COPD in Young People and Pre-COPD

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The Catholic University of Korea

Contents

- COPD in young people
  - Definition
  - Risk factors
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STATE OF THE ART

Treatment Trials in Young Patients with Chronic Obstructive Pulmonary Disease and Pre–Chronic Obstructive Pulmonary Disease Patients

Time to Move Forward

Fernando J. Martinez[1*‡], Alvar Agusti[2,3,4,5*], Bartolome R. Celli[6*], MeiLan K. Han[7], James P. Allinson[8‡], Surya P. Bhatt[9], Peter Calverley[10‡], Sanjay H. Chotirmall[11‡], Badrul Chowdhury[12], Patrick Darken[13], Carla A. Da Silva[14], Gavin Donaldson[8‡], Paul Dorinsky[13], Mark Dransfield[9], Rosa Faner[15], David M. Halpin[16], Paul Jones[17], Jerry A. Krishnan[18‡], Nicholas Locantore[19], Fernando D. Martinez[20‡], Hana Mullerova[21], David Price[22,23], Klaus F. Rabe[24,25‡], Colin Reisner[26], Dave Singh[27], Jørgen Vestbo[28], Claus F. Vogelmeier[29], Robert A. Wise[30], Ruth Tal-Singer[31‖], and Jadwiga A. Wedzicha[8‖‡]

Martinez FJ. Am J Respir Crit Care Med 2022; 205: 275-287.

Table 1. Nosology Used in This Review

Term	Definition

Martinez FJ. Am J Respir Crit Care Med 2022; 205: 275-287.

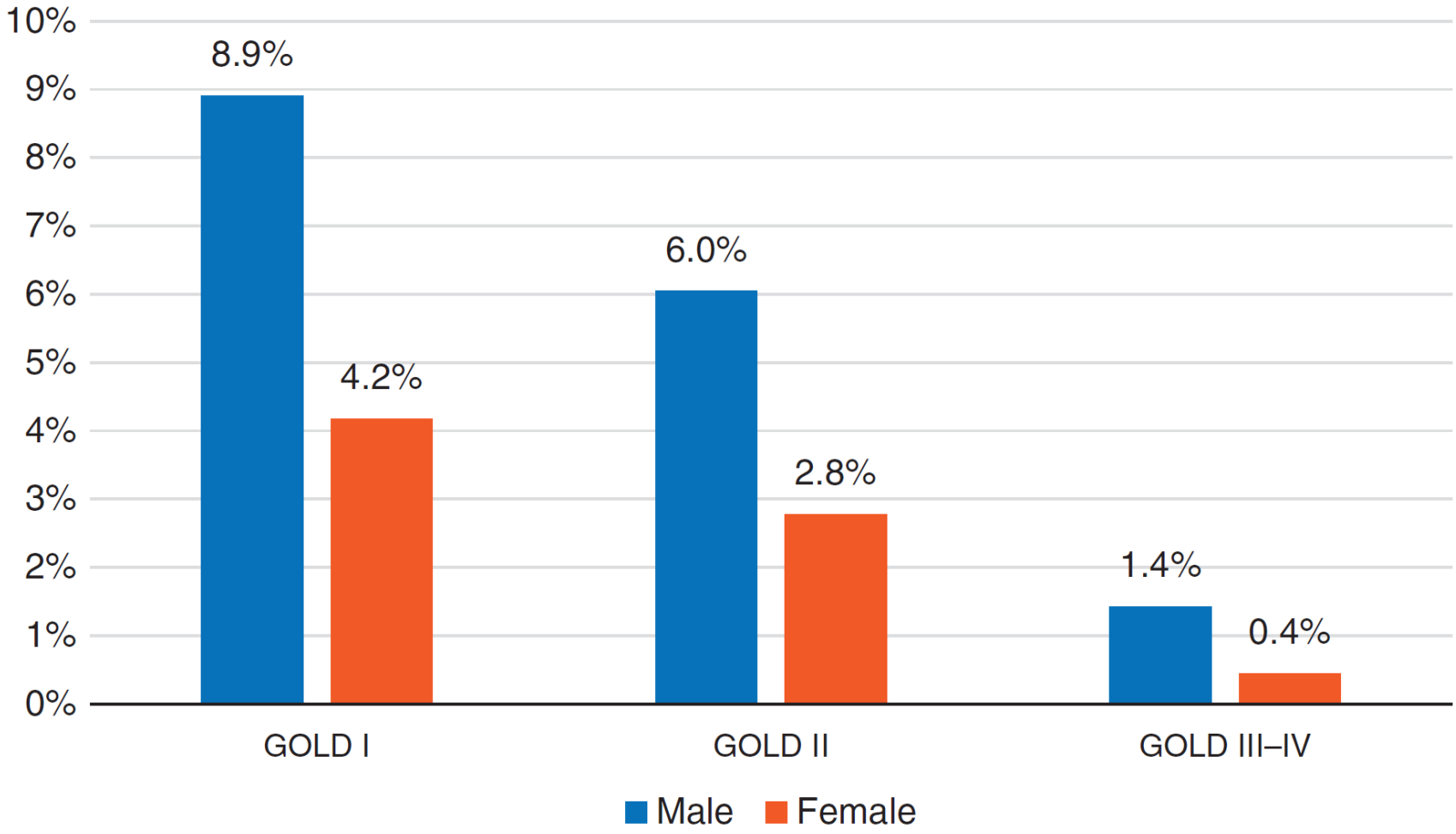


Figure 2. Prevalence of chronic obstructive pulmonary disease in young individuals (20–49 years) in the general population in China. Data are from Reference 44. GOLD = Global Initiative for Chronic Obstructive Lung Disease.

Table 3. Rate of FEV_1 Decline (ml/yr) Study Results

Study	Length (*yr*)	*n*	Mean FEV_1 (%)	Mean Age	Active	Placebo	Difference (95% CI)
SUMMIT (138)	1–4*	16,485	60	65	38	46	−8 (−15, −1)
Zhou and colleagues (15)	2	841	78	64	29	51	−22 (−37, −6)
Copenhagen CHS (166)	3	290	86	59	45	42	3 (−13, 19)
EUROSCOPE (167)	3	1,277	77	52	57	69	−12 NS
TORCH (168)	3	6,112	44	65	42/43/39	55	−16 (−25, −8)
BRONCUS (169)	3	523	57	62	56	47	8 (−10, 25)
ISOLDE (170)	3	751	50	64	50	59	−9 (−3, 20)
Lung Health Study II (171)	3.5–4.5*	1,116	68	56	44	47	−3 (−11, 5)
UPLIFT (40, 172)	4	5,993	48	65	40	42	−2 (−6, 2)
Lung Health Study I (68)	5	5,887	78	48	30	66	−31 UNK

Martinez FJ. Am J Respir Crit Care Med 2022; 205: 275-287.

ORIGINAL ARTICLE

Prevalence, Characteristics, and Prognosis of Early Chronic Obstructive Pulmonary Disease

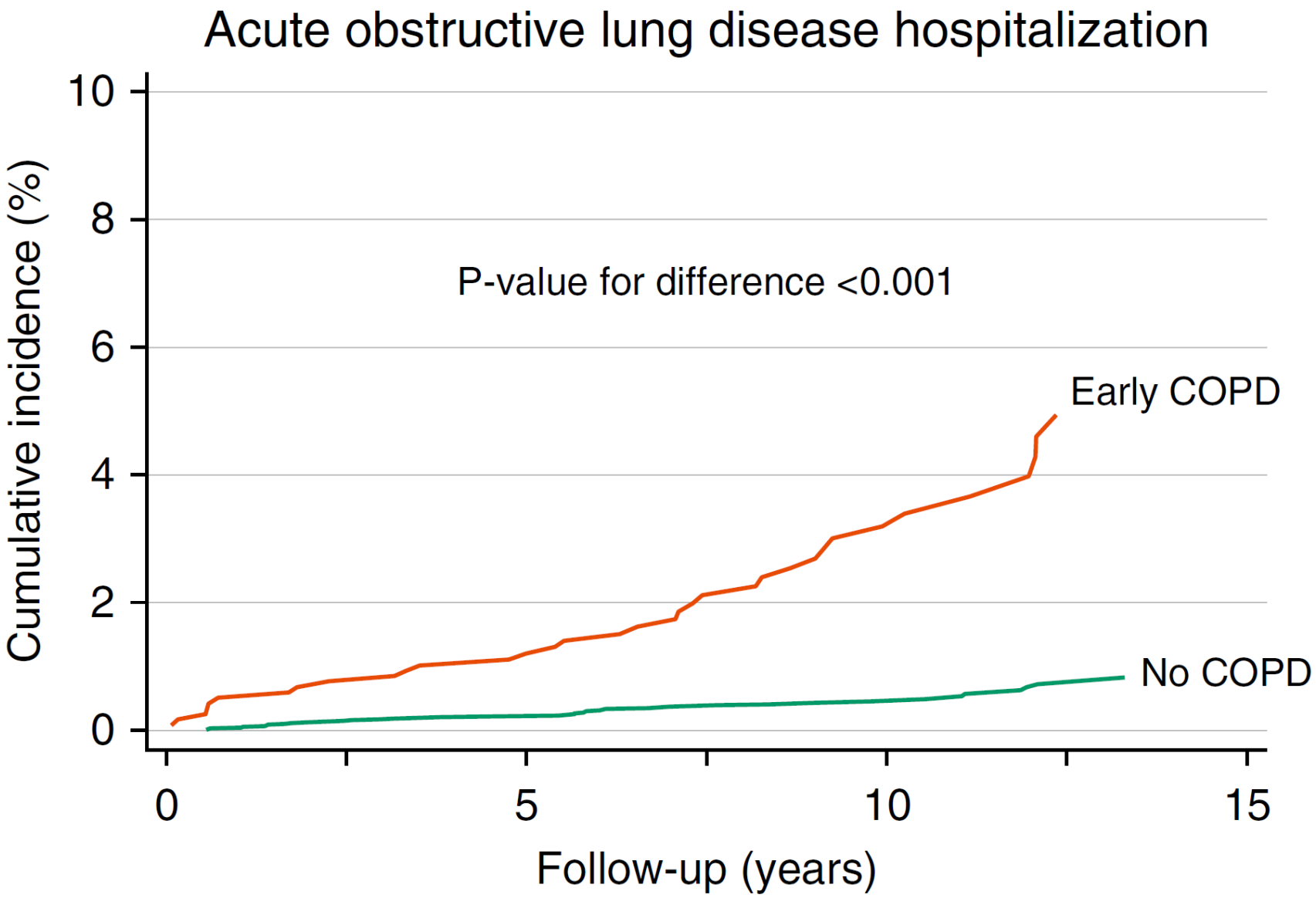
The Copenhagen General Population Study

Yunus Çolak[1,2,3], Shoaib Afzal[1,2,3], Børge G. Nordestgaard[1,2,3], Jørgen Vestbo[4], and Peter Lange[2,3,5,6]

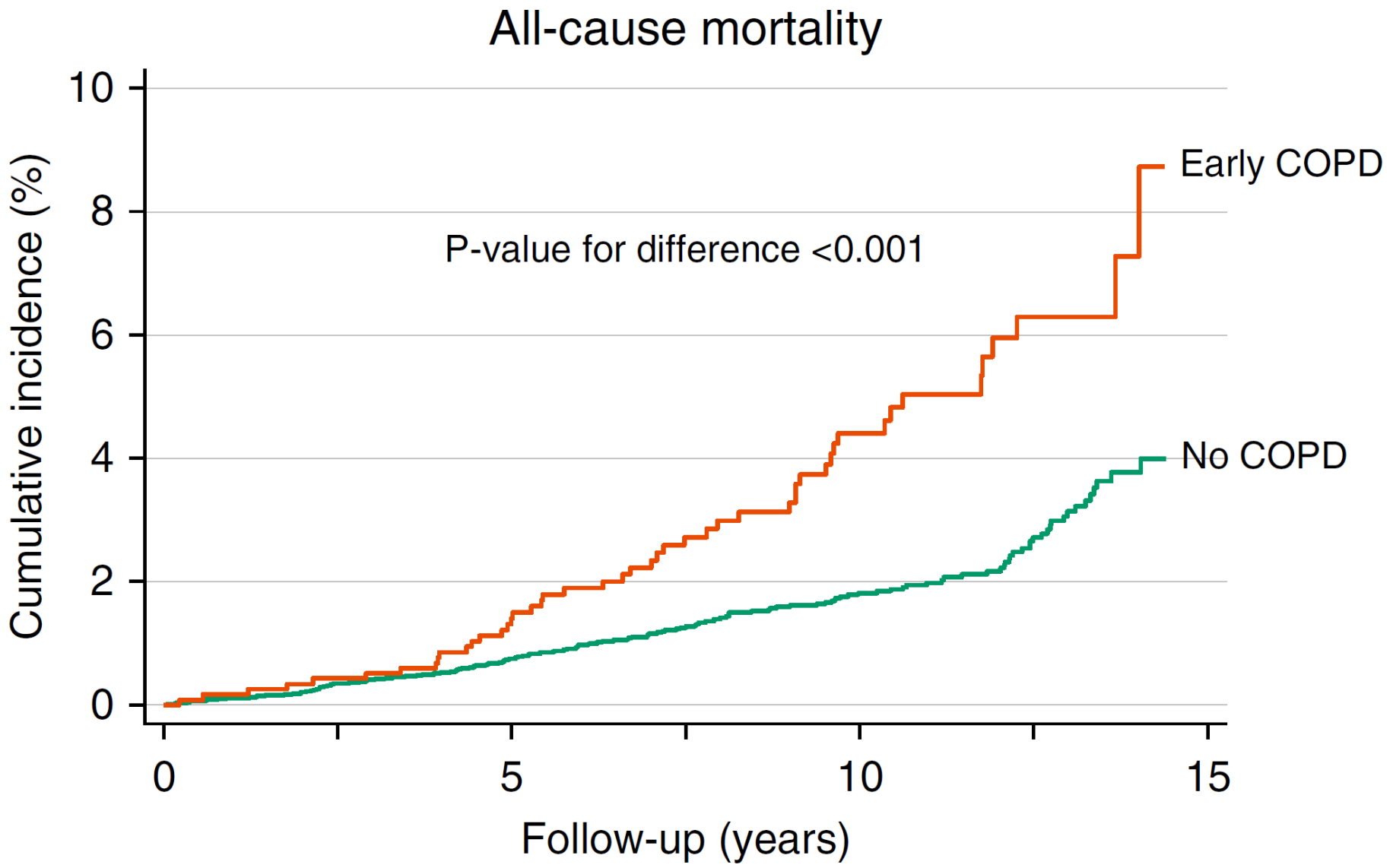
[1]Department of Clinical Biochemistry, [2]The Copenhagen General Population Study, and [6]Department of Internal Medicine, Section of Respiratory Medicine, Herlev and Gentofte Hospital, Copenhagen University Hospital, Herlev, Denmark; [3]Faculty of Health and Medical Sciences and [5]Department of Public Health, Section of Epidemiology, University of Copenhagen, Copenhagen, Denmark; and [4]Division of Infection, Immunity, and Respiratory Medicine, School of Biological Sciences, Manchester Academic Health Science Centre, University of Manchester, and Manchester University National Health Service Foundation Trust, Manchester, United Kingdom

Methods: We investigated 105,630 randomly chosen adults from a Danish contemporary population-based cohort. Early COPD was defined as FEV_1/FVC less than the lower limit of normal in individuals under 50 years of age with 10 pack-years or greater of tobacco consumption.

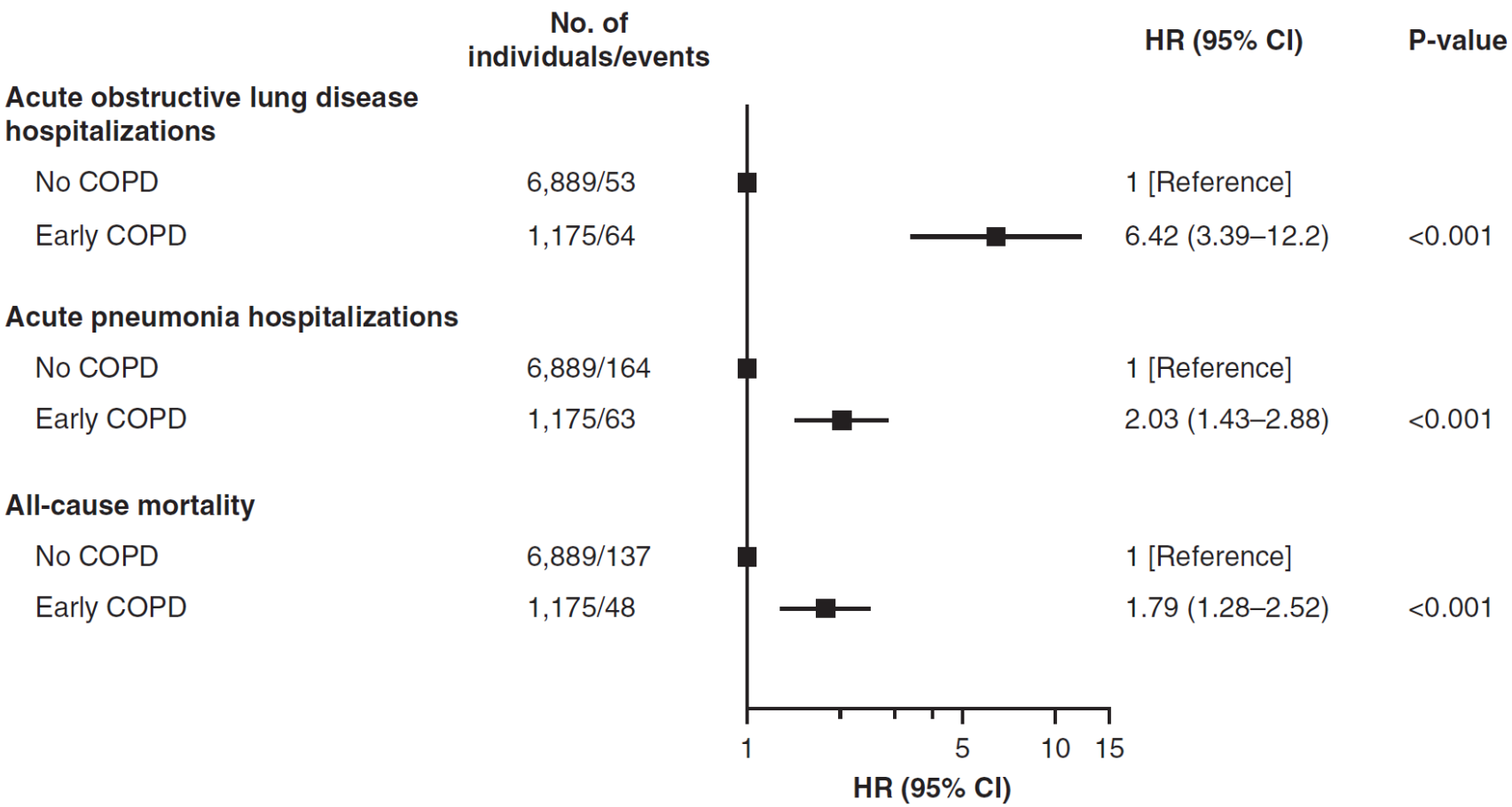
Colak Y. Am J Respir Crit Care Med 2020; 201: 671-680.



