Who are at risk for COPD?

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Factors that influence disease development and progression

- Genetic factors
- Age and sex
- Lung growth and development
- Exposure to particles
- Socioeconomic status
- Asthma and airway hyper-reactivity
- Chronic bronchitis
- Infections

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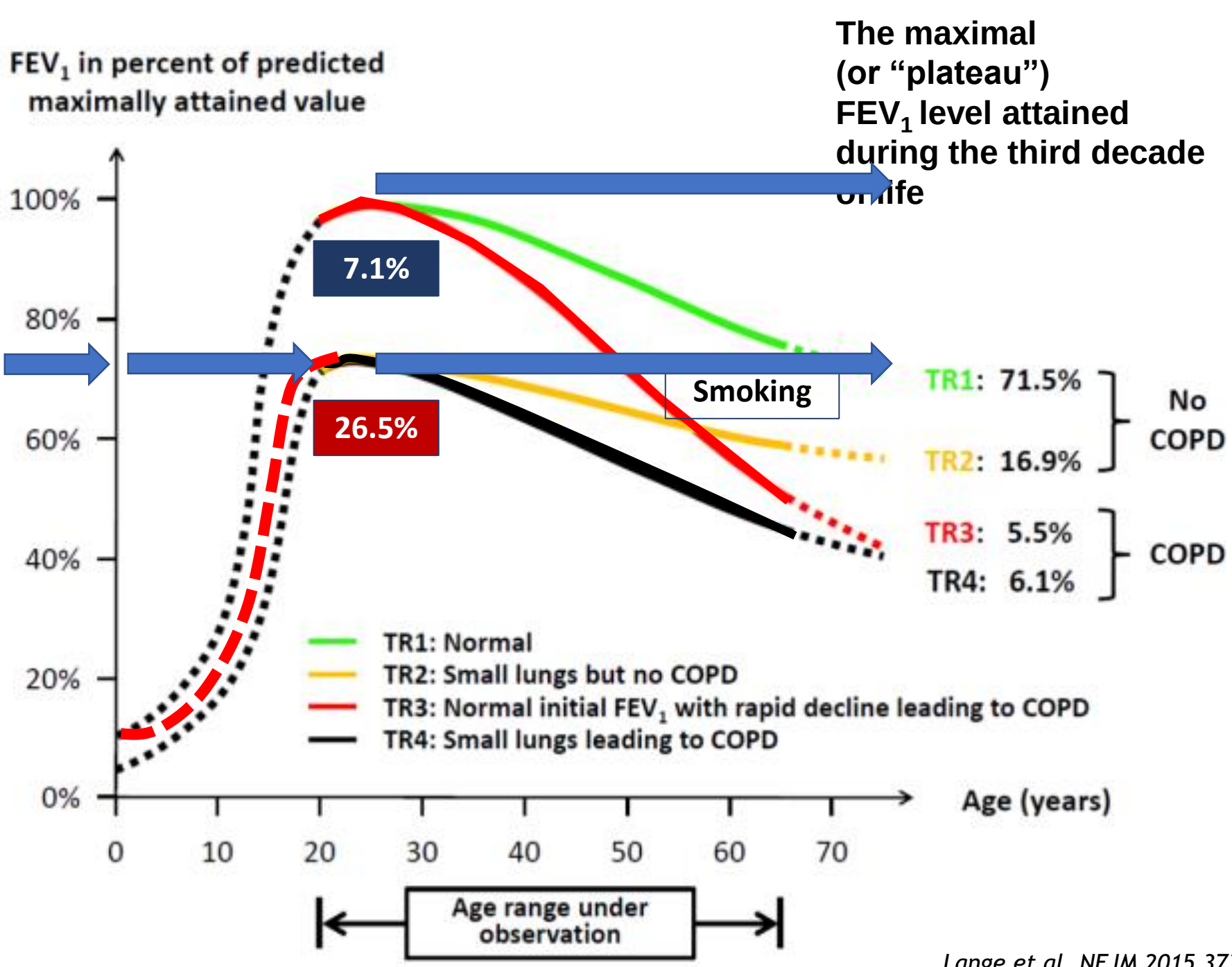
- **Preserved ratio impaired spirometry**



Lange et al. NEJM 2015 373;2

Combined Impact of Smoking and Early-Life Exposures on Adult Lung Function Trajectories

James P. Allinson[1], Rebecca Hardy[2], Gavin C. Donaldson[1], Seif O. Shaheen[3], Diana Kuh[2], and Jadwiga A. Wedzicha[1]

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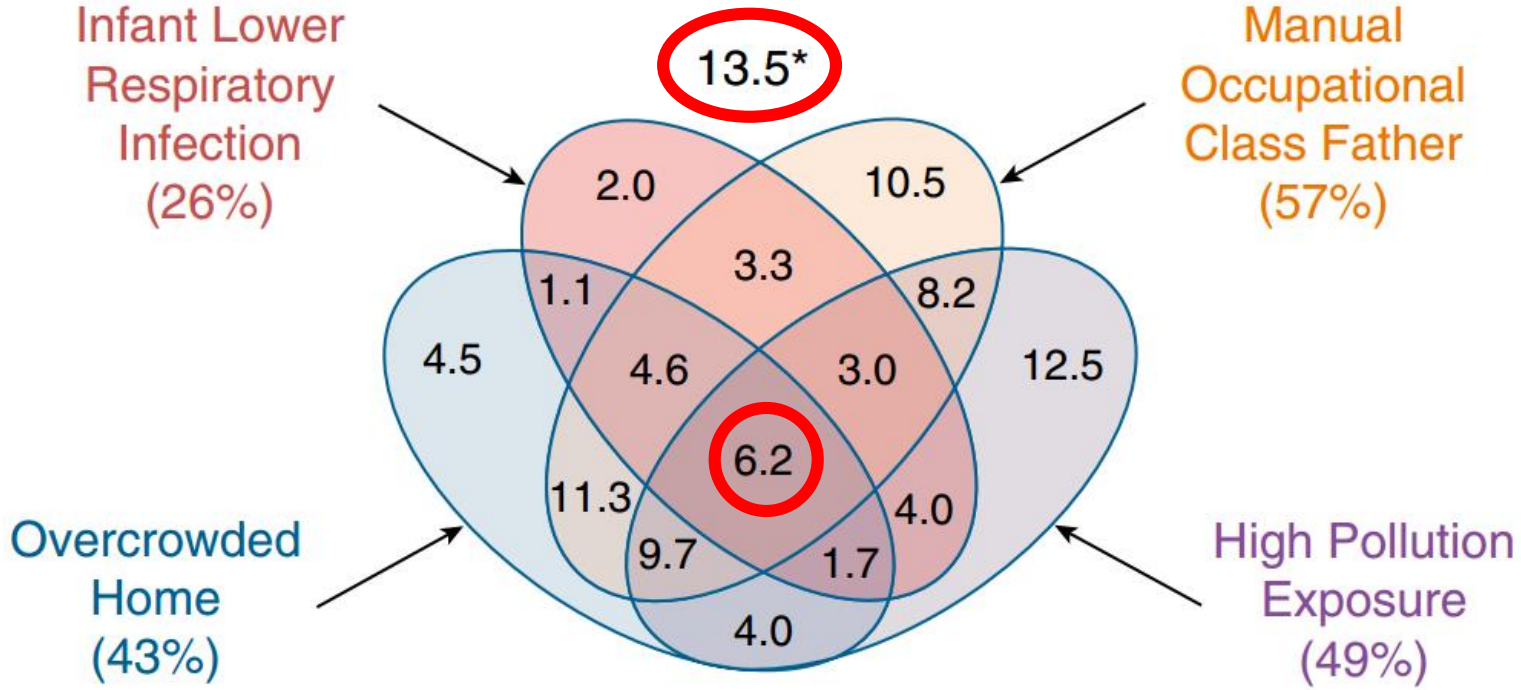
- National Survey of Health and Development (NSHD)
- 5,362 individuals; born during 1 wk in March 1946 within England, Scotland, and Wales
- **Early-life exposure**: infant lower respiratory infection (2yrs old), home overcrowding (2yrs old), father's social class (4, 11, or 15 yrs old), pollution exposure (domestic local coal consumption at ages 0 and 2 yrs)
- At age **43 yrs, 53 yrs and 60–64 years**; interviewed at home by research nurses.
- How **early-life exposures impacted adult FEV_1 and FVC level** and decline between ages 43 and 60–64 years and whether these relationships were modified by **smoking**.

