KU LEUVEN

Smoking and its effect on pulmonary function

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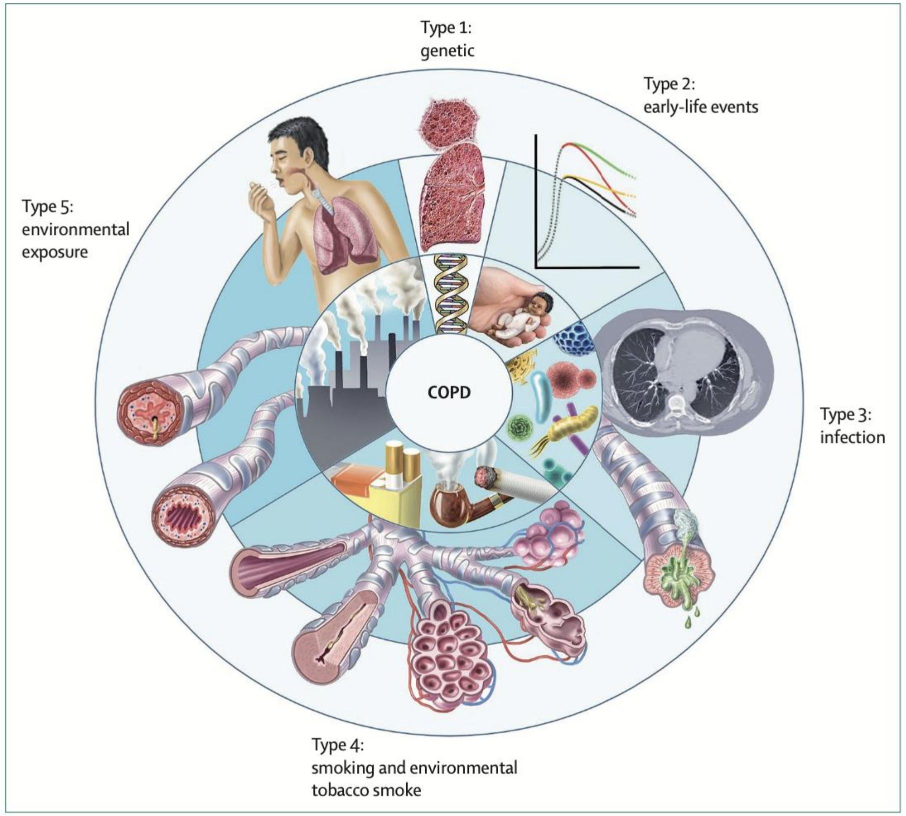
BREATHE - CHROMETA, KU Leuven

Conflicts of interest

- Received research grants from Chiesi, AZ, Roche, PulmonX, GSK
- Received consultancy and lecture fees from GSK, Chiesi, AZ, Griffols

Scientific disclosure 1



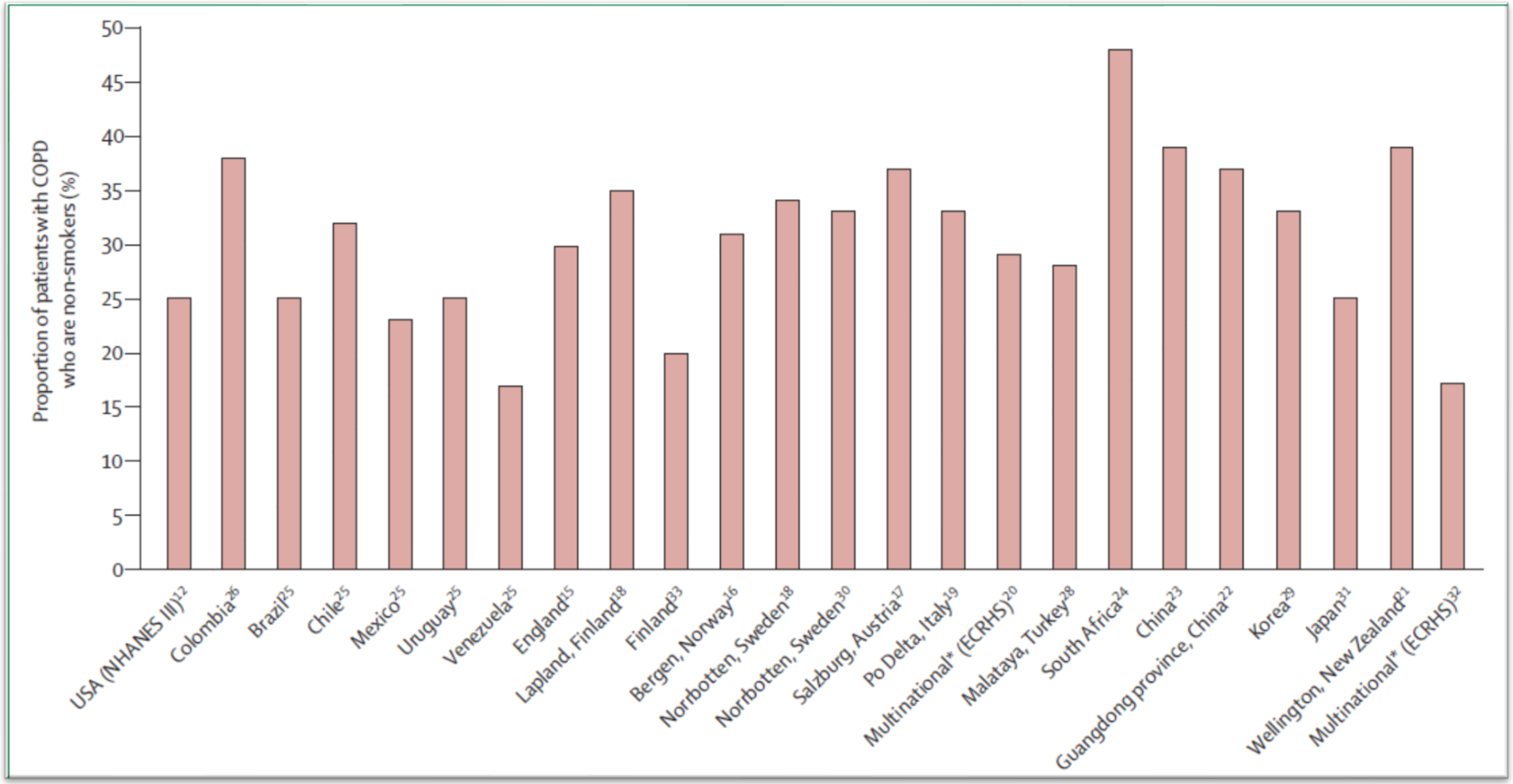
The Lancet Commissions

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, WHIV-associated COPD
COPD & asthma (COPD-A)	Particularly childhood asthma
COPD of unknown cause (COPD-U)	

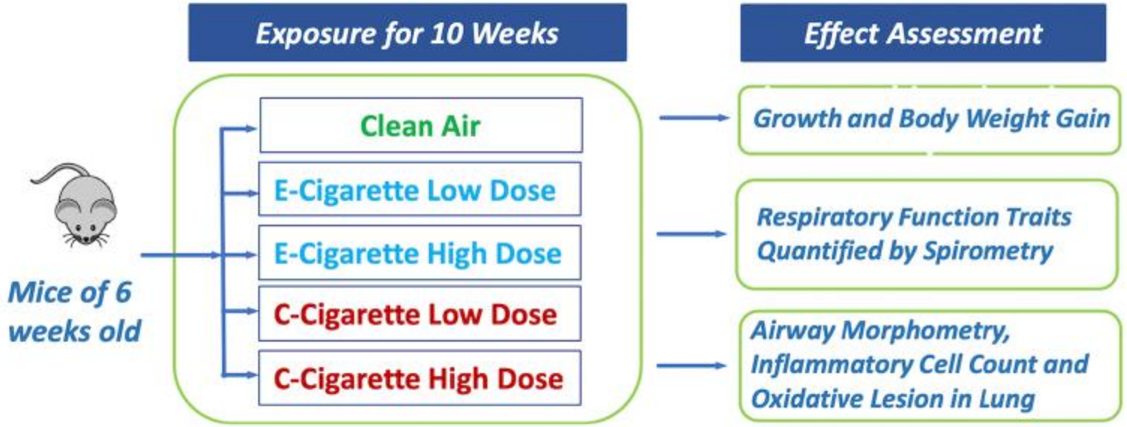
*Adapted from Celli et al. (2022) and Stolz et al. (2022)