Colak Y. Am J Respir Crit Care Med 2020; 201: 671-680.



Colak Y. Am J Respir Crit Care Med 2020; 201: 671-680.



Colak Y. Am J Respir Crit Care Med 2020; 201: 671-680.

ORIGINAL ARTICLE

Importance of Early COPD In Young Adults for Development of Clinical COPD

Findings from the Copenhagen General Population Study

Yunus Çolak[1,2,3], Shoaib Afzal[1,2,3], Børge G. Nordestgaard[1,2,3], Peter Lange[2,3,4,5], and Jørgen Vestbo[6]

Colak Y. Am J Respir Crit Care Med 2021; 203: 1245-1256.

At baseline examination before age 50

Early COPD = FEV_1/FVC <LLN

Smoking exposure ≥10 pack-years at baseline examination before age 50 (n=1,486)

Colak Y. Am J Respir Crit Care Med 2021; 203: 1245-1256.

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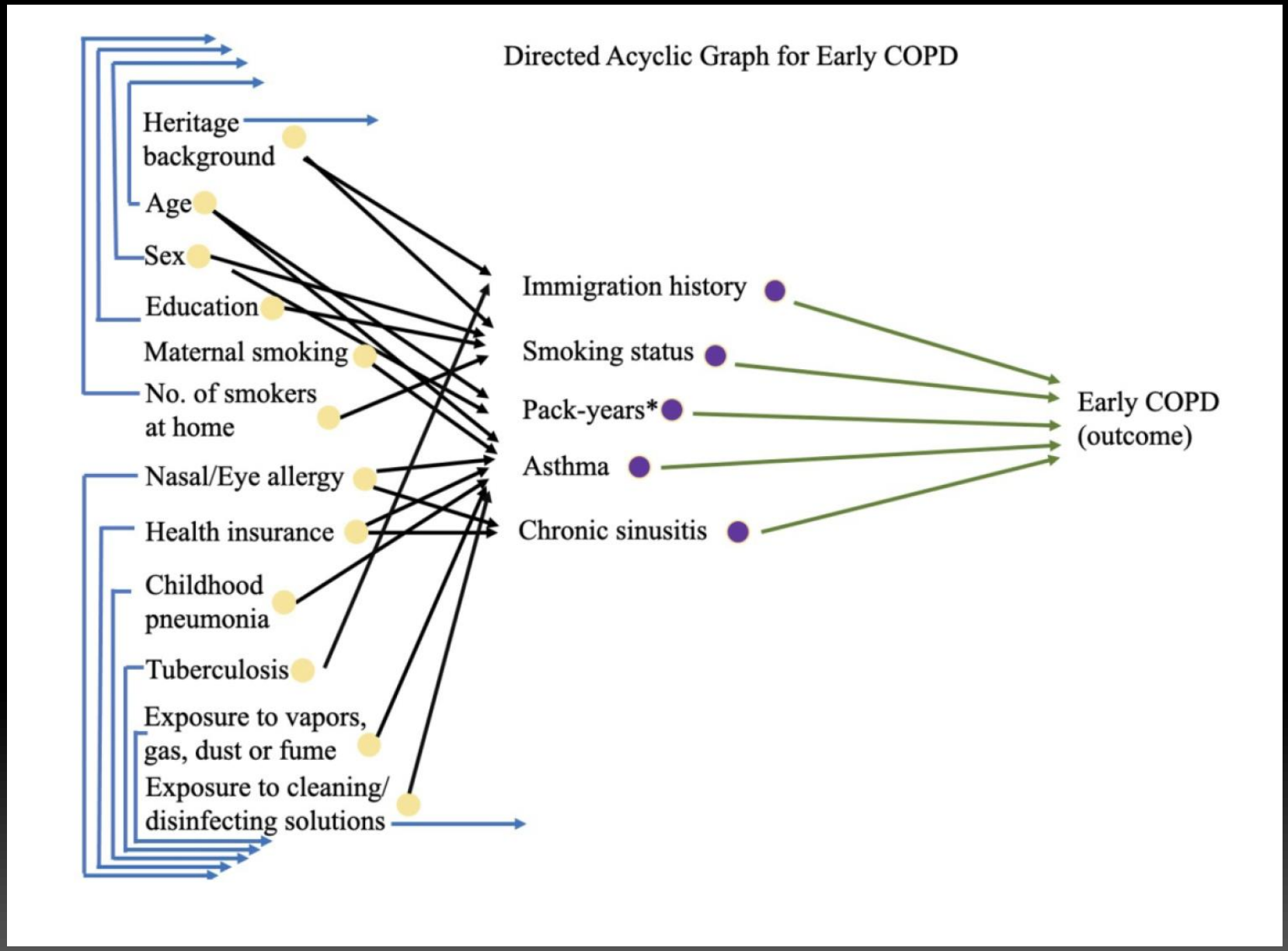
Prevalence and Population Attributable Risk for Early COPD in US Hispanics/Latinos

Fariha Khalid* MD, MPH,[1] Wei Wang* PhD,[2,3] David Mannino MD[4], Alejandro A. Diaz MD MPH[3,5]

[1]Department of Anesthesiology, Perioperative, and Pain Medicine, [2]Division of Sleep Medicine, and [5]Division of Pulmonary and Critical Care Medicine at Brigham and Women's Hospital, Boston, MA
[3]Harvard Medical School, Boston, MA;
[4]University of Kentucky, Lexington, KY.

Khalid F. Ann Am Thorac Soc 2021 [Epub].

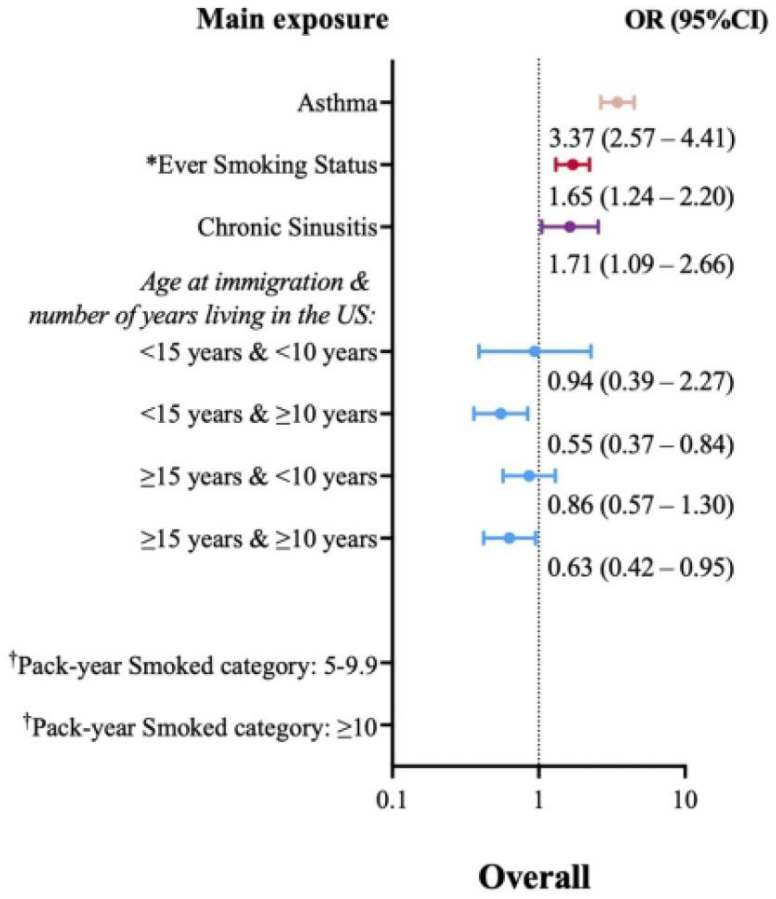


Khalid F. Ann Am Thorac Soc 2021 [Epub].

Table 2 Population attributable risk (PAR*) for early COPD by risk factor and sex among US Hispanics/Latinos aged 18-49 years

	Overall	Women	Men
Risk Factor	PAR (%) [95% Confidence Interval]	PAR (%) [95% Confidence Interval]	PAR (%) [95% Confidence Interval]
Asthma	26.3 [22.1 – 30.3]	35.6 [29.0 – 41.7]	19.4 [14.1 – 24.4]
Smoking Status (ever vs. never)	22.4 [17.4 – 27.1]	18.2 [11.3 – 24.6]	24.2 [16.9 – 30.9]
Chronic Sinusitis	6.9 [4.3 – 9.4]	5.2 [1.3 – 8.9]	8.4 [4.8 – 11.8]

Khalid F. Ann Am Thorac Soc 2021 [Epub].



Khalid F. Ann Am Thorac Soc 2021 [Epub].

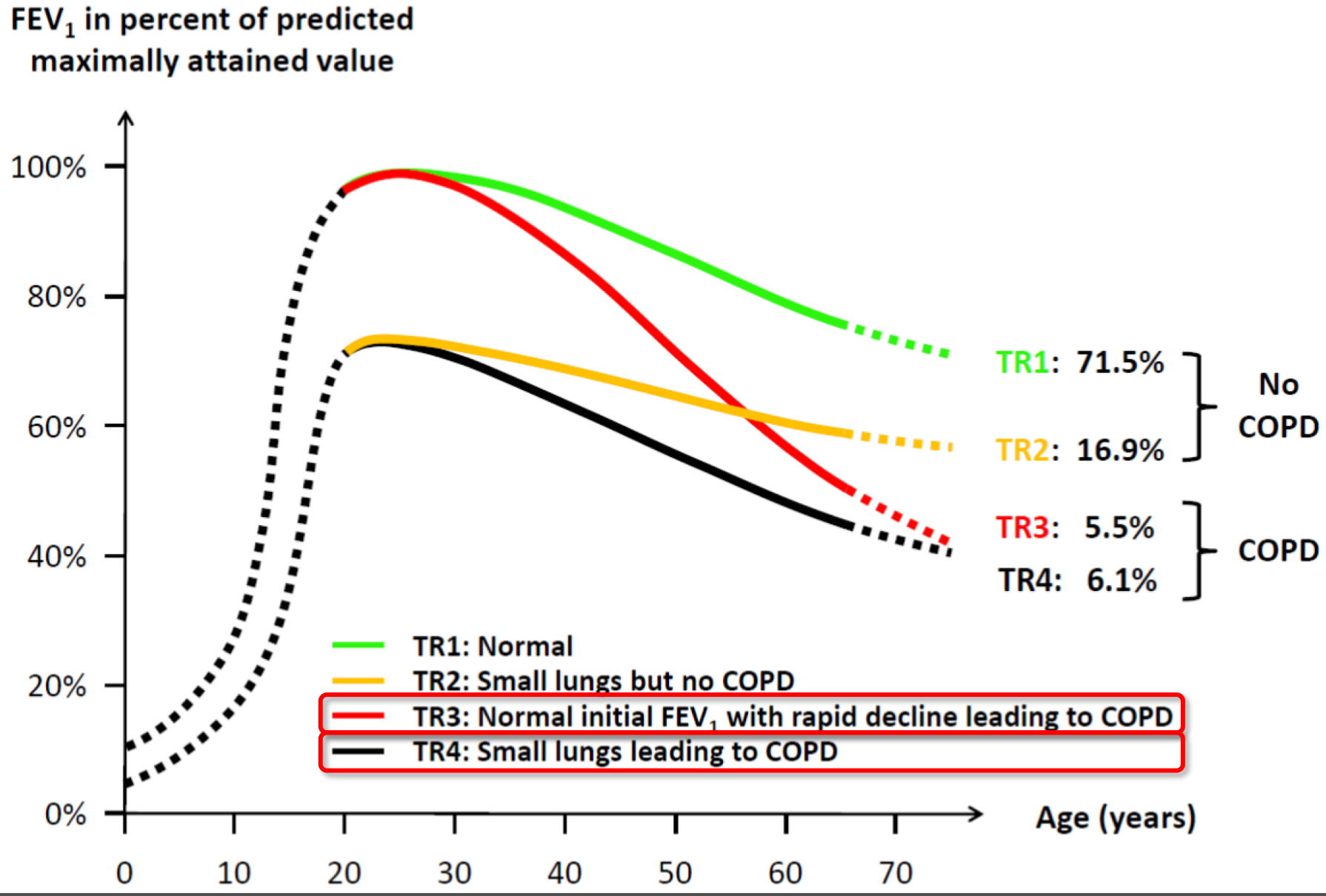
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 9, 2015 VOL. 373 NO. 2

Lung-Function Trajectories Leading to Chronic Obstructive Pulmonary Disease

Peter Lange, M.D., Dr. Med. Sc., Bartolome Celli, M.D., Alvar Agustí, M.D., Ph.D., Gorm Boje Jensen, M.D., Dr. Med. Sc., Miguel Divo, M.D., Rosa Faner, Ph.D., Stefano Guerra, M.D., Ph.D., Jacob Louis Marott, M.Sc., Fernando D. Martinez, M.D., Pablo Martinez-Camblor, Ph.D., Paula Meek, R.N., Ph.D., Caroline A. Owen, M.D., Ph.D., Hans Petersen, Ph.D, Victor Pinto-Plata, M.D., Peter Schnohr, M.D., Dr. Med. Sc., Akshay Sood, M.D., M.P.H., Joan B. Soriano, M.D., Yohannes Tesfaigzi, Ph.D., and Jørgen Vestbo, M.D., Dr. Med. Sc.

Lange P. N Engl J Med 2015; 373: 111-122.


FEV1 in percent of predicted maximally attained value
100%
80%
60%
40%
20%
0%
0
10
20
30
40
50
60
70
Age (years)
TR1: 71.5%
TR2: 16.9%
No COPD
TR3: 5.5%
TR4: 6.1%
COPD
TR1: Normal
TR2: Small lungs but no COPD
TR3: Normal initial FEV1 with rapid decline leading to COPD
TR4: Small lungs leading to COPD

Received: 16 March 2021 | Accepted: 29 August 2021

DOI: 10.1111/resp.14144

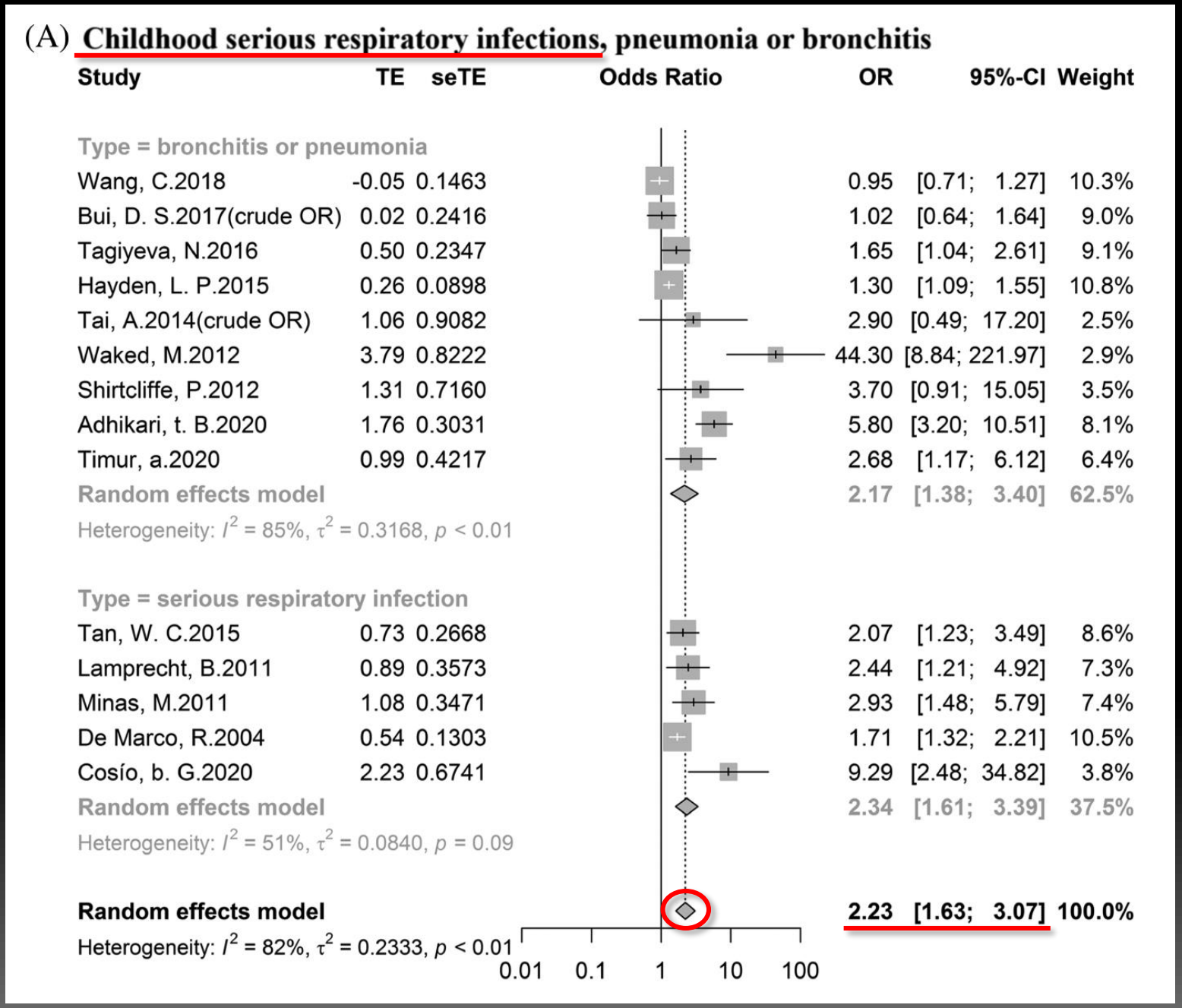
SYSTEMATIC REVIEW

Official Journal of the Asian Pacific Society of Respirology
Respirology
APSR
WILEY

