Bronchodilator (LABD) Therapy in Bronchiectasis

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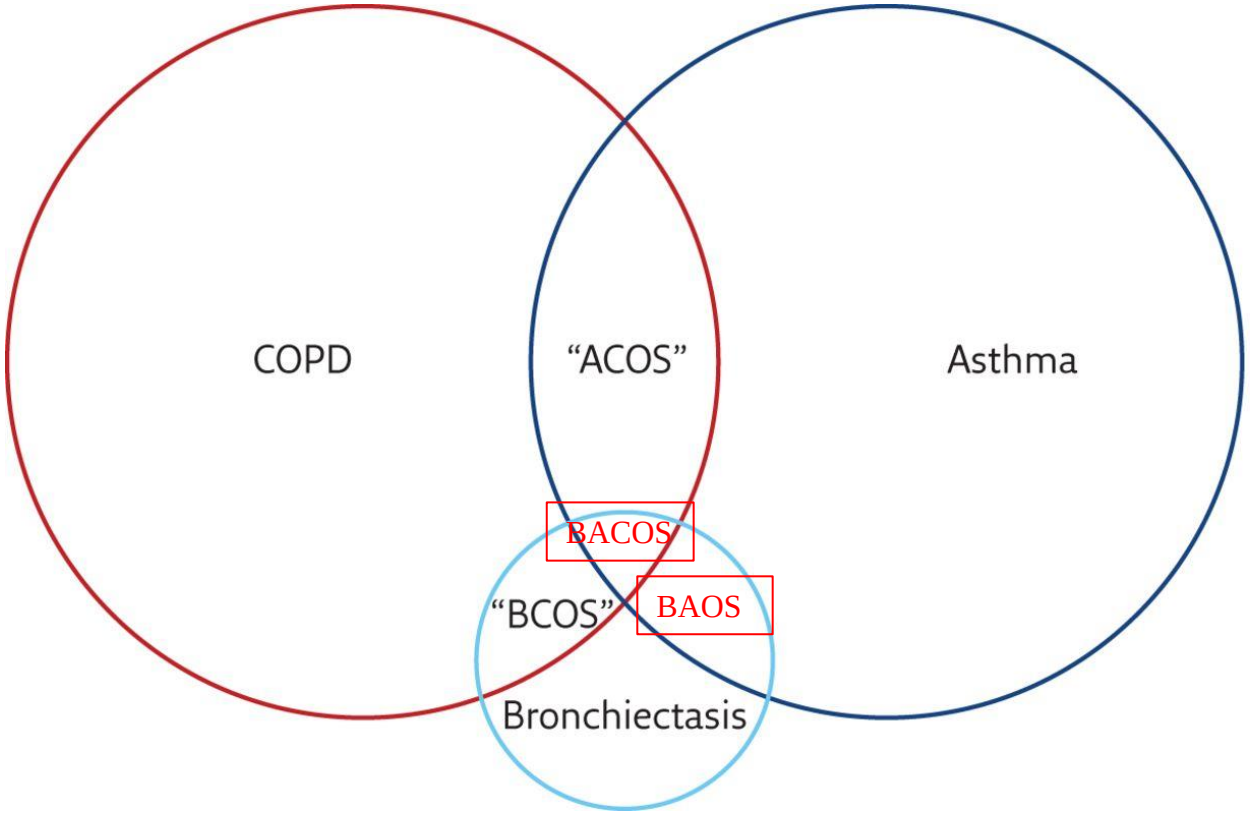
Venn diagram, chronic airway diseases



