiLan K. Han, MD, MS; Camden Lopez, MS; Susan Murray, ScD; David Mannino, MD; Stacey Anderson, MPH; Randall Brown, MD, MPH; Rowena Dolor, MD; Nancy Elder, MD, MPH; Min Joo, MD, MPH; Irfan Khan, MD; Lyndee M. Knox, PhD; Catherine Meldrum, PhD; Elizabeth Peters, BSN, RN; Cathie Spino, ScD; Hazel Tapp, PhD; Byron Thomashow, MD; Linda Zittleman, MPH; Barry Make, MD; Barbara P. Yawn, MD, MSc, MPH; for the CAPTURE Study Group

CAPTURE tool

- Questionnaire comprising 5 questions regarding respiratory exposure, symptoms, or acute respiratory illnesses + peak expiratory flow rate
- Positive screening result

(1) a questionnaire score of 5 or 6

(2) a questionnaire score of 2, 3, or 4 with a PEFR of <350 L/min for males or <250 L/min for females

Martinez FJ et al. JAMA 2023 Feb

eFigure 2. The CAPTURE screening tool[1]

For each question, place an X in the box with the answer that is best for you. There are no right or wrong answers, only answers which are right for you.

Respiratory exposure Living and working environment

Respiratory symptoms

Acute respiratory illness

Please answer each question	**No** *(0 points)*	**Yes** *(1 point)*	
1. Have you ever lived or worked in a place with dirty or polluted air, smoke, second-hand smoke, or dust?	☐	☐	
2. Does your breathing change with the seasons, weather, or air quality?	☐	☐	
3. Does your breathing make it difficult to do such things as carry heavy loads, shovel dirt or snow, jog, play tennis, or swim?	☐	☐	
4. Compared to others your age, do you tire easily?	☐	☐	
5. In the past 12 months, how many times did you miss work, school, or other activities due to a cold, bronchitis, or pneumonia?	**None** *(0 points)* ☐	**Once** *(1 point)* ☐	**2 or more** *(2 points)* ☐

Total Score (0-6): _____

Total Score (check **ONLY one box** based on above score)		**RECOMMENDED ACTION:**
0 or 1 ☐		**A.** Low likelihood of COPD based on CAPTURE: No further testing recommended at this time
2, 3, or 4 Record Highest Peak Flow (highest of 3): _____ L/min	(check one based on highest Peak Flow) Females ≥ 250 L/min Males ≥ 350 L/min ☐	**B.** Consider rescreening or reassessing in 12 months
	Females < 250 L/min Males < 350 L/min ☐	**C.** Evaluation including spirometry recommended
5 or 6 ☐		**D.** Significant likelihood of COPD: Evaluation including spirometry recommended

Peak expiratory flow rate

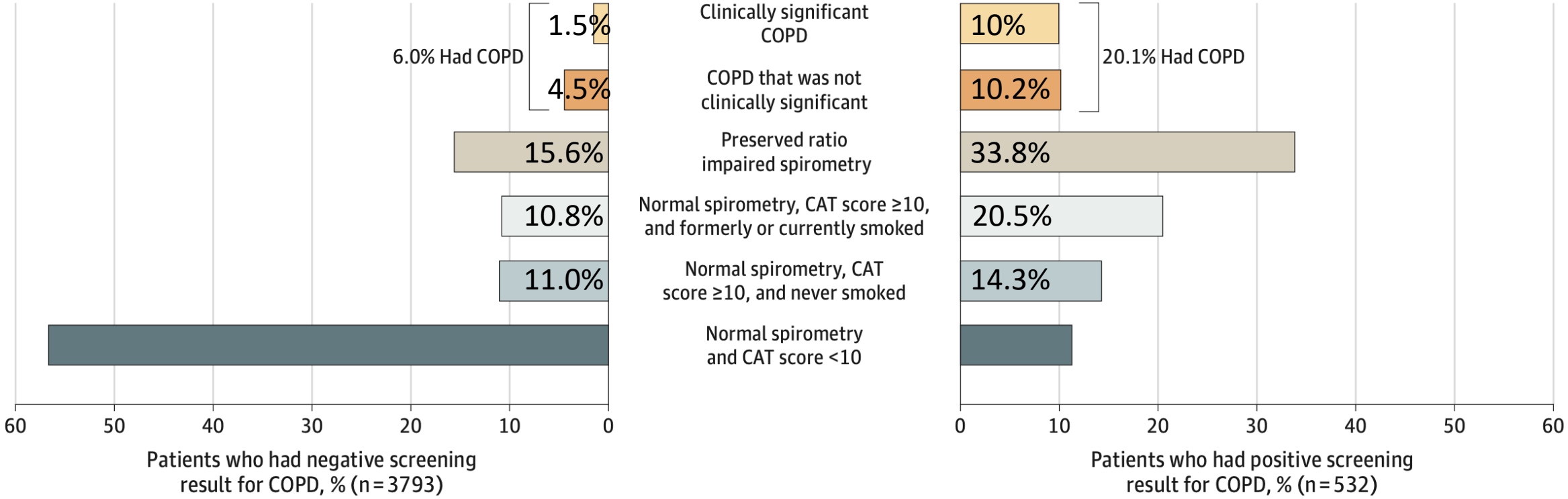
- For all study patients aged 45-80 years without a prior COPD diagnosis (n = 4,679)
  - 51.1% healthy
  - 17.8% PRISM
  - 12.0% symptomatic, normal spirometry, former/current smoker
  - 11.4% symptomatic, normal spirometry, never smoker
  - 5.2% non-clinically significant COPD
  - 2.5% clinically significant COPD

- **CAPTURE**

  Sensitivity 48.2% (95% CI, 38.6–57.9%)

  Specificity 88.6% (95% CI, 87.6–89.6%)

Figure 3. Spirometry- and Symptom-Based Classification of Patients With a Positive or Negative Screening Result for Detecting Clinically Significant Chronic Obstructive Pulmonary Disease (COPD)



Individuals with a variety of alternate respiratory diagnoses

ORIGINAL ARTICLE

Use of CAPTURE to Identify Individuals Who May or May Not Require Treatment for Chronic Obstructive Pulmonary Disease

Yun Li[1], Fuqiang Wen[2], Qianli Ma[3], Rongchang Chen[4], Yongchang Sun[5], Tiantian Liu[6], Chenjuan Gu[6], Shuling Hu[6], Jie Song[6], Chris Compton[7], Jinping Zheng[1], Nanshan Zhong[1], and Paul Jones[7]

Prospective COPD cohort study in China

- Usefulness of CAPTURE for identifying patients **who meet treatment thresholds** based on the level of symptoms and history of exacerbations or hospitalizations without the use of a spirometric severity criterion

- The cohort consists of individuals with COPD (85%), chronic bronchitis, and healthy never-smokers

Li Y et al. Am J Respir Crit Care Med 2023 Aug

Category	Questionnaire Score	PEF
Questions	⩾2	⩾250 L/min (female); ⩾350 L/min (male)
Questions + PEF	⩾2	<250 L/min (female); <350 L/min (male)
Variant 1	<2	⩾250 L/min (female); ⩾350 L/min (male)
Variant 1 + PEF	<2	<250 L/min (female); <350 L/min (male)
Variant 2	2–4	⩾250 L/min (female); ⩾350 L/min (male)
Variant 2 + PEF	2–4	<250 L/min (female); <350 L/min (male)
Variant 3	5/6	⩾250 L/min (female); ⩾350 L/min (male)
Variant 3 + PEF	5/6	<250 L/min (female); <350 L/min (male)