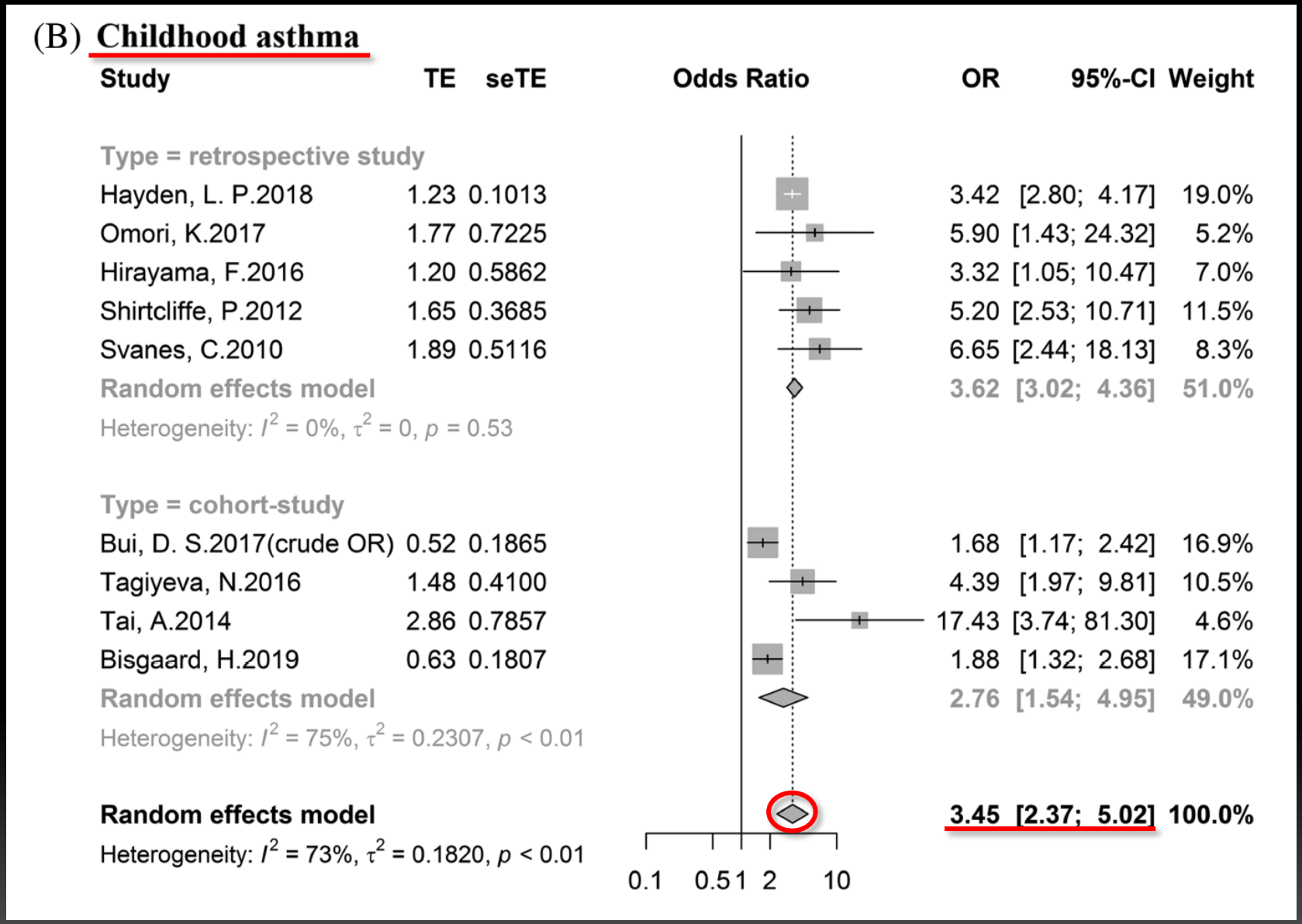
Impact of early life exposures on COPD in adulthood: A systematic review and meta-analysis

Pengfei Duan[1,2] | Yao Wang[1] | Rongqing Lin[1] | Yiming Zeng[3] | Chengshui Chen[4] | Li Yang[4] | Minghui Yue[1] | Shan Zhong[5] | Yun Wang[5] | Qingying Zhang[1,6]

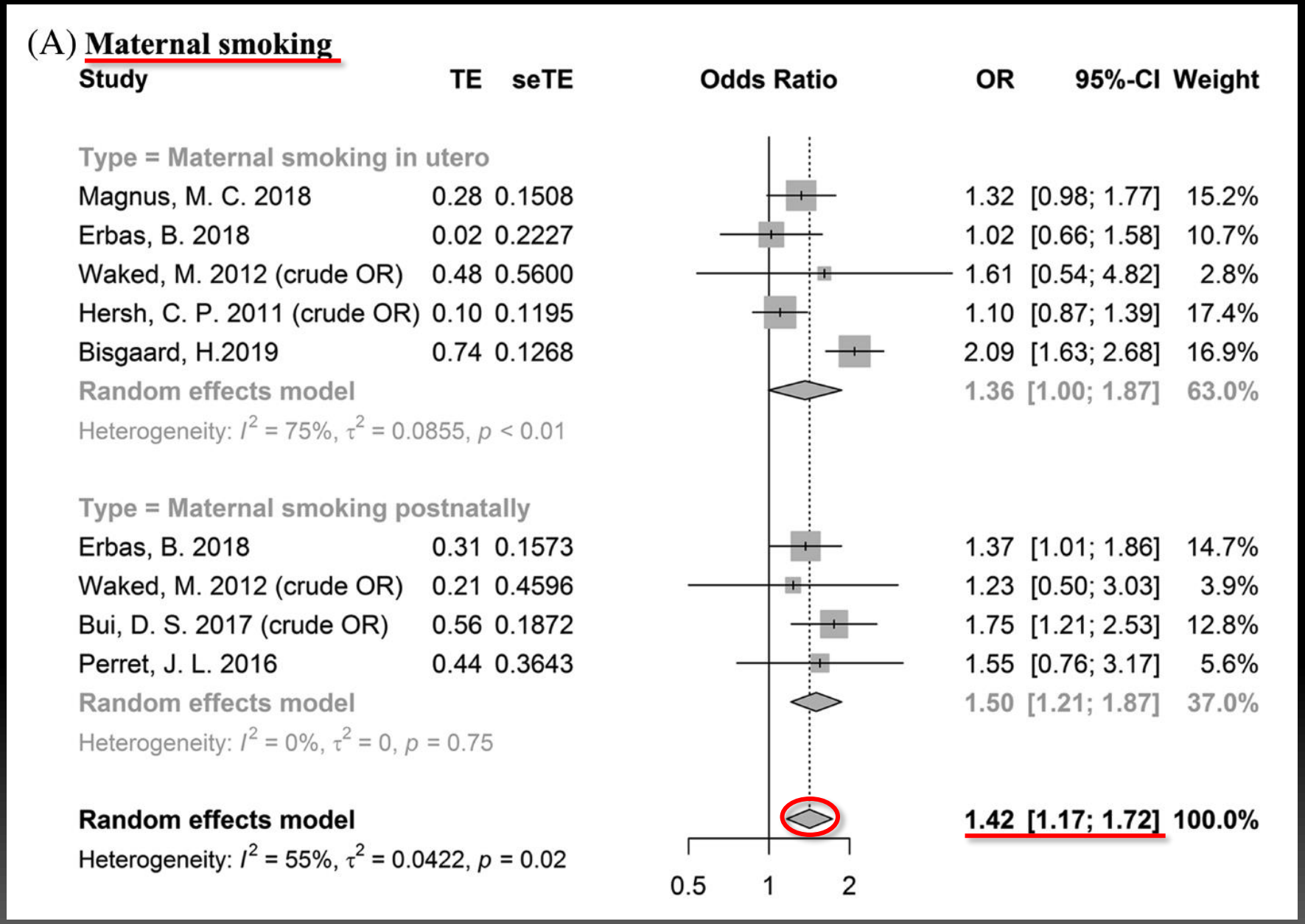
Duan P. Respirology 2021; 26: 1131-1151.



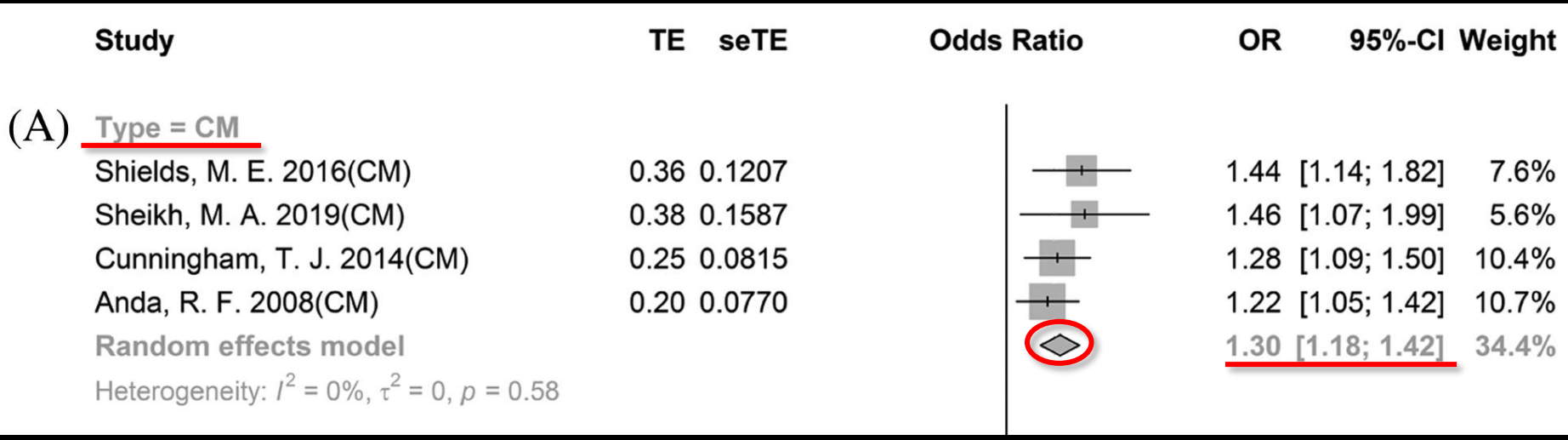
Duan P. Respirology 2021; 26: 1131-1151.



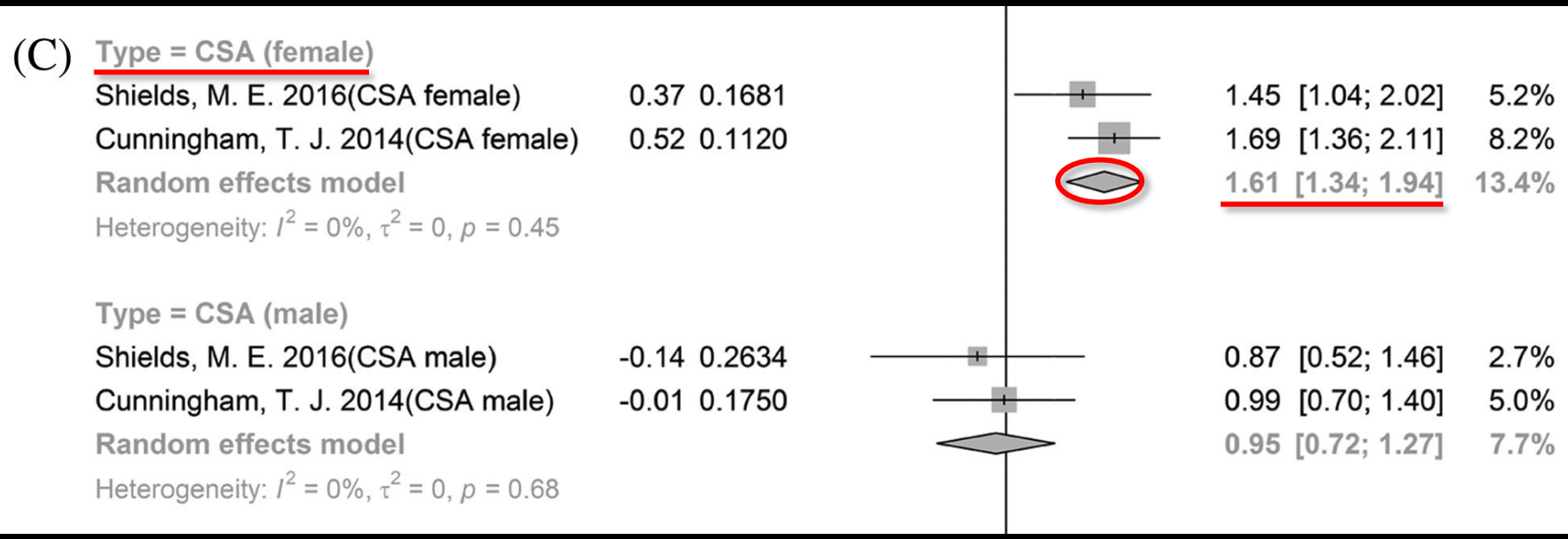
Duan P. Respirology 2021; 26: 1131-1151.



Duan P. Respirology 2021; 26: 1131-1151.

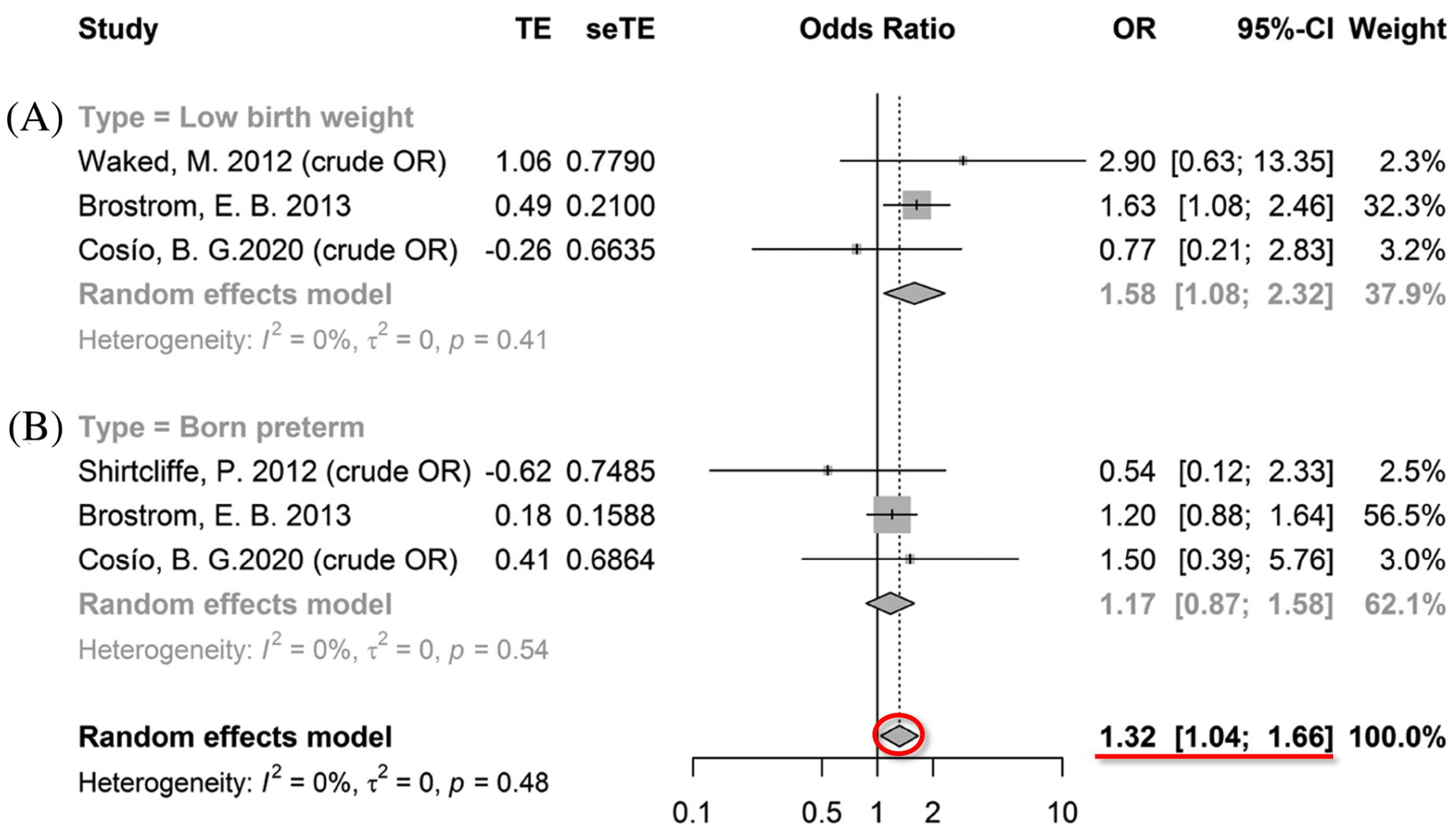


Duan P. Respirology 2021; 26: 1131-1151.



Duan P. Respirology 2021; 26: 1131-1151.

Low birth weight or premature birth



Duan P. Respirology 2021; 26: 1131-1151.