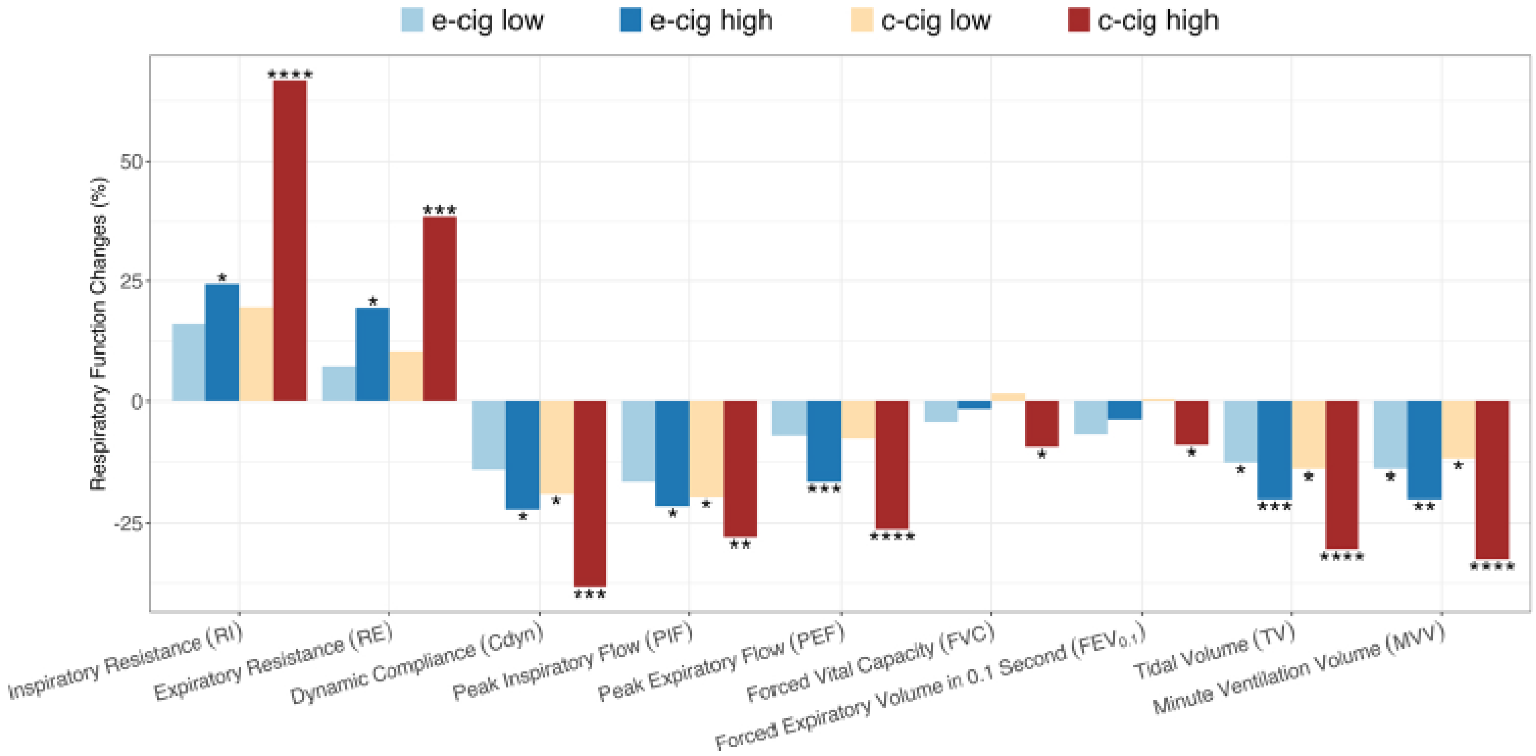
Scientific disclosure 2



Salvi S and Barnes P, Lancet 2009; 374:733-43

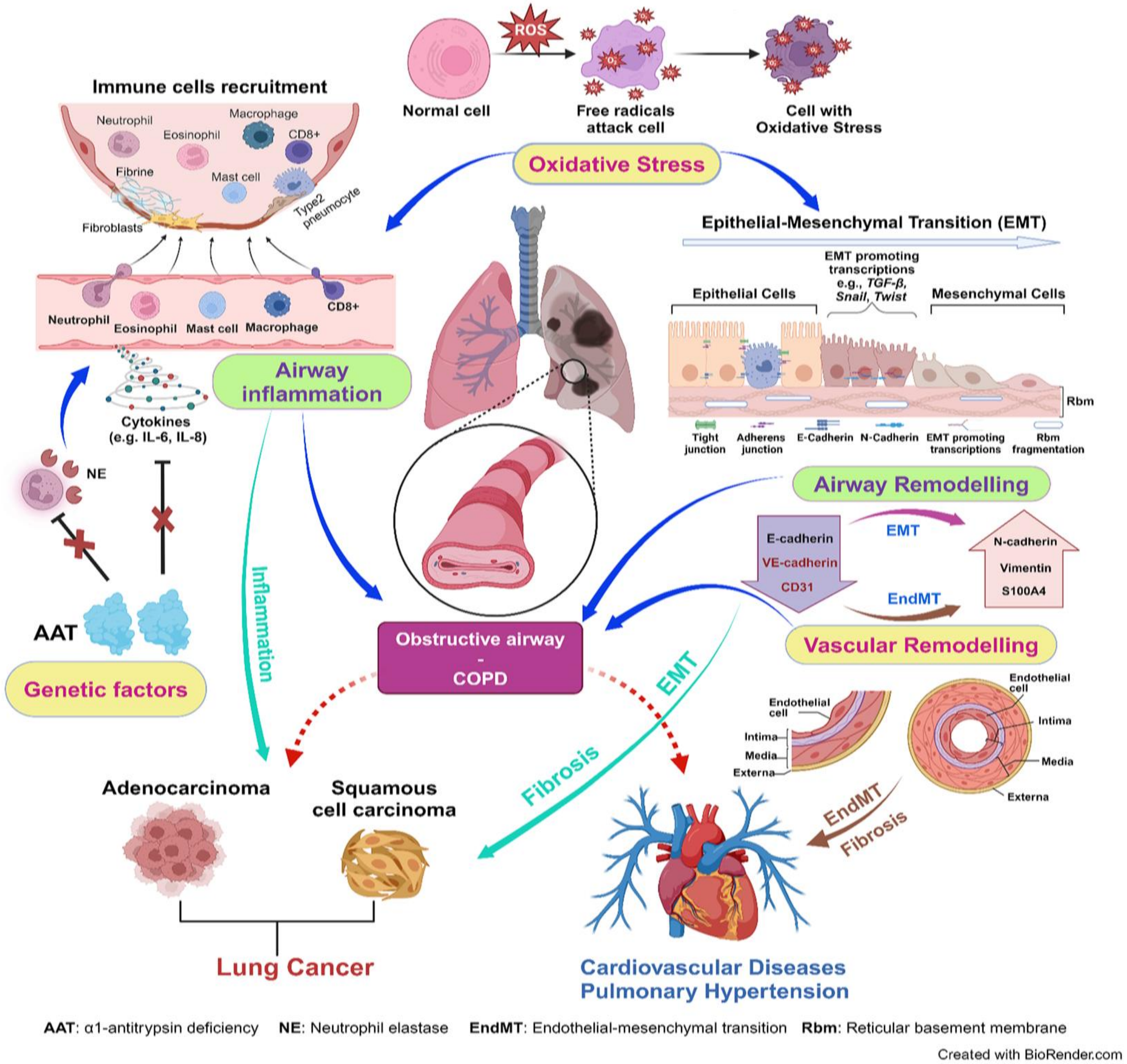
Scientific disclosure 3





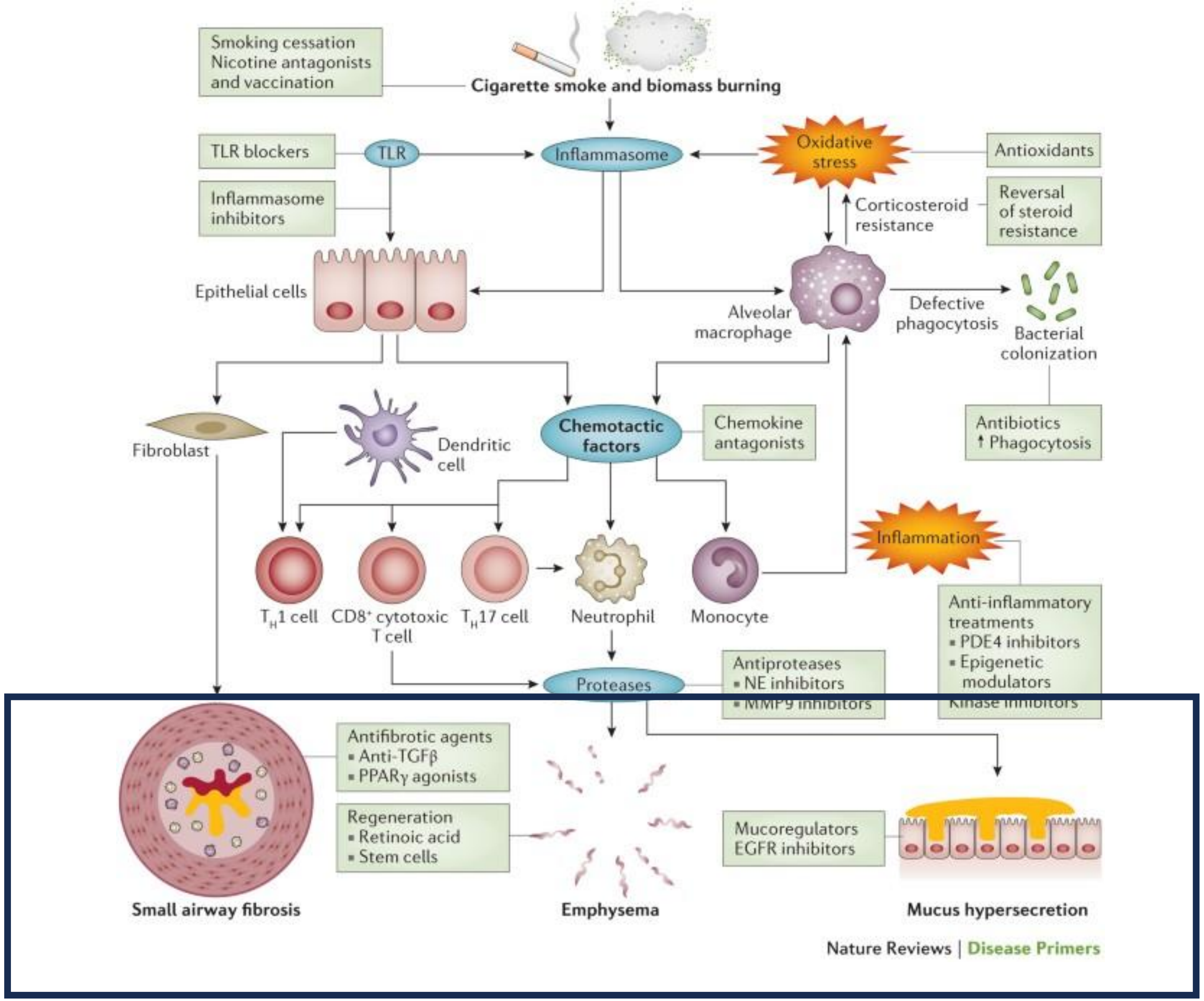
Zhang et al. Ecotoxicology 2023; 114426

Smoking and pathogenesis



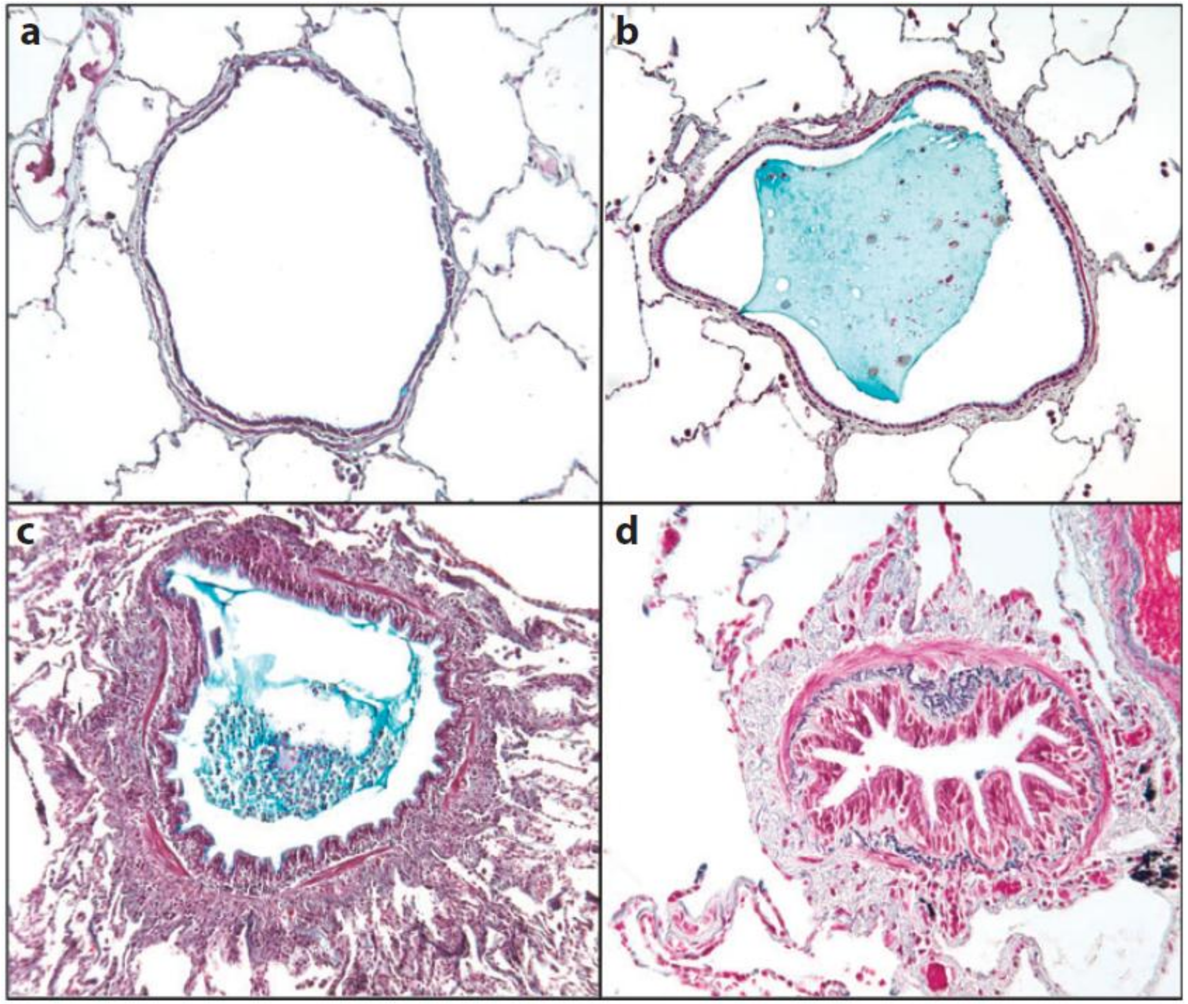
Lu W. Respiratory Research 25, 2024

Smoking and pathogenesis



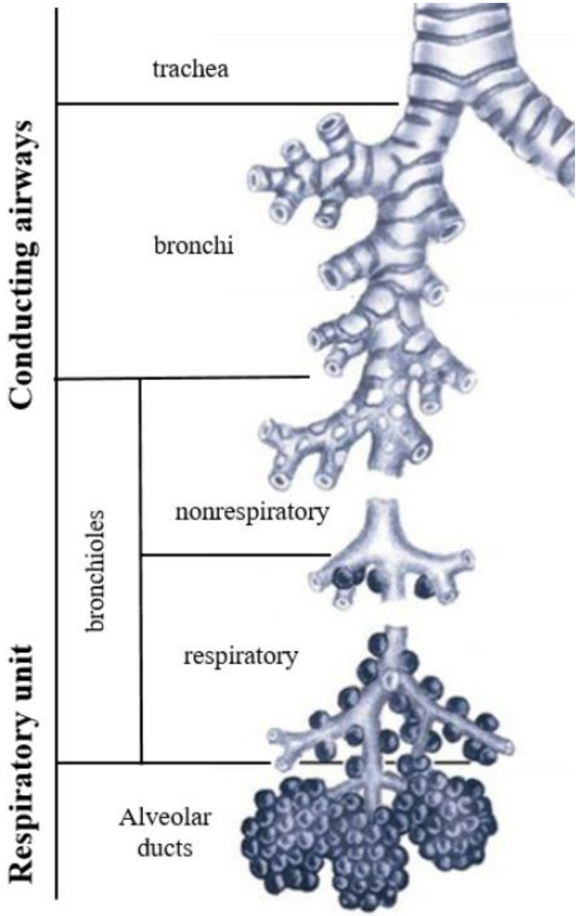
Barnes P et al. Nature reviews, 2015

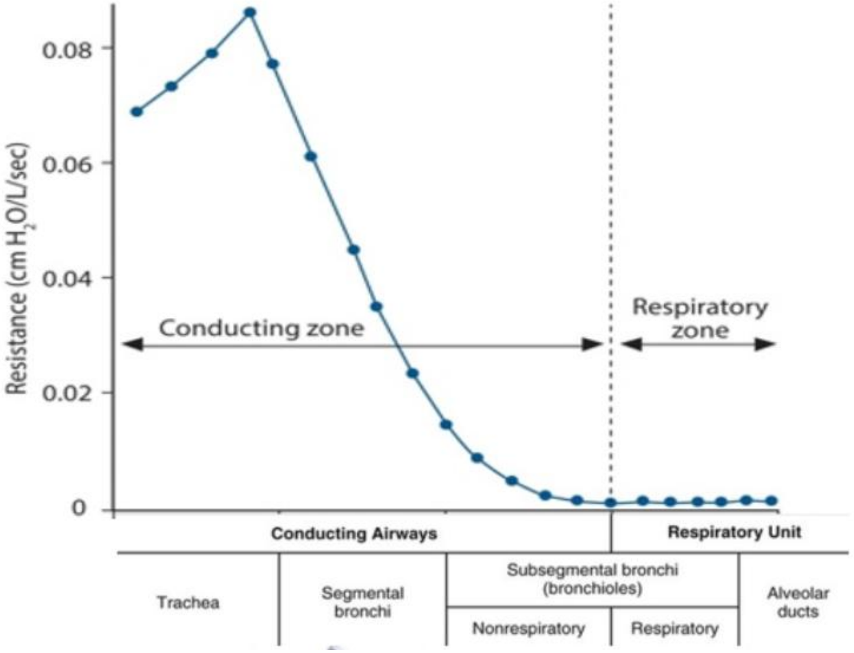
Smoking and airway pathology



Hogg JC. Lancet. 2004;364:709-721.