Chronic bronchitis
Healthy control

Table 3. Sensitivity of CAPTURE and Variants) to Detect COPD of Different Grades of Severity

	GOLD I vs. Control	GOLD II vs. Control	GOLD III vs. Control	GOLD IV vs. Control
Questions*	40.4 (35.8–45.0)	16.1 (13.8–18.5)	0.4 (0.0–2.5)	0.0 (0.0–3.7)
Questions + PEF*	17.1 (13.6–20.7)	59.1 (56.0–62.3)	89.2 (85.2–93.3)	95.9 (89.9–98.9)
Variant 1	32.0 (27.6–36.3)	7.8 (6.1–9.5)	0.0 (0.0–1.6)	0.0 (0.0–3.7)
Variant 1 + PEF	10.5 (7.6–13.4)	17.0 (14.6–19.4)	10.3 (6.3–14.3)	4.1 (1.1–10.1)
Variant 2	38.4 (33.8–42.9)	15.4 (13.1–17.7)	0.4 (0.0–2.5)	0.0 (0.0–3.7)
Variant 2 + PEF	14.6 (11.3–17.9)	51.0 (47.8–54.2)	72.2 (66.3–78.1)	65.3 (55.9–74.7)
Variant 3	2.1 (0.7–3.4)	0.7 (0.2–1.3)	0.0 (0.0–1.6)	0.0 (0.0–3.7)
Version 3 + PEF	2.5 (1.0–4.0)	8.1 (6.4–9.9)	17.0 (12.1–22.0)	30.6 (21.5–39.7)

Sensitivity 63.5–85.6%

Specificity 55.6–64.0%

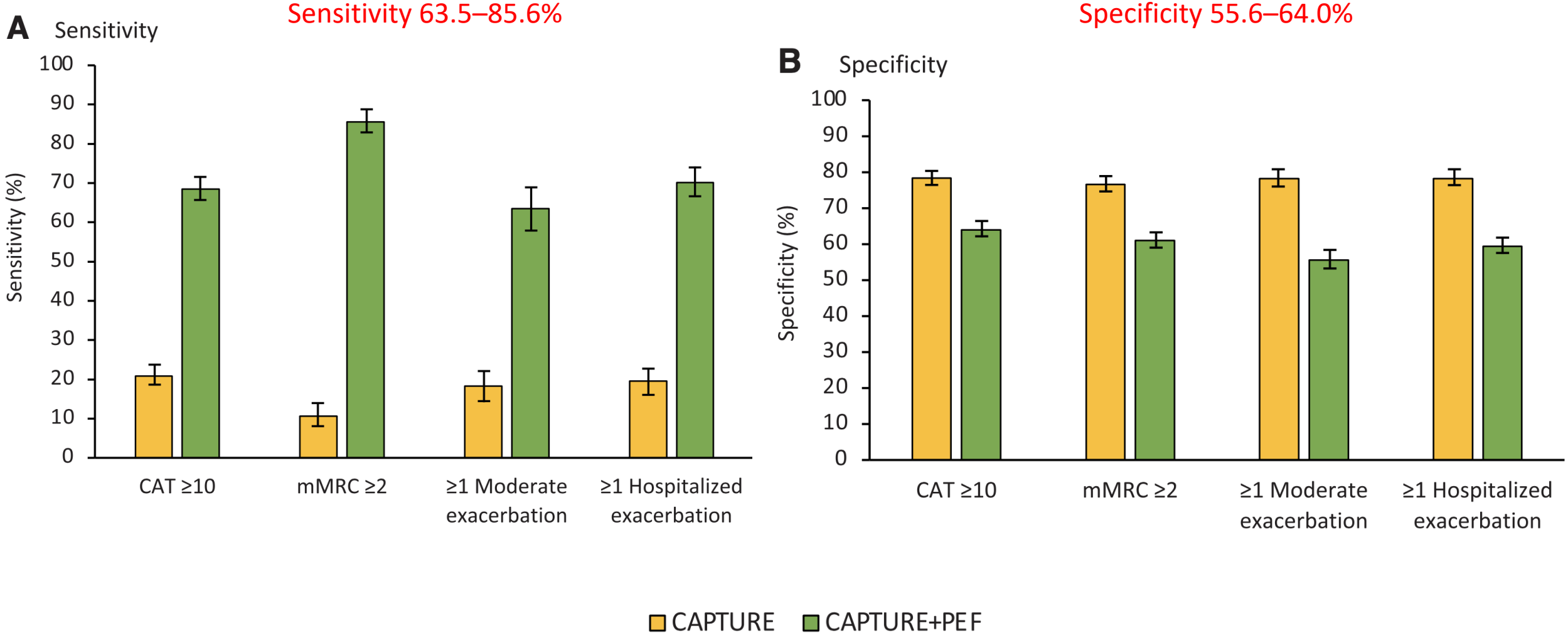


Table 6. PPV and NPV for Questions and PEF to Detect CAT (≥10 vs <10), mMRC (≥2 vs <2) and Exacerbations in the Previous Year (≥1 vs 0). Values are Mean (95% CI)

	CAT	mMRC	Moderate exacerbations	Severe exacerbations
PPV	47.8 (44.6–51.0)	29.9 (27.0–32.8)	15.6 (13.3–18.0)	30.3 (27.4–33.3)
NPV	80.8 (78.5–83.2)	95.6 (94.4–96.8)	92.1 (90.5–93.8)	88.8 (86.9–90.7)

- CAPTURE was developed to identify COPD patients with FEV_1 <60% in unselected primary care setting

- CAPTURE had **low PPV** but had **good NPV** for detecting **treatment-requiring COPD**
  - High NPV values give confidence that the **risk of missing a patient** with COPD who needs treatment is low
  - As prevalence decreases, NPV increases; therefore, it is unlikely to miss an individual who requires treatment for their COPD in a routine practice setting

- PEF was an essential component
  - Recommend the use of mini peak flow meters for case finding in community settings

ORIGINAL ARTICLE

FEV_1/FVC Severity Stages for Chronic Obstructive Pulmonary Disease

Surya P. Bhatt[1,2], Arie Nakhmani[1,3], Spyridon Fortis[4], Matthew J. Strand[5], Edwin K. Silverman[6], Frank C. Sciurba[7*], and Sandeep Bodduluri[1,2*]

COPDGene + Pittsburgh cohort

A new severity classification (STaging of Airflow obstruction by Ratio; STAR)

- Compared to the GOLD severity staging (based on FEV_1)
- FEV_1/FVC ratio
  1) 0.60 – 0.70
  2) 0.50 – 0.60
  3) 0.40 – 0.50
  4) <0.40

Mild	$FEV_1 \geq 80\%$ predicted
Moderate	$50\% \leq FEV_1 < 80\%$ predicted
Severe	$30\% \leq FEV_1 < 50\%$ predicted
Very Severe	$FEV_1 < 30\%$ predicted