EUROPEAN RESPIRATORY journal

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Early View

Original research article

A Polygenic Risk Score and Age of Diagnosis of Chronic Obstructive Pulmonary Disease

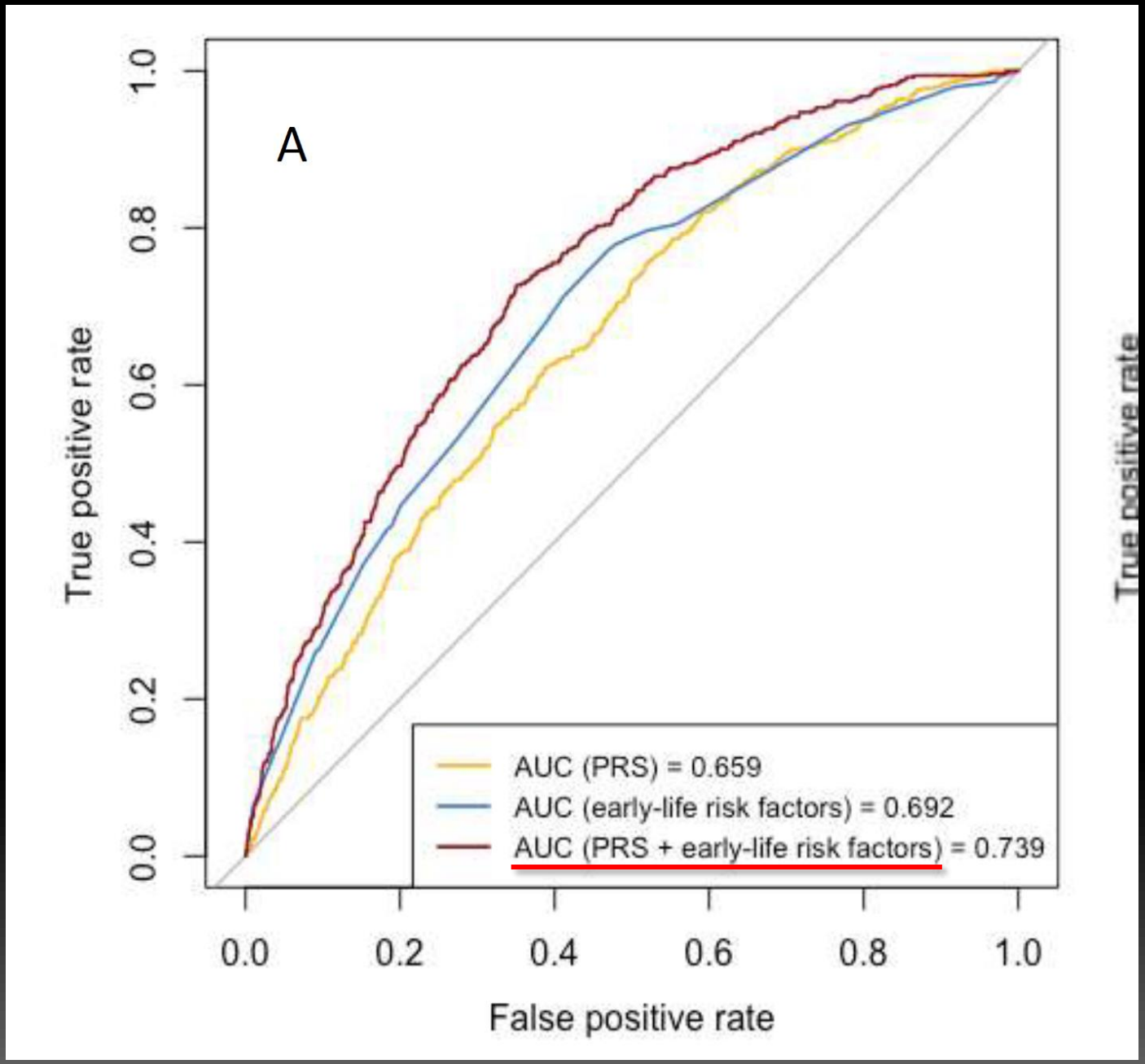
Jingzhou Zhang, Hanfei Xu, Dandi Qiao, Dawn L. DeMeo, Edwin K. Silverman, George T. O'Connor, Brian D. Hobbs, Josée Dupuis, Michael H. Cho, Matthew Moll

Zhang J. Eur Respir J 2022: 2101954.

Table 3. Associations between the PRS and other early-life risk factors and COPD occurring early in life (age < 50) in COPDGene non-Hispanic white participants.

Predictive variable	OR (95% CI)		
	model 1	model 2	model 3
Polygenic risk score *	1.60 (1.46-1.76)		1.55 (1.41-1.71)
Maternal smoking during pregnancy		1.48 (1.21-1.81)	1.51 (1.23-1.86)
Active smoking during adolescence		1.86 (1.42-2.43)	1.92 (1.46-2.52)
Childhood asthma		2.34 (1.72-3.19)	2.07 (1.51-2.83)
Family history of COPD		1.99 (1.64-2.41)	1.86 (1.52-2.26)
Education			
High school or below (reference)		1.00	1.00
College		0.53 (0.44-0.64)	0.55 (0.45-0.67)
Graduate		0.25 (0.16-0.39)	0.28 (0.18-0.44)

Zhang J. Eur Respir J 2022: 2101954.



Zhang J. Eur Respir J 2022: 2101954.

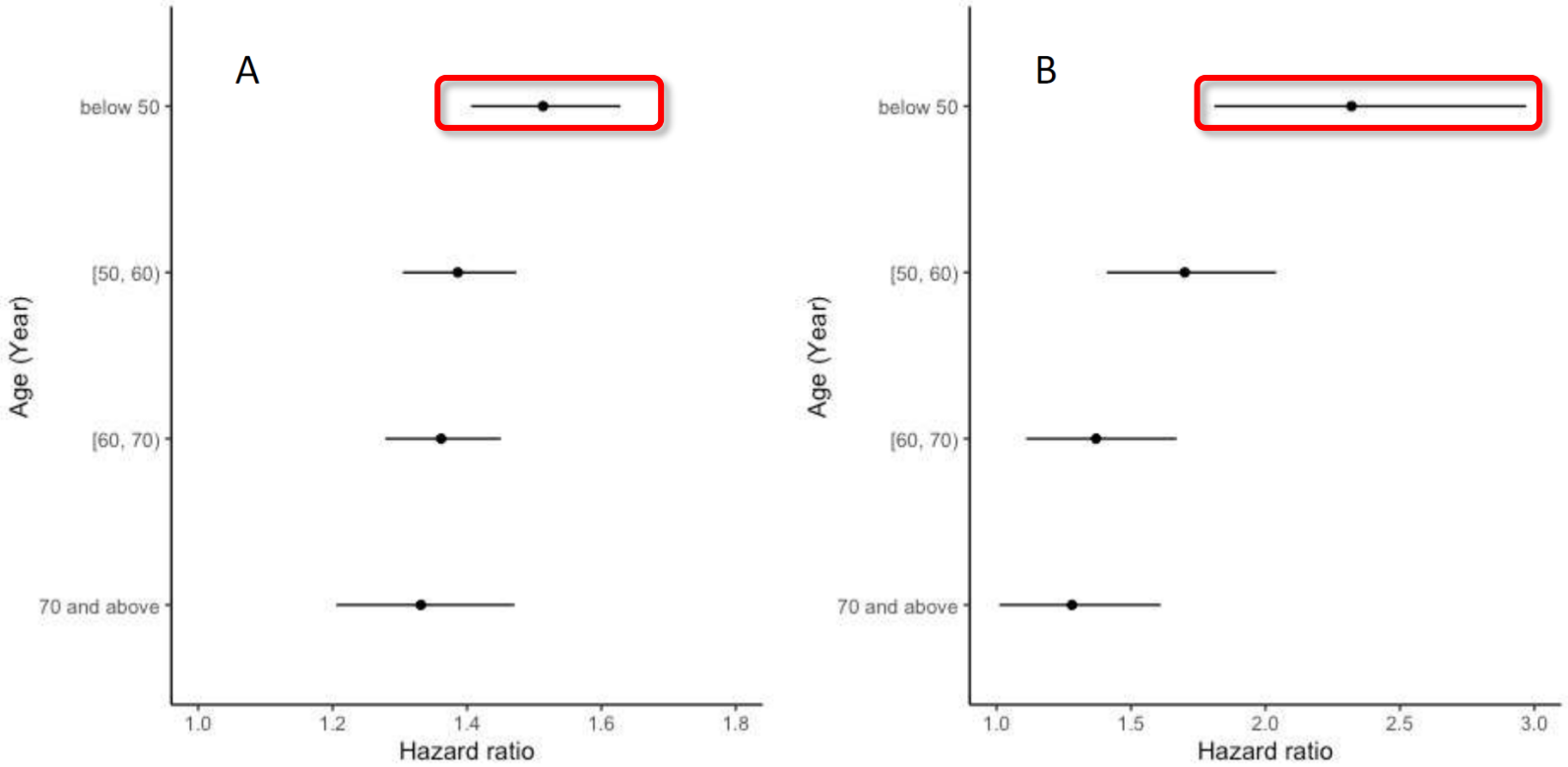


Figure 2. Risk estimates (points: hazard ratios, bars: 95% confidence intervals) associated with the polygenic risk score (per standard deviation) for incident COPD among age intervals of below 50, 50-60, 60-70, and 70 years and beyond in COPDGene non-Hispanic white (A) and Framingham Heart Study (B) participants.

Zhang J. Eur Respir J 2022: 2101954.

ORIGINAL ARTICLE

Increased Impact of Air Pollution on Lung Function in Preterm versus Term Infants

The BILD Study

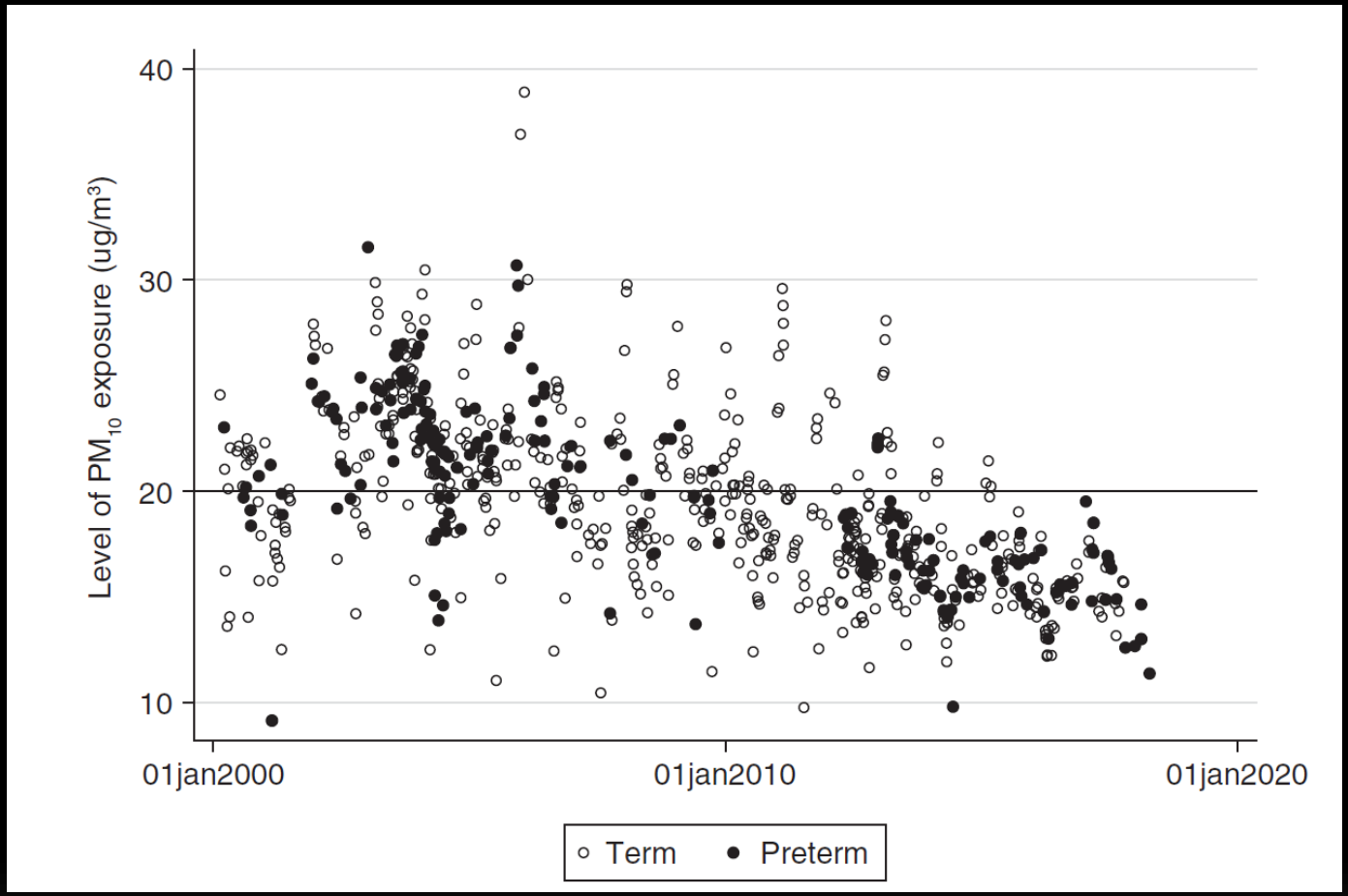
Fabienne Decrue[1,2], Olga Gorlanova[1,2], Yasmin Salem[1,2], Danielle Vienneau[3,4], Kees de Hoogh[3,4], Amanda Gisler[1], Jakob Usemann[1,2,5], Insa Korten[1,2], Uri Nahum[1,2], Pablo Sinues[1,6], Sven Schulzke[1], Oliver Fuchs[1,2], Philipp Latzin[1,2], Martin Röösli[3,4], and Urs Frey[1,2]; on behalf of the BILD study group

Decrue F. Am J Respir Crit Care Med 2022; 205: 99-107.

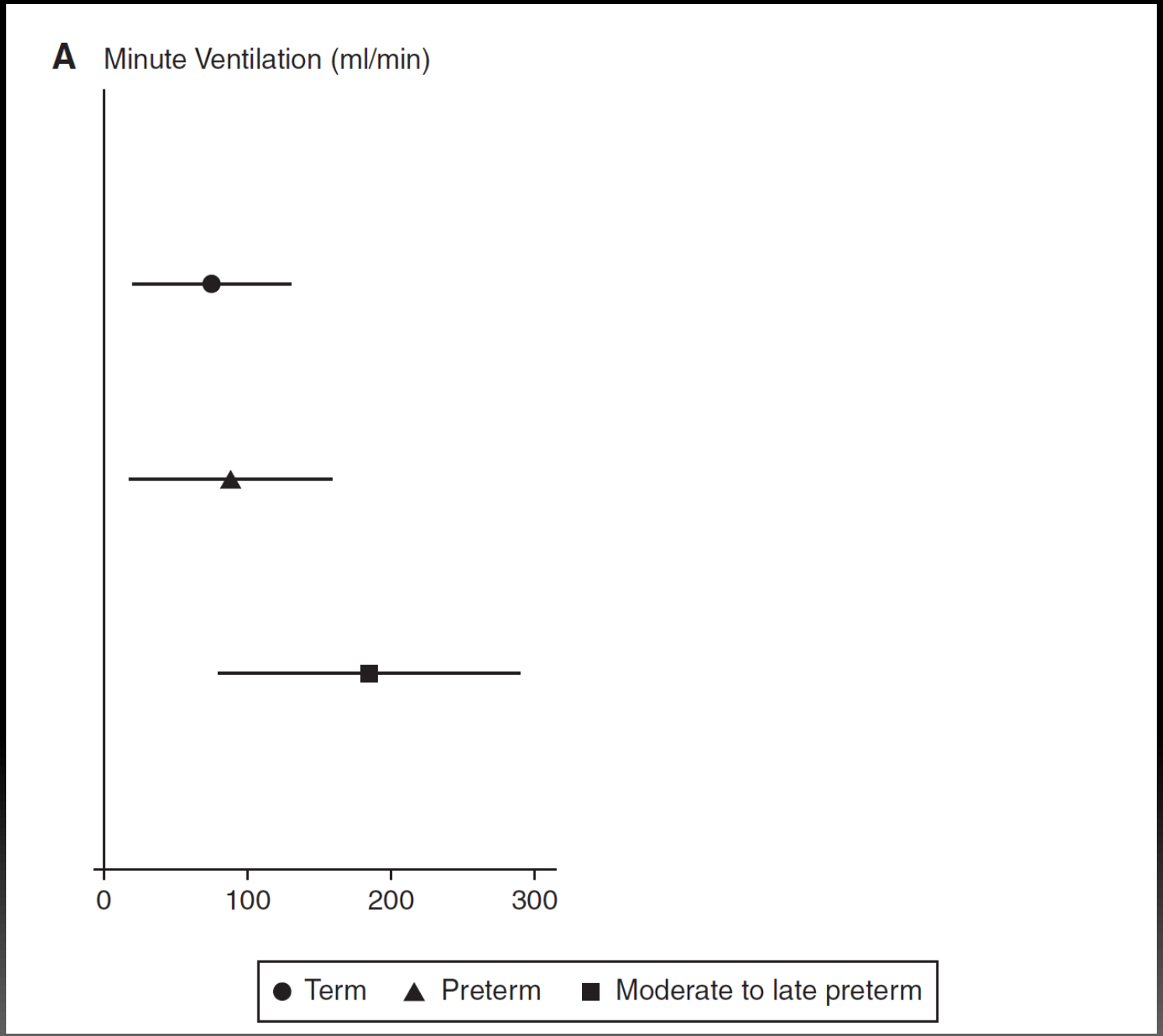
Eur Respir J 2011; 37: 1208–1216
DOI: 10.1183/09031936.00125510

Normative data for lung function and exhaled nitric oxide in unsedated healthy infants

O. Fuchs*,#, P. Latzin*,#, C. Thamrin*, G. Stern*, P. Frischknecht*, F. Singer*, E. Kieninger*, E. Proietti*, T. Riedel[¶] and U. Frey*,+



Decrue F. Am J Respir Crit Care Med 2022; 205: 99-107.



Decrue F. Am J Respir Crit Care Med 2022; 205: 99-107.