Overlapping prevalence (%)

N=2,172



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Odds ratios (95% CI) of having an infant lower respiratory infection

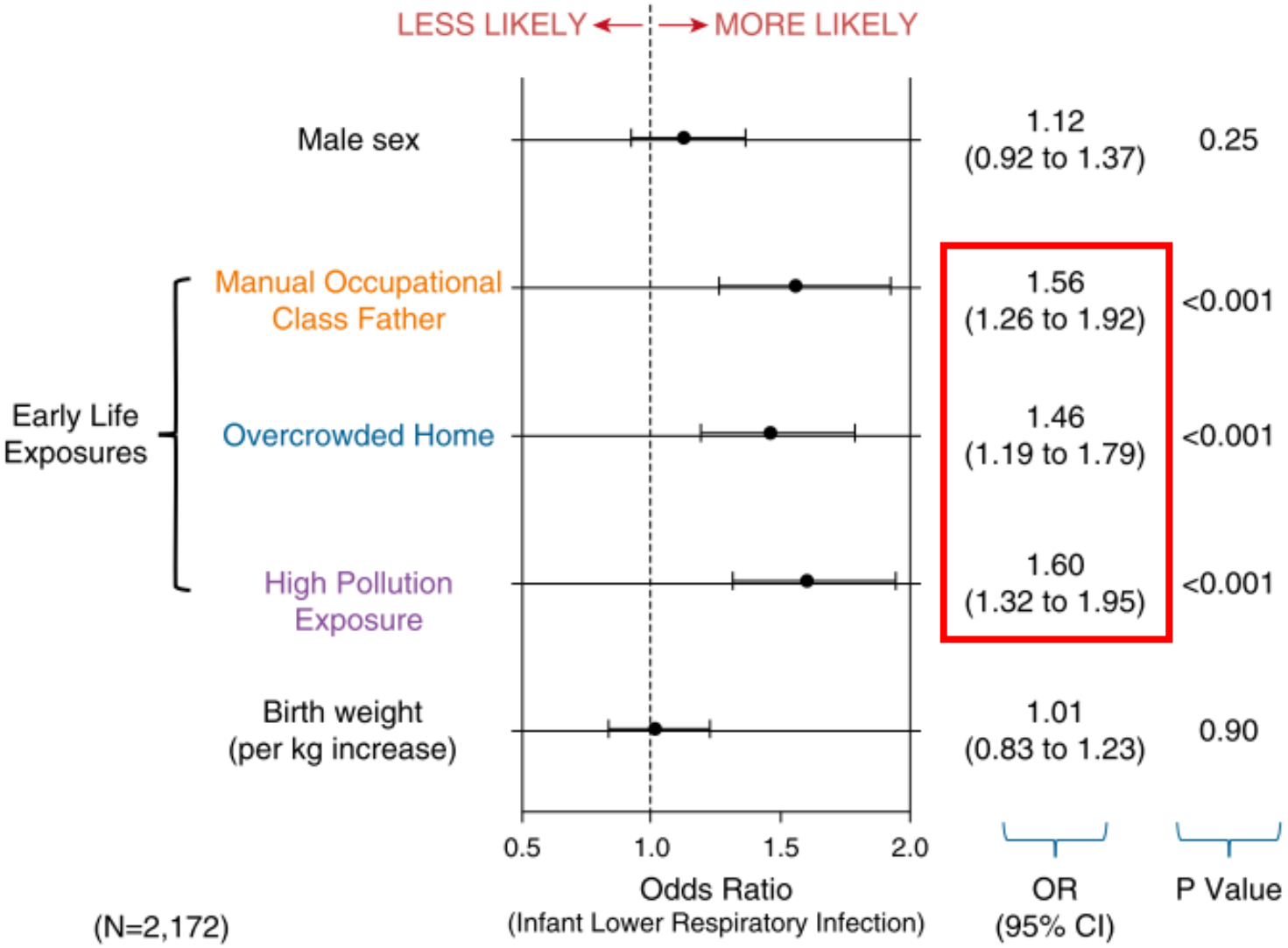

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Table 1. Estimated Associations between Early-Life Factors and Adult FEV_1 for Subjects between 43 and 60–64 Years of Age*

In models including only age,
estimated mean FEV1 at age 43 : 3.02 L
overall FEV1 decline: 24.8 ml/yr

	FEV_1 Intercept (*ml*) at Age 43 Years			FEV_1 Linear Change per Year (*ml/yr*) between Ages 43 and 60–64 Years		
	Coefficient	95% CI	*P* Value	Coefficient	95% CI	*P* Value
Ever-smokers (n = 1,299)						
Constant	−2,305.1	−2,952.8 to −1,657.5	—	−17.3	−29.4 to −5.1	0.001
Male sex	586.3	511.7 to 660.9	<0.001	−1.6	−5.0 to 1.8	0.34
Height at 43 yr (per cm)	31.0	26.8 to 35.3	<0.001	—	—	—
Weight at age 43 yr (per kg)	−2.9	−5.1 to −0.7	0.01	—	—	—
Infant lower respiratory infection, 0–2 yr (yes vs. no)	−108.2	−170.1 to −46.3	0.001	−1.2	−5.2 to 2.7	0.53
Father's occupational class at 4 yr (manual vs. nonmanual)	−71.6	−130.1 to −13.2	0.02	−1.8	−5.3 to 1.8	0.32
Home overcrowding at 2 yr (yes vs. no)	−89.2	−147.0 to −31.5	0.002	1.8	−1.8 to 5.3	0.33
High pollution exposure, 0–2 yr (yes vs. no)	27.0	−27.8 to 81.7	0.33	1.7	−1.7 to 5.1	0.32
Birth weight (per g)	0.07	0.01 to 0.12	0.02	−0.002	−0.005 to 0.002	0.28
Pack-years accrued between ages 20 and 43 yr (per pack-year)	−12.7	−15.4 to −10.0	<0.001	—	—	—
Smoking 43 and 64 yr (per cigarette smoked daily)	2.1	−0.3 to 4.6	0.09	−0.4	−0.6 to −0.2	<0.001
Never-smokers (n = 873)						
Constant	−2,089.8	−2,916.4 to −1,263.2	—	−15.8	−27.4 to −4.3	0.007
Male sex	561.6	468.6 to 654.7	<0.001	1.4	−1.8 to 4.7	0.39
Height at 43 yr (per cm)	28.7	23.4 to 34.1	<0.001	—	—	—
Weight at age 43 yr (per kg)	−1.6	−4.3 to 1.0	0.23	—	—	—
Infant lower respiratory infection, 0–2 yr (yes vs. no)	−15.9	−94.0 to 62.2	0.69	−1.2	−4.9 to 2.6	0.54
Father's occupational class at 4 yr (manual vs. nonmanual)	−39.1	−110.0 to 31.9	0.28	−2.2	−5.6 to 1.1	0.20
Home overcrowding at 2 yr (yes vs. no)	−13.7	−84.3 to 56.8	0.70	2.8	−0.6 to 6.2	0.10
High pollution exposure, 0–2 yr (yes vs. no)	−0.4	−66.4 to 65.7	0.99	−0.7	−3.8 to 2.5	0.69
Birth weight (per g)	0.06	−0.01 to 0.13	0.09	−0.002	−0.005 to 0.001	0.26
Pack-years accrued between ages 20 and 43 yr (per pack-year)	—	—	—	—	—	—
Smoking 43 and 64 yr (per cigarette smoked daily)	—	—	—	—	—	—

60%

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Table 2. Estimated Associations between Early-Life Factors and Adult FVC Decline Trajectory for Subjects between 43 and 60–64 Years of Age*

In models including only age
estimated mean FVC at age 43 years: 3.62 L
an overall FVC decline: 21.7 ml/yr

	FVC Intercept (*ml*) at Age 43 Years			FVC Linear Change per Year (*ml/yr*) between Ages 43 and 60–64 Years		
	Coefficient	95% CI	*P* Value	Coefficient	95% CI	*P* Value
Ever-smokers (n = 1,157)						
Constant	−3,802.6	−4,633.7 to −2,971.5	—	−12.6	−30.2 to 4.9	0.16
Male sex	701.7	601.0 to 802.3	<0.001	1.9	−3.1 to 6.9	0.46
Height at 43 yr (per cm)	45.0	39.5 to 50.4	<0.001	—	—	—
Weight at age 43 yr (per kg)	−7.1	−10.0 to −4.2	<0.001	—	—	—
Infant lower respiratory infection, 0–2 yr (yes vs. no)	−117.3	−204.7 to −29.8	0.009	0.4	−5.4 to 6.2	0.89
Father's occupational class at 4 yr (manual vs. nonmanual)	−80.6	−163.1 to 1.9	0.06	−2.4	−7.6 to 2.8	0.36
Home overcrowding at 2 yr (yes vs. no)	−93.1	−174.6 to −11.5	0.03	2.4	−2.8 to 7.6	0.37
High pollution exposure, 0–2 yr (yes vs. no)	44.4	−32.7 to 121.5	0.26	2.3	−2.6 to 7.3	0.36
Birth weight (per g)	0.08	0.005 to 0.16	0.04	−0.003	−0.008 to 0.002	0.18
Pack-years accrued between ages 20 and 43 yr (per pack-year)	−12.8	−16.2 to −9.4	<0.001	—	—	—
Smoking 43 and 64 yr (per cigarette smoked daily)	0.9	−2.6 to 4.5	0.60	−0.1	−0.4 to 0.1	0.34
Never-smokers (n = 803)						
Constant	−3,583.9	−4,605.5 to −2,562.3	—	−17.7	−37.3 to 1.9	0.08
Male sex	627.4	504.1 to 750.7	<0.001	5.9	0.3 to 11.6	0.04
Height at 43 yr (per cm)	42.3	35.8 to 48.8	<0.001	—	—	—
Weight at age 43 yr (per kg)	−6.0	−9.3 to −2.8	<0.001	—	—	—
Infant lower respiratory infection, 0–2 yr (yes vs. no)	−18.9	−126.1 to 88.2	0.73	2.9	−3.5 to 9.2	0.38
Father's occupational class at 4 yr (manual vs. nonmanual)	−58.4	−155.6 to 38.9	0.24	0.2	−5.5 to 5.9	0.94
Home overcrowding at 2 yr (yes vs. no)	−40.4	−137.0 to 56.2	0.41	−1.4	−7.2 to 4.3	0.63
High pollution exposure, 0–2 yr (yes vs. no)	−0.6	−91.4 to 90.2	0.99	2.2	−3.2 to 7.5	0.43
Birth weight (per g)	0.09	0.001 to 0.19	0.05	−0.002	−0.008 to 0.004	0.48
Pack-years accrued between ages 20 and 43 yr (per pack-year)	—	—	—	—	—	—
Smoking 43 and 64 yr (per cigarette smoked daily)	—	—	—	—	—	—