Bhatt SP et al. Am J Respir Crit Care Med 2023 Sep

Major redistributions

GOLD 2 → STAR 1

GOLD 2 → STAR 3

GOLD 3 → STAR 2

GOLD 3 → STAR 4

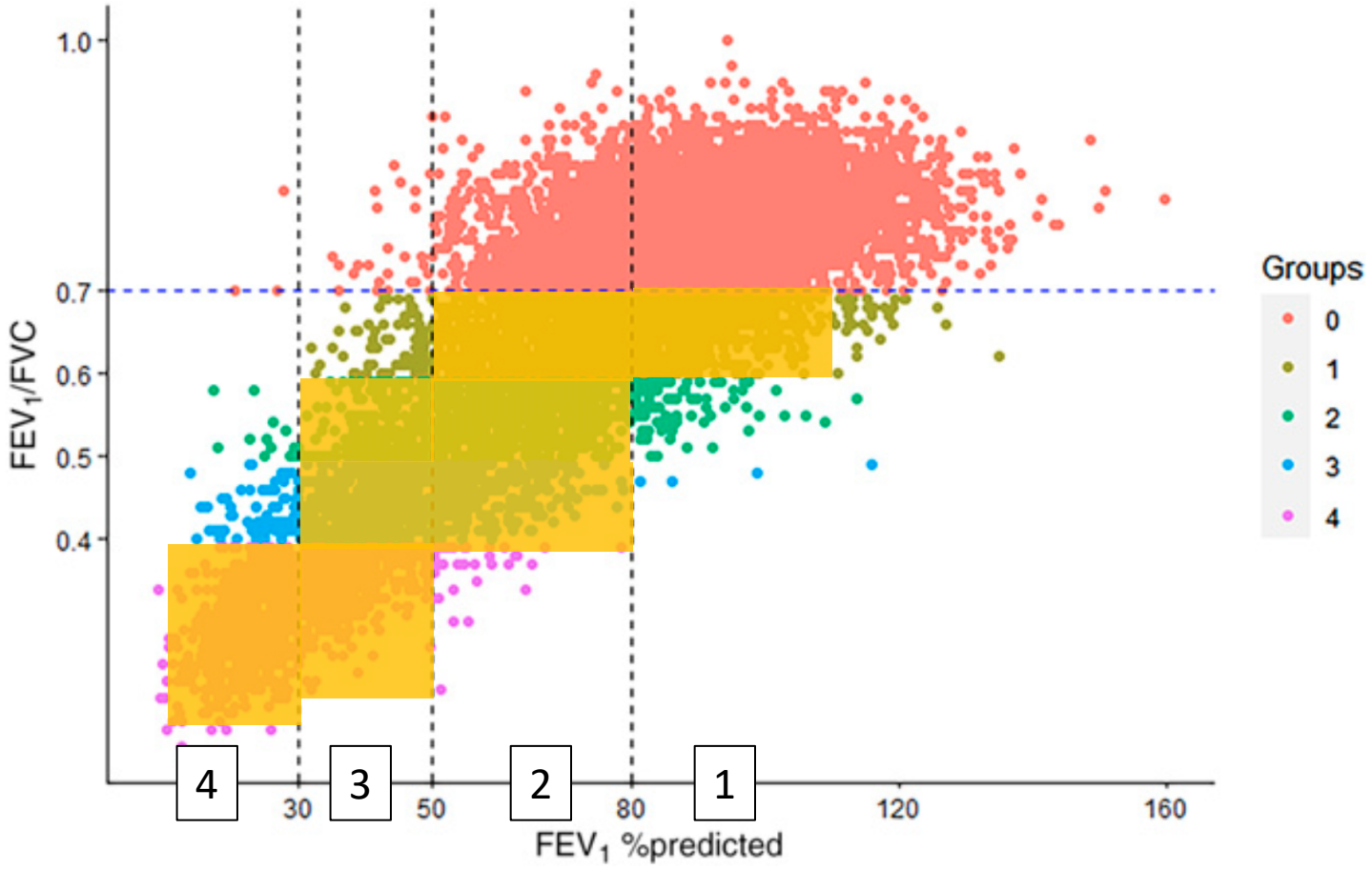
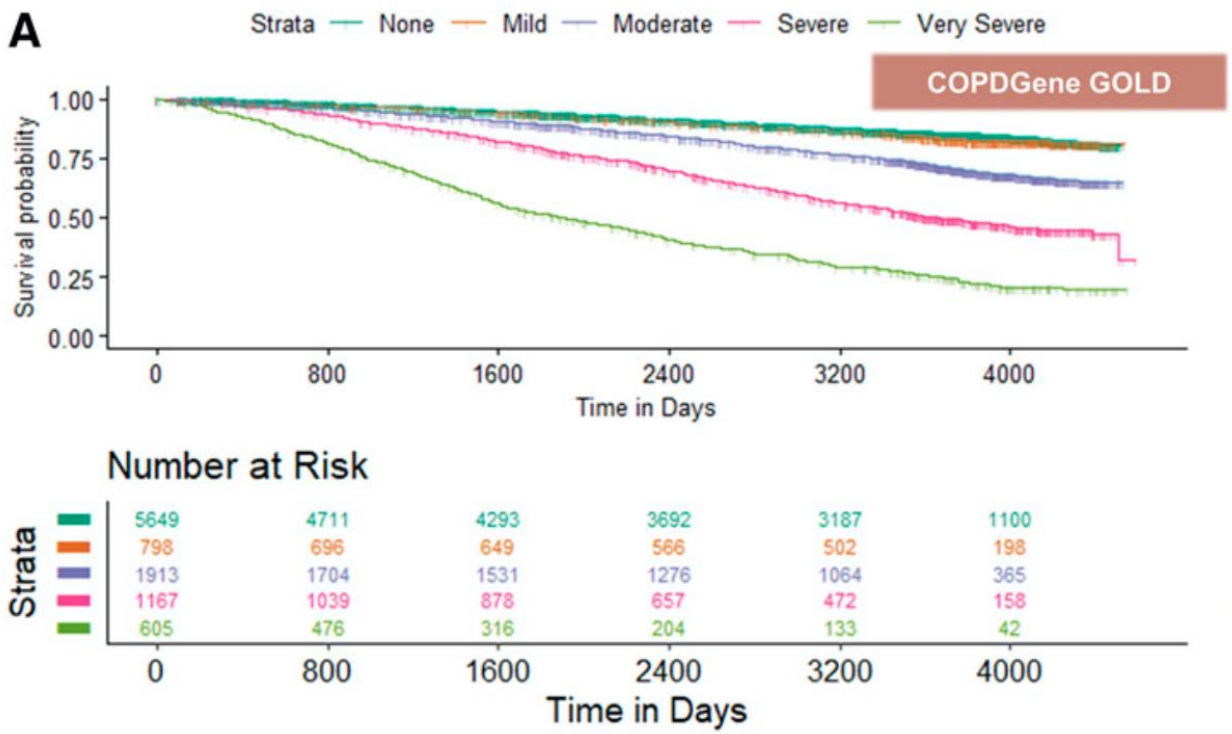