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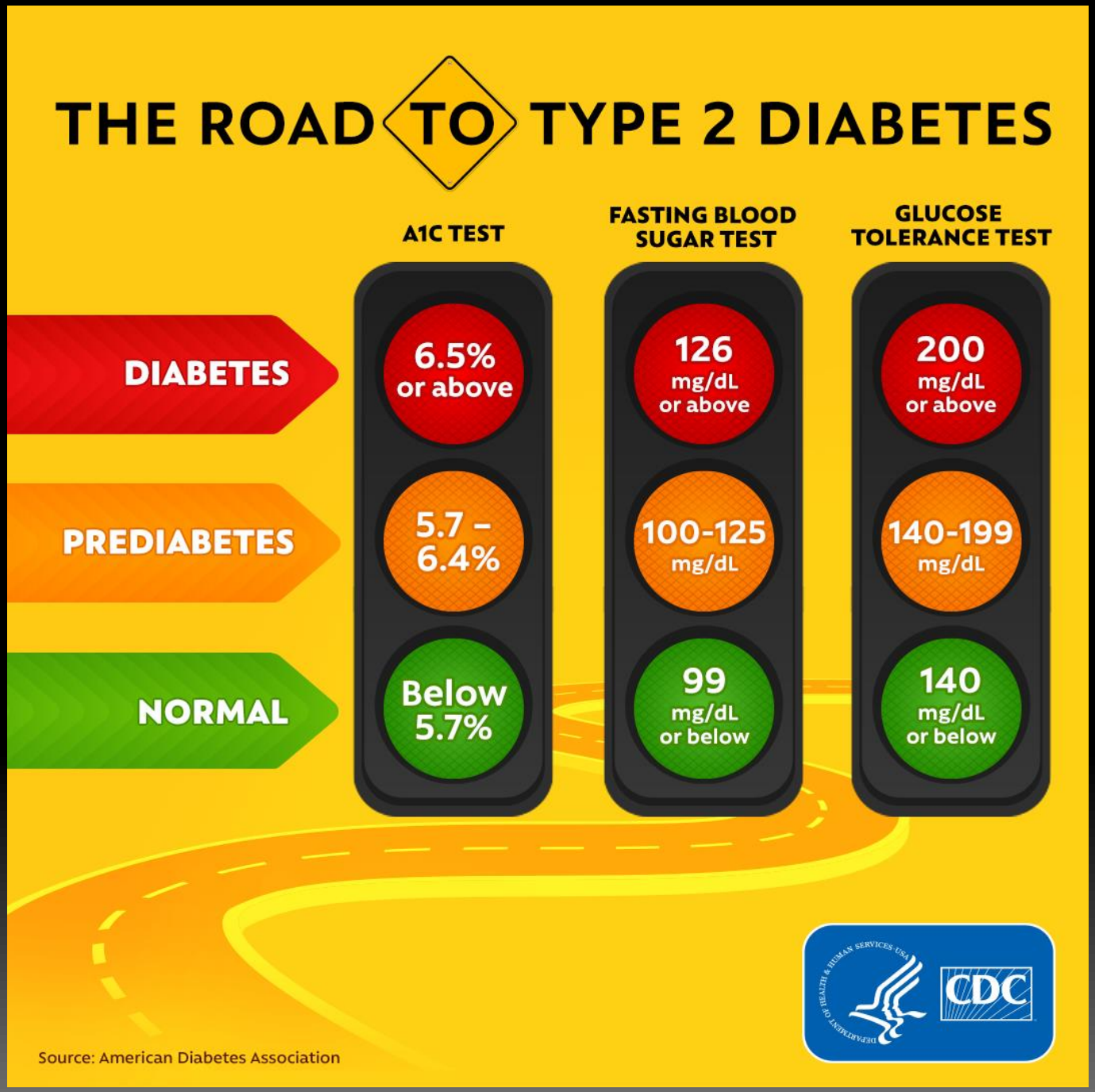
ERJ open research

COPD: time to improve its taxonomy?

Bartolomé R. Celli[1] and Alvar Agustí[2,3,4]

Number 2 in the series "Gaps in our understanding of COPD"
Edited by A. Agustí and B. Celli

Celli BR. ERJ Open Research 2018; 4: 00132-02017.



https://www.cdc.gov/diabetes/basics/getting-tested.html

Scadding conditions	Pre-COPDs	COPDs
Function	No airflow limitation	Airflow limitation
Symptoms	Cough; sputum; dyspnoea	Dyspnoea; cough; sputum
Structure	Emphysema; abnormal airways	Emphysema; abnormal airways
Aetiology	Genetic (AAT deficiency); cigarettes; biomass; infectious; asthma; developmental; unknown	

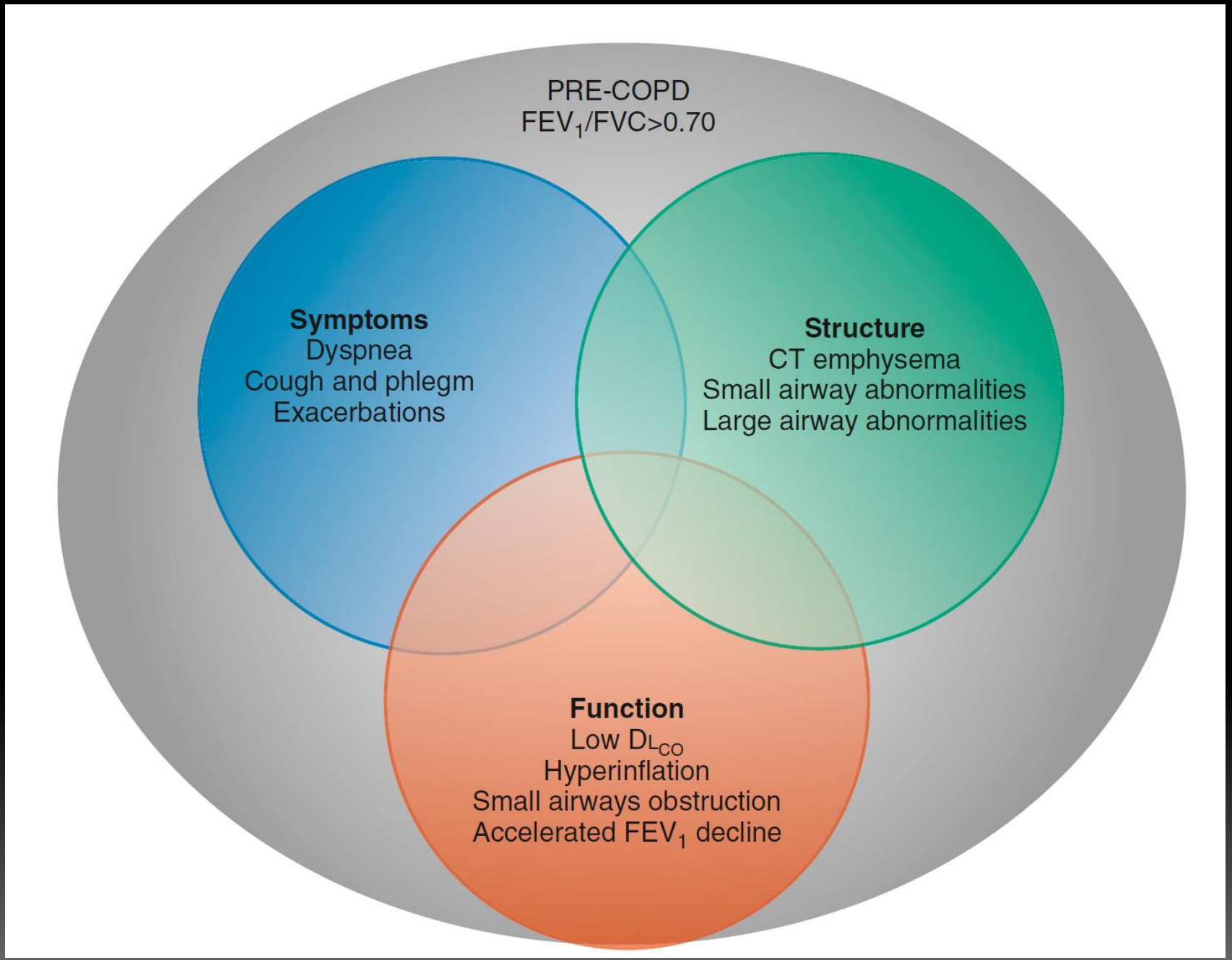
Celli BR. ERJ Open Research 2018; 4: 00132-02017.

PULMONARY PERSPECTIVE

From GOLD 0 to Pre-COPD

MeiLan K. Han[1]*, Alvar Agusti[2], Bartolome R. Celli[3], Gerard J. Criner[4]*, David M. G. Halpin[5], Nicolas Roche[6], Alberto Papi[7], Robert A. Stockley[8], Jadwiga Wedzicha[9]*, and Claus F. Vogelmeier[10]

Han MK. Am J Respir Crit Care Med 2021; 203: 414-423.



Han MK. Am J Respir Crit Care Med 2021; 203: 414-423.

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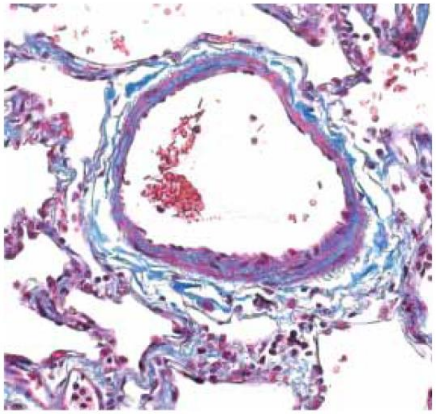
EDITORIAL
COPD

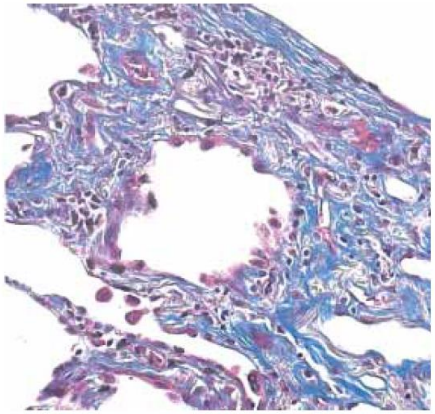
Small airways and early origins of COPD: pathobiological and epidemiological considerations

Francesca Polverino[1] and Joan B. Soriano[2,3]

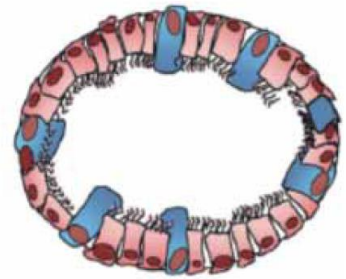
Polverino F. Eur Respir J 2020; 55: 1902457.

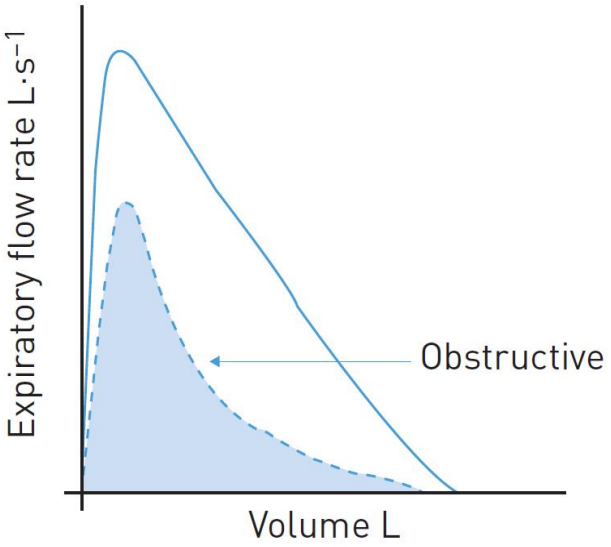


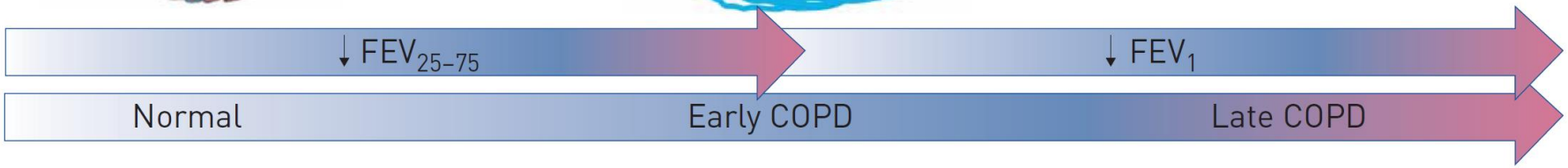
Normal small airways



Remodelling and loss of small airways







Polverino F. Eur Respir J 2020; 55: 1902457.

CHEST

Ratio of FEV_1/Slow Vital Capacity of < 0.7 Is Associated With Clinical, Functional, and Radiologic Features of Obstructive Lung Disease in Smokers With Preserved Lung Function

Spyridon Fortis, MD; Alejandro P. Comellas, MD; Surya P. Bhatt, MD; Eric A. Hoffman, PhD; MeiLan K. Han, MD; Nirav R. Bhakta, MD; Robert Paine III, MD; Bonnie Ronish, MD; Richard E. Kanner, MD; Mark Dransfield, MD; Daniel Hoesterey, MD; Russell G. Buhr, MD; R. Graham Barr, MD; Brett Dolezal, PhD; Victor E. Ortega, MD; M. Bradley Drummond, MD; Mehrdad Arjomandi, MD; Robert J. Kaner, MD; Victor Kim, MD; Jeffrey L. Curtis, MD; Russell P. Bowler, MD; Fernando Martinez, MD; Wassim W. Labaki, MD; Christopher B. Cooper, MD; Wanda K. O'Neal, PhD; Gerald Criner, MD; Nadia N. Hansel, MD; Jerry A. Krishnan, MD; Prescott Woodruff, MD; David Couper, PhD; Donald Tashkin, MD; and Igor Barjaktarevic, MD

Fortis S. Chest 2021; 160: 94-103.

TABLE 2] Factors Associated With Abnormal Postbronchodilator FEV_1/SVC Ratio of < 0.7 Among Smokers With Normal Spirometry Results[a] (n = 854)

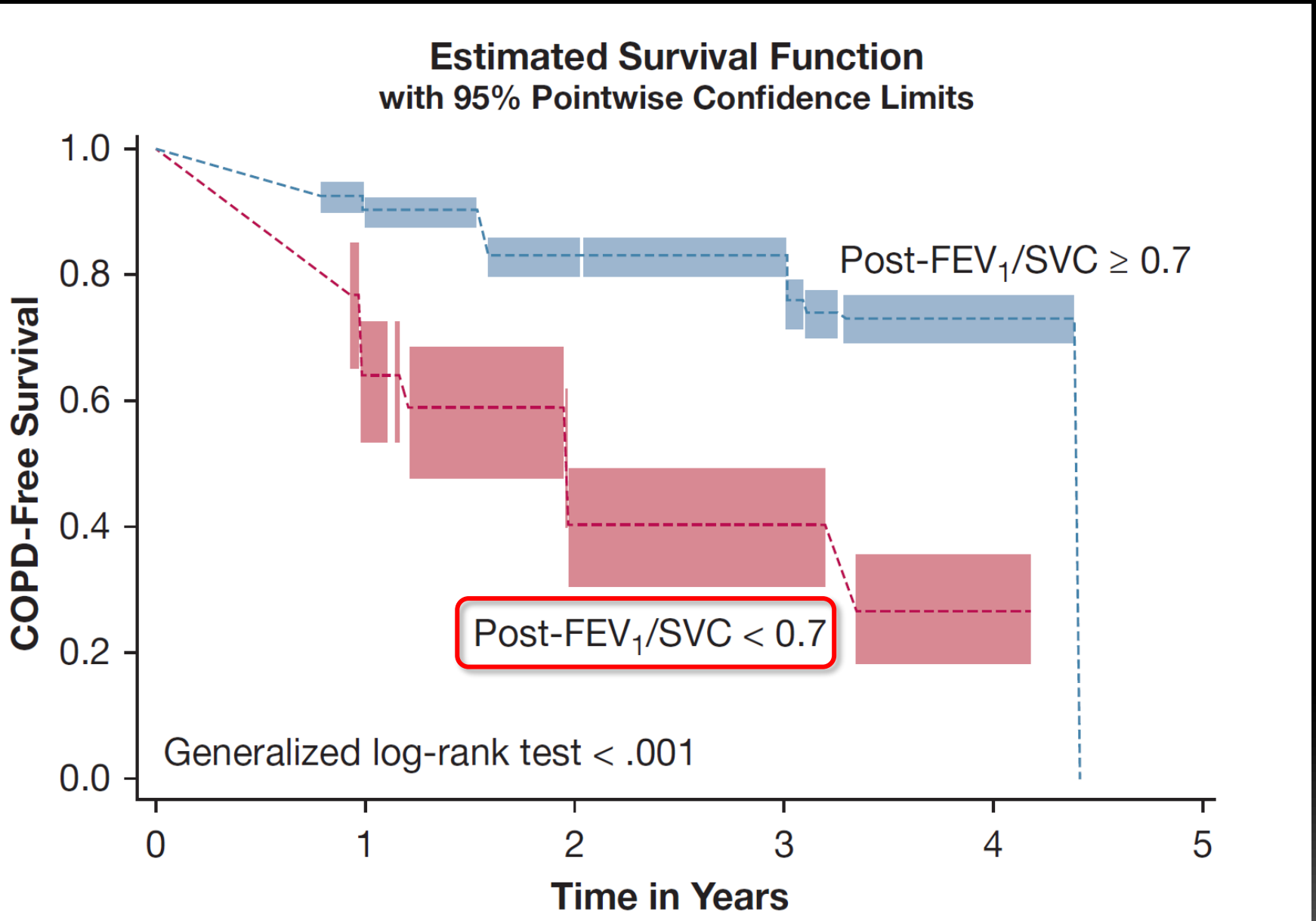
Variable	OR (95% CI)	*P* Value
Age, every 10 y	1.91 (1.51-2.45)	< .001
Pack-years, every 10 y	1.06 (0.99-1.14)	.09
Postbronchodilator FEV_1 % predicted	0.96 (0.94-0.97)	< .001
% Emphysema	1.13 (1.03-1.25)	.008
Female sex	0.68 (0.45-1.04)	.08

Fortis S. Chest 2021; 160: 94-103.

TABLE 4] Association of Postbronchodilator FEV_1 to SVC Ratio of < 0.7 With Exacerbations and Progression to COPD in Smokers With Normal Spirometry Results[a]

Variable	IRR (95% CI)	*P* Value
Total exacerbations	1.60 (0.97-2.64)	.07
Severe exacerbations	2.60 (1.04-4.89)	.040
	HR (95% CI)	
Progression to COPD	3.93 (2.71-5.72)	< .001
	OR (95% CI)	
Persistent COPD	5.08 (3.09-8.37)	< .001

Fortis S. Chest 2021; 160: 94-103.



Fortis S. Chest 2021; 160: 94-103.