Breathe 2016; 12: 222-235

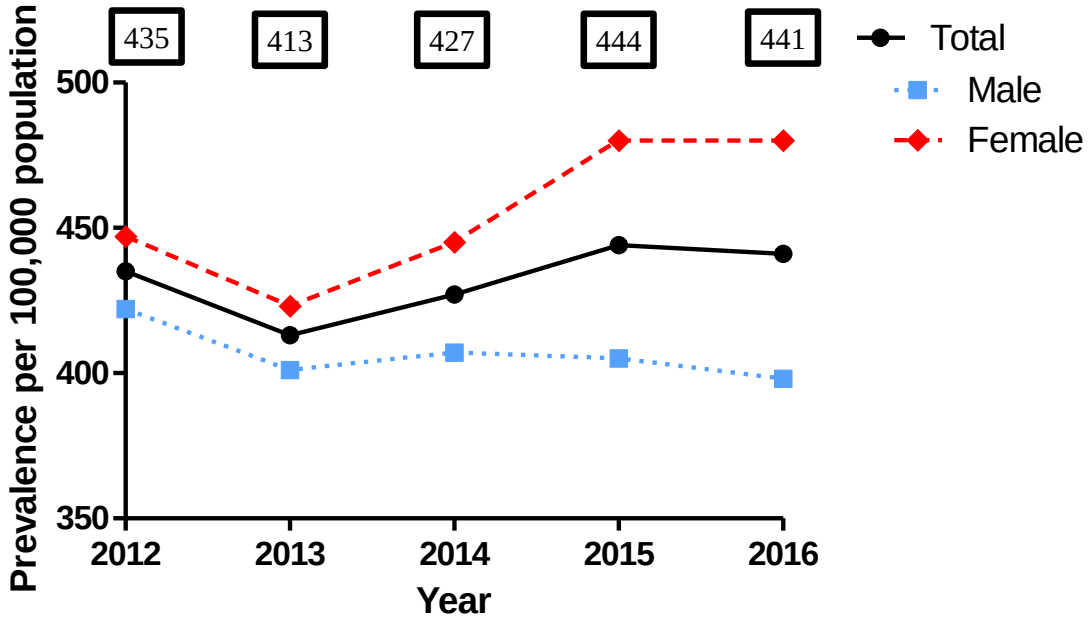
Prevalence, COPD vs Bronchiectasis

COPD: 국민건강영양조사, 2008

- 6,480 subjects ≥ 19 yrs
- 한국 COPD 유병율 (≥ 40 yrs and FEV1/FVC < 0.7): 13.4%
- 100,000명당 13,400명 (13.4%)

Yoo KH;Respirology;2011;16;659-65

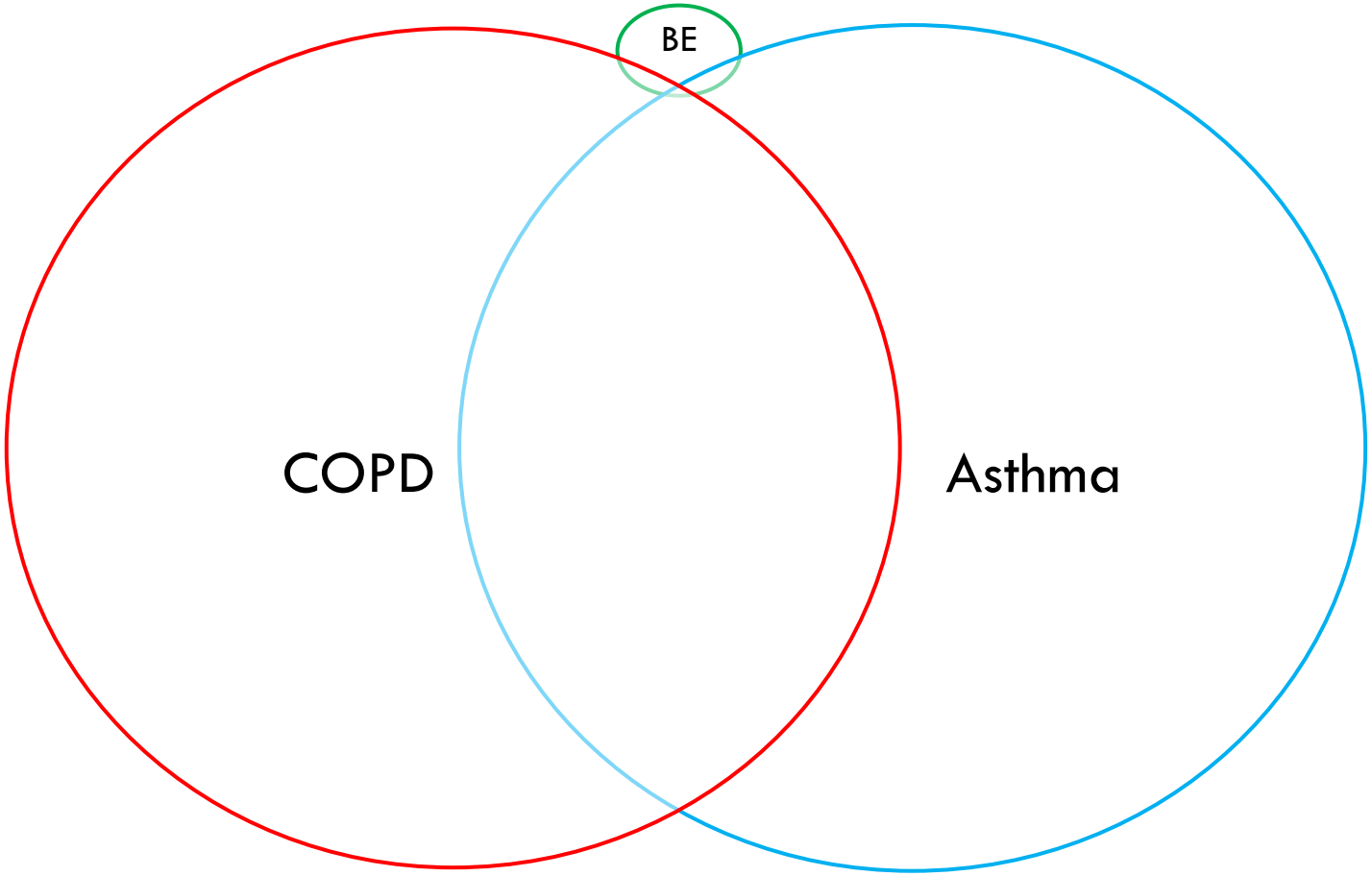
BE: 심평원 표본청구자료, 2012-2016



- 100,000명당 432명 (0.43%)

Lee SJ;CHEST 2021;159 (3);959-962

432 vs 13,400 = 3.22%



Dose long term bronchodilator treatment improve outcomes for patients with bronchiectasis ?