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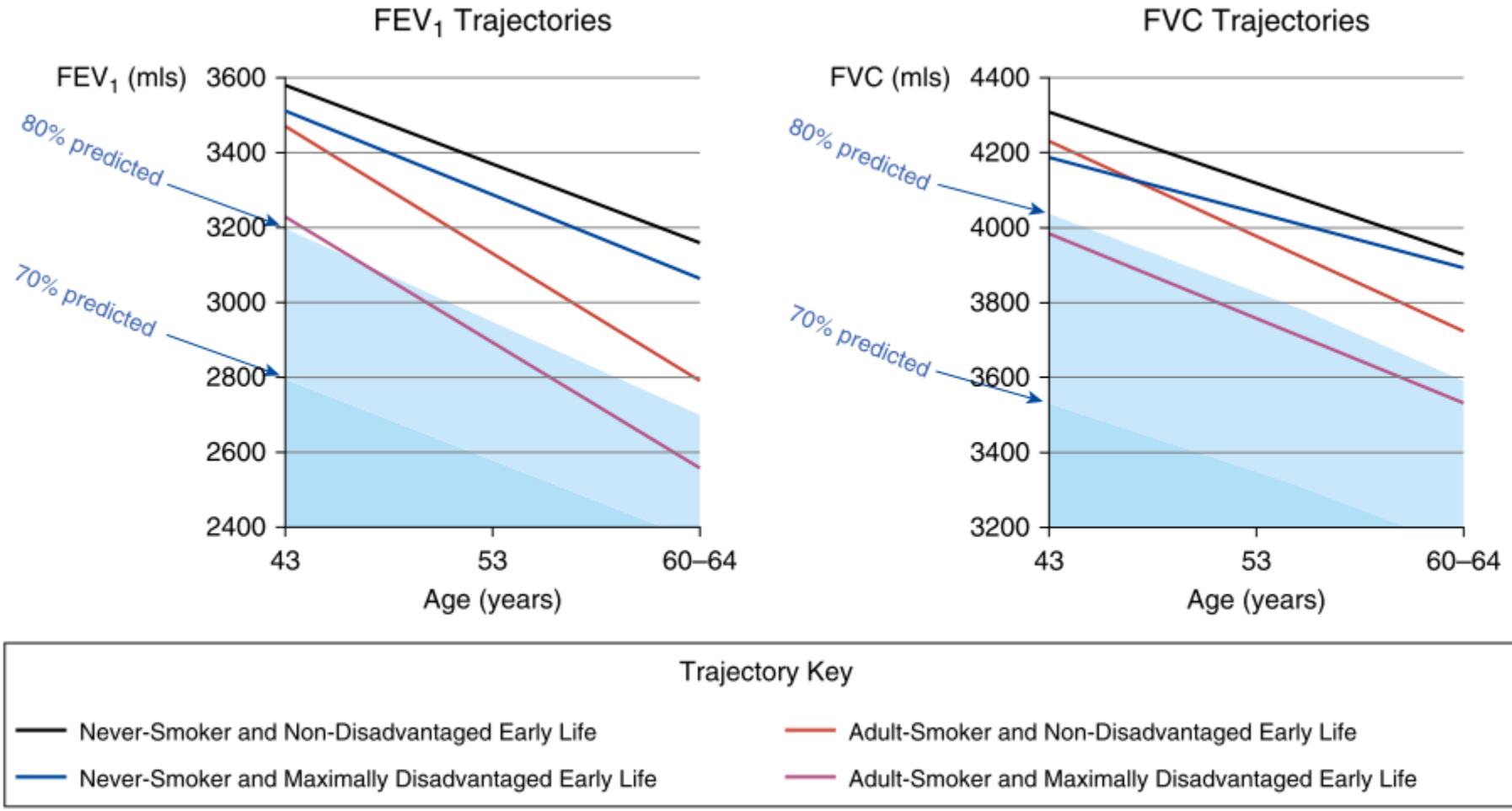
Estimated average FEV_1 and FVC trajectories ages 43 ~ 60–64 years

males of average height at age 43 years (175 cm), average weight at age 43 years (78 kg), and average birth weight (3.5 kg)



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PRISm (Preserved ratio impaired spirometry)

- post-BD $FEV_1/FVC \geq 0.7$ and an $FEV_1 < 80\%$ pred.

- post-BD $FEV_1/FVC \geq 0.7$ and increased lung volume
- post-BD $FEV_1/FVC \geq 0.7$ and decreased diffusion capacity
- post-BD $FEV_1/FVC \geq 0.7$ and imaging features

PFT with non-specific pattern

Table 1—*Different PF Pattern Possibilities Including the NS Pattern (N = 3,674)*

Column	FEV_1	FVC	Ratio	TLC	Classification
1	N	N	N	N	N (n = 87)
2	N	N	N	REDU	Restriction (n = 5)
3	N	N	REDU	N	BOO (n = 7)
4	N	N	REDU	REDU	Mixed, reduced ratio (n = 0)
5	REDU	N	N	N	NS, low FEV_1 (n = 307)
6	REDU	N	N	REDU	Restriction, low FEV_1 (n = 4)
7	REDU	REDU	REDU	N	Obstruction (n = 310)
8	REDU	REDU	REDU	REDU	Mixed (n = 41)
9	REDU	N	REDU	N	Obstruction (n = 98)
10	REDU	N	REDU	REDU	Mixed pattern FEV_1 (n = 1)
11	REDU	REDU	N	N	NS (n = 2,333)
12	REDU	REDU	N	REDU	Restriction, classic (n = 383)
13	N	REDU	N	N	NS, low FVC (n = 90)
14	N	REDU	N	REDU	Restriction FVC (n = 8)

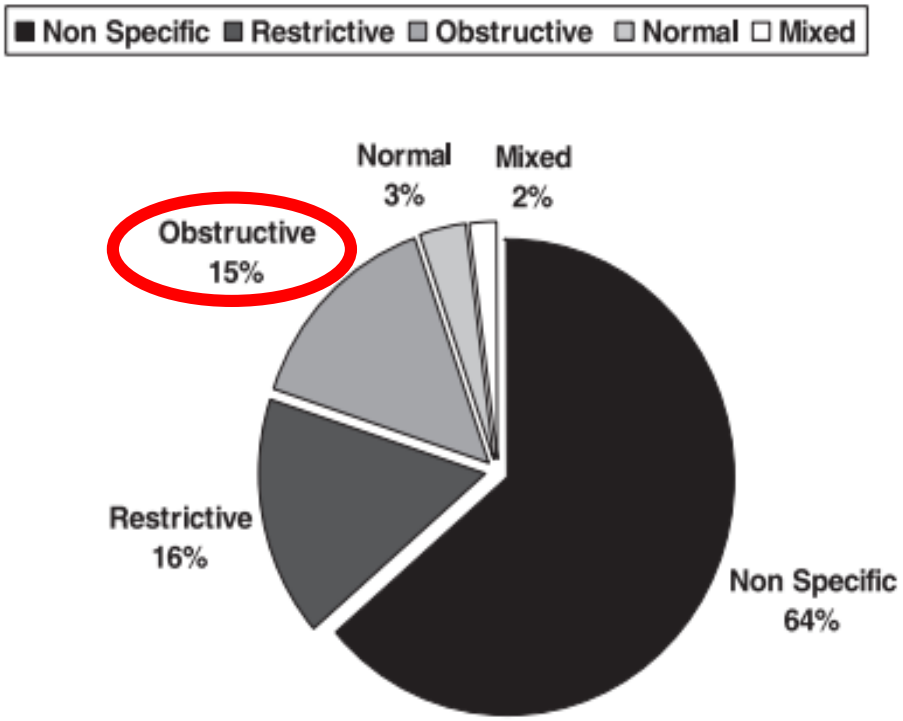
BOO = borderline obstruction; N = normal; NS = nonspecific; PF = pulmonary function; REDU = reduced; TLC = total lung capacity.

- 1990 – 2005
- 1,284 subjects with non-specific PFT
  - 3 Mayo Clinics
  - PFT f/u , 6 month apart (median f/u period = 3 years)

Iyer et al. Chest 2011

PFT with non-specific pattern

PF pattern at last follow-up



Characteristic	Obstructive OR	Obstructive 95% CI
Age, y		
≤49	Reference	0.3-2.4
50-59	0.9	0.4-2.2
60-69	0.9	0.3-2.1
≥70	0.9	…
Sex		
Female	Reference	0.5-1.6
Male	0.9	…
Smoking status		
Never	Reference	0.4-2.2
Former	0.9	0.7-2.1
Current	1.2	…
BMI, kg/m²		
≤24.9	Reference	0.3-1.5
25.0-29.9	0.7	0.4-2.1
30.0-34.9	0.9	0.2-1.1
≥35.0	0.5	…
BD responsive		
No	Reference	1.1-4.2
Yes	2.1	…
SVC − FVC		
Q1	Reference	0.5-2.4
Q2	1.1	0.7-3.4
Q3	1.6	0.8-3.8
Q4	1.7	…
TLC − VA		
Q1	Reference	0.7-4.5
Q2	1.8	1.2-6.8
Q3	2.9	1.5-8.3
Q4	3.6	…
Sraw		
Q1	Reference	0.5-5.9
Q2	1.7	1.4-13.2
Q3	4.2	3.0-28.1
Q4	9.2	…

Sraw: specific airway resistance

V_A: alveolar volume

Iyer et al. Chest 2011

Longitudinal Phenotypes and Mortality in Preserved Ratio Impaired Spirometry in the COPDGene Study

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Phase 1	**Phase 2**
(2008-2011) 45-80 yrs, ≥ 10 PY (n=6,284)	(2012-2016) 5 yr follow-up visit (n=5,593)