[COPD Original Research]

CHEST

Significance of FEV_3/FEV_6 in Recognition of Early Airway Disease in Smokers at Risk of Development of COPD

Analysis of the SPIROMICS Cohort

Nathan Yee, MD; Daniela Markovic, MS; Russell G. Buhr, MD, PhD; Spyridon Fortis, MD; Mehrdad Arjomandi, MD; David Couper, PhD; Wayne H. Anderson, MEd, PhD; Robert Paine III, MD; Prescott G. Woodruff, MD, MPH; Meilan K. Han, MD; Fernando J. Martinez, MD; R. Graham Barr, MD, DrPH; James M. Wells, MD; Victor E. Ortega, MD, PhD; Eric A. Hoffman, PhD; Victor Kim, MD; M. Bradley Drummond, MD, MHS; Russell P. Bowler, MD, PhD; Jeffrey L. Curtis, MD; Christopher B. Cooper, MD; Donald P. Tashkin, MD; and Igor Z. Barjaktarevic, MD, PhD

TABLE 1] Baseline Characteristics in Ever-Smokers With Post-Bronchodilator $FEV_1/FVC \geq 0.7$ Stratified According to Pre-Bronchodilator FEV_3/FEV_6

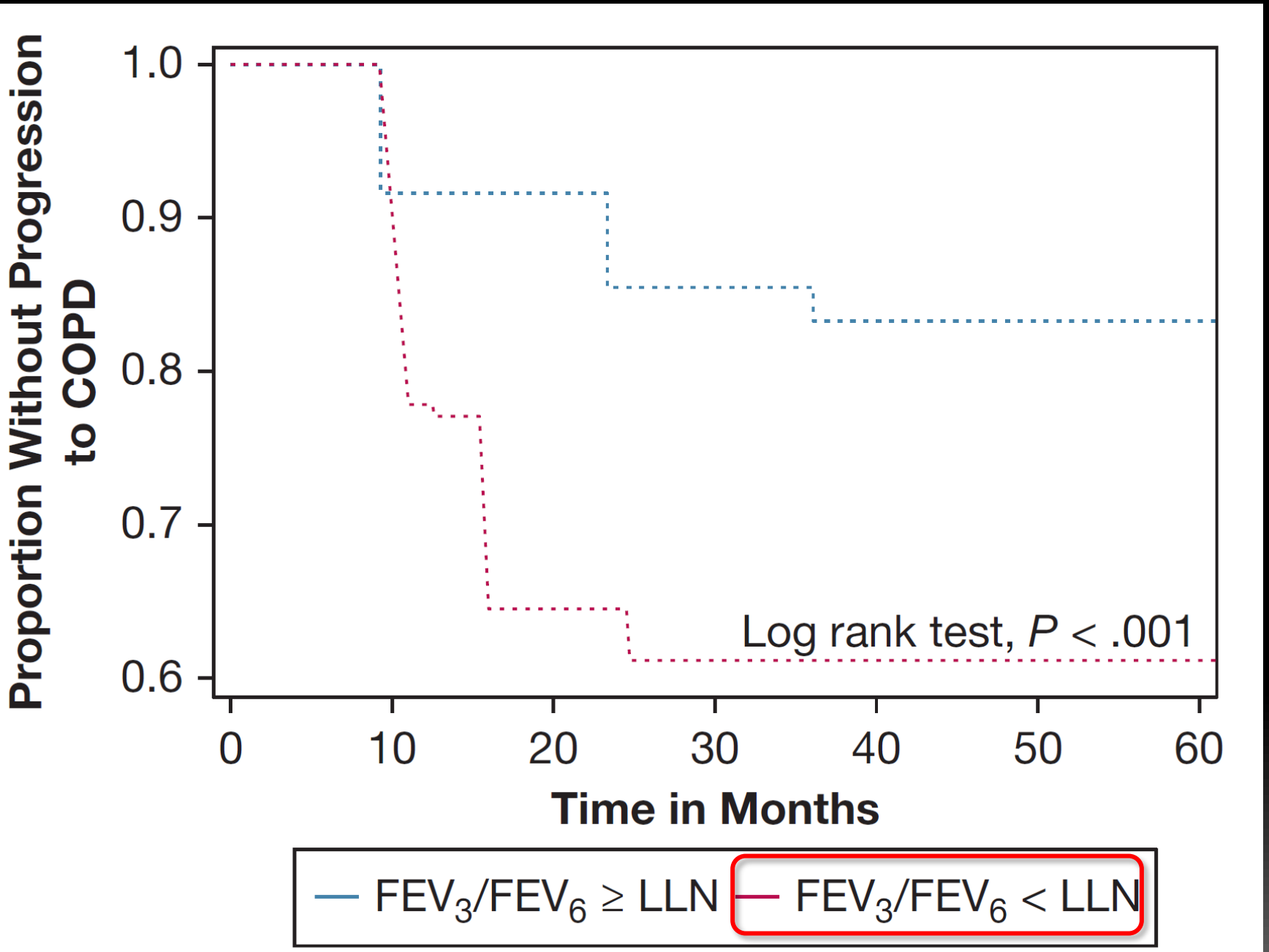
Baseline Variable	FEV_3/FEV_6 Less Than the LLN (n = 143)	FEV_3/FEV_6 at or Above the LLN (n = 689)	*P* Value
Age, y	57.1 ± 10.3	60.5 ± 9.4	<.001
Female sex	81 (56.6)	347 (50.4)	.17
Race:			
White	87 (60.8)	473 (68.7)	.34
African American	46 (32.2)	175 (25.4)	
Other	9 (6.3)	36 (5.2)	
BMI, kg/m^2	27.7 ± 5.3	29.5 ± 4.9	< .001
BODE index	0.6 ± 1.0	0.4 ± 0.7	.02
Smoking status			
Currently smoking	88 (61.5)	338 (49.1)	.025
Pack-years	46.8 (30.3)	41.6 (22.9)	.11
History of asthma	32 (22.4)	90 (13.8)	.049
Chronic bronchitis	29 (20.3)	79 (11.5)	.012
On ICS	26 (18.3)	73 (10.7)	.011
On bronchodilator	53 (37.3)	134 (19.6)	< .001
FEV_3/FEV_6	0.90 ± 0.02	0.93 ± 0.01	
FEV_1			
Liters	2.6 ± 0.7	2.9 ± 0.7	.001
Percent predicted	90.3 (11.3)	98.6 (13.2)	< .001
FVC			
Liters	3.6 ± 1.0	3.7 ± 0.9	.18
Percent (%) predicted	90.3 ± 11.3	98.6 ± 13.2	< .001
FEV_1/FVC	0.74 ± 0.03	0.78 ± 0.05	< .001
TLC_{CT}, L	5.5 ± 1.4	5.4 ± 1.3	.68
RV_{CT}, L	2.9 ± 0.7	2.8 ± 0.7	.16
mMRC dyspnea score ≥ 2	23 (16.1)	78 (11.3)	.26
CAT score ≥ 10	75 (52.5)	318 (46.2)	.37
SGRQ	29.1 ± 21.1	23.2 ± 18.3	.003
6MWD, m	428.3 ± 99.5	439.0 ± 95.8	.27
PRM^{Emph}, %	0.7 ± 1.2	0.4 ± 0.8	.001
PRM^{fSAD}, %	9.3 ± 9.5	7.8 ± 9.1	.017

Yee N. Chest 2021 [Epub].

TABLE 2] Exacerbation and COPD Progression Outcomes in Ever-Smokers With Post-Bronchodilator $FEV_1/FVC \geq 0.7$ Stratified According to Pre-Bronchodilator FEV_3/FEV_6

COPD Outcome Measure (FEV_3/FEV_6 Less than the LLN vs FEV_3/FEV_6 at or Above the LLN)	OR[a]	
	Unadjusted	Adjusted[b]
Any respiratory exacerbation (first 365 d following enrollment)	1.97 (1.13-3.44; $P = .016$)	1.75 (0.94-3.28; $P = .078$)
Severe respiratory exacerbation (first 365 d following enrollment)[c]	4.14 (1.37-12.52; $P = .012$)	4.28 (1.17-15.66; $P = .028$)
	Rate Ratio[d]	
	Unadjusted	Adjusted[b]
Any type of respiratory exacerbation (through the third annual follow-up visit)[e]	1.32 (1.01-1.71; $P = .04$)	1.00 (0.72-1.34; $P = .99$)
Severe respiratory exacerbation (through the third annual follow-up visit)[c,e]	1.73 (1.14-2.62; $P = .01$)	1.02 (0.68-1.53; $P = .93$)
	Hazard Ratio	
	Unadjusted	Adjusted[b]
Time to first exacerbation[f]	1.68 (1.15-2.44; $P = .006$)	1.52 (1.02-2.25; $P = .039$)
Risk of progression to COPD by GOLD criteria[g]	2.75 (2.00-3.78; $P < .001$)	2.11 (1.48-3.03; $P < .001$)

Yee N. Chest 2021 [Epub].



Yee N. Chest 2021 [Epub].

Prediction of COPD by the single-breath nitrogen test and various respiratory symptoms

Jan Olofson [1], Björn Bake [1], Bengt Bergman [1], Lowie E.G.W. Vanfleteren [2] and Kurt Svärdsudd [3]

[1]Unit of Respiratory Medicine and Allergology, Dept of Internal Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden. [2]COPD Center, Institute of Medicine, Sahlgrenska University Hospital, University of Gothenburg, Gothenburg, Sweden. [3]Dept of Public Health and Caring Sciences, Family Medicine and Preventive Medicine Section, Uppsala University, Uppsala, Sweden.

Olofson J. ERJ Open Res 2021; 7: 00383-02021.

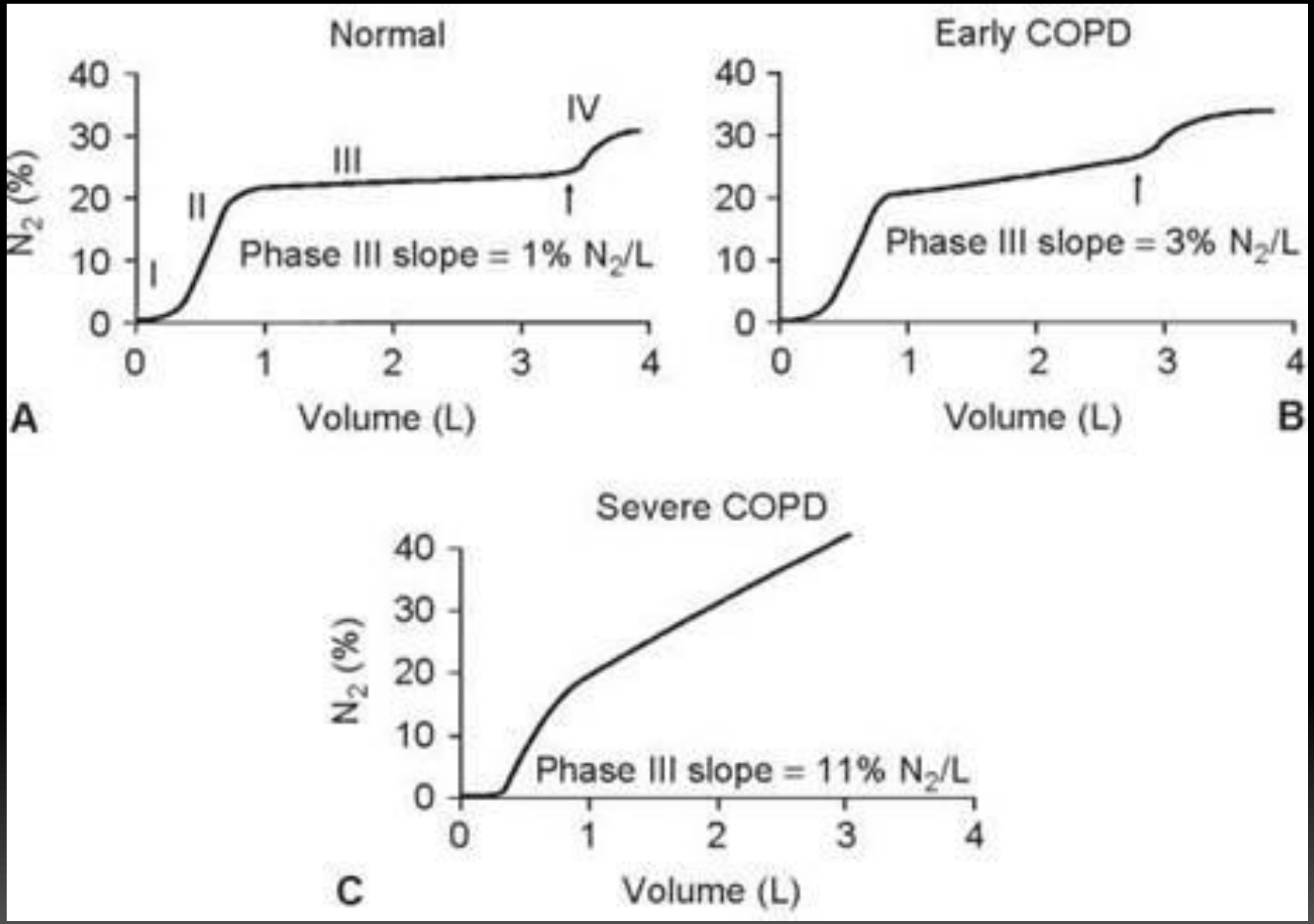

Normal
40
30
20
10
0
N_2 (%)
I
II
III
IV
Phase III slope = 1% N_2/L
0
1
2
3
4
Volume (L)
A
Early COPD
40
30
20
10
0
Phase III slope = 3% N_2/L
0
1
2
3
4
Volume (L)
B
Severe COPD
40
30
20
10
0
N_2 (%)
Phase III slope = 11% N_2/L
0
1
2
3
4
Volume (L)
C

TABLE 1 Characteristics of the study population

	All subjects		No incident COPD events[#]		Incident COPD events[#]		p-value for no COPD – COPD difference
Subjects n	615		561		54		
Person-years of observation	13553		12717		836		
Age at baseline (years)	625	56.8±4.8	571	56.8±4.7	54	56.4±4.9	0.53
BMI (kg·m^{-2})	625	25.6±3.3	571	25.6±3.2	54	25.2±3.5	0.34
FEV_1 (% pred)[¶]	615	88.7±16.4	561	90.2±15.0	54	72.2±20.9	<0.0001
FEV_1/VC (% pred)[¶]	615	99.6±11.4	561	100.0±9.8	54	87.0±17.8	<0.0001
N_2-slope (% N_2/L)[+]	604	2.0±1.5	552	1.9±1.4	52	3.1±2.1	<0.0001
N_2-slope (% pred)[+]	604	162±118	552	154±110	52	253±155	<0.0001
Smoking habits	625						<0.0001
Never-smoker (%)	125	20.0	121	21.2	4	7.4	
Ex-smoker (%)	194	31.0	181	31.4	13	24.1	
Current smoker (%)	306	49.0	269	47.1	37	68.5	
Non-productive cough (%)[§]	149	24.1	124	21.9	25	47.2	<0.0001
Productive cough (%)[§]	139	22.5	115	20.3	24	45.3	<0.0001
Wheezing (%)[§]	219	35.4	186	32.9	33	62.3	<0.0001
Dyspnoea (%)[§]	160	26.0	131	23.3	29	54.7	<0.0001
Total symptom score[f]	619	2.0±2.6	556	1.8±2.4	53	4.4±3.2	<0.0001

Data are presented as n or mean±SD, unless otherwise stated. Continuous variable differences were tested using the Mann–Whitney U-test; discrete variables were tested using the Chi-squared test. BMI: body mass index; FEV_1: forced expiratory volume in 1 s; VC: vital capacity; N_2-slope: alveolar slope of the single-breath nitrogen test. [#]: first admission to hospital or death related to COPD; [¶]: according to Hedenström *et al.* [16]; [+]: according to Sixt *et al.* [17]; [§]: percentage of subjects reporting any of the symptoms in each symptom group; [f]: mean of all the reported symptoms.

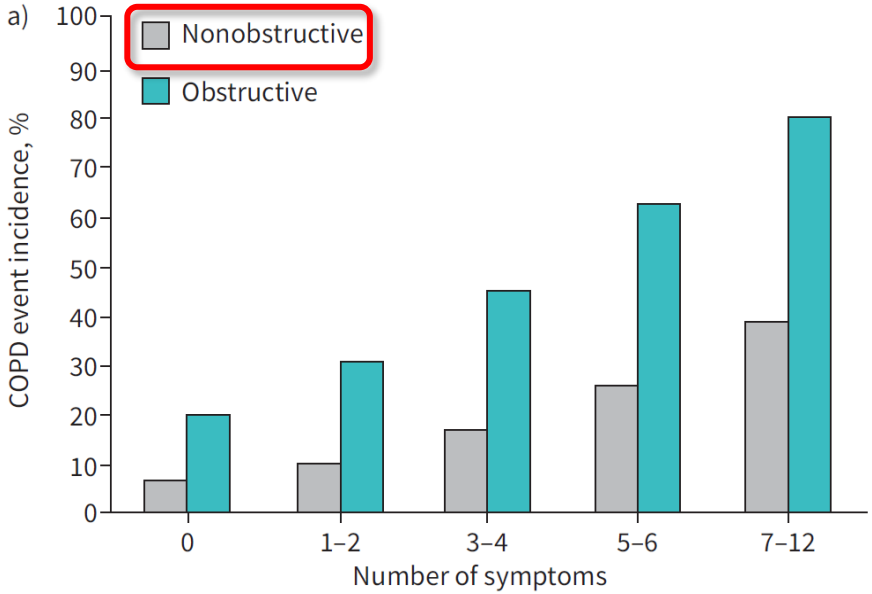
Olofson J. ERJ Open Res 2021; 7: 00383-02021.

TABLE 2 Multivariate proportional hazards regression of total symptom score, forced expiratory volume in 1 s (FEV_1), N_2-slope, attained age and smoking habit score on admission to hospital or death related to COPD

	Parameter estimate	Wald's Chi-squared[#]	p-value	Hazard ratio (95% CI)
Total symptom score[¶]	0.20	20.7	<0.0001	1.22 (1.12–1.33)
FEV_1 (quintiles)[+]	−0.35	5.6	<0.05	0.71 (0.53–0.94)
N_2-slope (quintiles)[§]	0.49	9.5	<0.005	1.63 (1.20–2.22)
Attained age[f]	0.02	0.5	NS	1.02 (0.96–1.08)
Smoking habit score[##]	0.03	0.1	NS	1.04 (0.79–1.37)

NS: nonsignificant. [#]: expresses impact of exposures on outcome with one degree of freedom for all variables; [¶]: sum of yes-responses from all 12 symptoms; [+]: FEV_1 in percentage of predicted normal according to Hedenström *et al.* [16] in quintiles; [§]: alveolar slope of the single-breath nitrogen test in percentage of predicted normal according to Sixt *et al.* [17] in quintiles; [f]: age at each year of follow-up; [##]: 1=never-smoker, 2=ex-smoker since >6 months, 3=currently smoking 1–14 $g \cdot day^{-1}$, 4=smoking 15–24 $g \cdot day^{-1}$, 5=smoking >24 $g \cdot day^{-1}$.