- There is limited supporting evidence for the use of bronchodilator
- Patients with bronchiectasis frequently have airflow obstruction and more than 60% of bronchiectasis patients have daily symptoms of breathlessness
- Offer a trial of long acting bronchodilator therapy in patients with symptoms of significant breathlessness
- Use of bronchodilators in patients with bronchiectasis and co-existing COPD or asthma should follow the guideline recommendations for COPD or asthma

Hill AT, *et al*. *Thorax* 2019;**74**(Suppl 1):1–69.

- 현재 기관지확장증 치료에 있어 기관지확장제의 주요 역할은 기도청결법 시행전 기도를 확장하여 기도 청결을 증진시키시 위해 사용하는 것이다
- 향후 기관지확장제의 효과에 대한 더 많은 연구가 필요하다

J Korean Med Assoc 2020 August; 63(8):486-492

Comorbidities of Bronchiectasis, KMBARC

	Korea (*n* = 598)	Australia (*n* = 653)	Europe[a] (*n* = 2596)	India[a] (*n* = 2195)
Demographics				
Age, years	66 (60–72)	73 (64–79)	67 (57–74)	56 (41–66)
Men	264 (44.1)	195 (29.9)	1010 (38.9)	1249 (56.9)
BMI, kg/m^2	22.9 (20.7–25.4)	25.0 (21.5–29.0)	24.8 (21.8–28.1)	21.5 (18.5–24.5)
Current or former smokers	211 (35.3)	145 (22.2)	990 (38.1)	619 (28.2)
Comorbidities				
Ischaemic heart disease	27 (4.5)	46 (7.0)	453 (17.5)	355 (16.2)
Stroke	11 (1.8)	20 (3.1)	152 (5.9)	9 (0.4)
Diabetes mellitus	73 (12.2)	42 (6.4)	260 (10.0)	315 (14.4)
Liver disease	13 (2.2)	5 (0.8)	41 (1.6)	18 (0.8)
Chronic renal failure	12 (2.0)	12 (1.8)	154 (5.9)	26 (1.2)
COPD	226 (37.8)	95 (14.5)	431 (16.6)	512 (23.3)
Asthma	134 (22.4)	94 (14.4)	226 (8.7)	485 (22.1)
Osteoporosis	70 (11.7)	151 (23.1)	192 (7.4)	130 (5.9)
GORD	89 (14.9)	224 (34.3)	394 (15.2)	346 (15.8)
Solid tumour	50 (8.4)	14 (2.2)	164 (6.3)	17 (0.8)

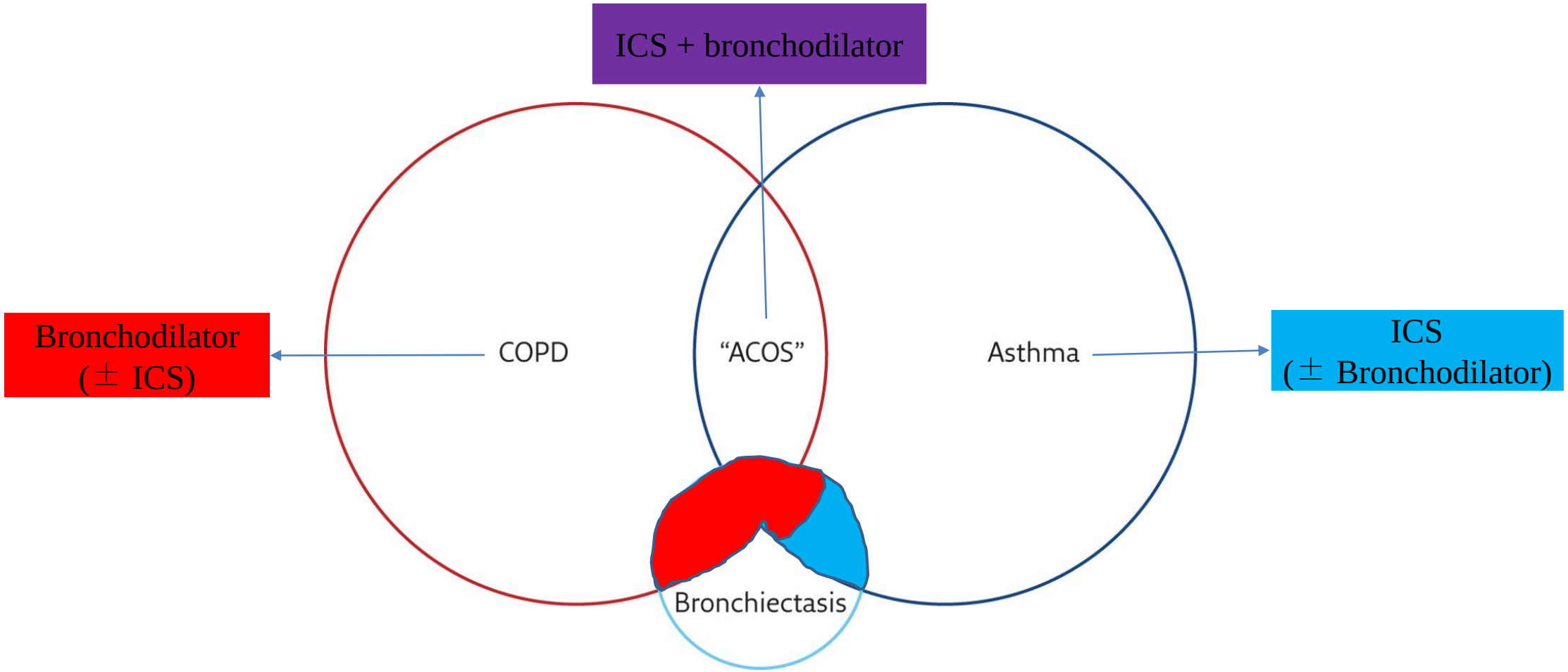
Lee & Choi et al. Respirology 2021; 26: 618-620