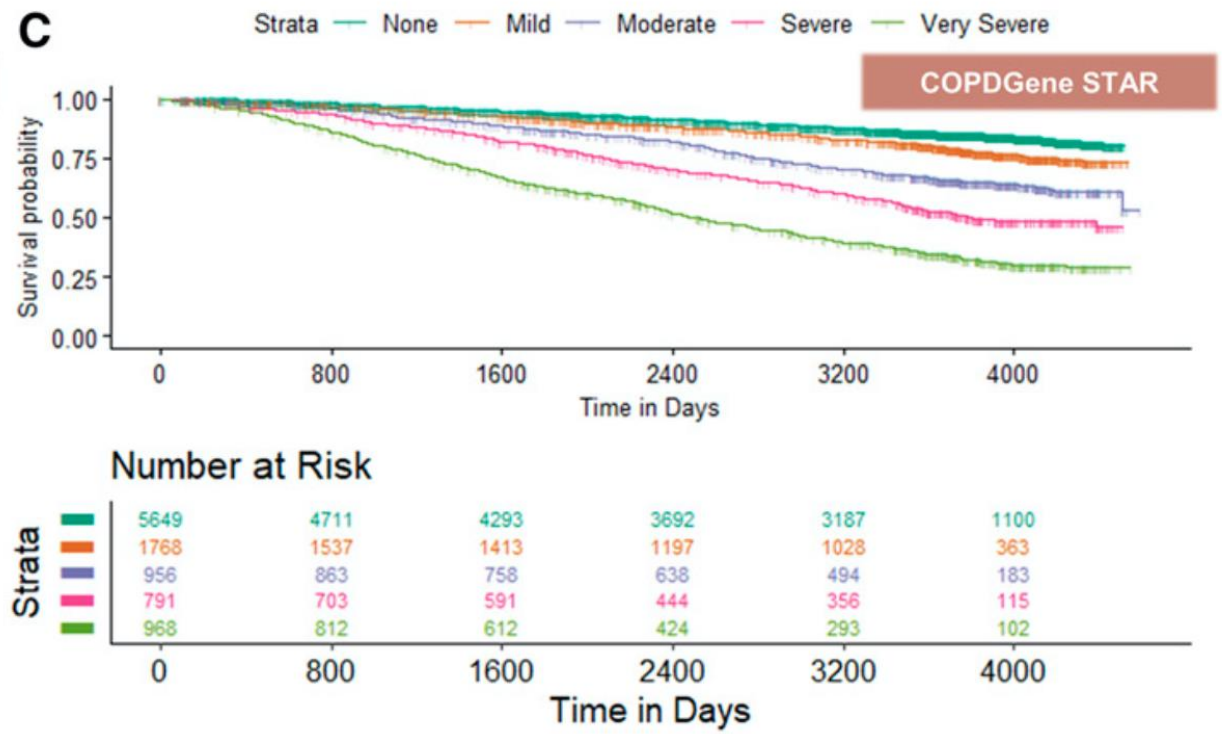
Figure 1. Distribution of disease severity by Global Initiative for Chronic Obstructive Lung Disease stage and STaging of Airflow obstruction using Ratio (STAR) severity category in the COPDGene (Genetic Epidemiology of COPD) study. Groups are STAR severity stages. COPD = chronic obstructive pulmonary disease.

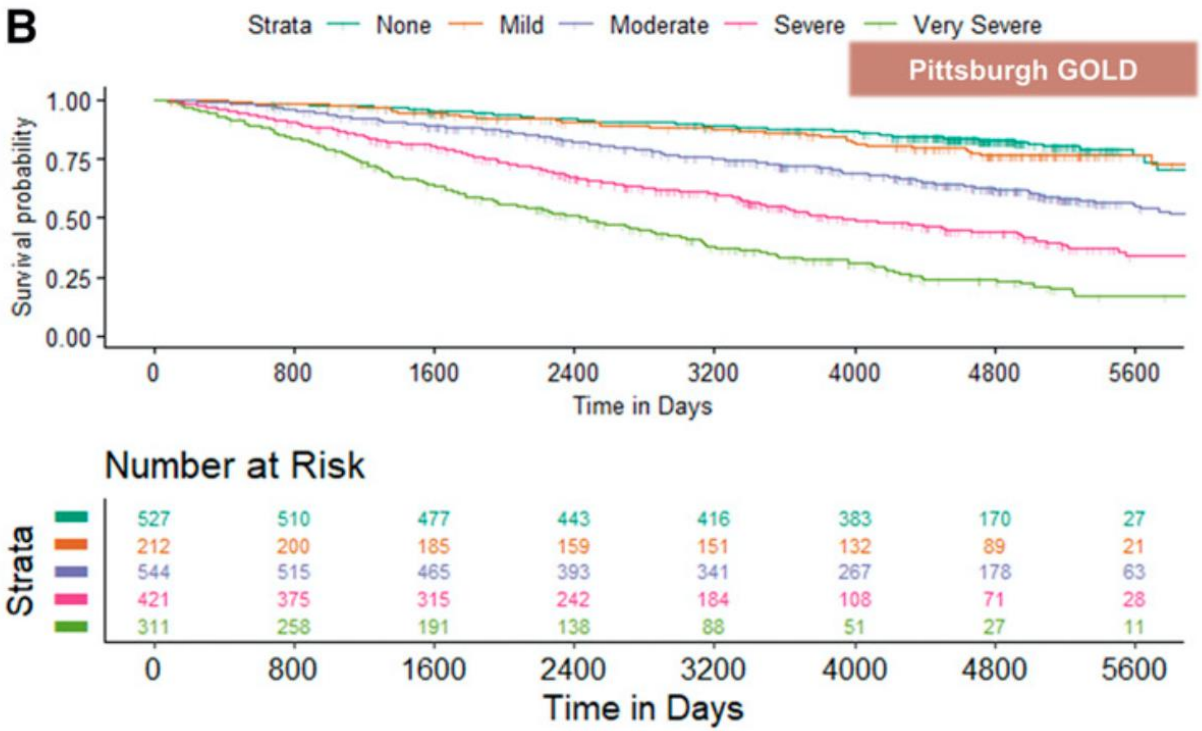
GOLD stage	STAR Stage	COPD Gene	Pittsburgh
1	1	87.5%	84.0%
	2	12.0%	15.5%
	3	0.5%	0.5%
	4	0%	0%
2	1	51.5%	32.2%
	2	32.8%	39.5%
	3	13.7%	24.1%
	4	2.0%	4.2%
3	1	7.3%	2.9%
	2	18.9%	10.5%
	3	39.2%	34.7%
	4	34.6%	52.0%
4	1	0%	0%
	2	1.8%	1.3%
	3	11.2%	6.8%
	4	86.9%	92.0%

None vs. Mild



None vs. Mild




B
Strata None Mild Moderate Severe Very Severe
Pittsburgh GOLD
Survival probability
1.00
0.75
0.50
0.25
0.00
0 800 1600 2400 3200 4000 4800 5600
Time in Days
Number at Risk
Strata
527 510 477 443 416 383 170 27
212 200 185 159 151 132 89 21
544 515 465 393 341 267 178 63
421 375 315 242 184 108 71 28
311 258 191 138 88 51 27 11
0 800 1600 2400 3200 4000 4800 5600
Time in Days