Olofson J. ERJ Open Res 2021; 7: 00383-02021.



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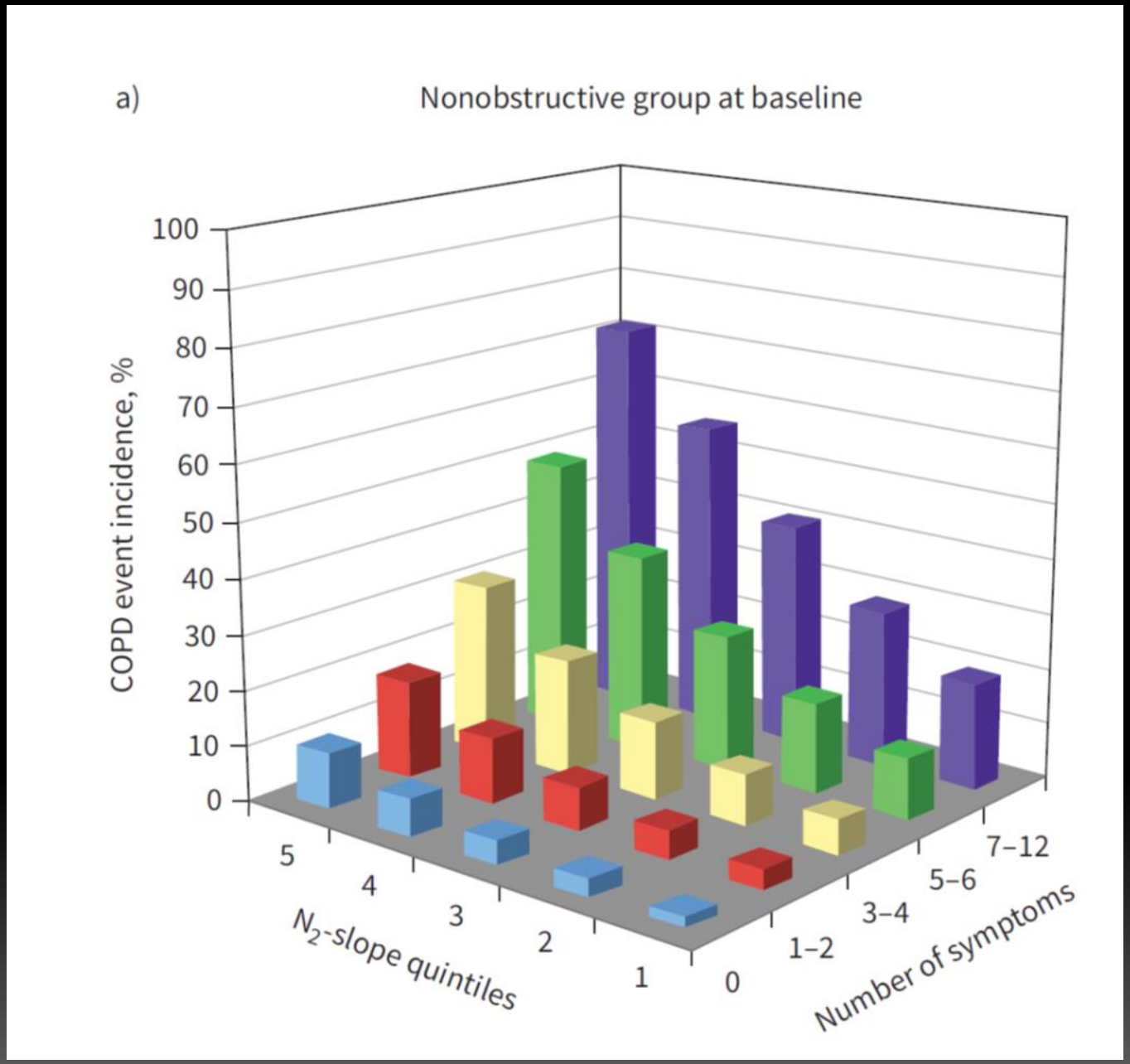


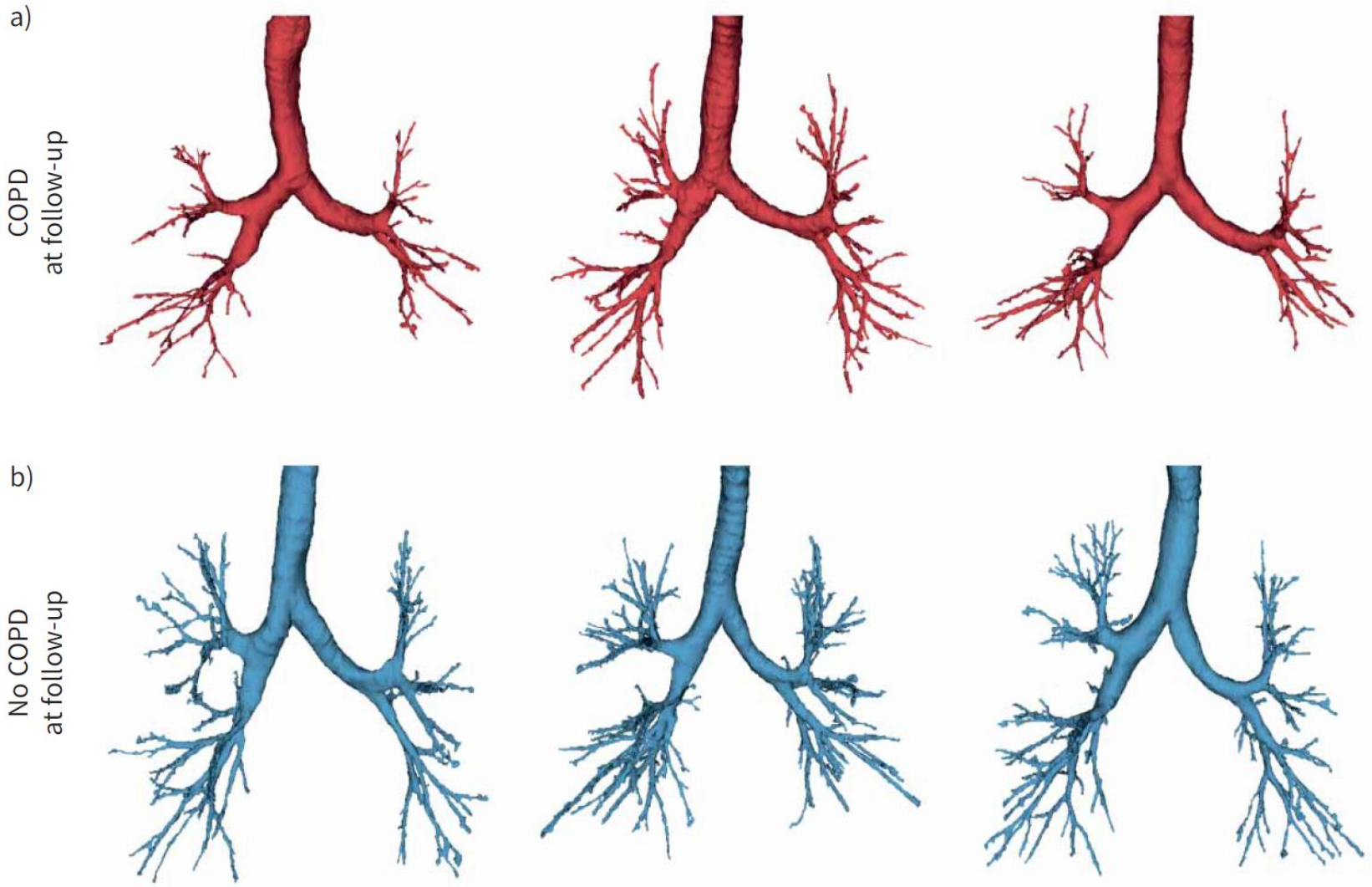
Olofson J. ERJ Open Res 2021; 7: 00383-02021.

Computed tomography total airway count predicts progression to COPD in at-risk smokers

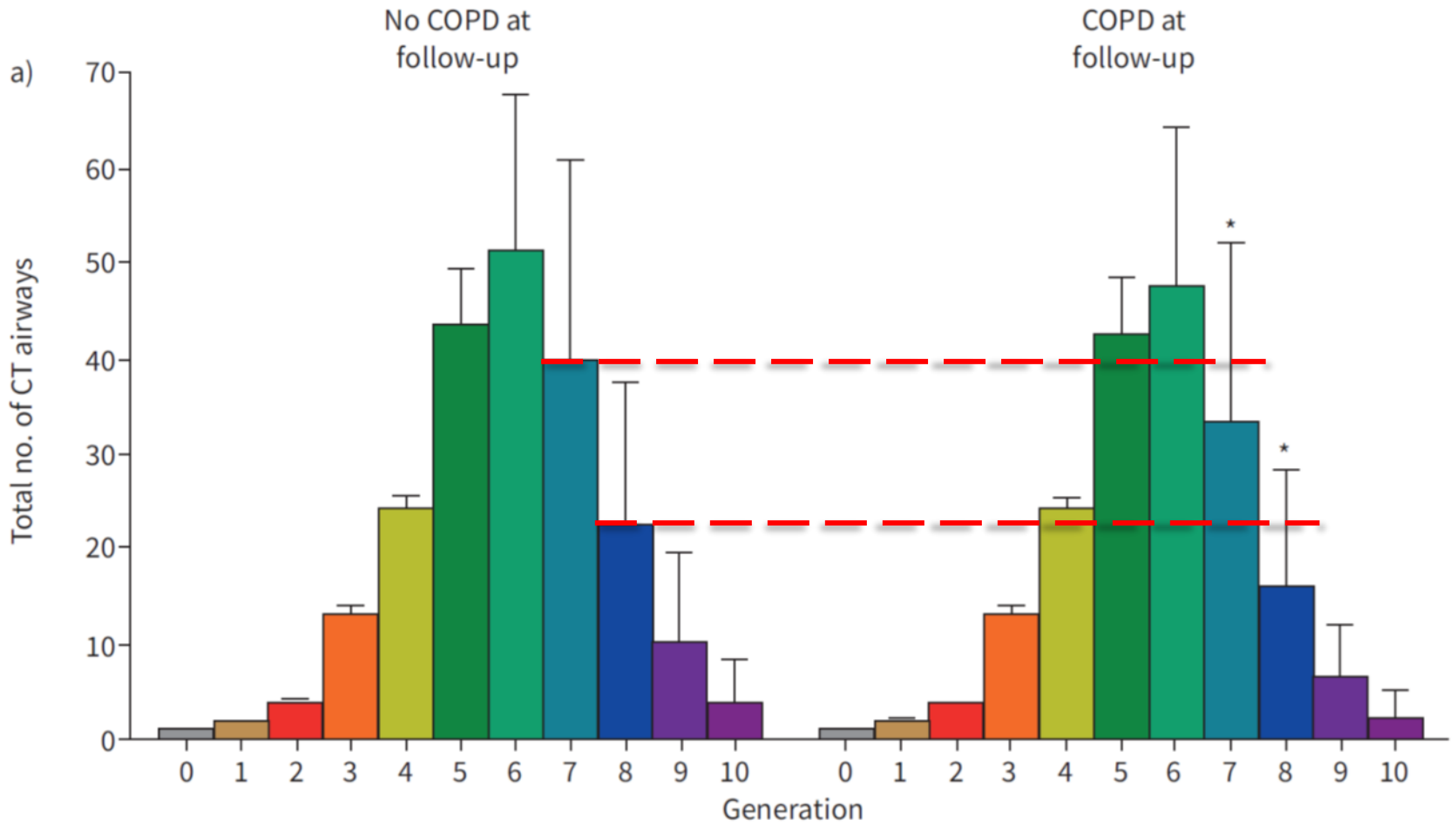
Miranda Kirby[1,2], Benjamin M. Smith[3,4,5], Naoya Tanabe[2], James C. Hogg[2], Harvey O. Coxson[2], Don D. Sin[2], Jean Bourbeau[6,7] and Wan C. Tan[2] for the CanCOLD Collaborative Research Group and the Canadian Respiratory Research Network

[1]Dept of Physics, Ryerson University, Toronto, ON, Canada. [2]UBC Centre for Heart Lung Innovation, St Paul's Hospital, Vancouver, BC, Canada. [3]Dept of Medicine, McGill University, Montreal, QC, Canada. [4]Dept of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, QC, Canada. [5]Dept of Medicine, Columbia University Medical Center, New York, NY, USA. [6]Montreal Chest Institute of the Royal Victoria Hospital, McGill University Health Centre, Montreal, QC, Canada. [7]Respiratory Epidemiology and Clinical Research Unit, Research Institute of McGill University Health Centre, Montreal, QC, Canada.

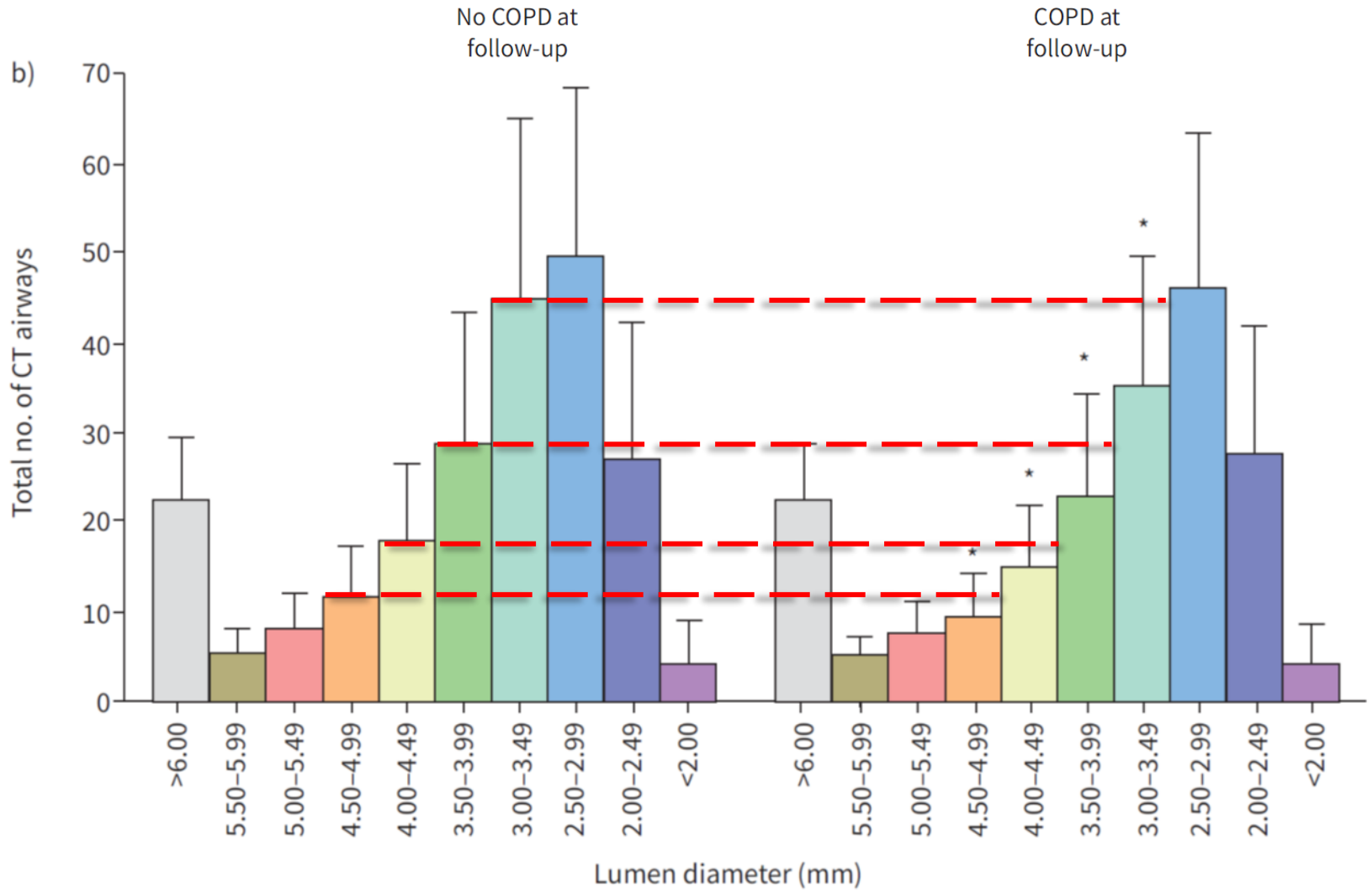
Kirby M. ERJ Open Res 2021; 7: 00307-02021.



Kirby M. ERJ Open Res 2021; 7: 00307-02021.



Kirby M. ERJ Open Res 2021; 7: 00307-02021.



Kirby M. ERJ Open Res 2021; 7: 00307-02021.

	COPD development at Visit 3			COPD development at last visit		
	Point estimate	95% confidence limits	p-value	Point estimate	95% confidence limits	p-value
N		285			316	
Time from Visit 1, years (±SD)		3.2 (0.3)			3.1 (0.6)	
Models[#]						
TAC	1.82	1.14–2.92	0.01	1.66	1.05–2.60	0.03
Pi10	1.02	0.69–1.51	0.92	0.95	0.65–1.38	0.78
Wall area percent	0.96	0.67–1.36	0.80	1.00	0.71–1.41	0.99
LAA_{856}	1.03	0.57–1.85	0.92	0.97	0.54–1.72	0.91

Kirby M. ERJ Open Res 2021; 7: 00307-02021.