Prevalence of PRISm → 12.4% → 12.5%

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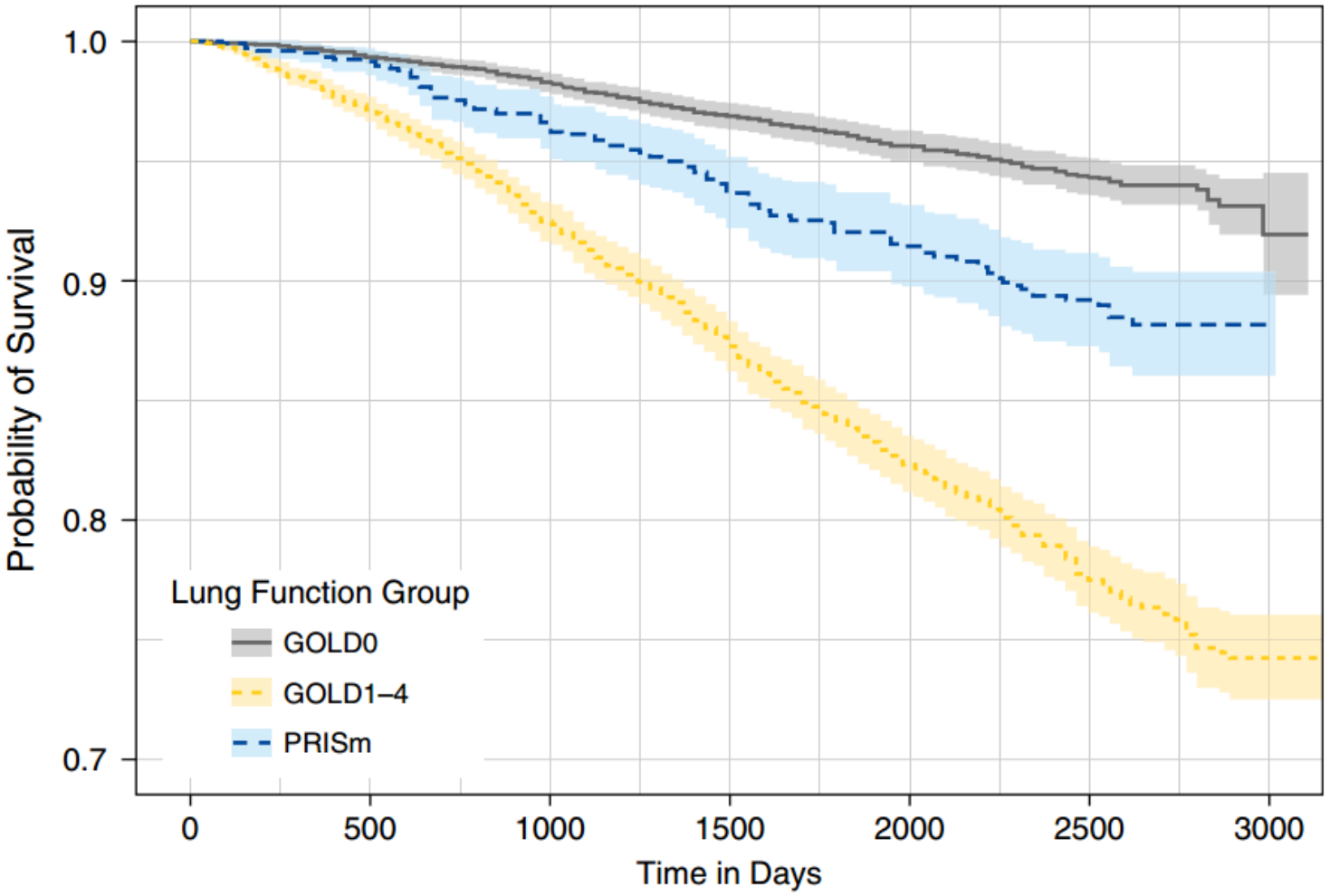
Kaplan-Meier plot of mortality by lung function category in the COPDGene cohort



GOLD 0

PRISm

GOLD 1-4

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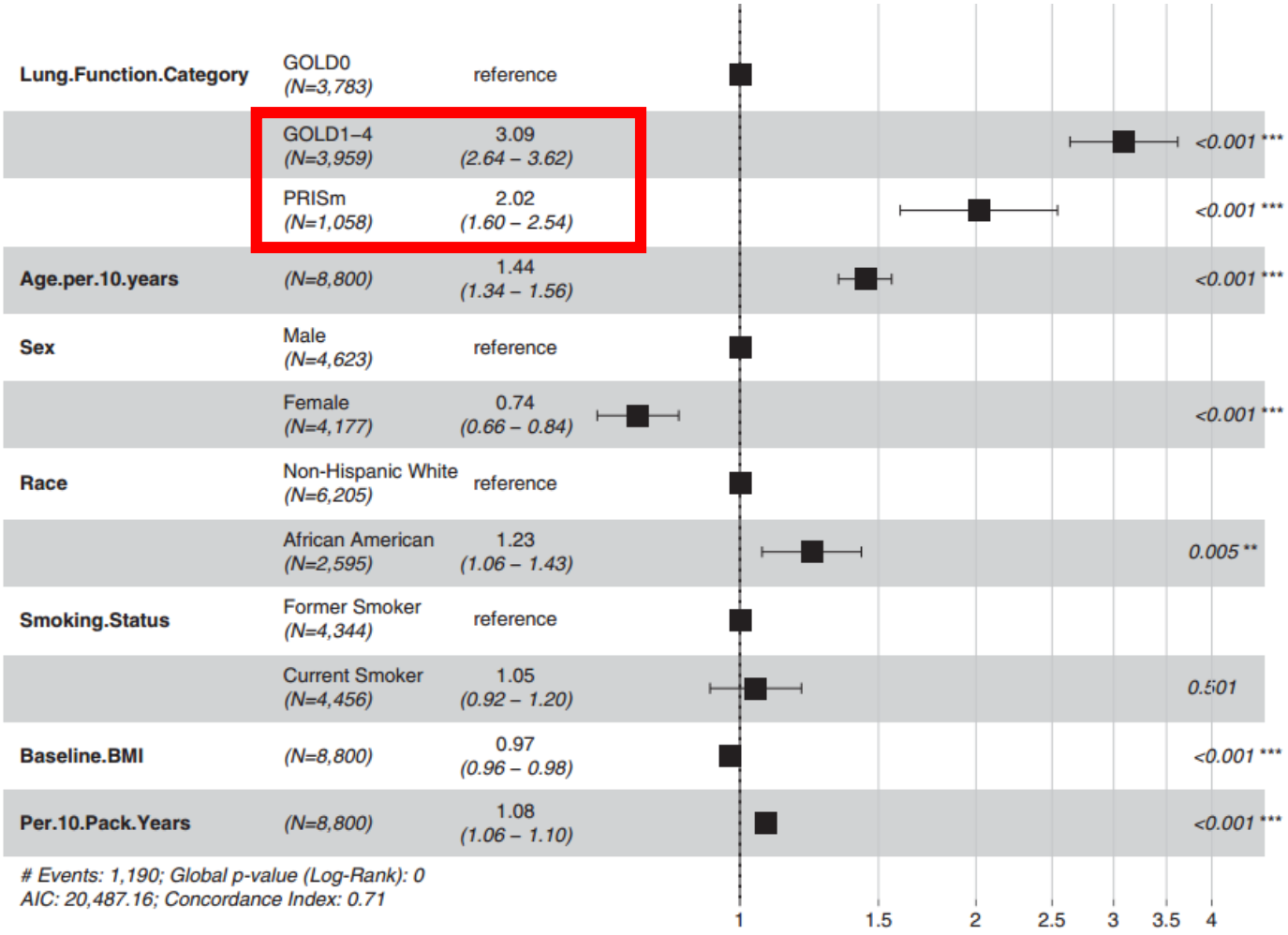
Forest plot of hazard ratios for mortality from Cox proportional hazards model



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Rate of Lung Function Decline by Lung Function Category at Enrollment

	Lung Function Category at Phase 1		
	PRISm (*n* = 684)	GOLD0 (*n* = 2,641)	GOLD1–4 (*n* = 2,268)
ΔFEV_1, ml/yr	−18.9 (52.6)	−41.8 (47.1)*	−38.9 (54.5)*
ΔFVC, ml/yr	−9.8 (68.1)	−41.9 (63.5)*	−63.4 (90.4)*

Definition of abbreviations: GOLD = Global Initiative for Chronic Obstructive Lung Disease; PRISm = Preserved Ratio Impaired Spirometry.
Data are expressed as mean (SD).
*$P < 0.05$ relative to PRISm.

Change in lung function categories among subjects with PRISM

A

Phase 1*	Phase 2*	N	%
PRISm	GOLD 0	152	22.2%
	COPD (GOLD 1–4)	172	25.1%
	PRISm	360	52.6%

*Among participants with lung function data at both Phase 1 and Phase 2

B

Phase 1*	N	%	Phase 2*
PRISm	360	51.9%	PRISm
GOLD 0	223	32.1%	
COPD (GOLD 1–4)	111	16%	

*Among participants with lung function data at both Phase 1 and Phase 2

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Table 3. Characteristics of Subjects with Preserved Ratio Impaired Spirometry at Phase 1 by Lung Function Category at Phase 2

	Lung Function Category at Phase 2		
	PRISm (*n* = 360)	**GOLD0 (*n* = 152)**	**GOLD1–4 (*n* = 172)**
Months between phase 1 and phase 2 visits	67.6 (9.6)	67.5 (9.4)	67.3 (9.0)
Age, yr	56.7 (8.1)*†	58.6 (8.1)	59.3 (8.8)
Female sex, *n* (%)	200 (55.6)	94 (61.8)	89 (51.7)
African American race, *n* (%)	141 (39.2)	61 (40.1)	69 (40.1)
BMI, kg/m^2	32.7 (7.7)†	32.4 (6.7)	31.2 (7.2)
Current smoker, *n* (%)	219 (60.8)*	77 (50.7)	97 (56.4)
Pack-years	40.4 (22.3)†	38.8 (20.6)‡	45.9 (25.0)
FEV_1% predicted, baseline	69.5 (8.1)*	74.8 (5.5)‡	68.2 (8.8)
FVC% predicted, baseline	70.2 (8.9)*†	75.0 (6.8)‡	71.9 (9.7)
TLC_{CT} % predicted§	79.3 (13.2)†	80.5 (13.9)‡	84.2 (15.0)
Chronic bronchitis, *n* (%)	63 (17.5)*	15 (9.9)	28 (16.3)
mMRC	1.4 (1.4)	1.4 (1.4)	1.4 (1.4)
SGRQ	28.1 (23.2)	25.2 (19.5)	29.1 (23.5)
6MWD, m	402.1 (111.4)	401.7 (102.6)	384.4 (106.6)
Percent emphysema§	1.5 (3.2)†	1.6 (2.1)‡	2.2 (2.9)
Percent gas trapping‖	8.2 (6.6)†	9.7 (7.6)‡	12.6 (8.2)
Pi10, mm**	3.72 (0.12)	3.72 (0.12)	3.71 (0.14)
Acute respiratory events/yr††	0.3 (0.6)†	0.3 (0.8)	0.4 (0.8)
ΔFEV_1, ml/yr	−27.2 (42.2)*†	28.0 (44.5)‡	−42.9 (53.8)
ΔFVC, ml/yr	−32.6 (56.8)*†	35.7 (59.4)‡	−2.6 (75.2)
ΔBMI, kg/m^2	0.0 (3.8)*	−1.3 (3.8)‡	−0.4 (3.5)
ΔAdjusted lung density, g/L‡‡	−0.2 (12.5)	−2.4 (11.2)	−2.7 (12.1)

*$P < 0.05$ between PRISm-P2 and GOLD0 spirometry at P2.
†$P < 0.05$ between PRISm-P2 and GOLD1–4 spirometry at P2.
‡$P < 0.05$ between GOLD0 and GOLD1–4 at P2.