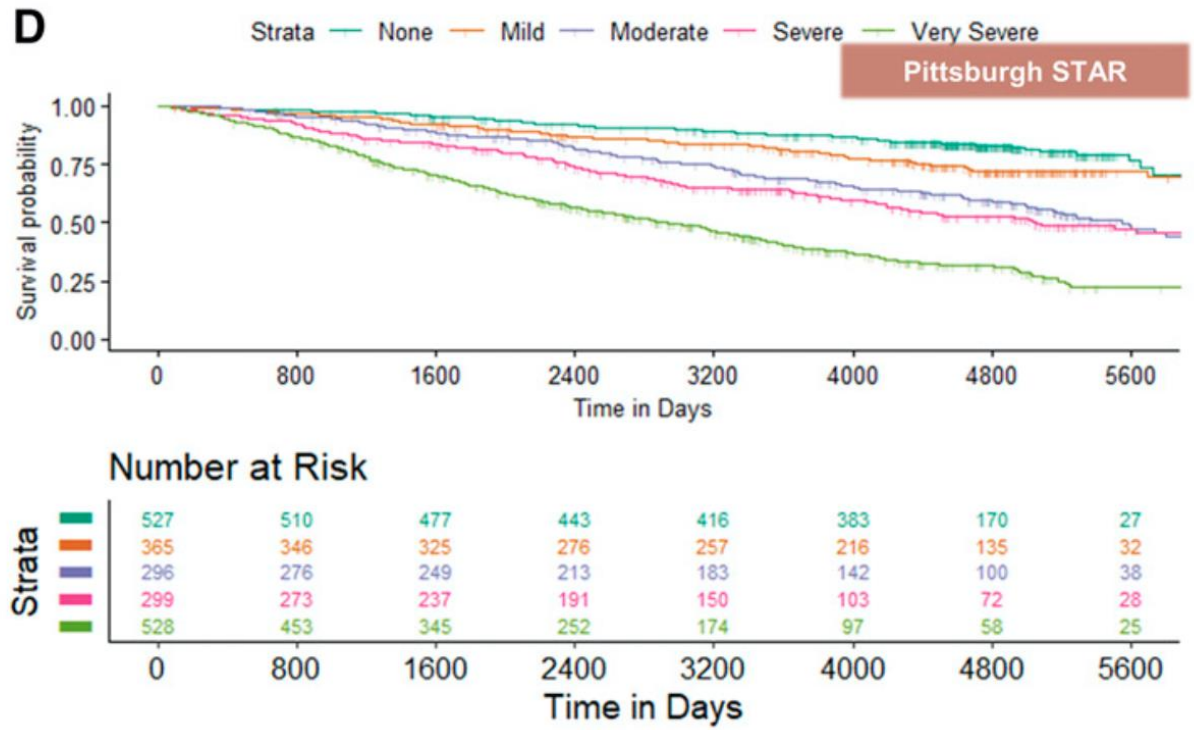

D
Strata None Mild Moderate Severe Very Severe
Pittsburgh STAR
Survival probability
1.00
0.75
0.50
0.25
0.00
0 800 1600 2400 3200 4000 4800 5600
Time in Days
Number at Risk
Strata
527 510 477 443 416 383 170 27
365 346 325 276 257 216 135 32
296 276 249 213 183 142 100 38
299 273 237 191 150 103 72 28
528 453 345 252 174 97 58 25
0 800 1600 2400 3200 4000 4800 5600
Time in Days

Table 1. Comparison of All-cause Mortality by Severity Stage

	COPDGene				Pittsburgh			
	Unadjusted HR (95% CI)		Adjusted HR* (95% CI)		Unadjusted HR (95% CI)		Adjusted HR* (95% CI)	
Stage	GOLD	STAR	GOLD	STAR	GOLD	STAR	GOLD	STAR
1	1.11† (0.91–1.35)	1.47 (1.29–1.68)	0.95† (0.78–1.17)	1.34 (1.66–1.53)	1.28* (0.89–1.84)	1.64 (1.22–2.19)	1.02† (0.71–1.48)	1.49 (1.11–1.99)
2	2.09 (1.86–2.35)	2.52 (2.19–2.89)	1.77 (1.57–1.99)	2.15 (1.87–2.48)	2.43 (1.89–3.13)	2.76 (2.10–3.63)	2.18 (1.69–2.80)	2.40 (1.82–3.16)
3	4.20 (3.75–4.72)	3.92 (3.44–4.47)	3.42 (3.05–3.87)	3.25 (2.84–3.73)	4.38 (3.41–5.63)	3.32 (2.53–4.35)	3.98 (3.09–5.12)	3.09 (2.35–4.06)
4	9.41 (8.32–10.64)	6.89 (6.17–7.70)	7.92 (6.98–8.98)	5.79 (5.15–6.51)	7.73 (6.02–9.94)	6.32 (4.98–8.02)	7.32 (7.67–9.44)	5.65 (4.43–7.19)

Reference: no airflow obstruction

*Model adjusted for age, sex, race, and height

- The greatest discrepancy in classification lay between GOLD 1 and STAR 1 grades
- **Mortality in the STAR grade 1 was higher** than that in individuals without COPD, whereas there was no difference between non-COPD and GOLD 1 patients

- STAR stage seems to be more useful in milder COPD patients
- Offer some important insights, particularly **about the transition** from normal lung function to established COPD

- View the FEV_1/FVC ratio **as a continuous variable** rather than a simple threshold used to identify those with airflow obstruction

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
M.J. DIVO ET AL.

From pre-COPD to COPD: a Simple, Low cost and easy to IMplement (SLIM) risk calculator

Miguel J. Divo [1], Congjian Liu [1], Francesca Polverino [2], Peter J. Castaldi [3,4], Bartolome R. Celli [1,5] and Yohannes Tesfaigzi [1,5]

Lovelace Smokers' Cohort

- 677 participants with normal spirometry at baseline and a minimum of three spirometries, each 1 year apart
- Building a practical predictive model for developing chronic airflow limitation
- Validated in the COPDGene cohort