TABLE 3 Mixed effects multivariable regression models for longitudinal FEV_1, FVC and FEV_1/FVC change with CT measurements

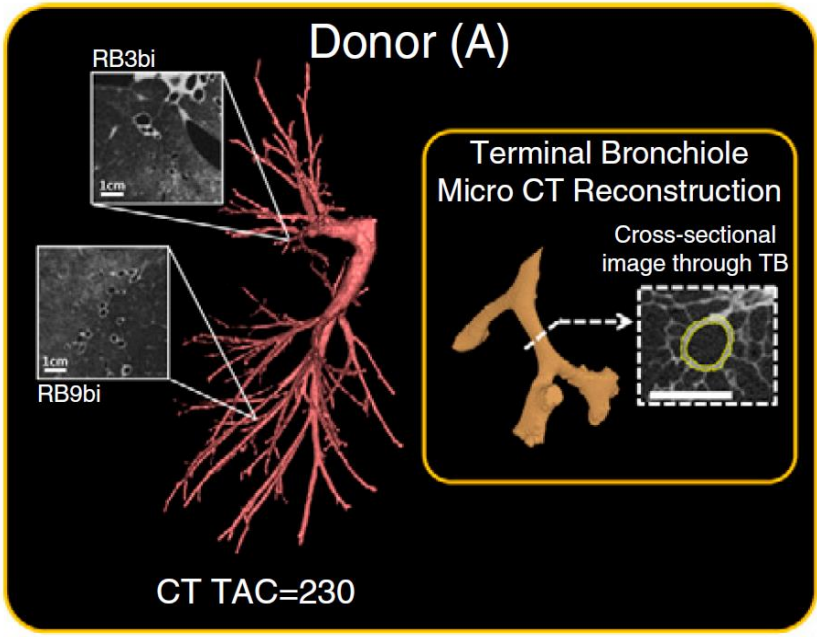
Interactions	Estimate (95% CI)	SE	p-value
FEV_1, mL			
TAC×time	−0.052	0.058	0.37
Pi10×time	−15.80	25.14	0.53
Wall area percent×time	−0.70	1.40	0.62
LAA_{856}×time	−0.32	0.26	0.22
FVC, mL			
TAC×time	−0.18	0.08	0.02
Pi10×time	−42.37	36.00	0.24
Wall area percent×time	0.73	1.97	0.71
LAA_{856}×time	−0.36	0.36	0.33
FEV_1/FVC, %			
TAC×time	0.003	0.001	0.03
Pi10×time	−0.67	0.49	0.17
Wall area percent×time	−0.03	0.03	0.33
LAA_{856}×time	−0.002	0.005	0.75

Kirby M. ERJ Open Res 2021; 7: 00307-02021.

Computed Tomography Total Airway Count Is Associated with the Number of Micro–Computed Tomography Terminal Bronchioles

To the Editor:

Kirby M. Am J Respir Crit Care Med 2020; 201: 613-615.



Kirby M. Am J Respir Crit Care Med 2020; 201: 613-615.

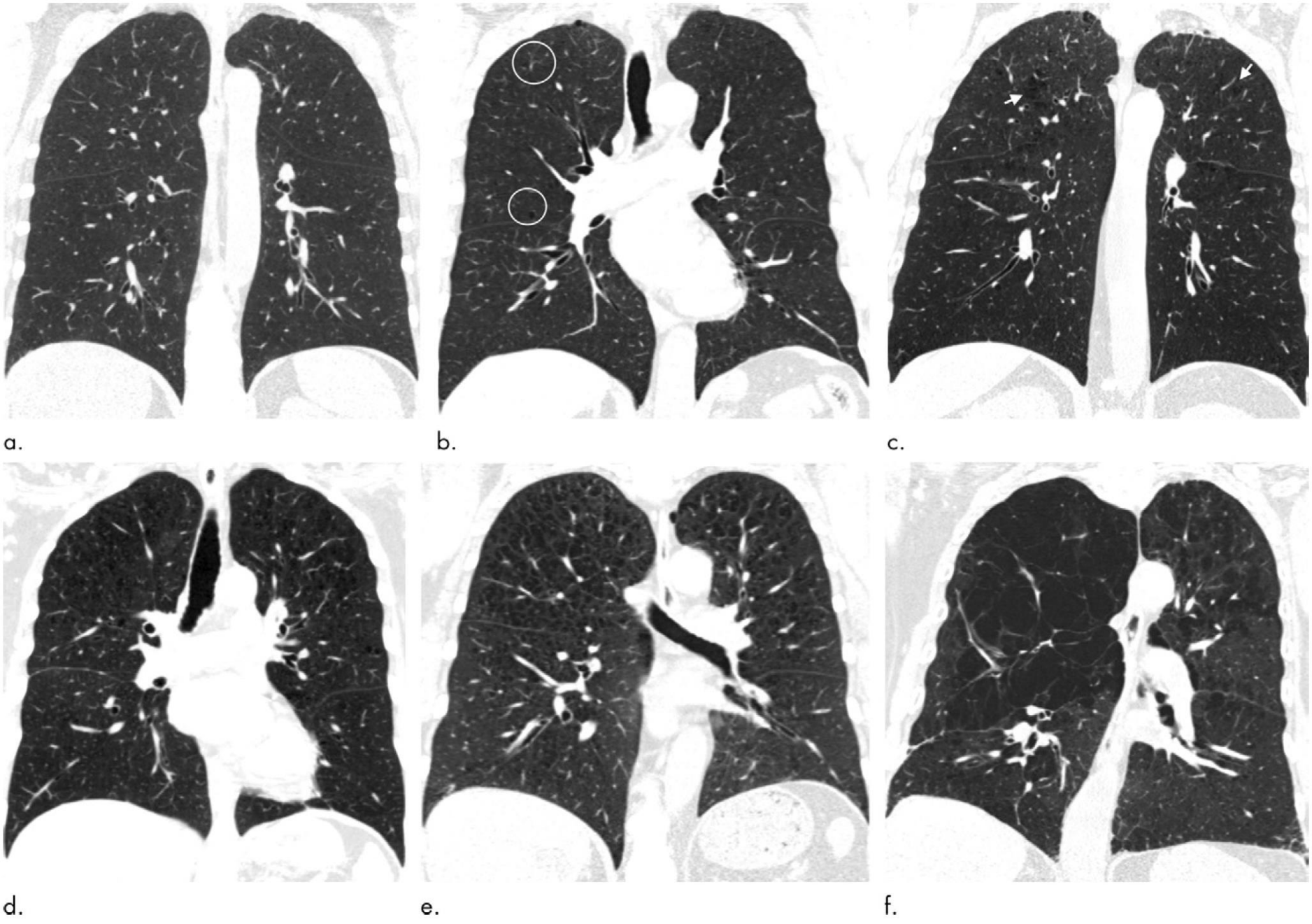
Radiology

ORIGINAL RESEARCH • THORACIC IMAGING

Visual Emphysema at Chest CT in GOLD Stage 0 Cigarette Smokers Predicts Disease Progression: Results from the COPDGene Study

Andrea S. Oh, MD • Matthew Strand, PhD • Katherine Pratte, MSPH • Elizabeth A. Regan, MD, PhD • Stephen Humphries, PhD • James D. Crapo, MD • David A. Lynch, MB • For the Genetic Epidemiology of COPDGene Investigators

Oh AS. Radiology 2020; 296: 641-649.



Oh AS. Radiology 2020; 296: 641-649.

Table 1: Baseline Characteristics according to Absence versus Presence of Visually Evident Emphysema on CT

Parameter	No Visually Evident Emphysema	Visually Evident Emphysema*	*P* Value†
No. of participants	2116 (51.7)	1979 (48.3)	
No. of deaths	127 (6.0)	166 (8.4)	.003
Demographics			
Age (y)	56 ± 8	57 ± 8	<.001
Height (cm)	170 ± 10	170 ± 9	.70
Weight (kg)	87 ± 19	81 ± 17	<.001
BMI (kg/m^2)	30 ± 6	28 ± 5	<.001
No. of men	1068 (50.5)	1096 (55.4)	.002
Ethnicity			
No. of non-Hispanic white participants	1347 (63.7)	1070 (54.1)	<.001
No. of African American participants	769 (36.3)	909 (45.9)	<.001
Smoking status			
No. of current smokers	1111 (52.5)	1313 (66.3)	<.001
No. of pack-years smoked‡	30 (21)	38 (23)	<.001
Comorbidities			
No. of exacerbations in past year	187 (8.8)	168 (8.5)	.69
No. with chronic bronchitis	155 (7.7)	189 (10)	<.01
Functional parameters			
Percentage predicted FEV_1	98 ± 12	97 ± 11	<.001
FEV_1-to-FVC ratio	0.8 ± 0.1	0.8 ± 0.0	<.001
6-minute walk distance (m)‡	461.1 (132.6)	445.5 (128.7)	<.001
No. of participants with mMRC dyspnea score answer of yes	736 (34.8)	776 (39.2)	.004
SGRQ‡	9 (21)	11 (26)	<.001
$\%LAA_{-950}$‡	0.90 (2.3)	0.98 (2.3)	<.03
Adjusted lung density (g/L)	94 ± 20	96 ± 21	<.001
FRC_{CT}-to-TLC_{CT} ratio	0.5 ± 0.1	0.5 ± 0.1	<.001

Oh AS. Radiology 2020; 296: 641-649.

Table 4: Estimated 5-year Mean Change in CT Parameters, Lung Function, and Clinical Status for Participants Stratified by Emphysema Grade according to the Fleischner Society Classification System

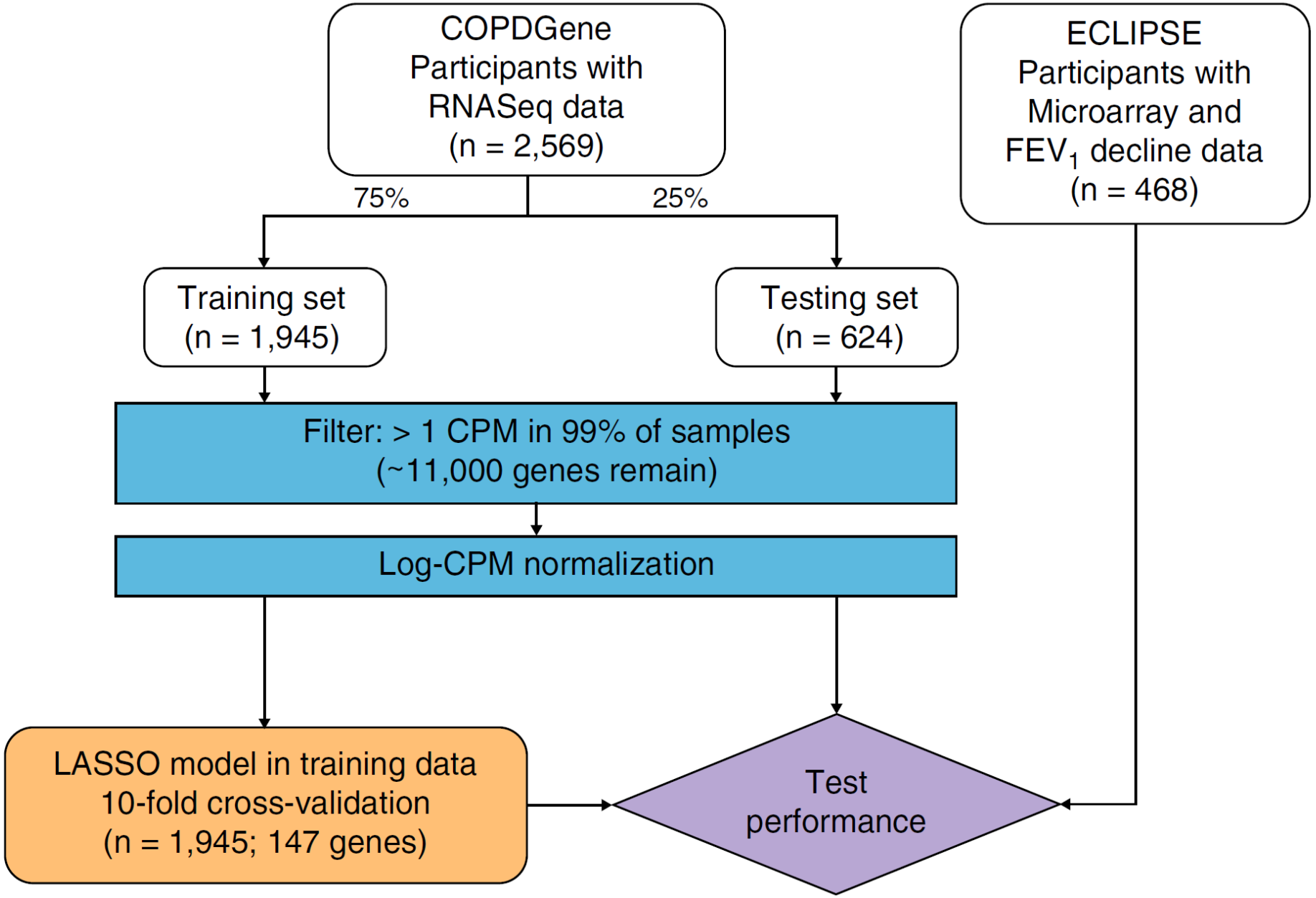
Parameter	Trace	Mild	Moderate	Confluent and Advanced Destructive	*P* Value
ALD (g/L)	−2.01 (−3.11, −0.91)	−4.13 (−5.28, −2.98)	−3.79 (−5.52, −2.05)	−5.63 (−10.09, −1.17)	.006
Perc15 (HU)	−2.68 (−4.37, −1.00)	−4.05 (−5.82, −2.28)	−2.71 (−5.45, 0.03)	−5.77 (−12.97, 1.42)	.50
Natural log $\%LAA_{-950}$	0.01 (−0.09, 0.10)	0.26 (0.17, 0.36)	0.35 (0.20, 0.50)	0.37 (−0.02, 0.77)	<.001
FRC_{CT}-to-TLC_{CT} ratio	−0.50 (−1.37, 0.38)	0.13 (−0.80, 1.06)	−1.14 (−2.63, 0.34)	−4.12 (−8.04, −0.21)	.10
(FEV_1-to-FVC ratio) · 100	−1.5 (−2.0, −1.0)	−1.9 (−2.4, −1.4)	−3.2 (−4.0, −2.3)	−1.1 (−3.4, 1.1)	.005
FEV_1 (mL)	−85 (−112, −58)	−97 (−126, −68)	−81 (−128, −34)	−98 (−221, 24)	.90
6MWD (m)	−10.8 (−20.4, −1.5)	−15.0 (−25.5, −4.8)	−15.0 (−31.8, 1.8)	−9.0 (−54.6, 36.6)	.92
SGRQ total	0.67 (−0.83, 2.16)	1.39 (−0.23, 3.00)	−0.04 (−2.63, 2.55)	−0.78 (−7.75, 6.20)	.74
SF36 general	−1.51 (−2.56, −0.47)	−0.73 (−1.85, 0.39)	−1.71 (−3.51, 0.09)	0.66 (−4.28, 5.61)	.56

ORIGINAL ARTICLE

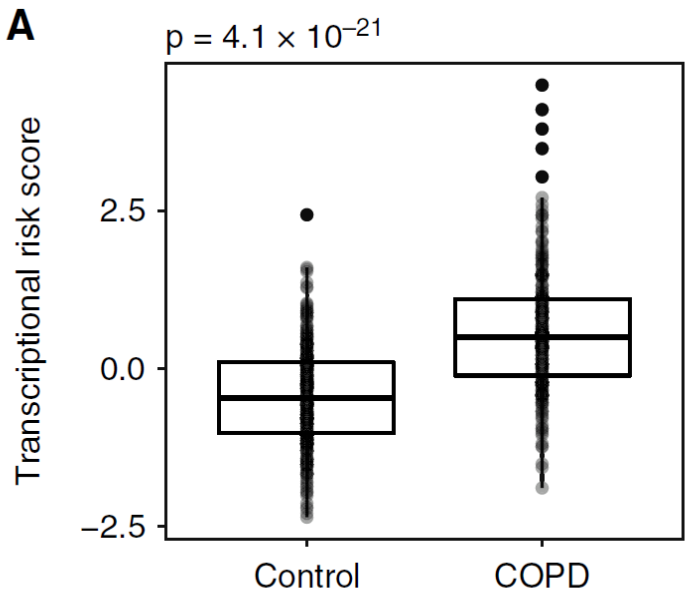
Development of a Blood-based Transcriptional Risk Score for Chronic Obstructive Pulmonary Disease

Matthew Moll[1,2], Adel Boueiz[1,2], Auyon J. Ghosh[1,2], Aabida Saferali[1], Sool Lee[1,3], Zhonghui Xu[1], Jeong H. Yun[1,2], Brian D. Hobbs[1,2], Craig P. Hersh[1,2], Don D. Sin[4,5], Ruth Tal-Singer[6], Edwin K. Silverman[1,2], Michael H. Cho[1,2*], and Peter J. Castaldi[1,7*]; on behalf of the COPDGene Investigators

Moll M. Am J Respir Crit Care Med 2022; 205: 161-170.



Moll M. Am J Respir Crit Care Med 2022; 205: 161-170.



Moll M. Am J Respir Crit Care Med 2022; 205: 161-170.

Table 3. Multivariable Models Including Clinical Factors, PRS, and TRS for Moderate-to-Severe COPD and Change in FEV_1

	COPDGene Testing Sample				ECLIPSE	
	Moderate to Severe COPD		Change in FEV_1 (*ml/yr*)		Change in FEV_1 (*ml/yr*)	
Variable	OR (95% CI)	*P* Value	β (95% CI)	*P* Value	β (95% CI)	*P* Value
PRS	1.67 (1.31 to 2.13)	<0.0001	−4.2 (−14 to 5.1)	0.37	1.3 (−5.3 to 8)	0.69
TRS	3.27 (2.38 to 4.5)	<0.0001	−17 (−28 to −6.6)	0.002	−8.2 (−15 to −1)	0.025
Baseline FEV_1, L	N/A	N/A	−24 (−38 to −9.9)	0.0011	−34 (−50 to −19)	1.90×10^{-5}

Moll M. Am J Respir Crit Care Med 2022; 205: 161-170.

Conclusions

- COPD in young people
  - Definition: FEV1/FVC<0.7, age: 20~50
  - Risk factors: early life disadvantage, smoking, genetic susceptibility, asthma, chronic sinusitis
- Pre-COPD
  - Definition: FEV1/FVC≥0.7, syptom/abnormality
  - Risk factors for progression to COPD: FEV1/FVC<0.7, FEV3/FVC<LLN, high phase 3 slope, low TAC, emphysema in CT, TRS