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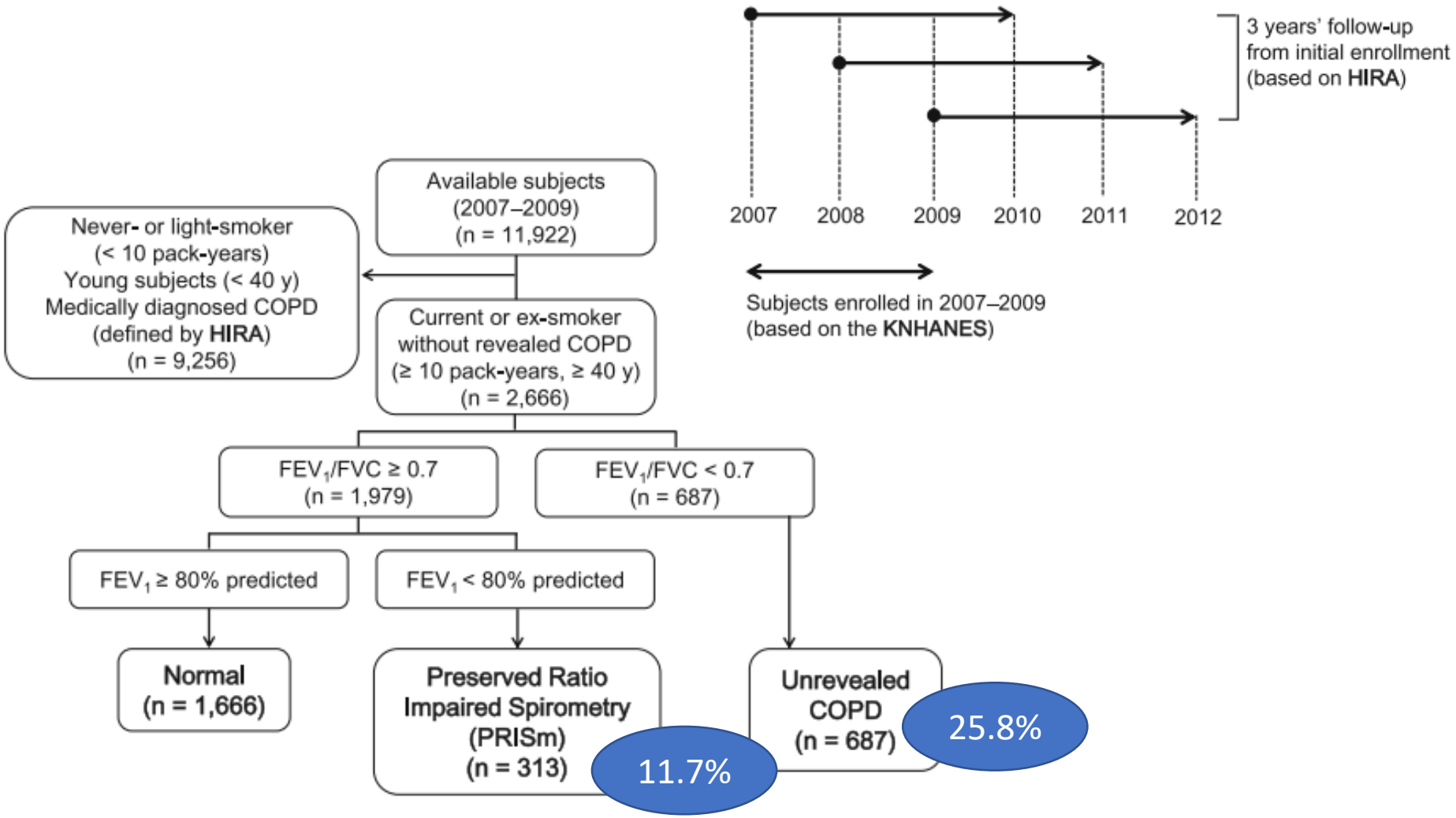
PRISm in Korea: 3-yr cohort study



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PRISm in Korea: 3-yr cohort study

Table 1 Demographics of subjects according to the group

	Normal	PRISm	Unrevealed COPD
Age	54.57 ± 10.52	55.97 ± 10.85	64.48 ± 9.54
Male, *n* (%)	1560 (93.6)	286 (91.4)	654 (95.2)
Height (cm)	167.14 ± 6.94	166.79 ± 6.94	165.97 ± 6.56
Weight (kg)	68.29 ± 9.91	68.66 ± 11.6	63.7 ± 9.8
Smoking history			
Current smoking, *n* (%)	858 (51.5)	193 (61.7)	367 (53.4)
Pack-years	28.62 ± 17.11	33.20 ± 20.34	36.58 ± 21.14
Co-morbidity, *n* (%)			
Hypertension	453 (27.2)	91 (29.1)	209 (30.4)
Hyperlipidemia	166 (10.0)	34 (10.9)	47 (6.8)
Stroke	48 (2.9)	14 (4.5)	18 (2.6)
Acute coronary syndrome	17 (1.0)	8 (2.6)	16 (2.3)
Diabetes mellitus	174 (10.4)	63 (20.1)	84 (12.2)
Pulmonary tuberculosis	124 (7.4)	21 (6.7)	109 (15.9)
Asthma	20 (1.2)	15 (4.8)	65 (9.5)
Lung function test			
FVC % predicted	92.96 ± 10.02	72.55 ± 9.45	88.51 ± 15.02
FEV_1% predicted	94.66 ± 9.14	72.8 ± 6.72	74.18 ± 16.57
FEV_1/FVC	0.79 ± 0.05	0.77 ± 0.06	0.61 ± 0.09
Respiratory symptoms, *n* (%)			
Cough for more than 3 months	1 (0.1)	2 (0.6)	19 (2.8)
Sputum for more than 3 months	4 (0.2)	2 (0.6)	18 (2.6)
Dyspnea	10 (0.6)	3 (1.0)	31 (4.5)
Wheezing	116 (7.0)	37 (11.8)	154 (22.4)
Chronic bronchitis	4 (0.2)	2 (0.6)	21 (3.1)
Total	1666	313	687

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PRISm in Korea: 3-yr cohort study

Table 2 COPD incidence, medication and hospital utilization, and cost

	Normal	PRISm	Unrevealed COPD
COPD incidence (/1000PY)	4.4	17.0	45.1
OPD visit, *n* (%)	51 (3.1)	22 (7.0)	131 (19.1)
No. of OPD visit	0.10 ± 0.91	0.48 ± 2.96	1.86 ± 6.37
Hospitalization, *n* (%)	79 (4.7)	29 (9.3)	83 (12.1)
ER visit, n (%)	23 (1.4)	12 (3.8)	36 (5.2)
ICU admission, n (%)	12 (0.7)	6 (1.9)	19 (2.8)
Total hospital visit, n (%)	121 (7.3)	41 (13.1)	169 (24.6)
ICS, n (%)	4 (0.2)	5 (1.6)	20 (2.9)
ICS + LABA, n (%)	2 (0.1)	11 (3.5)	50 (7.3)
LAMA, n (%)	–	4 (1.3)	44 (6.4)
SAMA, n (%)	12 (0.7)	12 (3.8)	36 (5.2)
SABA, n (%)	14 (0.8)	11 (3.5)	54 (7.9)
Systemic bronchodilator, n (%)	28 (1.7)	11 (3.5)	72 (10.5)
Methylxanthine, n (%)	33 (2.0)	17 (5.4)	101 (14.7)
Total prescribed medication, n (%)	57 (3.4)	26 (8.3)	127 (18.5)
Hospitalization medical Cost (for 3 years) (USD)	186.17 ± 1411.24	398.61 ± 1975.51	750.71 ± 3216.02

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PRISm in Korea: 3-yr cohort study

Table 4 Significant factors for COPD diagnosis in all subjects

	Multivariate analysis		
	OR	95% CI	*P*-value
Age (years)	**1.10**	**(1.07,1.13)**	**< 0.001**
Male			
Height (cm)	1.01	(0.97,1.05)	0.786
Weight (kg)	0.98	(0.95,1.01)	0.143
Smoking history			
Current smoking			
Pack-years	1.01	(1.00,1.02)	0.059
Co-morbidity			
Pulmonary tuberculosis	1.17	(0.66,2.10)	0.587
Asthma	1.88	(0.97,3.64)	0.060
Lung function test			
FVC % predicted	**1.03**	**(1.01,1.05)**	**0.006**
FEV_1% predicted	**0.95**	**(0.93,0.96)**	**< 0.001**
FEV_1/FVC			
Self-reported respiratory symptoms			
Cough for more than 3 months	2.40	(0.24,24.32)	0.458
Sputum for more than 3 months	0.48	(0.02,10.90)	0.647
Dyspnea	**3.07**	**(1.23,7.68)**	**0.017**
Wheezing	**2.90**	**(1.76,4.78)**	**< 0.001**
Chronic bronchitis	2.76	(0.07,109.05)	0.588