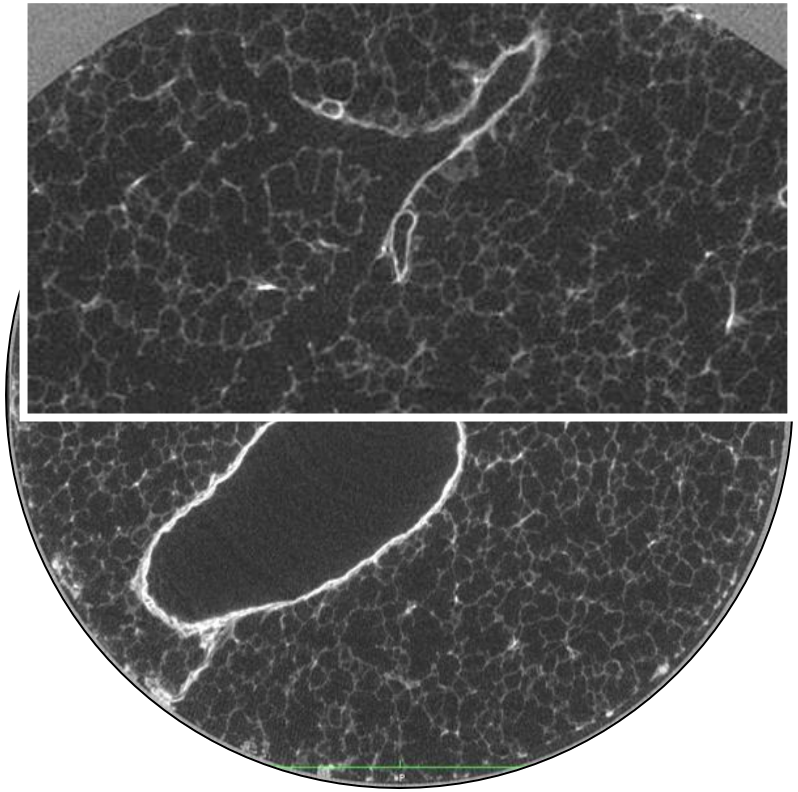
Small airways – silent zone

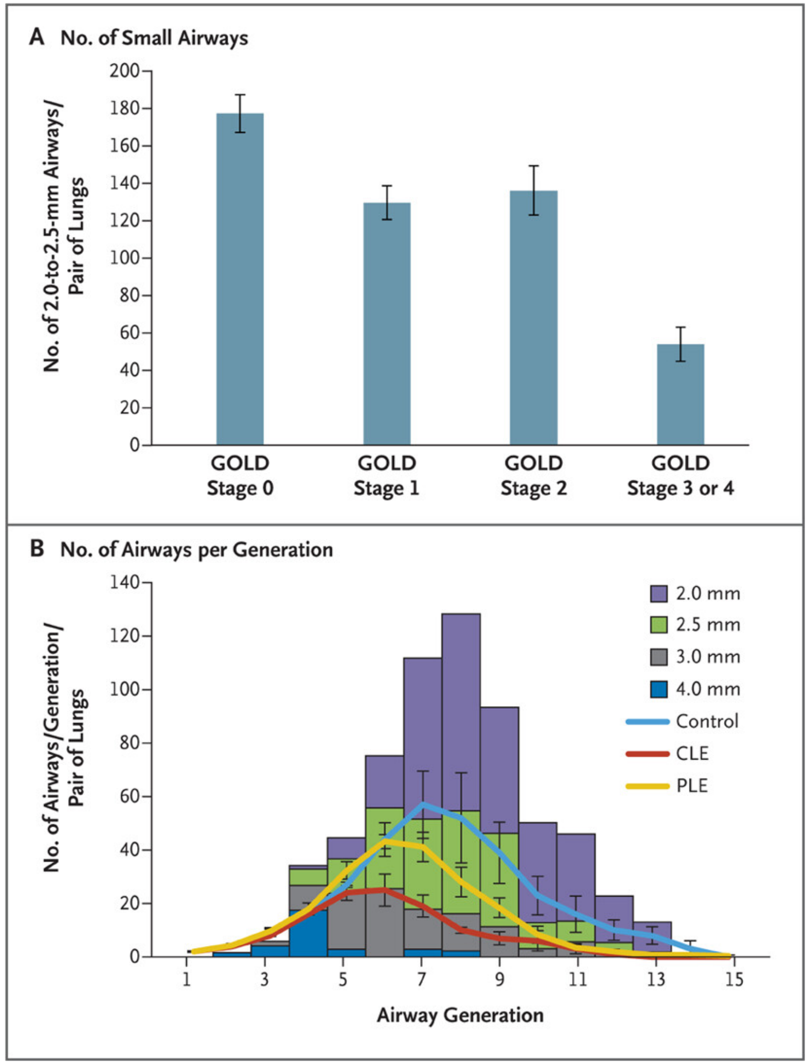




Impact van vernauwing luchtweg >>> Impact van vernauwing luchtweg

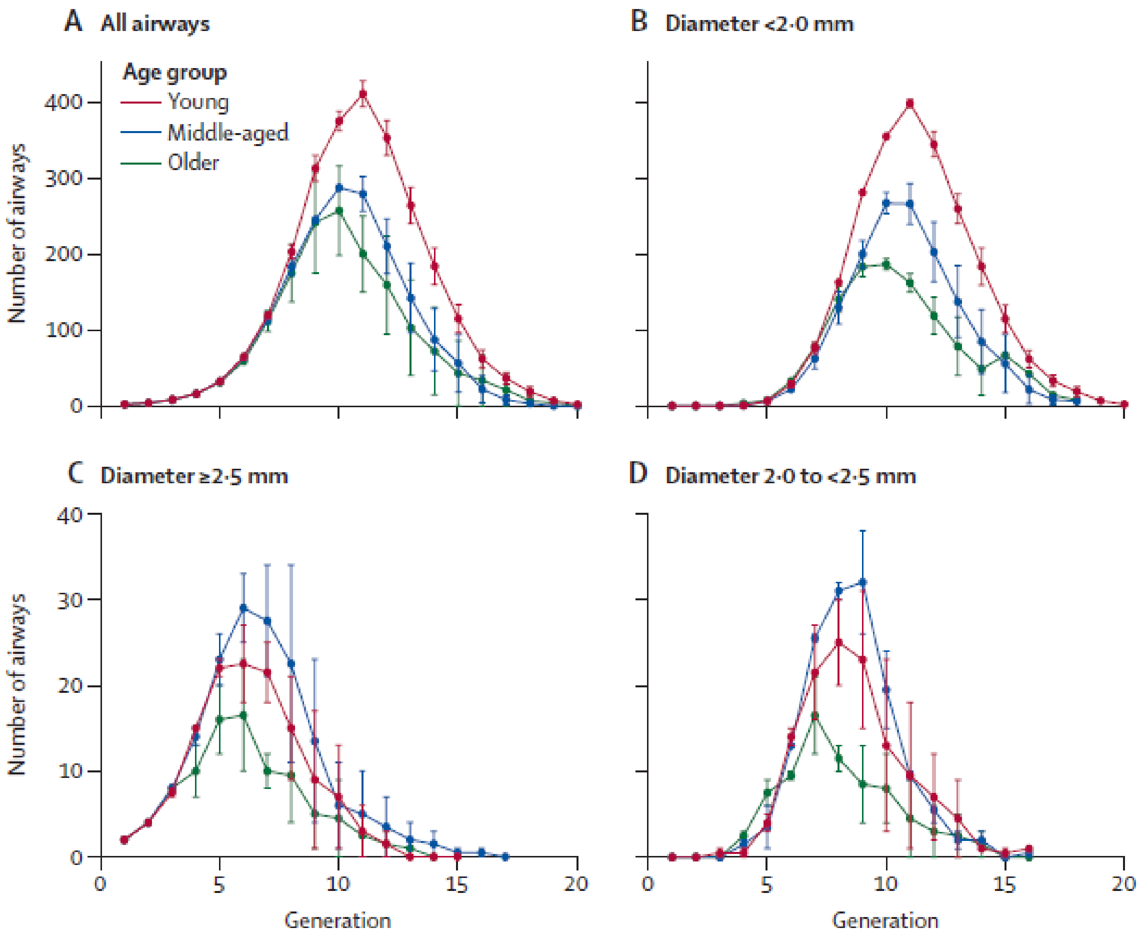
Small airways disappear

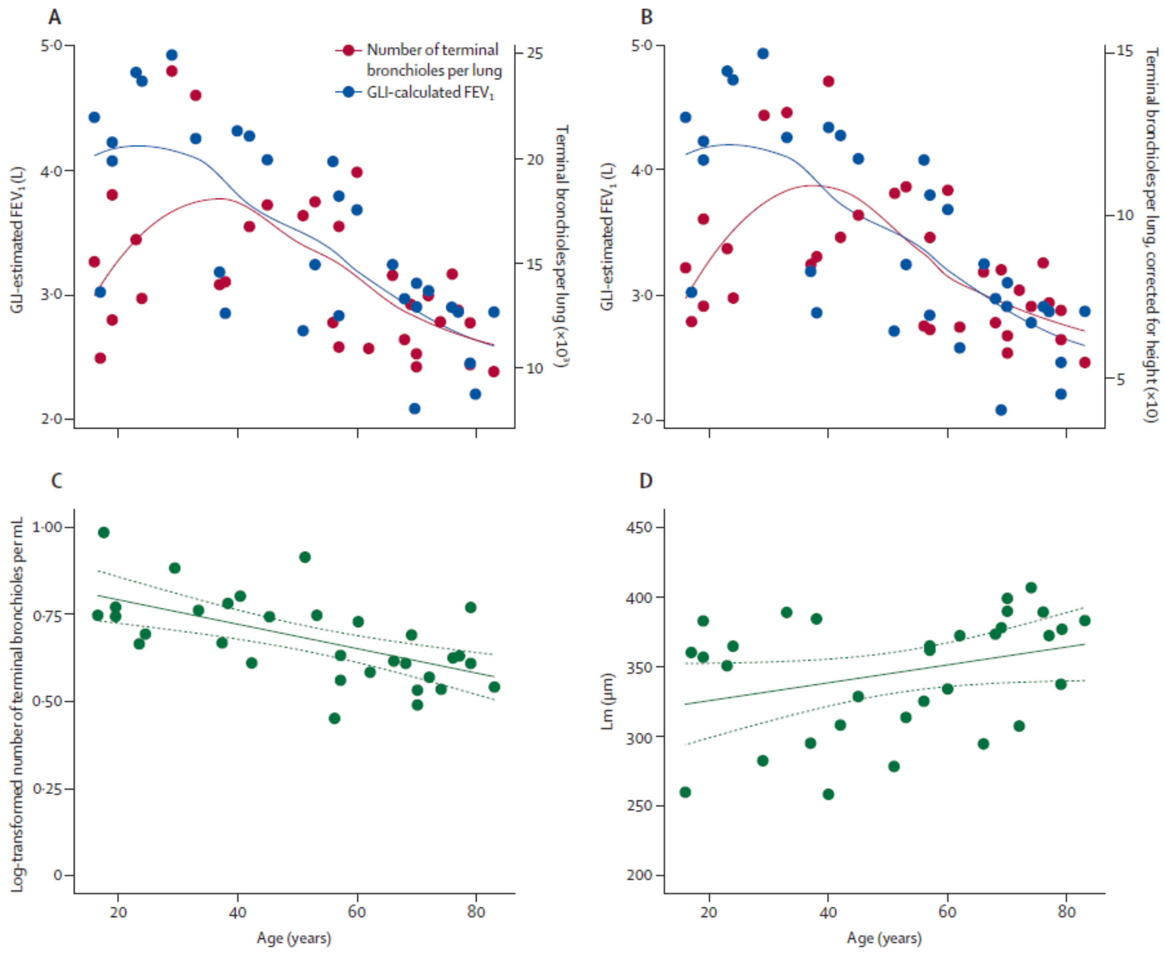




McDonough JE et al. N Engl J Med 2011;365:1567-1575

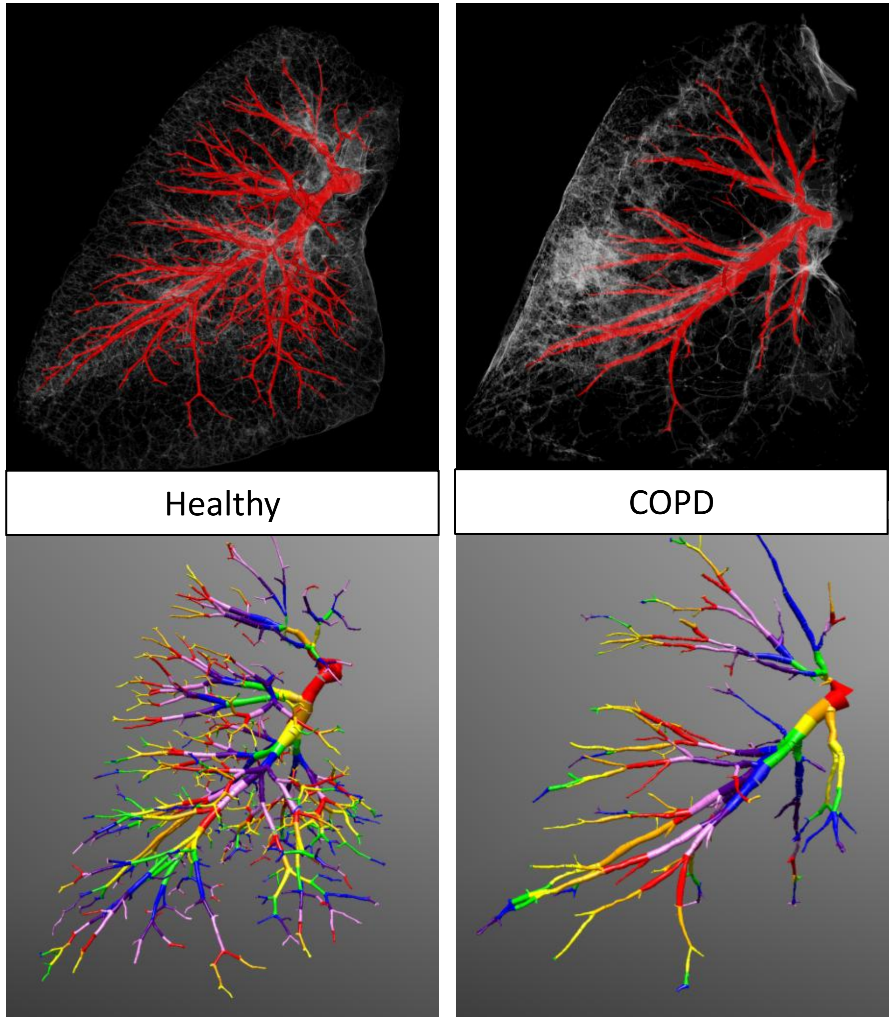
Small airways disappear with ageing





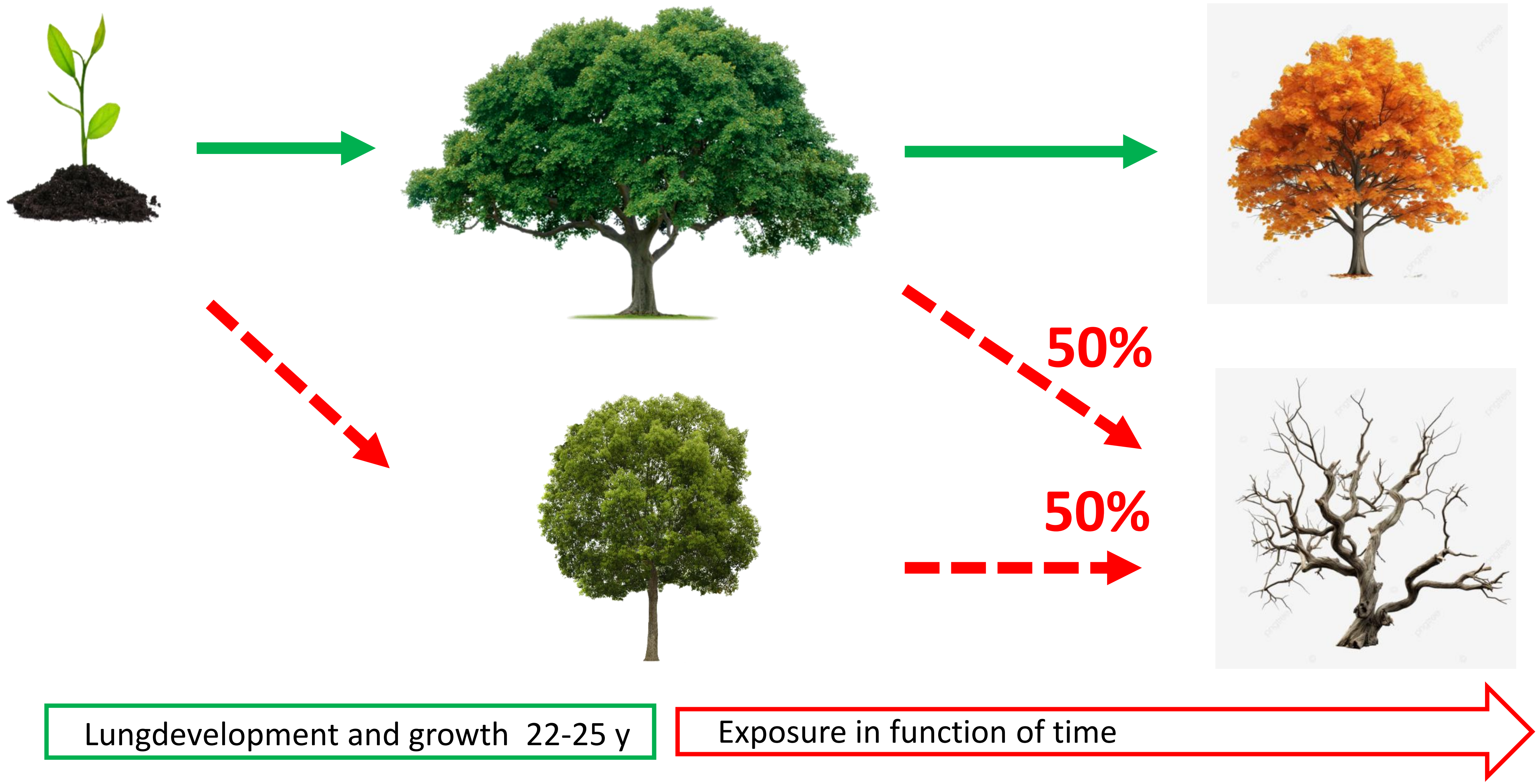
Verleden S et al. Lancet Respir Med 2021

Disappearance of small airways on whole lung



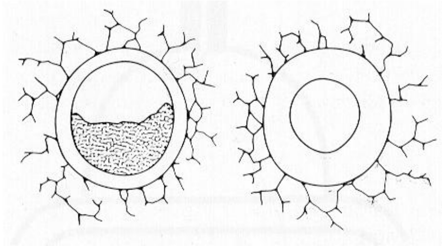
Everaerts et al. ERJ 2019

Exposure at early age and adolescence



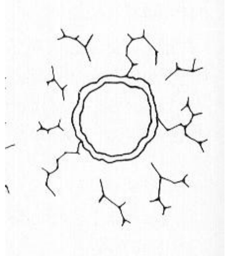
Spirometry as comprehensive tool for measuring disease

- Bronchial wall thickening by inflammation
- Muscular contraction and airway remodelling
- Intraluminal secretions and mucus plugs



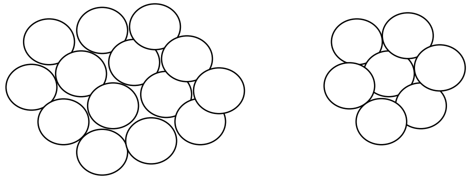
Intraluminal diameter of airway reduces

- Loss of elasticity and alveolar pressure – driving pressure for expiration