Comorbidities of Bronchiectasis, EMBARC

	EMBARC cohort (n=16 963)	UK (n=8163)	Southern Europe (n=4295)	Northern and western Europe (n=3444)	Central and eastern Europe (n=1061)
Age, years	67 (57–74)	69 (61–75)	66 (54–74)	65 (52–73)	62 (53–70)
Age >65 years	9943 (58·6%)	5465 (66·9%)	2174 (50·6%)	1841 (53·5%)	463 (43·6%)
Female	10 335 (60·9%)	4938 (60·5%)	2766 (64·4%)	2101 (61·0%)	530 (50·0%)
Male	6628 (39·1%)	3225 (39·5%)	1529 (35·6%)	1343 (39·0%)	531 (50·0%)
BMI, kg/m²*	24·9 (21·7–28·7)	25·7 (22·4–29·8)	24·3 (21·4–27·7)	23·8 (21·4–27·7)	24·8 (21·2–28·4)
Comorbidities					
Cardiovascular diseases	5509 (32·5%)	2413 (29·6%)	1397 (32·5%)	1135 (33·0%)	564 (53·2%)
Stroke	600 (3·5%)	388 (4·8%)	79 (1·8%)	101 (2·9%)	32 (3·0%)
Liver disease	103 (0·6%)	35 (0·4%)	15 (0·3%)	40 (1·2%)	13 (1·2%)
Osteoporosis	2228 (13·1%)	1255 (15·4%)	460 (10·7%)	398 (11·6%)	115 (10·8%)
Depression	2377 (14·0%)	1401 (17·2%)	493 (11·5%)	350 (10·2%)	133 (12·5%)
Anxiety	2428 (14·3%)	1290 (15·8%)	660 (15·4%)	339 (9·8%)	139 (13·1%)
Neoplastic disease	1863 (11·0%)	885 (10·8%)	435 (10·1%)	429 (12·5%)	114 (10·7%)
Chronic renal failure	667 (3·9%)	280 (3·4%)	173 (4·0%)	199 (5·8%)	15 (1·4%)
Diabetes	1724 (10·2%)	880 (10·8%)	403 (9·4%)	302 (8·8%)	139 (13·1%)
Asthma	5267 (31·0%)	3208 (39·3%)	811 (18·9%)	1046 (30·4%)	202 (19·0%)
COPD	4324 (25·5%)	2225 (27·3%)	828 (19·3%)	862 (25·0%)	409 (38·5%)

Chalmers et al. Lancet Respir Med 2023; 11: 637-49

Use of Bronchodilator in Bronchiectasis



Common Treatment in Real World

	EMBARC cohort (n=16 963)	UK (n=8163)	Southern Europe (n=4295)	Northern and western Europe (n=3444)	Central and eastern Europe (n=1061)
Inhaled corticosteroid	8700 (51·3%)	4796 (58·8%)	1779 (41·4%)	1630 (47·3%)	395 (37·2%)
LABA	8632 (50·9%)	4311 (52·8%)	2104 (49·0%)	1764 (51·2%)	453 (42·7%)
LAMA	4707 (27·7%)	2231 (27·3%)	1278 (29·8%)	911 (26·5%)	287 (27·0%)
LTRA	1007 (5·9%)	665 (8·1%)	135 (3·1%)	169 (4·9%)	38 (3·6%)
Theophylline	483 (2·8%)	298 (3·7%)	53 (1·2%)	70 (2·0%)	62 (5·8%)
Antibiotic treatments					
Inhaled antibiotic	1310 (7·7%)	620 (7·6%)	365 (8·5%)	306 (8·9%)	19 (1·8%)
Macrolide	2940 (17·3%)	1615 (19·8%)	475 (11·1%)	840 (24·4%)	10 (0·9%)
Other oral antibiotic prophylaxis	794 (4·7%)	574 (7·0%)	99 (2·3%)	101 (2·9%)	20 (1·9%)
Cyclical antibiotics	604 (3·6%)	297 (3·6%)	127 (3·0%)	116 (3·4%)	64 (6·0%)
Mucoactive drugs					
Carbocisteine or N-acetylcysteine	2910 (17·2%)	2389 (29·3%)	208 (4·8%)	256 (7·4%)	57 (5·4%)
Hypertonic saline	1454 (8·6%)	537 (6·6%)	224 (5·2%)	662 (19·2%)	31 (2·9%)
Isotonic saline	872 (5·1%)	356 (4·4%)	92 (2·1%)	373 (10·8%)	51 (4·8%)
Mannitol	4 (0%)	2 (0·0%)	0 (0%)	2 (0·1%)	0 (0%)
DNAse	75 (0·4%)	36 (0·4%)	19 (0·4%)	12 (0·3%)	8 (0·8%)
Sodium hyaluronate	24 (0·1%)	2 (0·0%)	16 (0·4%)	5 (0·1%)	1 (0·1%)