Park et al. Respir Res 2018

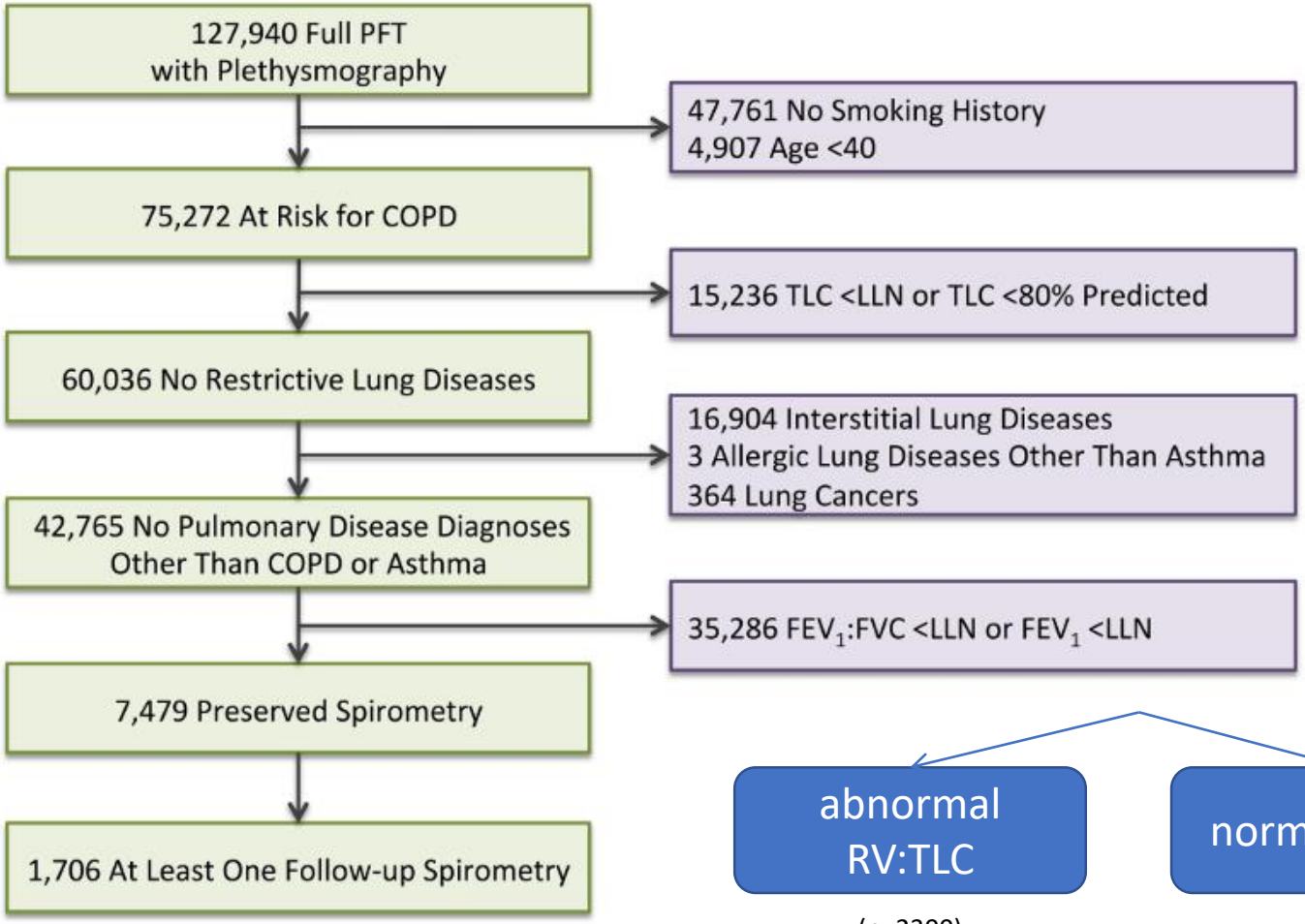
ORIGINAL ARTICLE

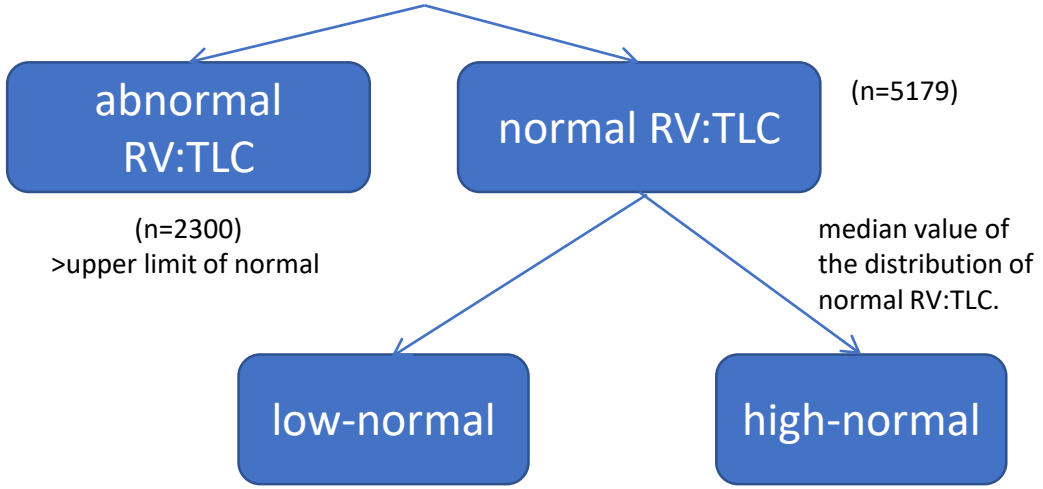
Lung volume indices predict morbidity in smokers with preserved spirometry

Siyang Zeng,[1,2] Andrea Tham,[1,3] Bruce Bos,[1,4] Joan Jin,[1,5] Brian Giang,[1,2] Mehrdad Arjomandi[1,2]

- Retrospective EHR from nationwide Veterans Administration Informatics and Computing Infrastructure (VINCI) database: 7,479 patients
  - at risk for COPD; current or former smokers >40 years of age
  - Preserved PFT; FEV_1:FVC or FEV_1> LLN
  - full PFT between 1985 and 2017
- Healthcare outcomes
  - clinical diagnoses, respiratory medication prescribed, outpatient office visits, ER visits, hospital admissions and ICU admissions with a COPD diagnosis
  - all-cause mortality