Divo MJ et al. Eur Respir J 2023 Sep

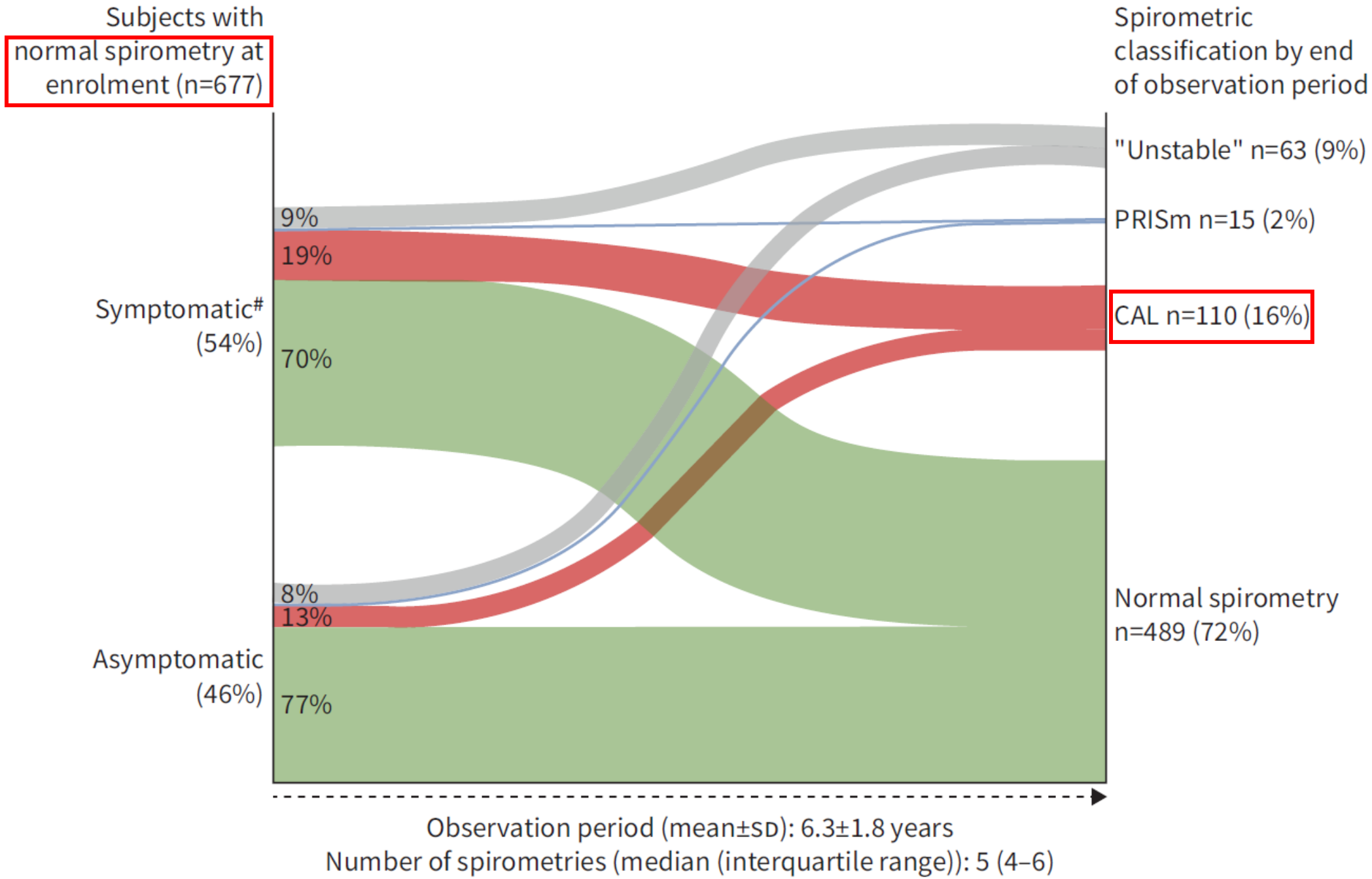

Subjects with normal spirometry at enrolment (n=677)
Spirometric classification by end of observation period
Symptomatic# (54%)
Asymptomatic (46%)
9%
19%
70%
8%
13%
77%
"Unstable" n=63 (9%)
PRISm n=15 (2%)
CAL n=110 (16%)
Normal spirometry n=489 (72%)
Observation period (mean±SD): 6.3±1.8 years
Number of spirometries (median (interquartile range)): 5 (4–6)

TABLE 1 Baseline characteristics of the Lovelace Smokers' Cohort (LSC) (derivation cohort) and the subjects of the COPDGene cohort (validation cohort)

	LSC (n=677)	COPDGene (n=830)
Age (years)	54±9	57±8
Female	571 (82)	435 (52)
Race/ethnicity		
White	508 (75)	558 (67)
Hispanic	125 (18)	
Black (African American)		272 (33)
BMI ($kg \cdot m^{-2}$)	28.0±5.4	28.9±5.6
Current smoker	346 (51)	453 (45)
Pack-years of smoking	35±18	38±19
Age of smoking initiation (years)	17±4	17±2
Pre-COPD[#]	273 (54)	416 (50)
Spirometries (n)	5 (4–6)	3
FEV_1/FVC	0.79±0.05	0.79±0.05
FEV_1 (L)	2.8±0.6	2.9±0.7
FEV_1 (% pred)	97±10	98±11
Follow-up (years)	6.3±1.8	10.1±0.6

[#]Pre-COPD: normal spirometry + chronic sputum production, cough, or mMRC grade >2

TABLE 4 Estimates (odd ratios) and weight of predictors for the incidence of chronic airway limitation analysed by multivariate logistic regression in the Lovelace Smokers' Cohort

	OR (95% CI)	p-value	Total effect on model
Model 2			
FEV1/FVC <0.75	13.75 (8.15–23.17)	<0.0001	0.72
⩾30 pack-years cumulative smoking	3.38 (1.94–5.89)	<0.0001	0.15
BMI ⩽25 kg·m^{-2}	2.41 (1.43–4.06)	0.001	
FEV1 % pred <100%	2.07 (1.17–3.67)	0.0130	
Chronic bronchitis (yes)	1.89 (1.09–3.27)	0.0231	
Model 3			
FEV_1/FVC <0.75	15.32 (9.14–25.69)	<0.0001	0.80
⩾30 pack-years cumulative smoking	3.38 (1.96–5.86)	<0.0001	0.15
BMI ⩽25 kg·m^{-2}	2.40 (1.43–4.03)	0.0009	0.07
Chronic bronchitis (yes)	1.87 (1.09–3.22)	0.0234	0.04

Sn 72% Sp 85%
PPV 52% NPV 93%

Model 2: continuous variables dichotomised and five predictors; model 3: continuous variables dichotomised and four predictors (parsimonious model). FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; BMI: body mass index.

FEV_1/FVC <0.75	≥30 pack-years	BMI ≤25 kg·m^{-2}	Chronic bronchitis (yes)	Probability of incident CAL (%) / Probability maintaining normal lung function (%)
+	+	+	+	85% / 15%
+	+	+	–	76% / 24%
+	+	–	+	71% / 29%
+	–	+	+	63% / 37%
+	+	–	–	56% / 44%
+	–	+	–	48% / 52%
+	–	–	+	42% / 58%
+	–	–	–	28% / 72%
–	+	+	+	27% / 73%
–	+	+	–	17% / 83%
–	+	–	+	14% / 86%
–	–	+	+	10% / 90%
–	+	–	–	8% / 92%
–	–	+	–	6% / 94%
–	–	–	+	4% / 96%
–	–	–	–	2% / 98%

Your COPD risk at 6 year is _____%

CHEST

Bronchodilator Responsiveness in Tobacco-Exposed People With or Without COPD

*Spyridon Fortis, MD; Pedro M. Quibrera; Alejandro P. Comellas; Surya P. Bhatt; Donald P. Tashkin; Eric A. Hoffman; Gerard J. Criner; MeiLan K. Han; R. Graham Barr; Mehrdad Arjomandi; Mark B. Dransfield; Stephen P. Peters; Brett A. Dolezal; Victor Kim; Nirupama Putcha; Stephen I. Rennard; Robert Paine III; Richard E. Kanner; Jeffrey L. Curtis; Russell P. Bowler; Fernando J. Martinez; Nadia N. Hansel; Jerry A. Krishnan; Prescott G. Woodruff; Igor Z. Barjaktarevic; David Couper; Wayne H. Anderson; and Christopher B. Cooper; for the Subpopulations and Intermediate Outcome Measures in COPD Study Investigators**