Data are n (%). LABA=long-acting beta agonist. LAMA=long-acting muscarinic antagonist. LTRA=leukotriene receptor antagonist.

Table 3: **Commonly used treatments between different European regions**

Chalmers et al. Lancet Respir Med 2023; 11: 637-49

Overuse of Bronchodilator in Bronchiectasis

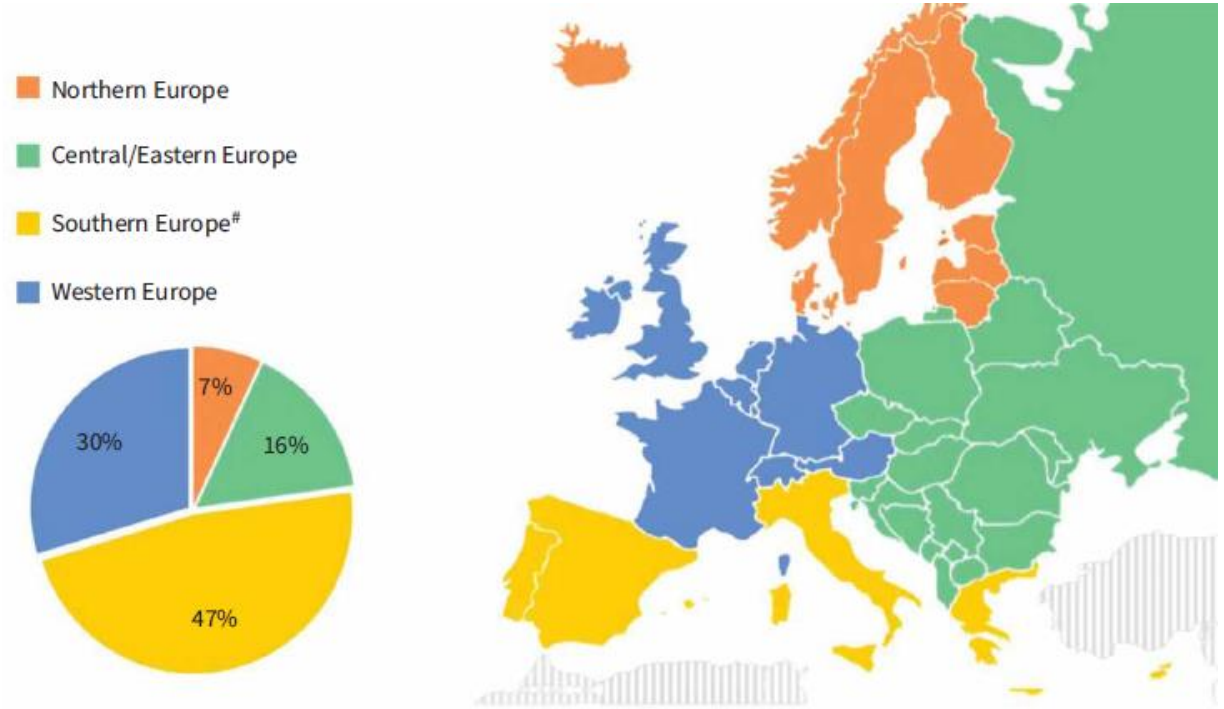
Registry	n	Age	FEV_1,%pred Median (IQR)	Airflow obstruction	SABA	LABA	LAMA
Indian Registry	2195	56 (41–66)	61.4 (42–80.1)	34.8% (92.4% fixed)	–	60%*	40%*
Spanish BE Research Registry (RIBRON)	1912	67.6 (± 15.2)	73.9 (55–92)	53.1% (17% severe)	67%	68%	44%
US BE Research Registry	1826	64 (± 14)	–	51% (15% severe)	–	61% LABA or LAMA	61% LABA or LAMA
Australian BE Registry	589	71 (64–77)	75 (57–91)	34%	38%	50%	15%