- Loss of lung tissue and airway interdependence – loss of alveolar attachments

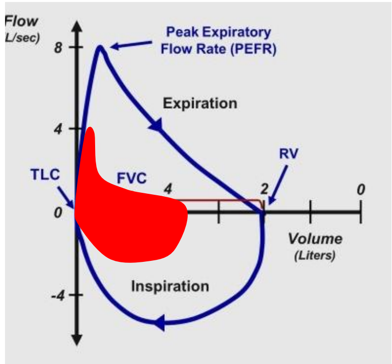


Collapse of small airways with forced expiration

- Underdevelopment of airway tree – differentiation
- Loss of airways generations



Reduced total airway surface –
increase in total airways resistance



FEV$_1$, forced expiratory volume in 1 second; FVC, forced vital capacity
Speaker's own figure

Spirometry as comprehensive tool for measuring disease

- Bronchial wall thickening by inflammation
- Muscular contraction and airway remodelling
- Intraluminal secretions and mucus plugs

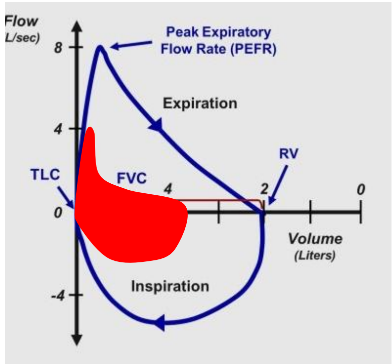
Intraluminal diameter of airway reduces

Large airway pathology

- Loss of elasticity and alveolar pressure – driving pressure for expiration
- Loss of lung tissue and airway interdependence – loss of alveolar attachments

Collapse of small airways with forced expiration

Alveolar pathology: emphysema



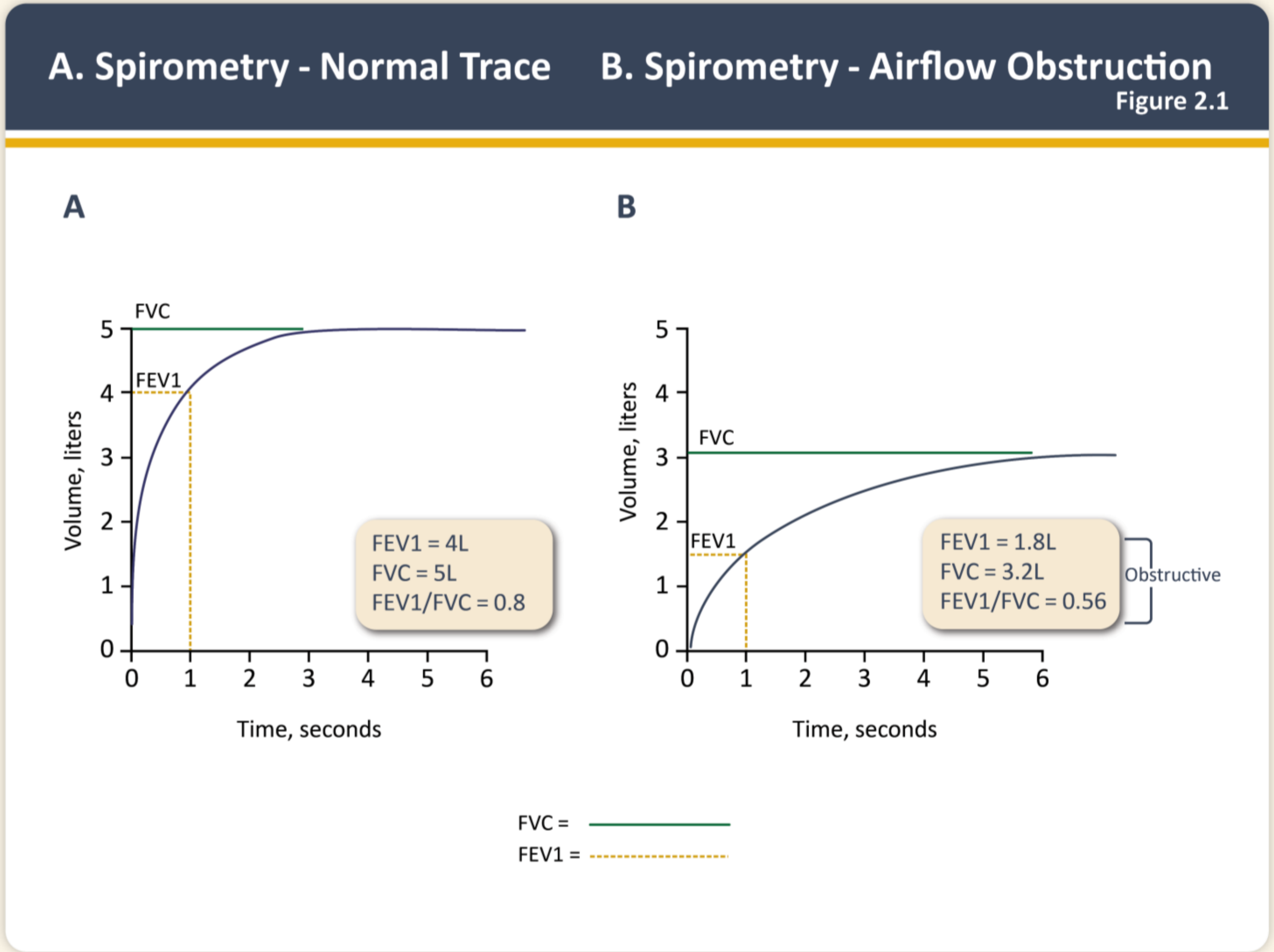
- Underdevelopment of airway tree – differentiation
- Loss of airways generations