SPIROMICS

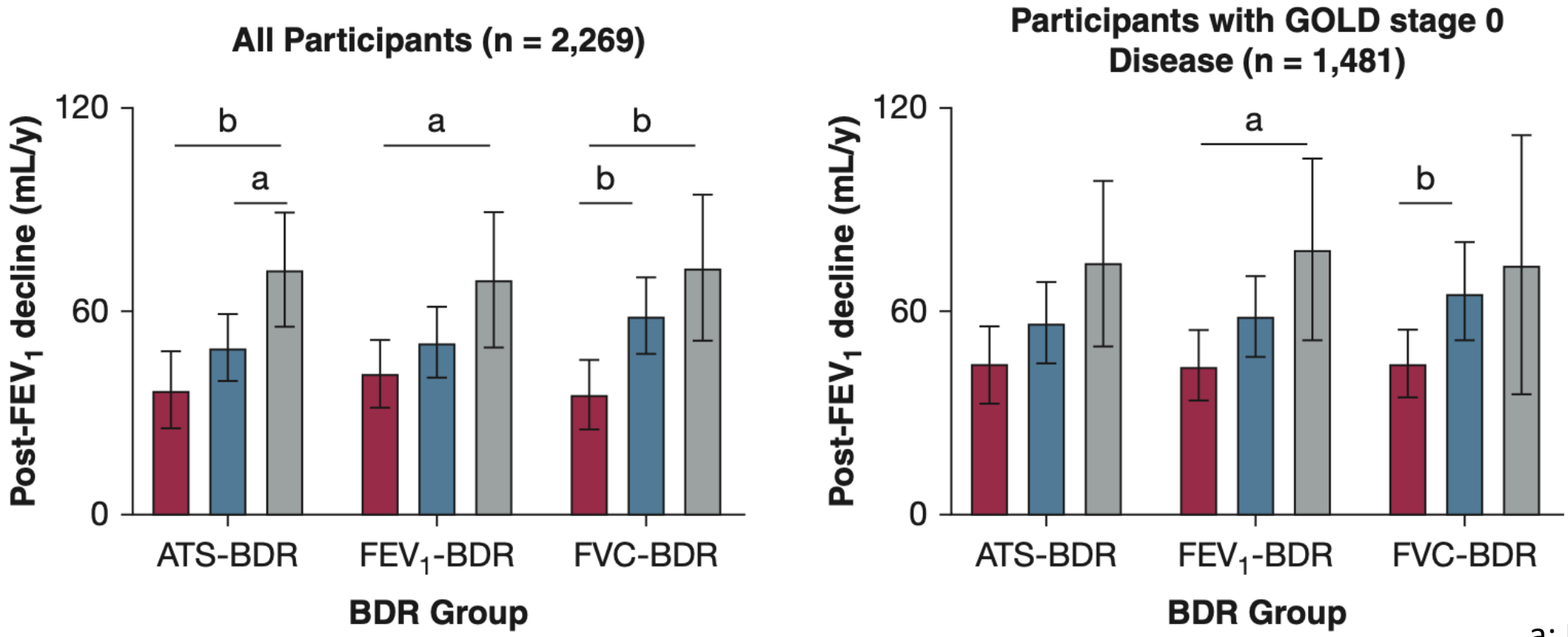
- 2,269 tobacco-exposed participants with or without COPD
- BDR definition: change of ≥200 mL and ≥12% in FEV_1 and/or FVC
- BDR classification
  (1) consistent BDR, (2) inconsistent BDR, and (3) never BDR

Fortis S et al. Chest 2023 Mar

TABLE 1] Baseline Characteristics of Participants With GOLD Stage 0 Disease[a] Categorized by Bronchodilator Responsiveness (n = 1,481)

Characteristics at Visit 1	ATS-BDR			*P* Value[b]
	Never	Inconsistent	Consistent	
No. of patients	725	629	127	. . .
Age, y	62.7 ± 9.5	64.0 ± 8.9	63.5 ± 8.6	.026
Female sex	334 (46.1)	301 (47.9)	51 (40.2)	.28
White race	547 (75.4)	486 (77.3)	108 (85.0)	.06
BMI, kg/m^2	28.7 ± 5.1	28.6 ± 5.2	28.6 ± 5.4	.94
Pack-years of smoking	45.3 ± 26.4	48.3 ± 23.0	52.3 ± 22.8	.004
Current individuals who smoke	288 (40.1)	261 (42.4)	61 (48.4)	.20
Asthma	91 (12.6)	136 (21.6)	27 (21.3)	< .001
Childhood asthma	33 (4.6)	69 (11.0)	12 (9.4)	< .001
Bronchodilator	186 (25.9)	262 (42.1)	61 (48.4)	< .001
Inhaled corticosteroids	106 (14.8)	162 (26.0)	37 (29.6)	< .001