Drugs 2022; 82: 1-13

ROSE: radiology, obstruction, symptoms and exposure – a Delphi consensus definition of the association of COPD and bronchiectasis by the EMBARC Airways Working Group

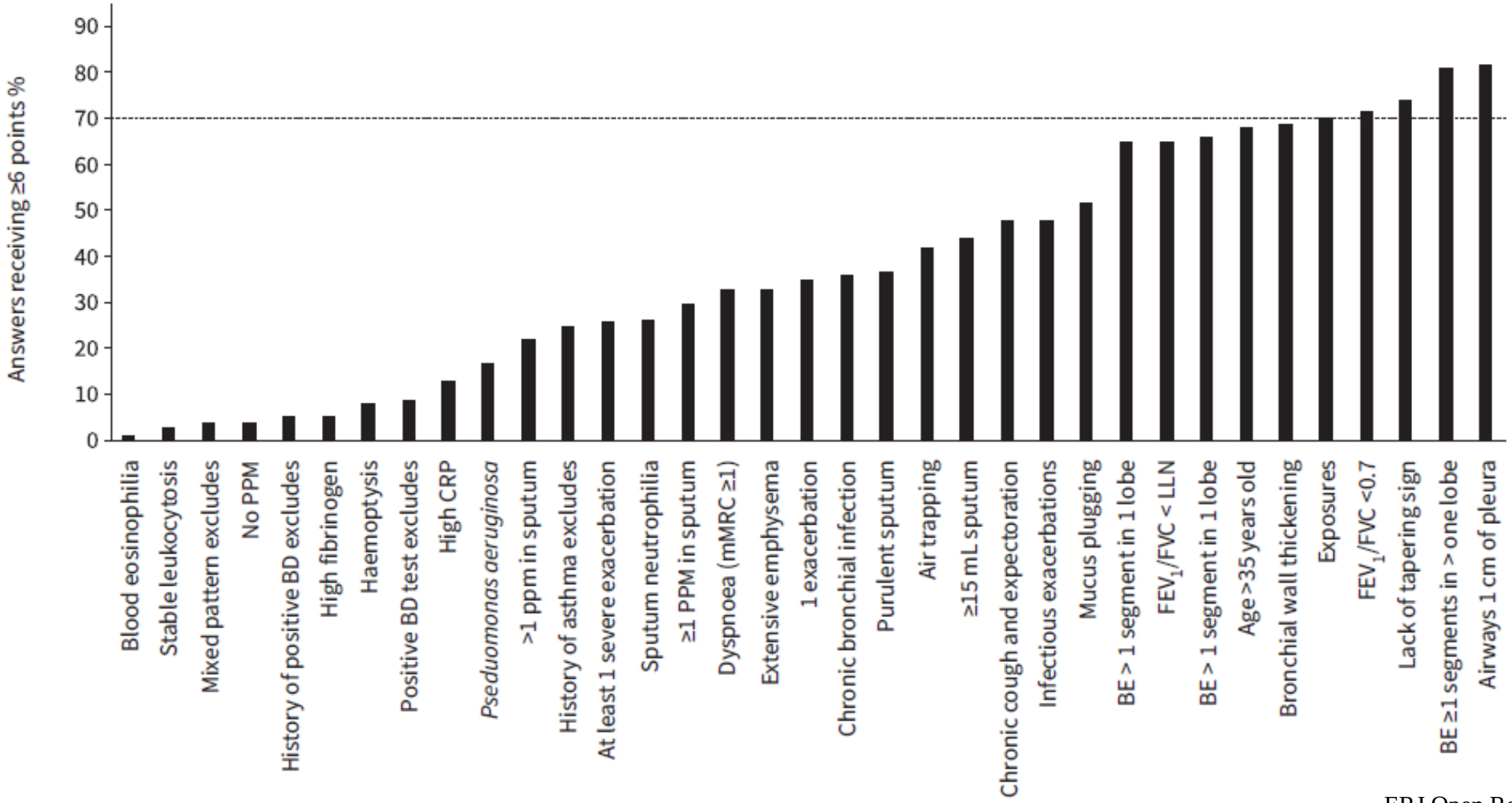
*

- Delphi survey with the objective of developing an international consensus definition of the COPD–BE association
- Panel of 16 experts in COPD and bronchiectasis from the EMBARC Airways Working Group: target number of 100 participants



ERJ Open Res 2021;7;00399-2021

Results from first round



ERJ Open Res 2021;7;00399-2021

Final Consensus Definition

TABLE 5 Final consensus definition

The association of COPD and bronchiectasis is defined as the presence of at least four elements

1. RADIOLOGICAL: Abnormal bronchial dilatation in one or more pulmonary segment in more than one lobe and specific radiological findings (airways visible within 1 cm of pleura and/or lack of tapering sign) plus
2. OBSTRUCTION: a functional obstructive pattern (post-bronchodilator $FEV_1/FVC < 0.7$), plus
3. SYMPTOMS: two or more of the following symptoms: cough, expectoration, dyspnoea, fatigue, frequent lower airway infections (≥2/year) plus
4. EXPOSURE: current or past smoking habit (≥10 pack-years) or other toxic exposure (biomass, industrial, *etc.*)