Reduced total airway surface – increase in total airways resistance

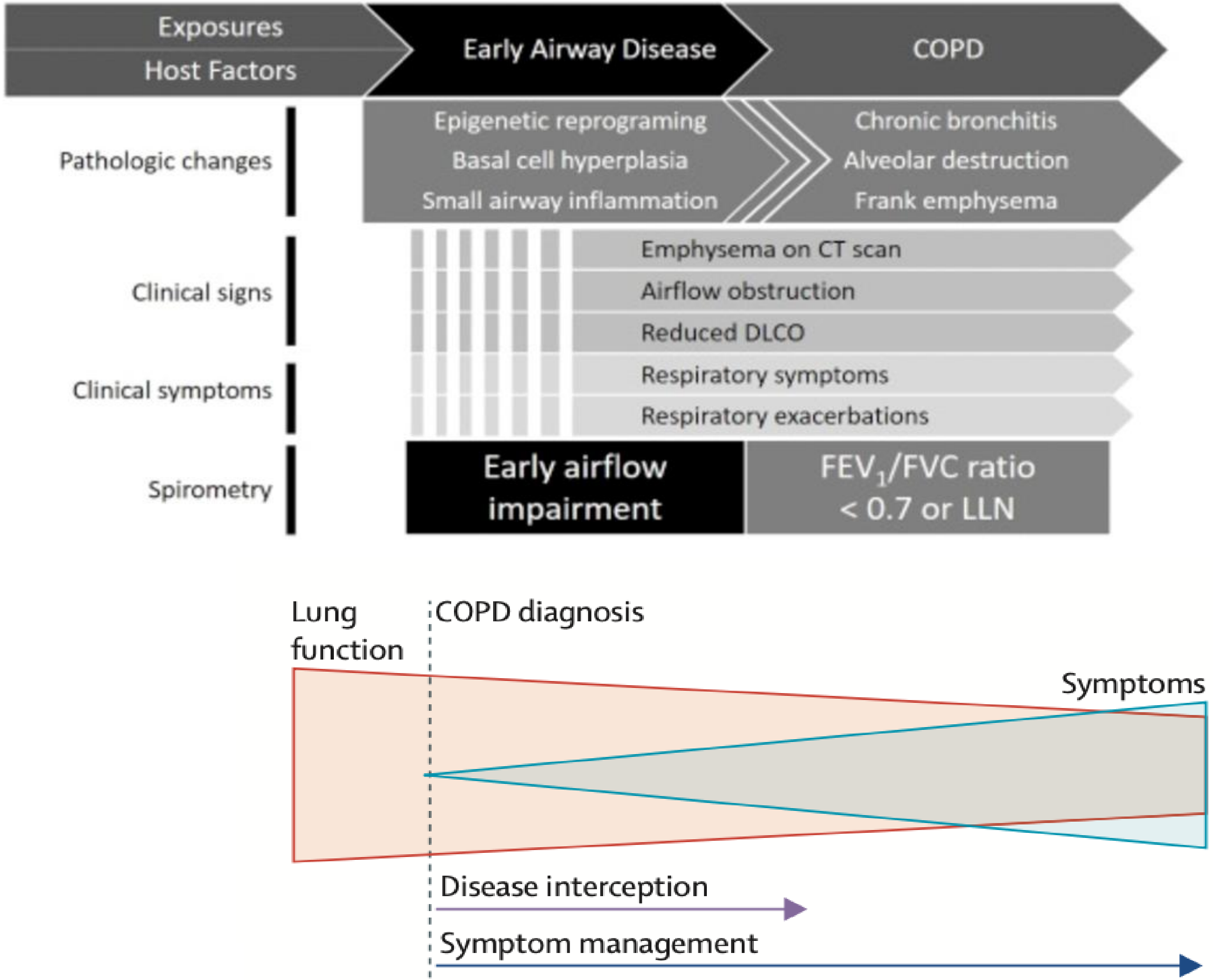
Reduced airway numbers

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity
Speaker's own figure

Spirometry diagnosis



Airways /lung disease prior to the diagnosis of COPD

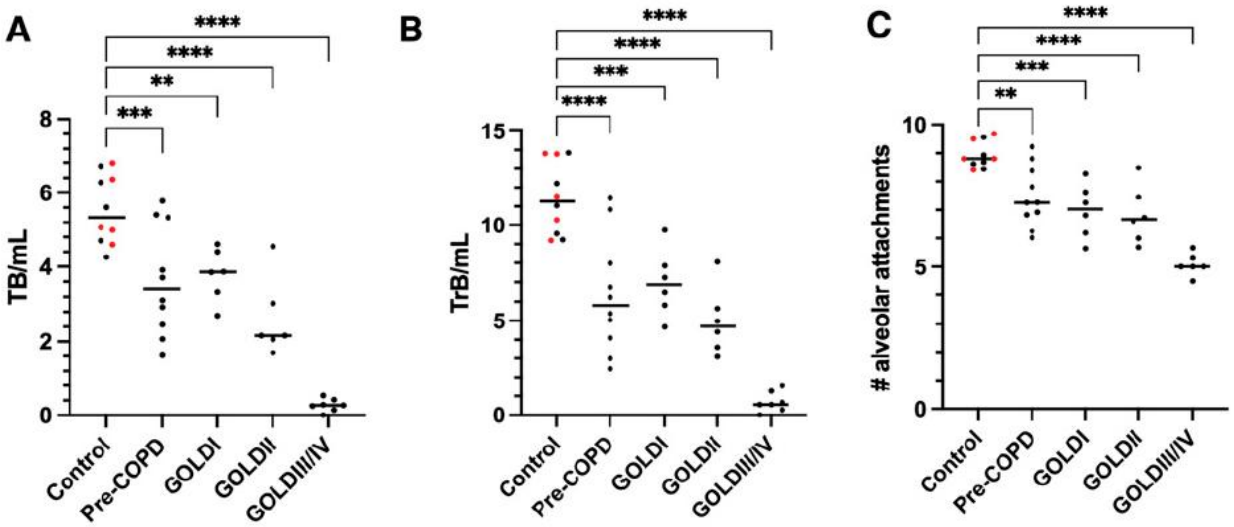


The Lancet Commissions

Airways /lung disease in PRE COPD

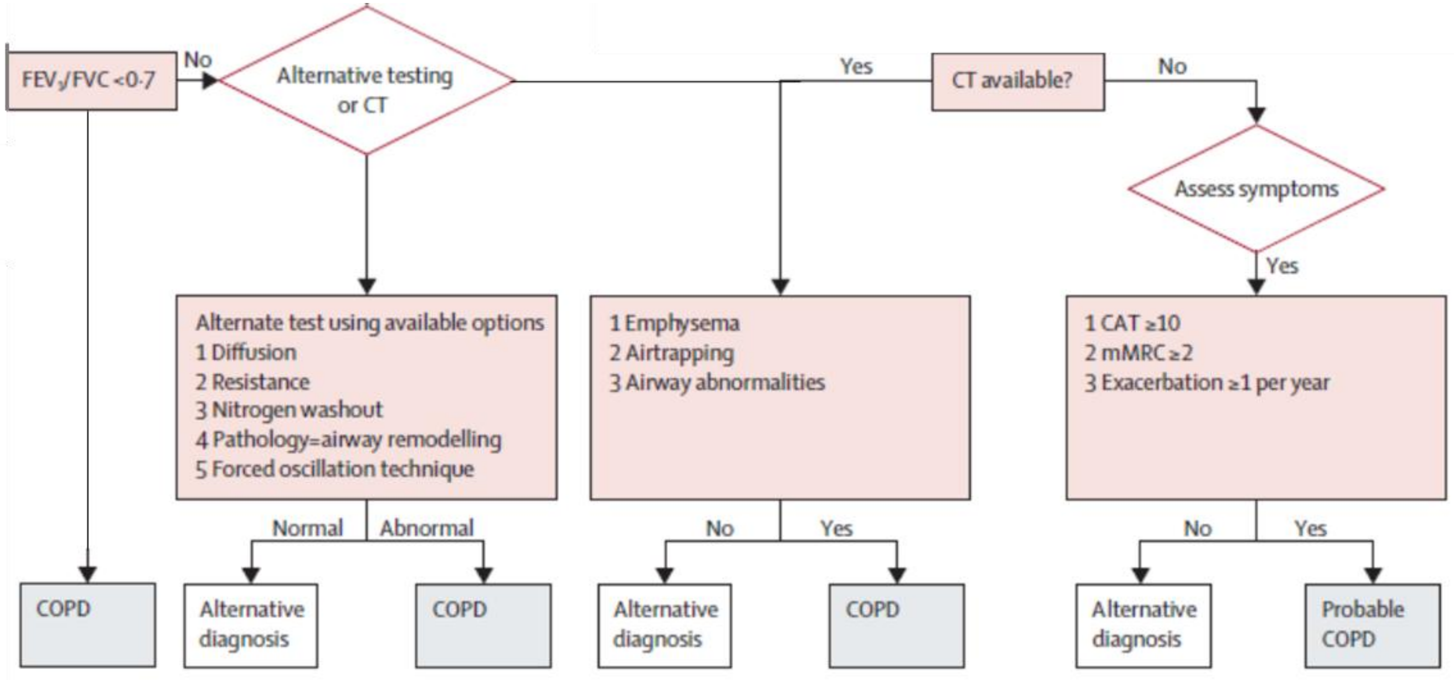
Table 1. Patient Characteristics

Characteristic	Control	Pre-COPD	GOLD I	GOLD II	GOLD III/IV
Number of patients	10	10	6	6	7
Age, yr	65 ± 10	66 ± 7	64 ± 7	67 ± 6	63 ± 4
BMI, kg/m^2	26.1 ± 4.1	25.0 ± 3.0	22.4 ± 3.3	23.5 ± 2.5	22.1 ± 3.0
Sex (M//F)	4//6	5//5	3//3	5//1	0//7
Ever-smoker	5	10	6	6	7
>5% CT emphysema	0	10	5	6	7

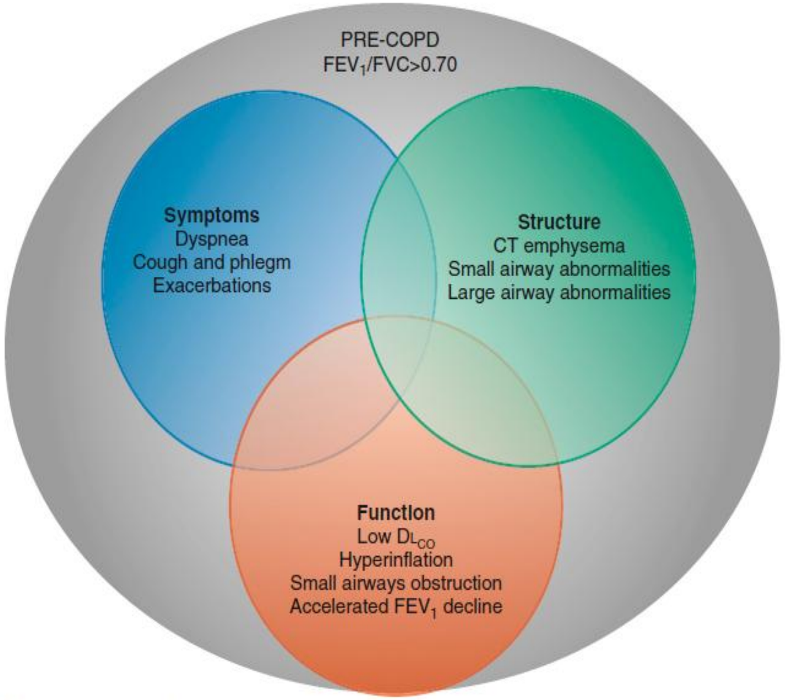


Verleden S, et al. AJRCCM 2024

Diagnosis: other test than spirometry vs. pre-COPD



The Lancet Commissions



Han M, et al. AJRCCM 2021; 203: 414-23

Lung function trajectories

The NEW ENGLAND JOURNAL of MEDICINE

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

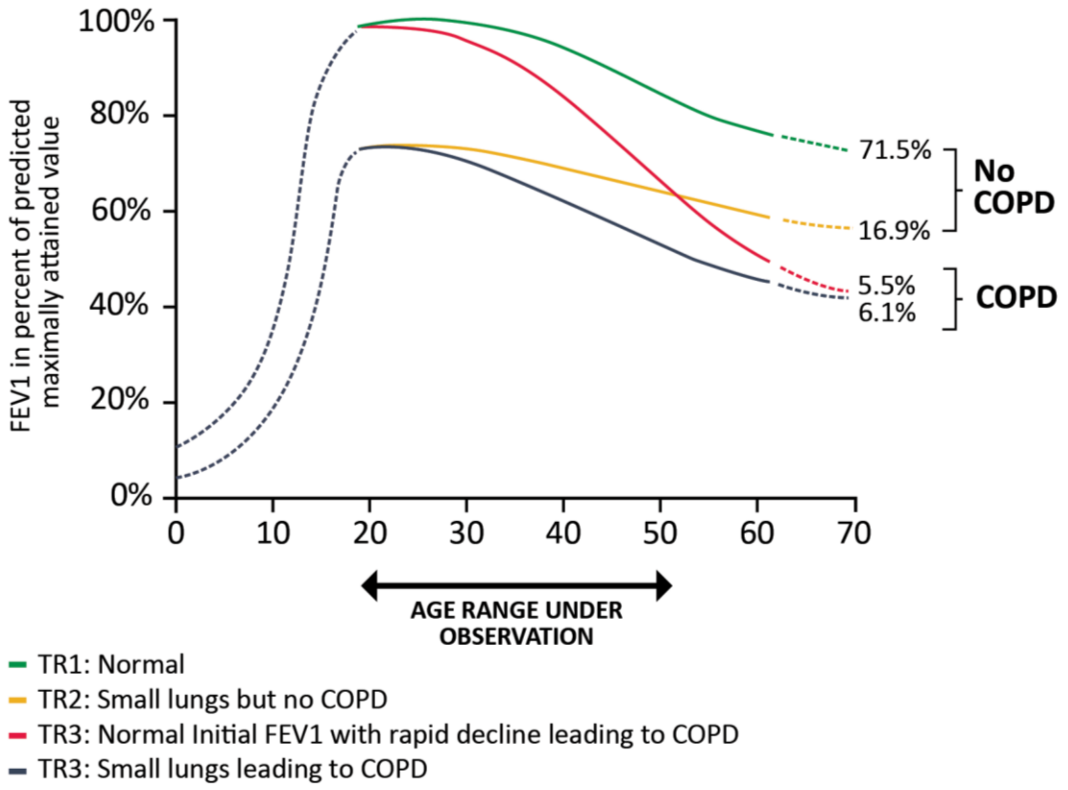
Lung-Function Trajectories Leading to Chronic Obstructive Pulmonary Disease

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.