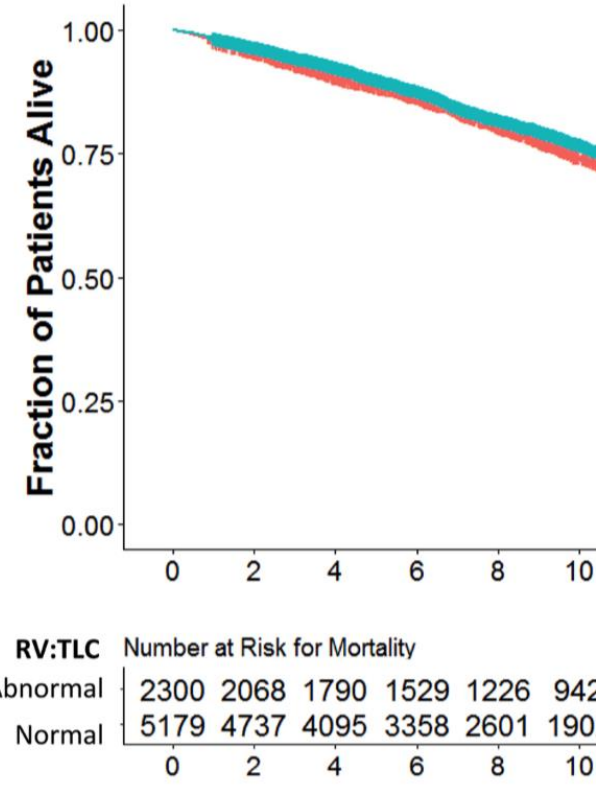
Zeng et al. Thorax 2019

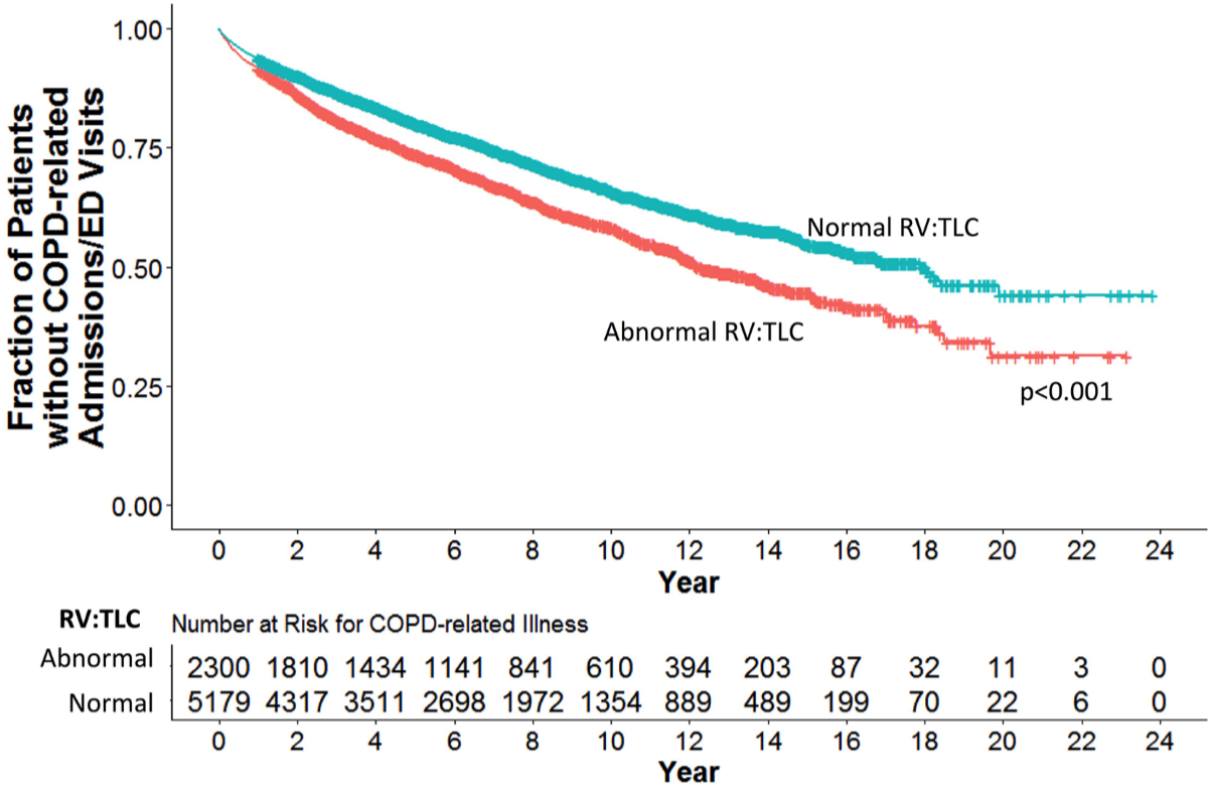




Zeng et al. Thorax 2019

Survival curves and Respiratory-related illness





Zeng et al. Thorax 2019

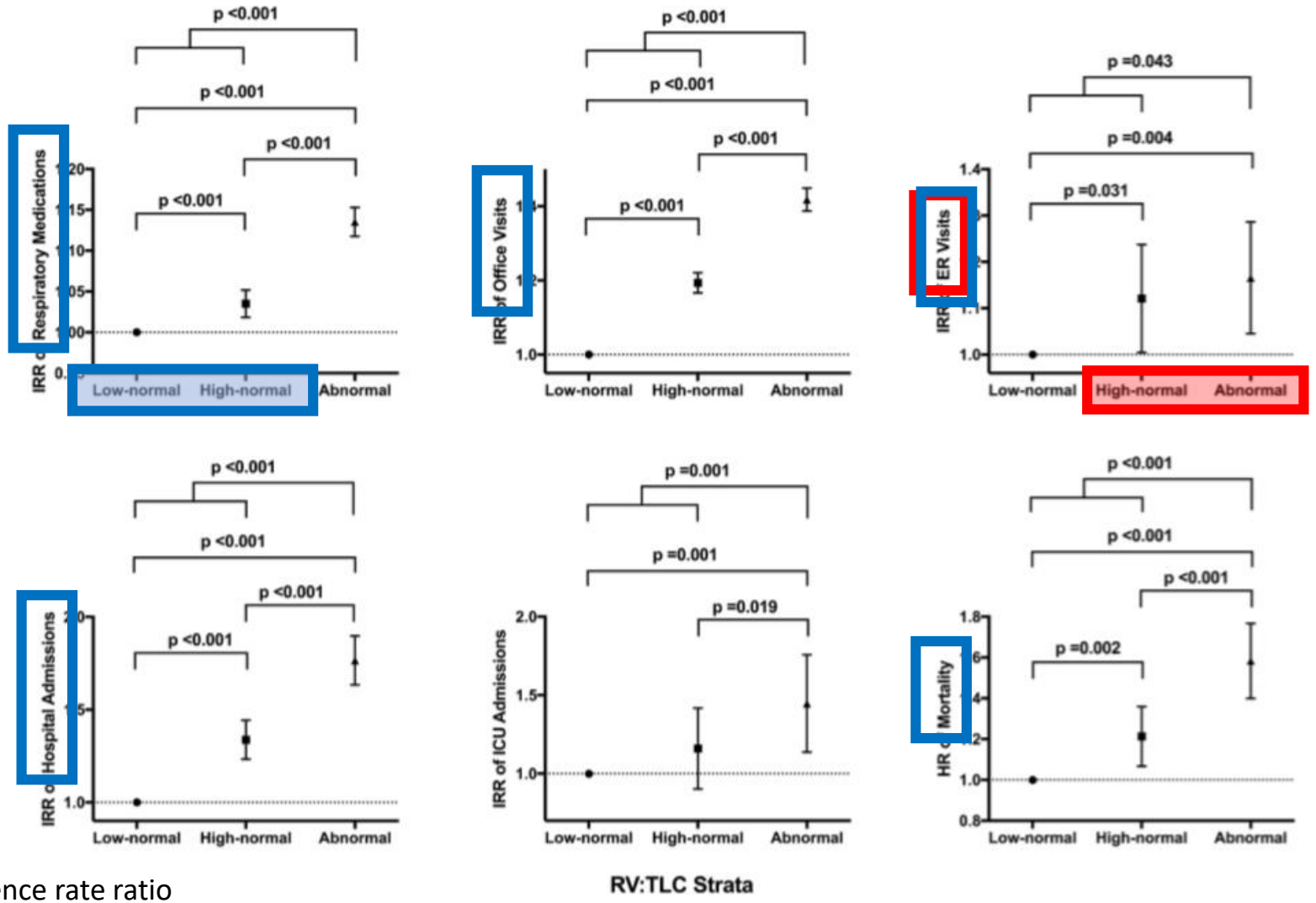
Association of RV:TLC and health outcomes

Respiratory-related health outcomes	Abnormal RV:TLC (%)	RV:TLC (%) continous
Clinical diagnosis of COPD	1.41 (1.29-1.55)	1.033(1.03-1.04)
Respiratory medications	1.07 (1.05-1.08)	1.005 (1.004-1.006)
Office visits	1.16 (1.14-1.18)	1.016 (1.014-1.017)
ER visits	0.95 (0.87-1.03)	1.007 (1.002-1.013)
Hospital admissions	1.34 (1.26-1.42)	1.031 (1.027-1.035)
ICU admissions	1.12 (0.95-1.33)	1.016 (1.004-1.029)
Mortality	1.31 (1.19-1.44)	1.019 (1.013-1.025)
COPD on fu spirometry	1.3 (1.00-1.69)	1.022 (1.003-1.041)

Adjusted by age, sex, height and years of follow-up

Zeng et al. Thorax 2019

Associations of healthcare outcomes with RV:TLC strata



IRR: incidence rate ratio

Zeng et al. Thorax 2019

Conclusions

- Prevalent air trapping: 1/3 of those at risk for COPD with PRISM having RV:TLC>ULN
- Patients with air trapping (RV:TLC>ULN)
  - more likely to receive clinical diagnoses of COPD and to progress to develop spirometric COPD
  - higher all-cause mortality
  - increased healthcare utilisation and hospitalisation associated with COPD diagnosis
- Without overt air trapping (normal RV:TLC), high-normal RV:TLC - worse outcomes compared with their low-normal counterparts
- Lung volume measurements and air trapping: predictive usefulness of in PRISm

Zeng et al. Thorax 2019

Risk of COPD with obstruction in active smokers with normal spirometry and reduced diffusion capacity

Ben-Gary Harvey[1,2,4], Yael Strulovici-Barel[1,4], Robert J. Kaner[1,2], Abraham Sanders[2], Thomas L. Vincent[1], Jason G. Mezey[1,3] and Ronald G. Crystal[1,2]

- Smokers recruited from NY metropolitan area
- 1570 active smokers
  - 1173: normal spirometry/normal Dlco
  - 397: normal spirometry/low Dlco

- Return for additional PFT assessments
  - 59 smokers with normal spirometry/normal Dlco
  - 46 smokers with normal spirometry/low Dlco

Harvey et al. ERJ 2015

	Normal spirometry/low Dlco	Normal spirometry/normal Dlco
Change in FEV_1/FVC per month	-0.14 ± 0.18%	-0.07 ± 0.11%

(P<0.02)

TABLE 2 Progression to chronic obstructive pulmonary disease (COPD) in active smokers with normal spirometry/low diffusing capacity of the lung for carbon monoxide (*D*LCO) *versus* active smokers with normal spirometry/normal *D*LCO

Group#	At end of evaluation period	
	Normal	With COPD
Normal spirometry, normal *D*LCO	97 (57/59)	3 (2/59)
Normal spirometry, low *D*LCO	78 (36/46)	22 (10/46)
p-value¶	0.009	

Isolated impairment in gas transfer may precede COPD

Harvey et al. ERJ 2015

Disease Severity Dependence of the Longitudinal Association Between CT Lung Density and Lung Function in Smokers