*Missing radiologic criteria: Bronchial wall thickening, Broncho-arterial ratio

ERJ Open Res 2021;7;00399-2021

The label of COPD in bronchiectasis is often incorrect

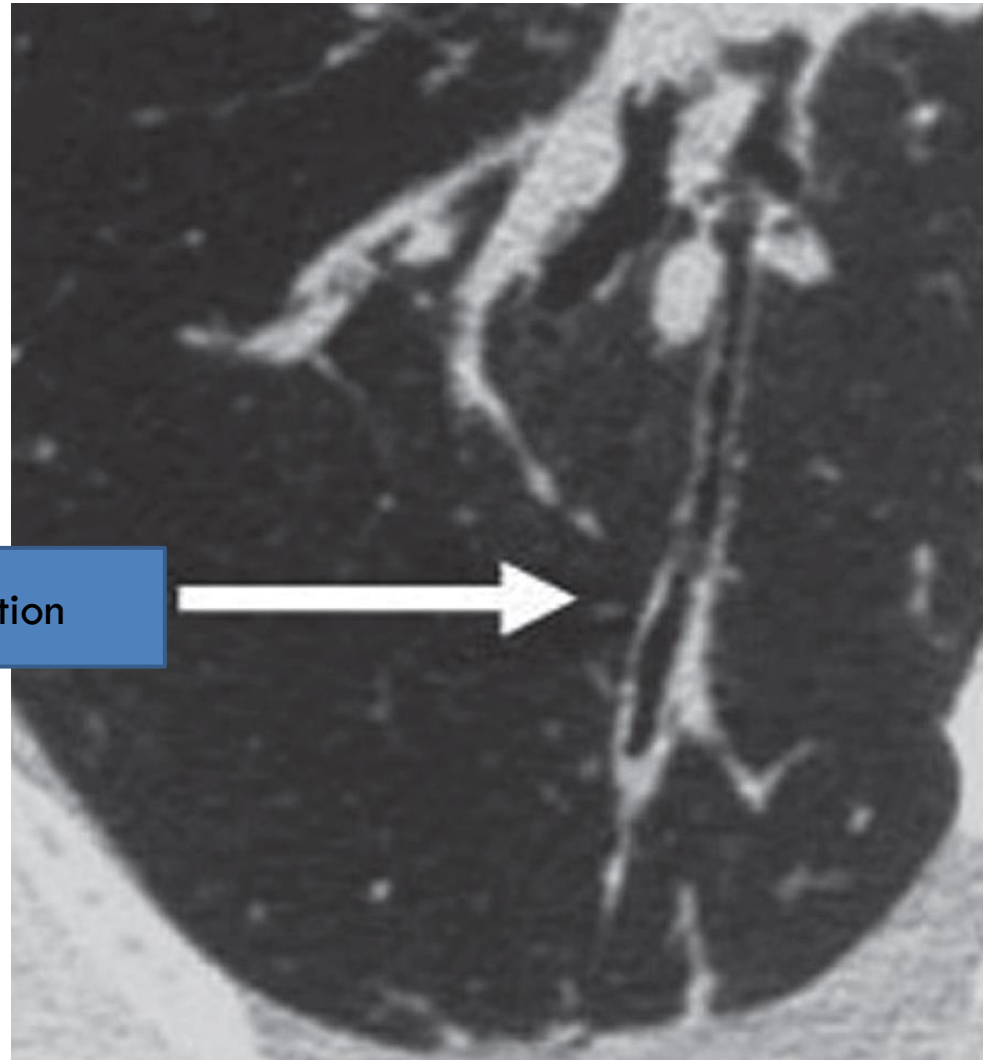
The Association Between Bronchiectasis and Chronic Obstructive Pulmonary Disease: Data from the European Bronchiectasis Registry (EMBARC)

	Reported COPD	No reported COPD
N	4324	12639
N with complete lung function data	3832 (88.6%)	11369 (90.0%)
FEV1/FVC ratio <0.7	2986 (77.9%)	4694 (41.3%)
10 or more pack year smoking history	2652 (69.2%)	2241 (19.7%)
ROSE criteria (Fixed ratio)	2130 (55.6%)	877 (7.7%)

Table 2. COPD diagnosis and objective criteria. Abbreviations FEV1= forced expiratory volume in 1 second, FVC= forced vital capacity.