Different trajectories towards COPD

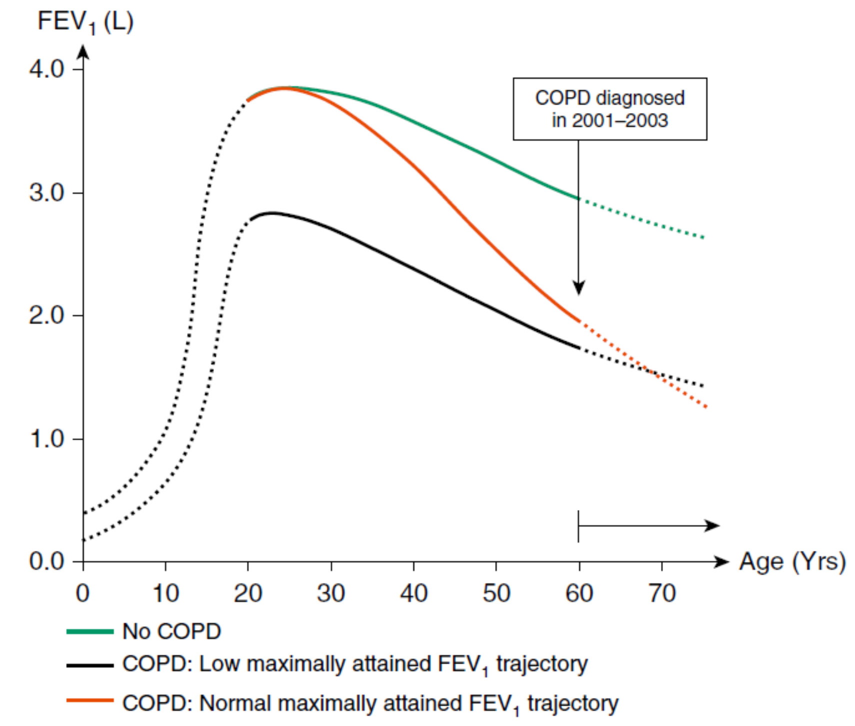
Framingham offspring cohort (n= 1849)
Copenhagen City Heart study (n= 1397)
Lovelace Smokers cohort (n=1553)

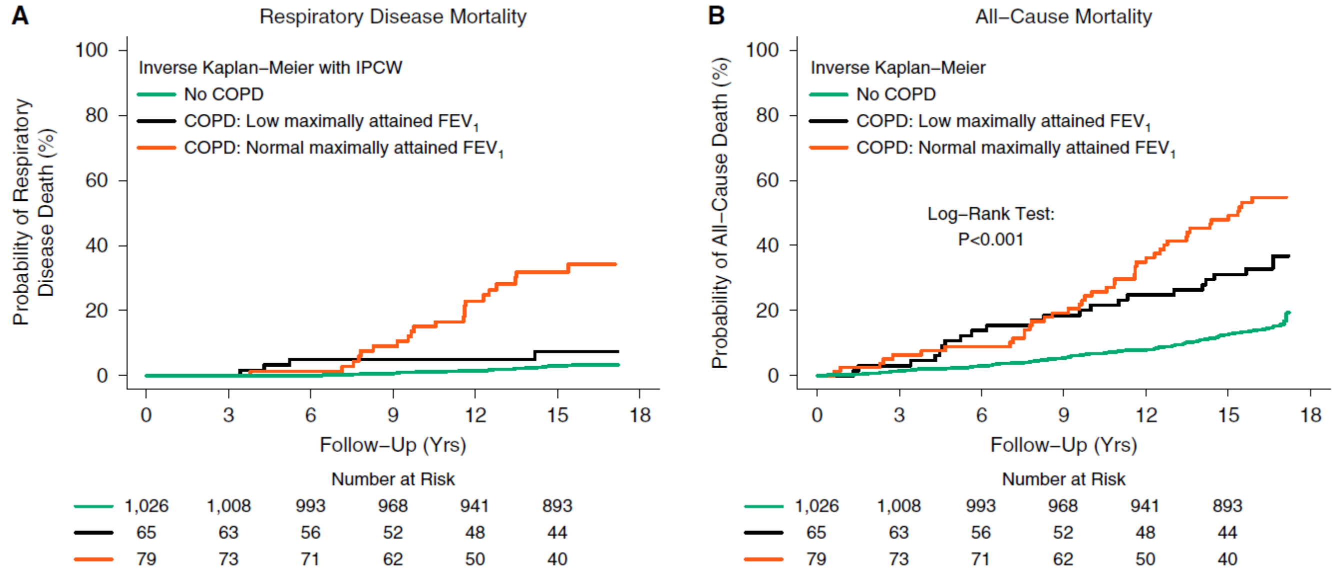
Identification of 4 trajectories



Lange et al. NEJM 2015; 373: 11-22

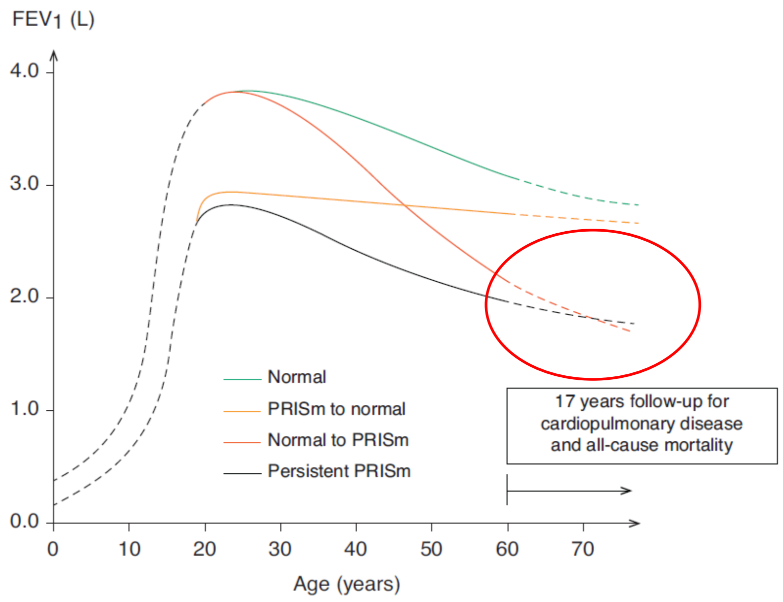
Different trajectories – Different prognosis