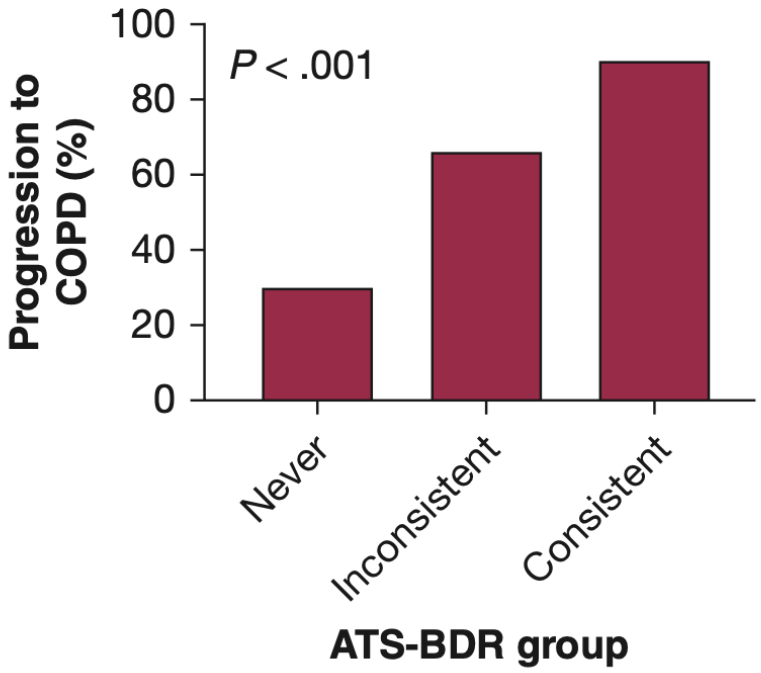
Lung function decline

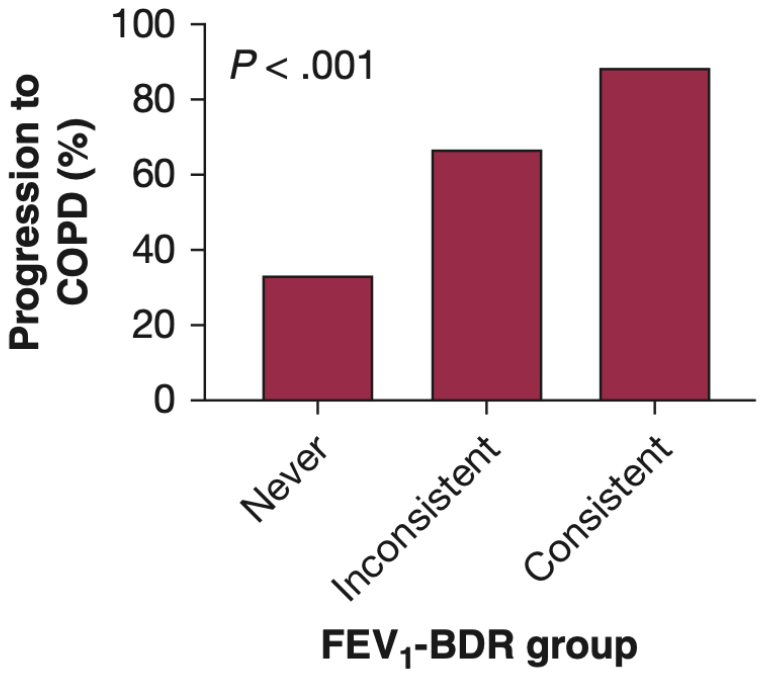


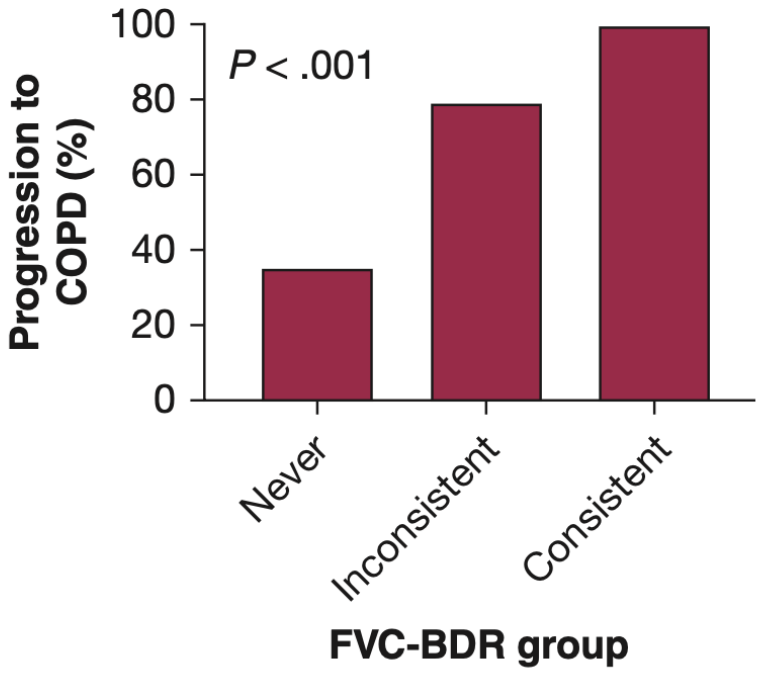
AST-BDR	
Never	–44 mL/y
Inconsistent	–66 mL/y
Consistent	–79 mL/y

a: P <0.05
b: P <0.01

Progression to COPD







- First study examining the association of **BDR over time** with clinical features
- Inconsistent and consistent BDR
  - Associated with self-reported history of asthma
  - Greater lung function decline

- **Small airways smooth muscle pathologic features** playing a role in the **inflammatory** and **remodeling** process of the airway

- BDR even at one visit (inconsistent BDR) describes an obstructive lung disease phenotype with a history of asthma and small airways disease

- Consistent BDR provides additional characterization of this phenotyping by indicating a high risk of lung function decline over time

Radiology

ORIGINAL RESEARCH • THORACIC IMAGING

Radiomics for Improved Detection of Chronic Obstructive Pulmonary Disease in Low-Dose and Standard-Dose Chest CT Scans

Praneeth Reddy Amudala Puchakayala, MS • Venkata L. Sthanam, MS • Arie Nakhmani, PhD • Muhammad F. A. Chaudhary, BS • Abhilash Kizhakke Puliyakote, PhD • Joseph M. Reinhardt, PhD • Chengcui Zhang, PhD • Surya P. Bhatt, MD, MSPH • Sandeep Bodduluri, PhD**

COPDGene study

- To determine if radiomics features (related to lung parenchymal texture and air-way geometry) from inspiratory CT scans can be used to detect the presence of COPD
- PyRadiomics (open-source Python package) was used to extract features from the lung regions identified by the lung and airway mask
- Using standard CT and low-dose CT

Amudala Puchakayala PR et al. Radiology 2023 Jun

Table 2: COPD Detection Results for Model I Using Standard-Dose CT Data

Feature	AUC	PRAUC	Brier Score	PPV	NPV	*P* Value
Demographics	0.73 (0.71, 0.76)	0.70	0.21	0.65	0.69	<.001
CT emphysema	0.82 (0.80, 0.84)	0.82	0.17	0.78	0.73	<.001
Radiomics	0.90 (0.88, 0.91)	0.91	0.12	0.83	0.83	Reference
Combined	0.90 (0.89, 0.92)	0.91	0.12	0.86	0.83	.16

Note.—Data in parentheses are 95% CIs. *P* values indicate AUCs compared using the DeLong method, with radiomics as the reference feature set. AUC = area under the receiver operating characteristic curve, COPD = chronic obstructive pulmonary disease, NPV = negative predictive value, PPV = positive predictive value, PRAUC = area under the precision-recall curve.

Table 4: COPD Detection Results for Model II Using Low-Dose CT Data

Feature	AUC	PRAUC	Brier Score	PPV	NPV	*P* Value
Demographics	0.70 (0.64, 0.75)	0.64	0.23	0.57	0.66	.001
CT emphysema	0.74 (0.69, 0.79)	0.72	0.20	0.63	0.72	.002
Radiomics	0.87 (0.83, 0.91)	0.88	0.14	0.79	0.80	Reference
Combined	0.88 (0.85, 0.92)	0.88	0.14	0.79	0.80	.32

Note.—Data in parentheses are 95% CIs. *P* values indicate AUCs compared using the DeLong method, with radiomics as the reference feature set. AUC = area under the receiver operating characteristic curve, COPD = chronic obstructive pulmonary disease, NPV = negative predictive value, PPV = positive predictive value, PRAUC = area under the precision-recall curve.

Table S1

Top 10 Radiomics Features Contributing to the Detection of COPD

High-Dose CT	Low-Dose CT
10th percentile of lung density	Sphericity of airways
Gray-level energy	Sphericity of right lung
Sphericity of airways	Normalized gray-level nonuniformity
Sphericity of right lung	10th percentile of lung density
Run-length entropy of gray levels	Sphericity of left lung
Complexity of lung texture	Low gray-level run emphasis
Minor axis length of airways	Airway surface area to volume ratio
Surface area of airways	Run-length entropy of gray levels
Normalized gray-level nonuniformity	Right lung flatness
Low gray-level run emphasis	Least axis length of airways

Texture features

Shape features

Summary

- **Preterm birth**

  COPD is linked to preterm gestational age and births classified as SGA

- **Indoor air pollution**

  Indoor air pollution is associated with rapid FEV_1 decline in former smokers

- **Childhood cigarette smoking**

  Initiation before the age of 15 has a greater risk of COPD

Summary

- **Screening and case finding studies**
  - CAPTURE has a low sensitivity for detecting clinically significant COPD in primary care setting
  - CAPTURE has a high negative predictability for COPD patients requiring treatment
- **New strategy using the FEV_1/FVC ratio severity**
  - STAR (FEV_1/FVC) grade may be more useful to differentiate non-COPD and mild COPD
- **Prediction of COPD development and lung function decline**
  - Prediction model with 4 clinical variables can be useful to predict a future COPD risk
  - Presence of BDR is related to rapid FEV_1 decline and COPD development
  - Prediction model with radiomics features has good accuracy for detecting COPD