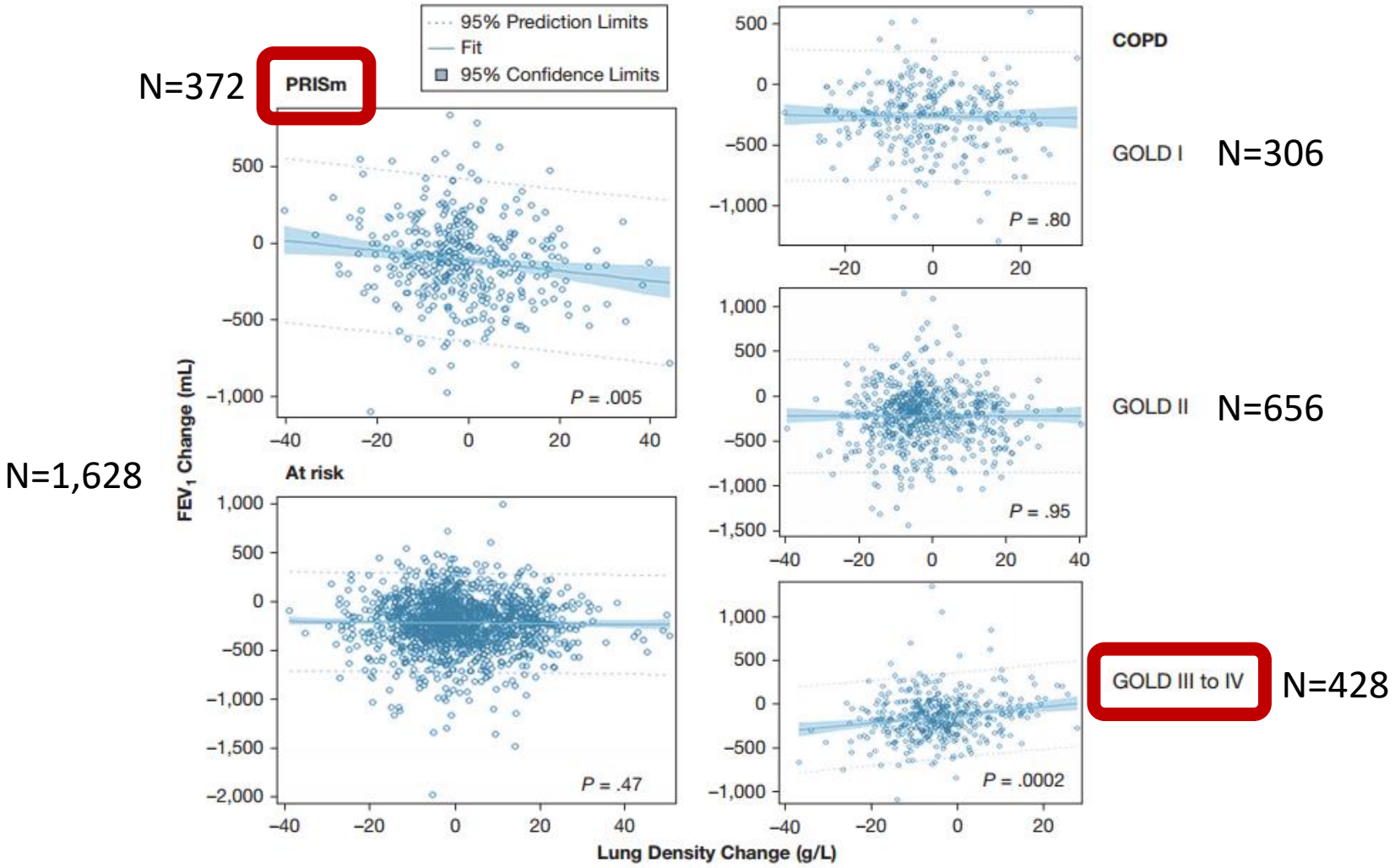
Alejandro A. Diaz, MD, MPH; Matthew Strand, PhD; Harvey O. Coxson, PhD; James C. Ross, PhD; Raul San Jose Estepar, PhD; David Lynch, MD; Eva M. van Rikxoort, PhD; Ivan O. Rosas, MD; Gary M. Hunninghake, MD, MPH; Rachel K. Putman, MD, MPH; Hiroto Hatabu, MD, PhD; Andrew Yen, MD; Gregory L. Kinney, PhD; John E. Hokanson, PhD; Edwin K. Silverman, MD, PhD; James Crapo, MD; and George R. Washko, MD

- COPDGene study
- 3,390 smokers with baseline and 5-year fu
- Total lung capacity-adjusted lung density (TLC-PD15)
  - lung density at 15th percentile (PD15) of the Hounsfield unit distribution adjusted for predicted total lung capacity (TLC)

- At Risk, PRISm, GOLD I, GOLD II, GOLD III-IV

Diaz et al. Chest 2018

Plots of 5-year changes in FEV_1 as a function of TLC-PD15 changes according to smoking group



N=372

N=1,628

N=306

N=656

N=428

Diaz et al. Chest 2018

Effects of Within-Subject TLC-PD15 on FEV_1 Over 5 Years of Follow-up According to Smoking Group

Smoking Group/COPD Severity Group	TLC-PD15 Effect (per 1 g/L)		
	Estimate (mL of FEV_1)	SE	*P* Value
PRISm	−2.8	1.3	.03
At risk	−0.9	0.7	.23
COPD stage			
GOLD I	0.5	1.7	.77
GOLD II	2.4	1.3	.06
GOLD III-IV	3.8	1.4	.01

Gain of tissue → No net change → Loss of tissue

- inflammation
- irregular deposition of matrix
- remodeling of respiratory bronchiole/surrounding alveolar structures
- fibrosis

- gains d/t inflammation and remodeling
- loss of healthy parenchyma

Diaz et al. Chest 2018

Imaging Features of Chronic Bronchitis with Preserved Ratio and Impaired Spirometry (PRISm)

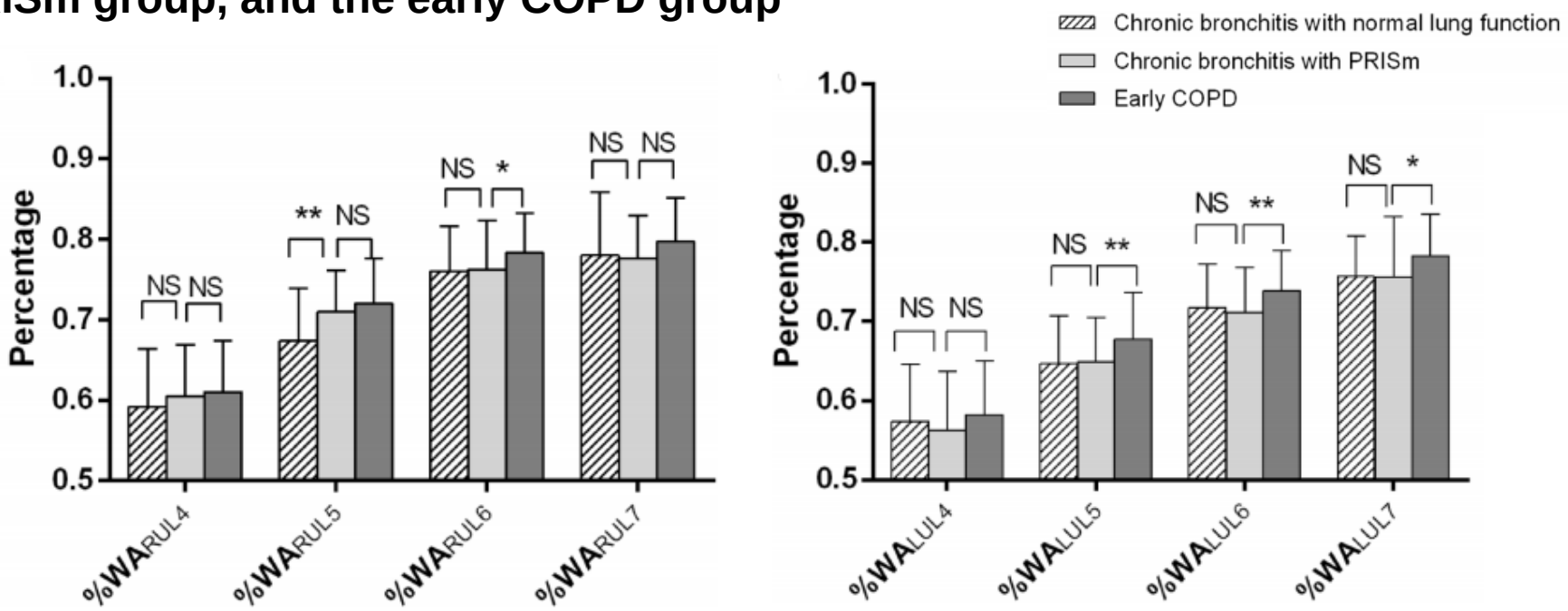
Xia Wei[1,2] · Qi Ding[1] · Nan Yu[3] · Jiuyun Mi[1] · Jingting Ren[1] · Jie Li[1] · Shudi Xu[1] · Yanzhong Gao[4] · Youmin Guo[1]

- Chinese Han nationality; Ninth Hospital of Xi'an Affiliated Hospital of Xi'an Jiaotong University between Oct 2014 and Sep 2017
- risk factors for COPD and had respiratory symptoms
- 77 CB with normal lung function ($FEV_1/FVC > 70\%$, &$FEV_1\% \geq 80\%$)
- 80 CB with PRISm ($FEV_1/FVC > 70\%$, & FEV_1%pred < 80%)
- 186 early COPD (GOLD 1+2)
- CT
  - %WA: 4-7th generation (BUL, BML), 4-9th generation (BLL)
  - %LAA−950, the mean emphysema density (MLD), the lung capacity (LC), and emphysema heterogeneity index (HI).

%WA: % of wall area
%LAA-950: % of low attenuation value below -950 HU

Wei et al. Lung 2018

Comparison of %WA in the CB group, the PRISm group, and the early COPD group



Comparison of emphysema related parameters among the three groups

	CB c NL	CB c PRISm	early COPD	*P*-value
LC_{whole}	4306	4029*	5264	< 0.001
$\%LAA_{whole}$	10.7	9.77	16.6	< 0.001
MLD_{whole}	-816.4	-799.9	-834.5	0.003
HI_{whole}	0.2	0.15	0.12	0.075

P-value: compared to the group of CB c NL and CB c PRISm

LC: lung capacity
%LAA−950,
MLD: mean emphysema density
HI: emphysema heterogeneity index

Wei et al. Lung 2018

SUMMARY

- Strategy for prevention of COPD
  - Start from fetus

- High risk for COPD but spirometrically impaired with preserved ratio

Worse clinical outcomes
More medical expenses
Higher mortality

than those with normal lung function

Distinct subgroups?

Transitory state?

risk stratification tool

Wan et al. AJRCCM 2018

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