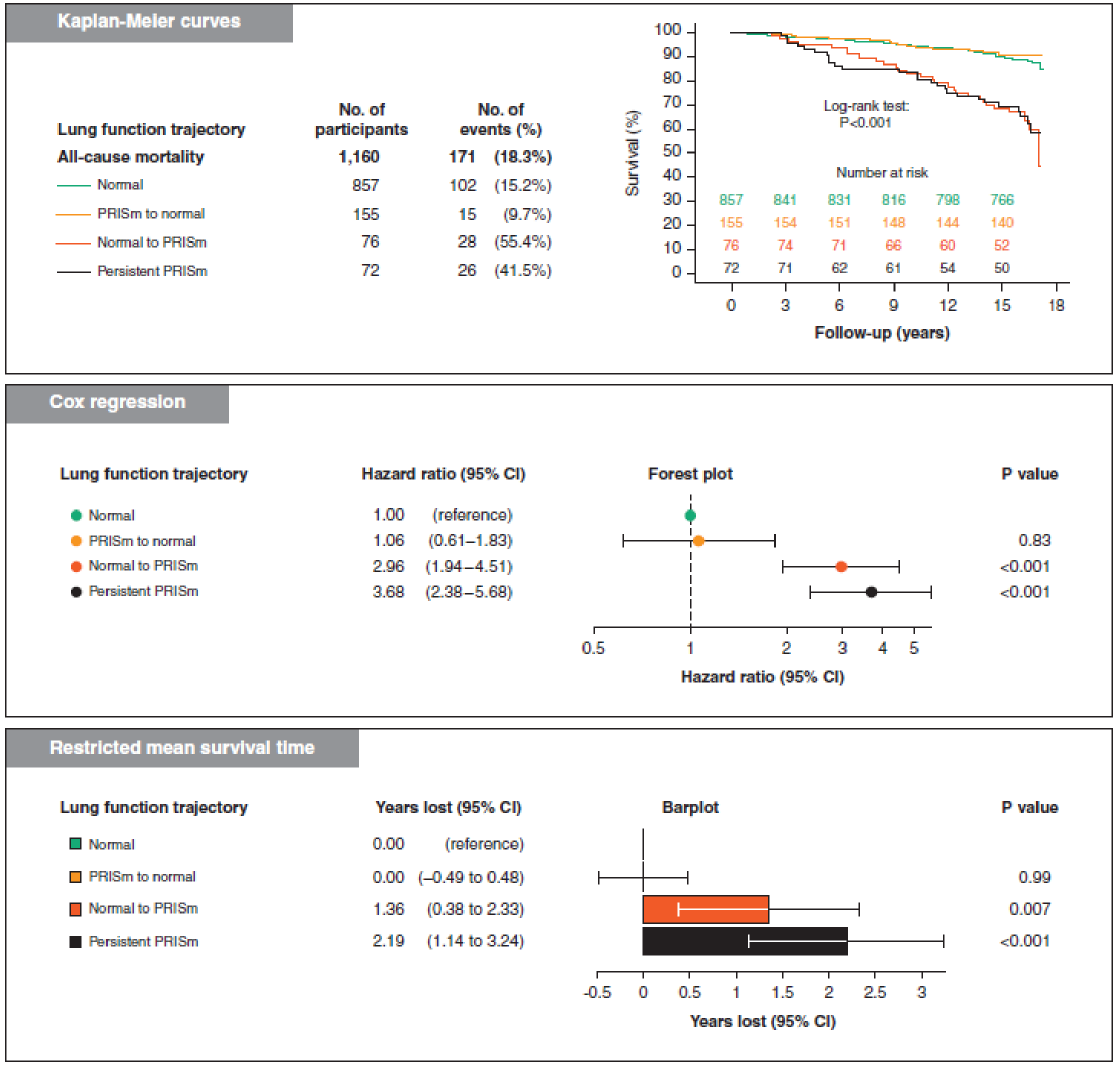




Lange et al. AJRCCM 2020; 202: 210-18

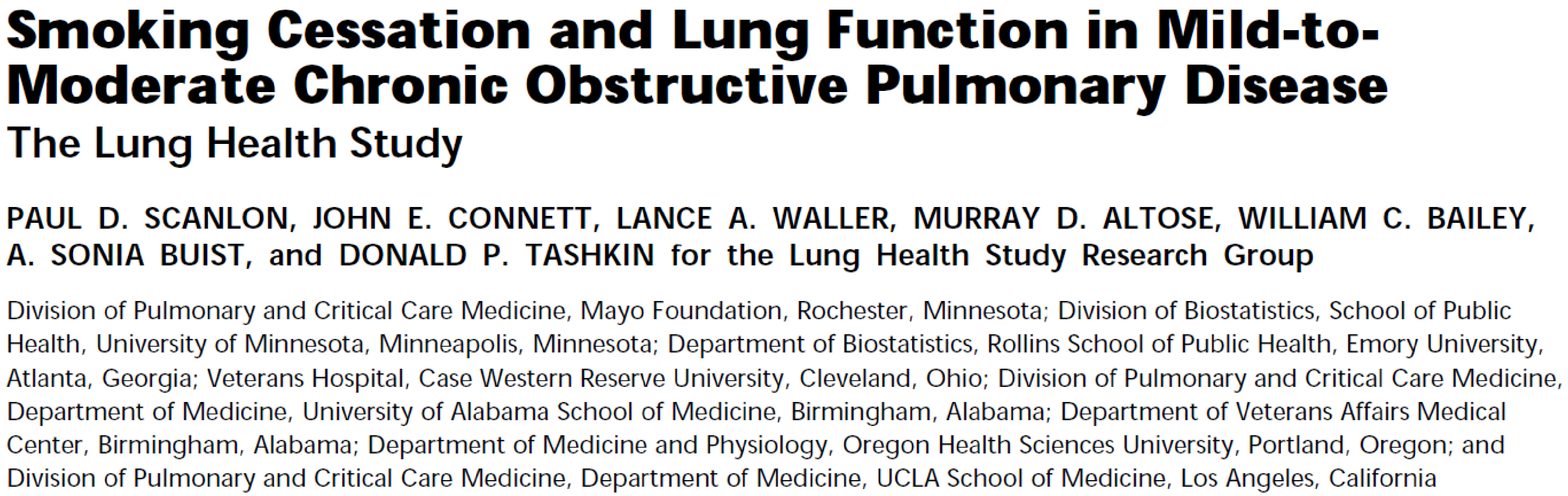
Pre- COPD (PRISM) with mortality





Marrot et al. AJRCCM 2021: 204; 910-920

Lung function decline



Scanlon PD et al. AJRCCM 2000;161:381-90

Quantification of lung function decline

TABLE 2

MEAN ANNUAL CHANGE IN FEV_1 FROM YEAR 1 TO YEAR 5, BY YEAR 5 SMOKING STATUS*

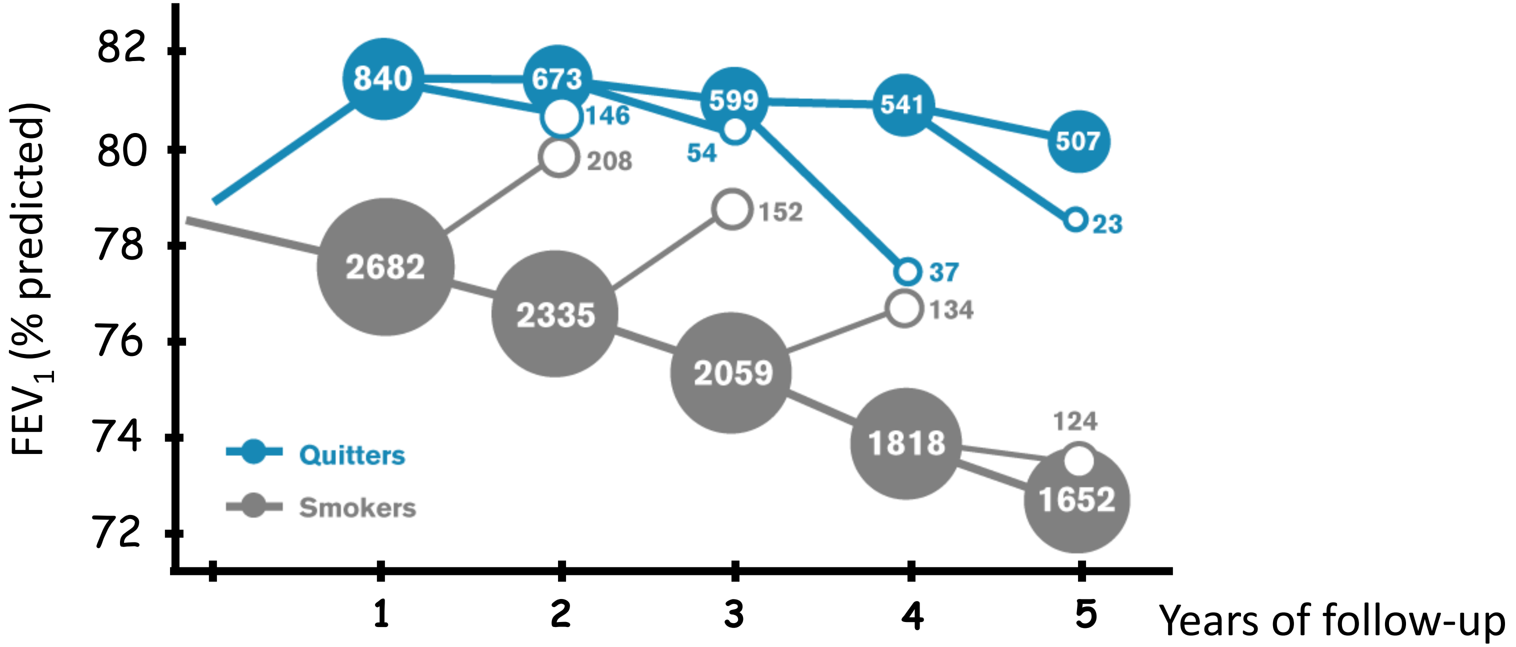
	Sustained Quitters	Intermittent Quitters	Continuing Smokers	All Smoking Groups
SI-P	−32 (46)	−47 (57)	−62 (55)	−50 (55)
UC	−30 (54)	−39 (57)	−62 (55)	−55 (57)
Total	−31 (48)	−43 (57)	−62 (55)	−52 (56)

Definition of abbreviations: FEV_1 = forced expiratory volume in 1 s; SI-P = special intervention and placebo; UC = usual care.

* Data presented are means (SD); change in FEV_1 is presented as milliliters per year.

Scanlon PD et al. AJRCCM 2000;161:381-90

Smoking cessation and impact on functional decline



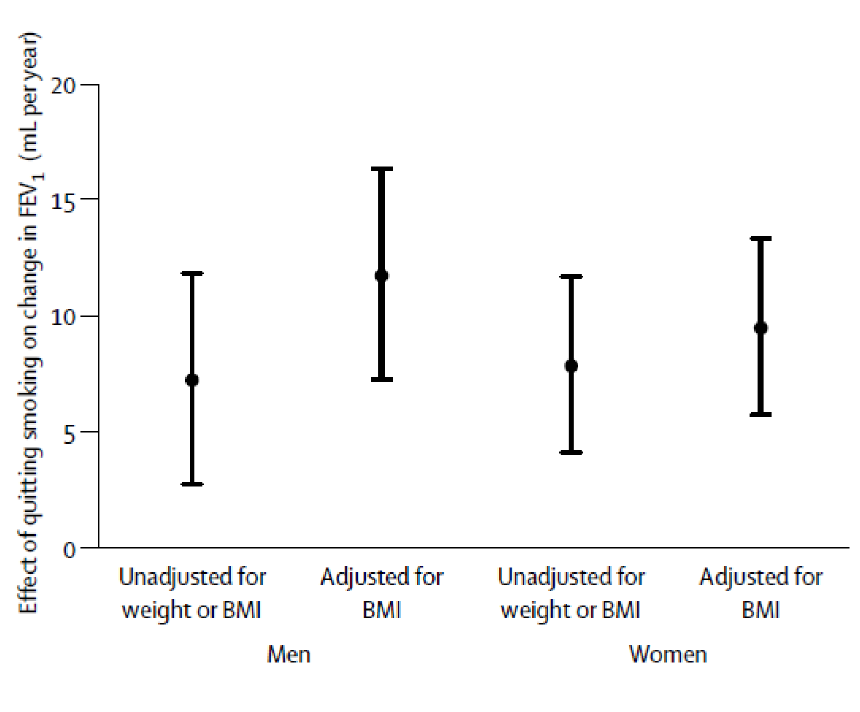
Scanlon PD et al. AJRCCM 2000;161:381-90

Smoking cessation and impact on lung function decline

Smoking cessation, lung function, and weight gain: a follow-up study

Susan Chinn, Deborah Jarvis, Roberto Melotti, Christina Luczynska, Ursula Ackermann-Liebrich, Josep M Antó, Isa Cerveri, Roberto de Marco,

Lancet 2005; 365: 1629–35



Smoking cessation and impact of lung function

SMOKING

Smokers with airway obstruction are more likely to quit smoking

M Bednarek, D Gorecka, J Wielgomas, M Czajkowska-Malinowska, J Regula, G Mieszko-Filipczyk, M Jasionowicz, R Bijata-Bronisz, M Lempicka-Jastrzebska, M Czajkowski, G Przybylski, J Zielinski

Thorax 2006;**61**:869–873. doi: 10.1136/thx.2006.059071

Table 3 Smoking cessation rates after 12 months of follow up stratified by baseline spirometric results

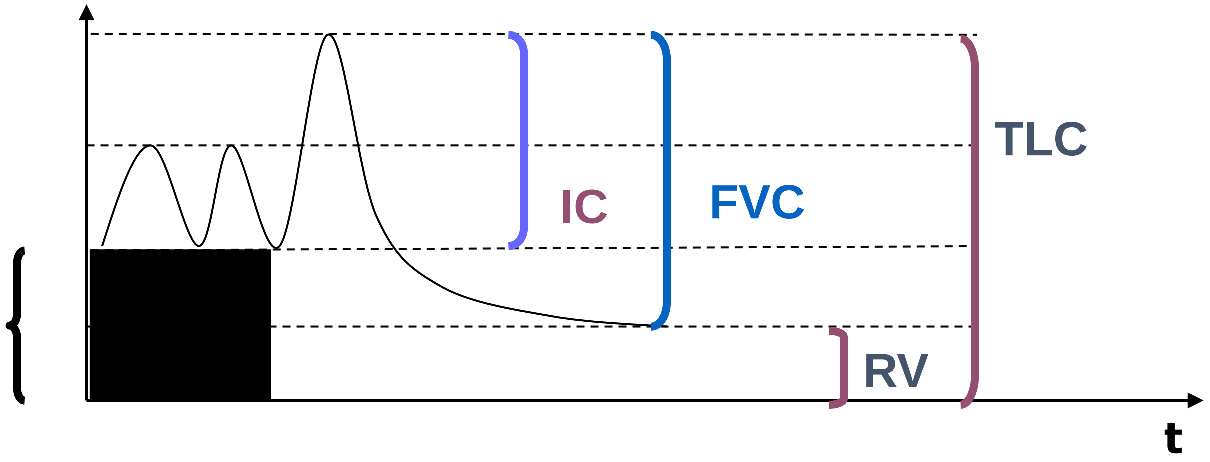
		Airway obstruction			
Spirometric results	**Normal**	**Mild**	**Moderate**	**Severe**	**Any**
All subjects (n)	3441	384	939	357	1680
Quitters (n)	413	56	151	66	273
Cessation rate (%)	12.0%	14.6%	16.1%	18.5%	16.3%
p value*	–	0.229	0.005	0.003	0.0003

*The p value compares the cessation rate in smokers with airway obstruction with the rate in smokers with normal spirometric results.

What about other lung function tests

FRC:

Functional residual capacity



FRC + IC = TLC : Total lungcapacity

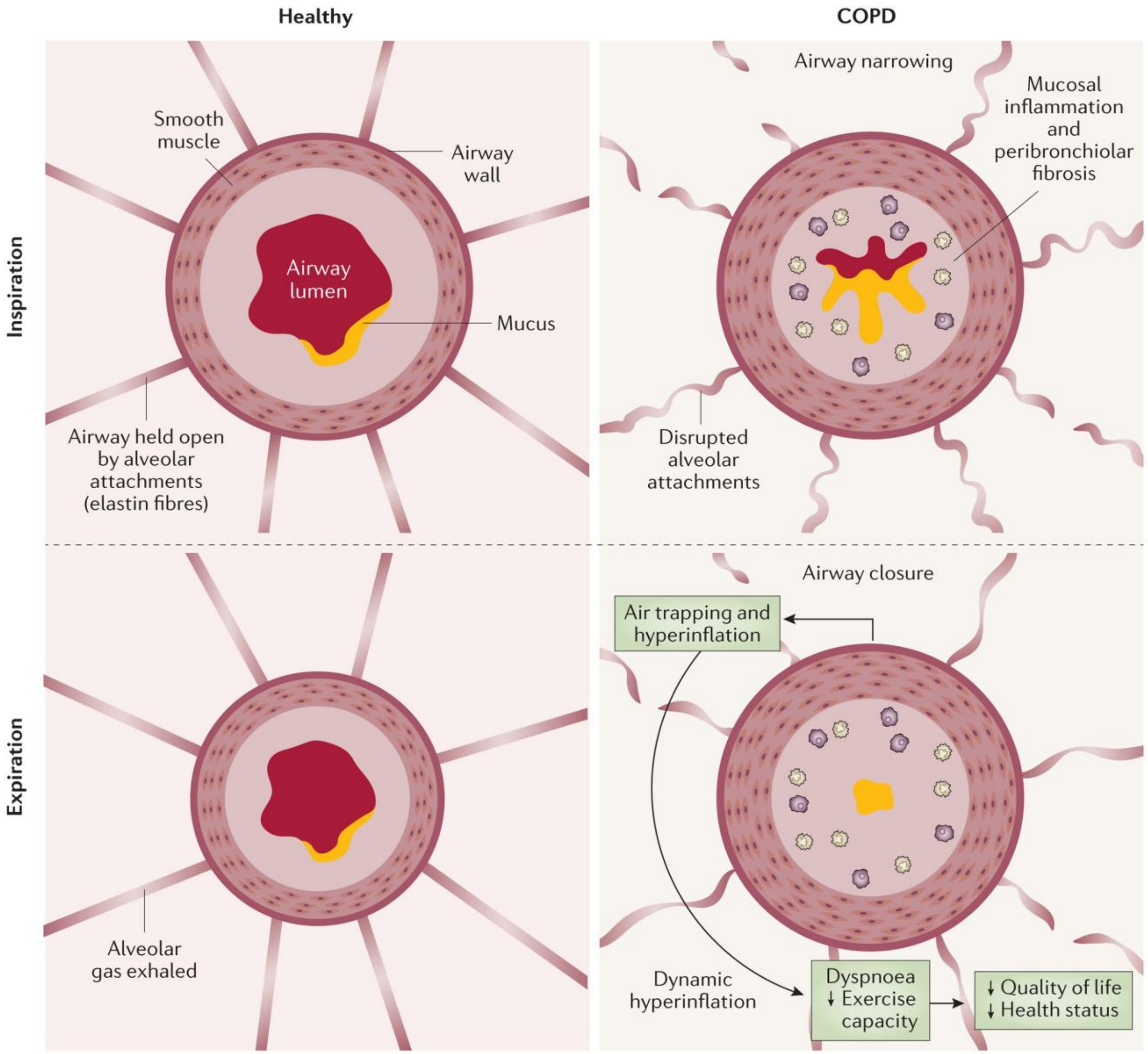
TLC- VC = RV: Residual volume

Calculated from FRC

Heliumdilution, N2 wash-out

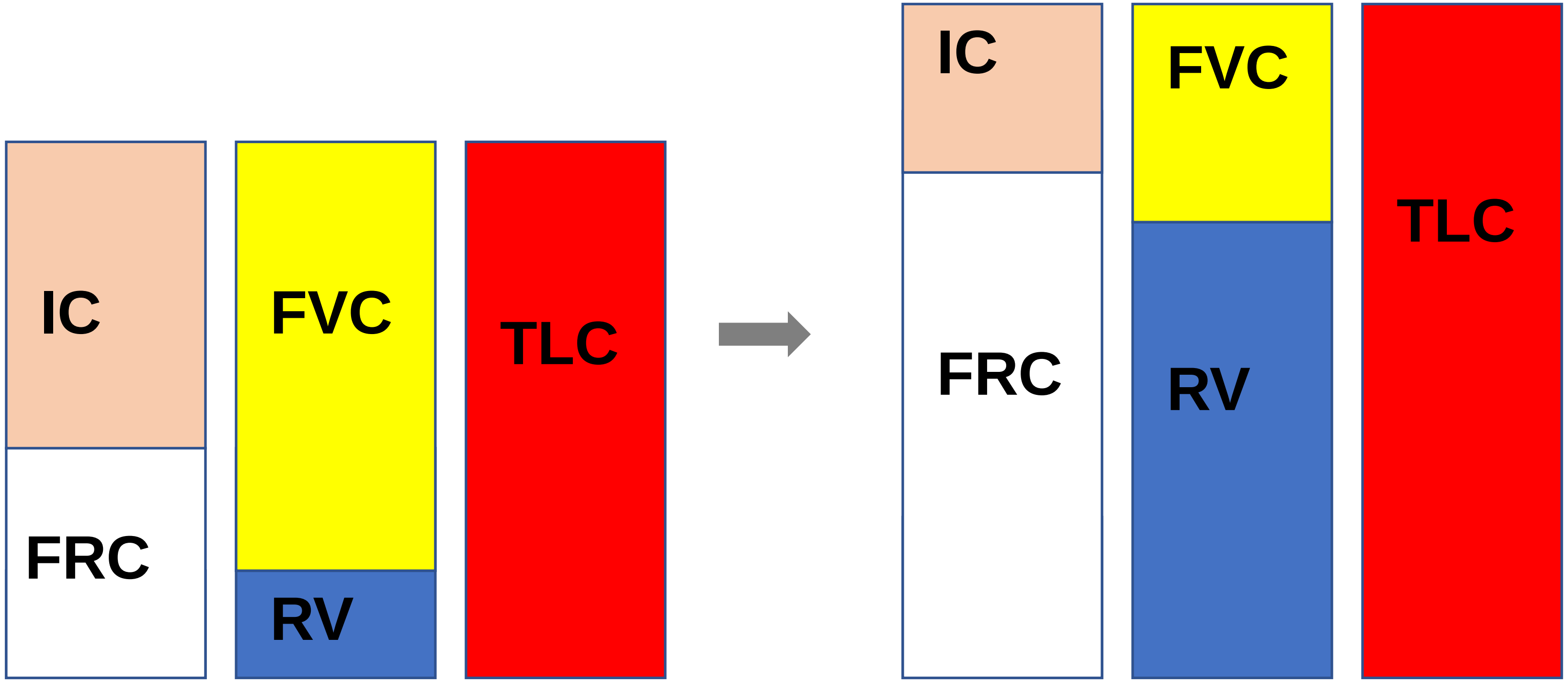
plethysmography (bodybox)

Airtrapping and hyperinflation



Nature Reviews | Disease Primers

Airtrapping and hyperinflation



RV / TLC ratio = 0,3

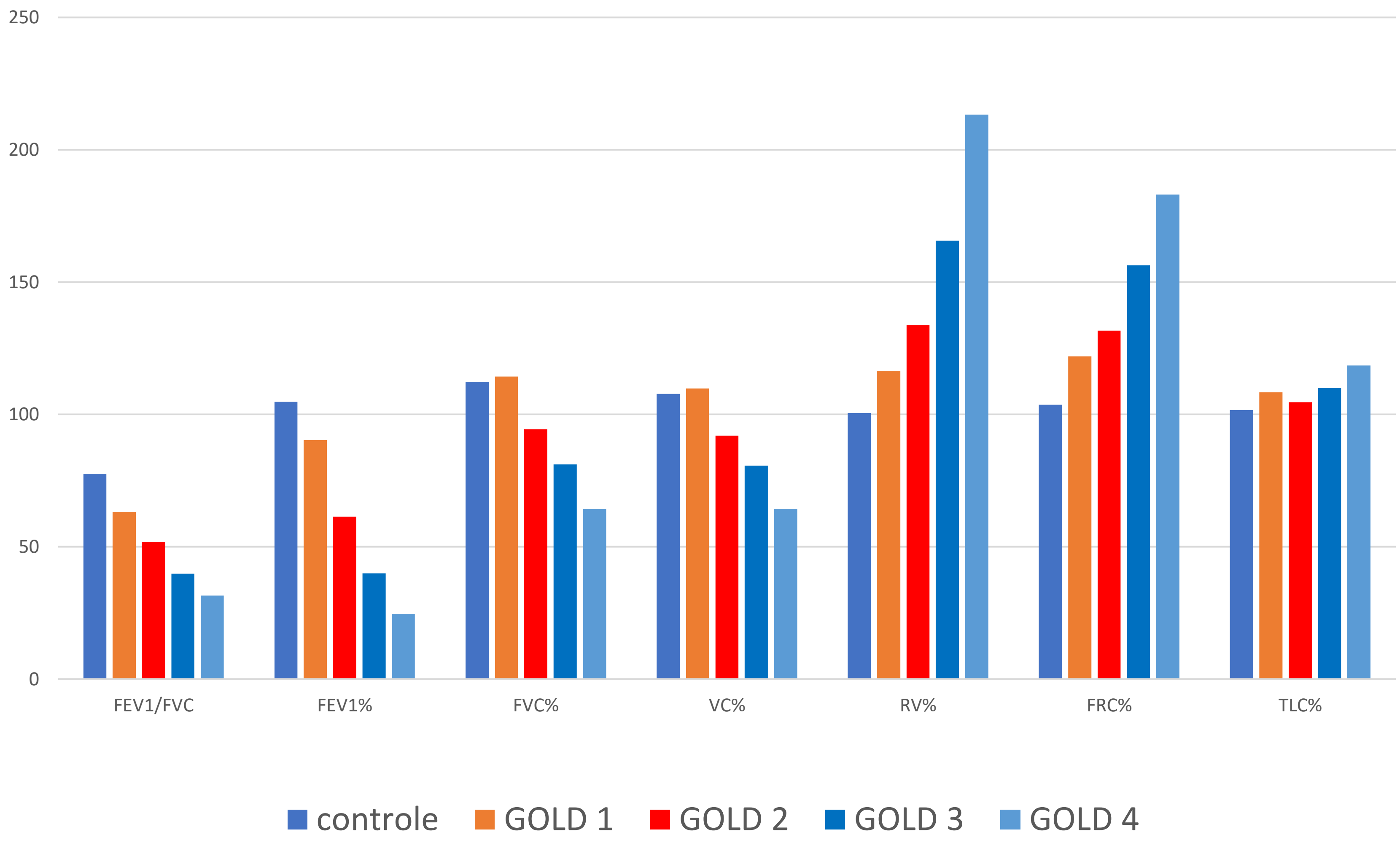
RV / TLC ratio = 0,6

RV/TLC ratio as a proxy for airtrapping

Airtrapping and hyperinflation

Leuven COPD cohort
GOLD 0: n = 70
GOLD 1: n = 70
GOLD 2: n = 70
GOLD 3: n = 70
GOLD 4: n = 70

Matched for age, gender and smoking status



Airtrapping and hyperinflation

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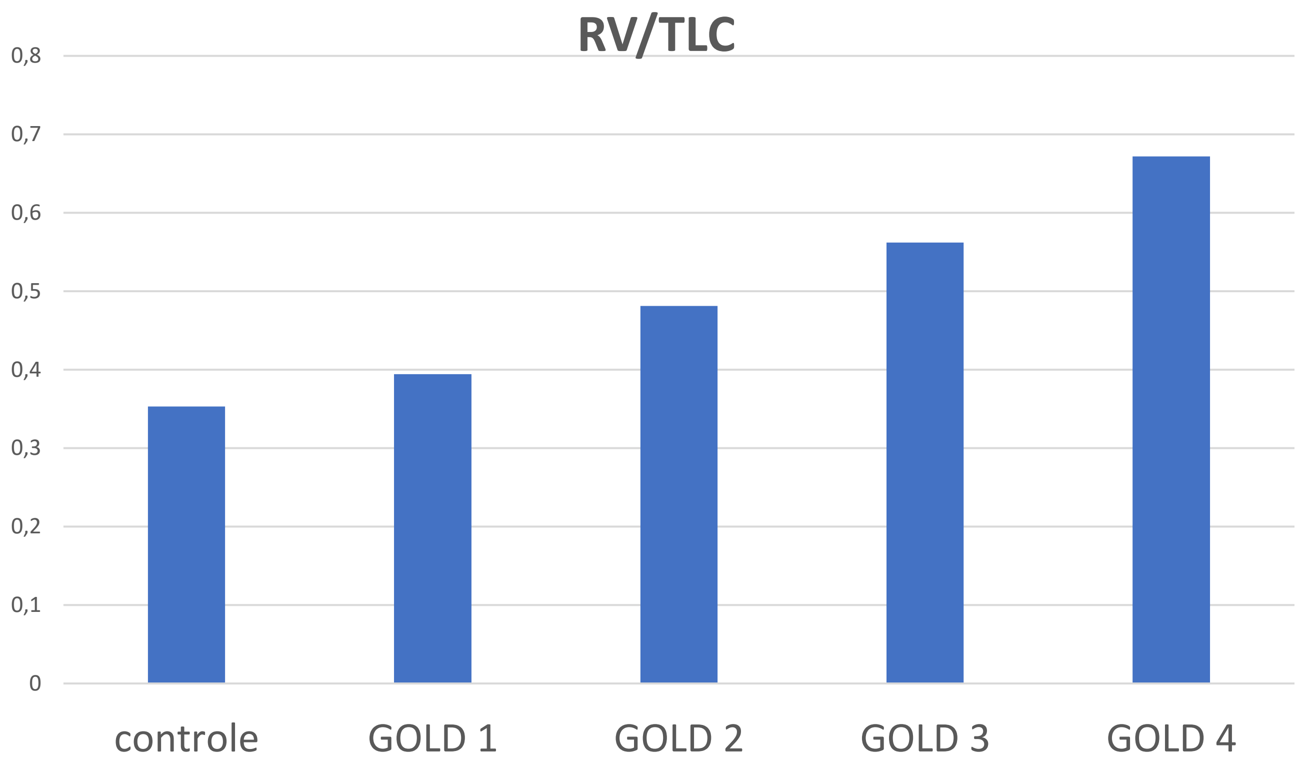


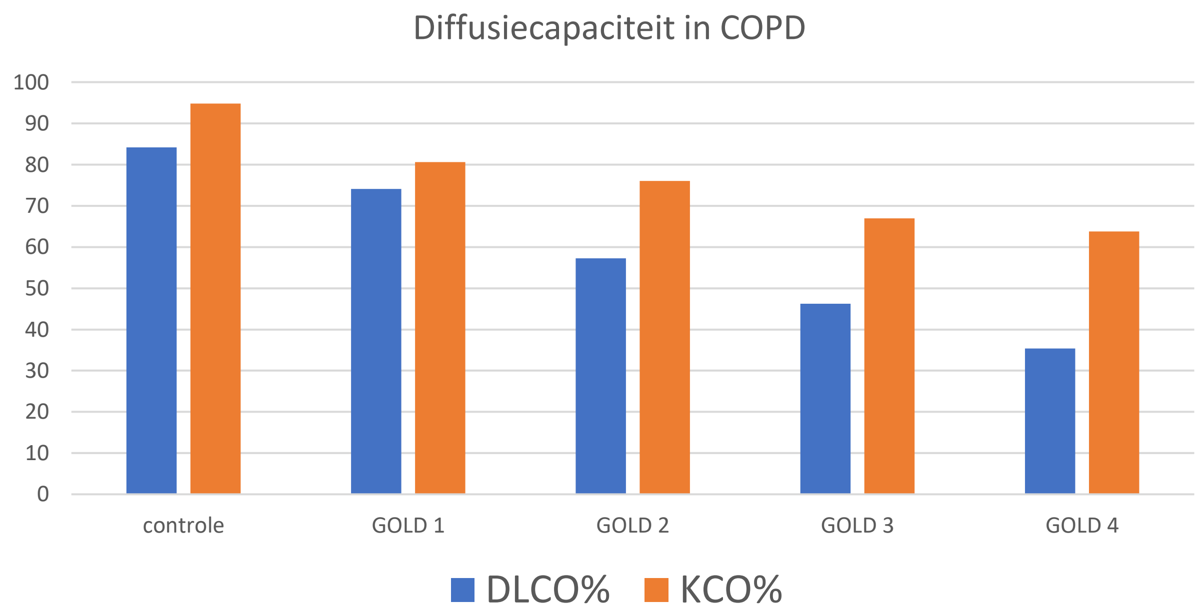
Diffusing capacity

Smoking

- ❑ Disturbed alveolar ventilation (high RV/TLC with low FVC)
- ❑ Reduced alveolo-capillary membrane
- ❑ Impaired V/Q matching
- ❑ Increased Carboxy Hb

Leuven COPD cohort
GOLD 0: n = 70
GOLD 1: n = 70
GOLD 2: n = 70
GOLD 3: n = 70
GOLD 4: n = 70

Matched for age, gender and smoking status



Conclusion and take-home message