Am J Respir Crit Care Med 2024 in press

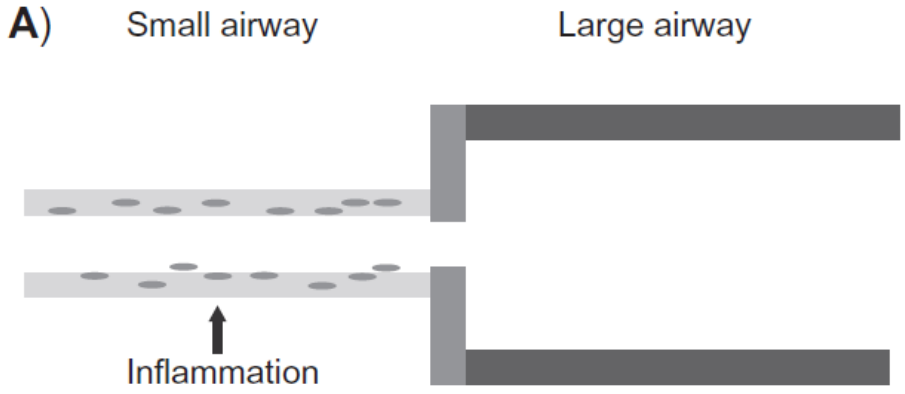
Airway Narrowing & Obstruction in Bronchi-ectasis ???

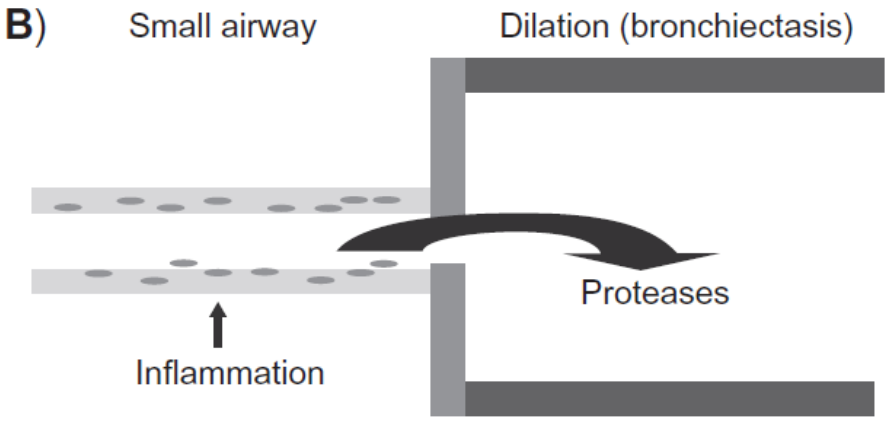


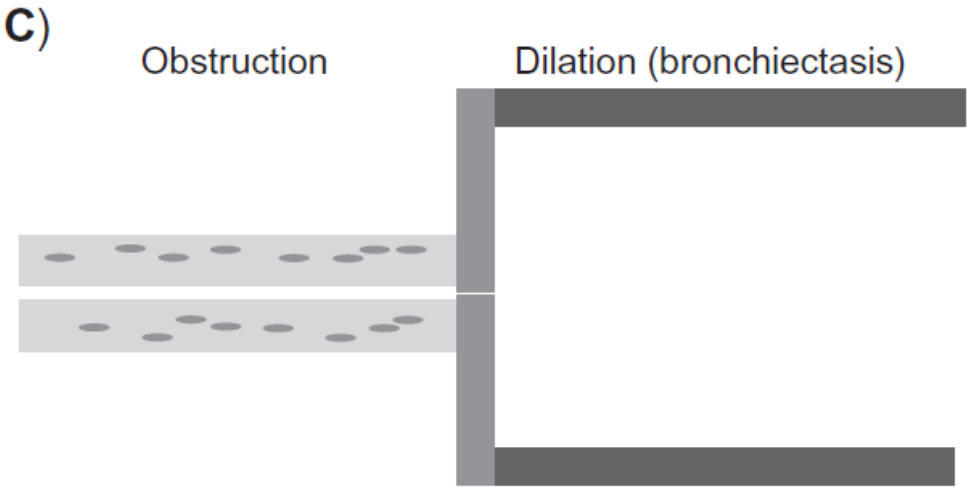
Airway Dilatation

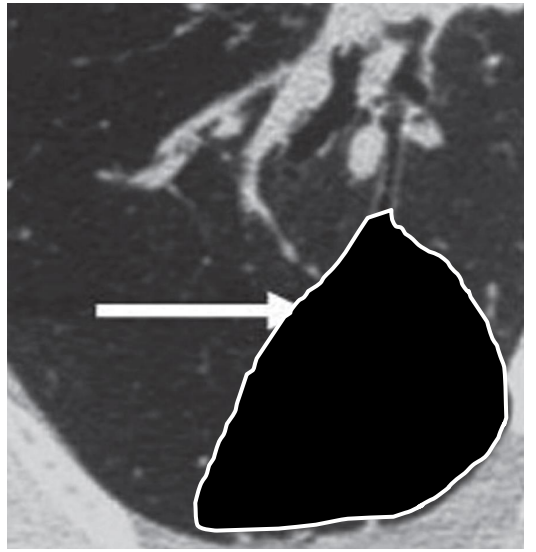
Bronchodilator in broncho-dilatory airway disease?

Airway Obstruction in Bronchiectasis









International Journal of COPD 2009:4

ORIGINAL ARTICLE

Proximal and Distal Bronchioles Contribute to the Pathogenesis of Non–Cystic Fibrosis Bronchiectasis

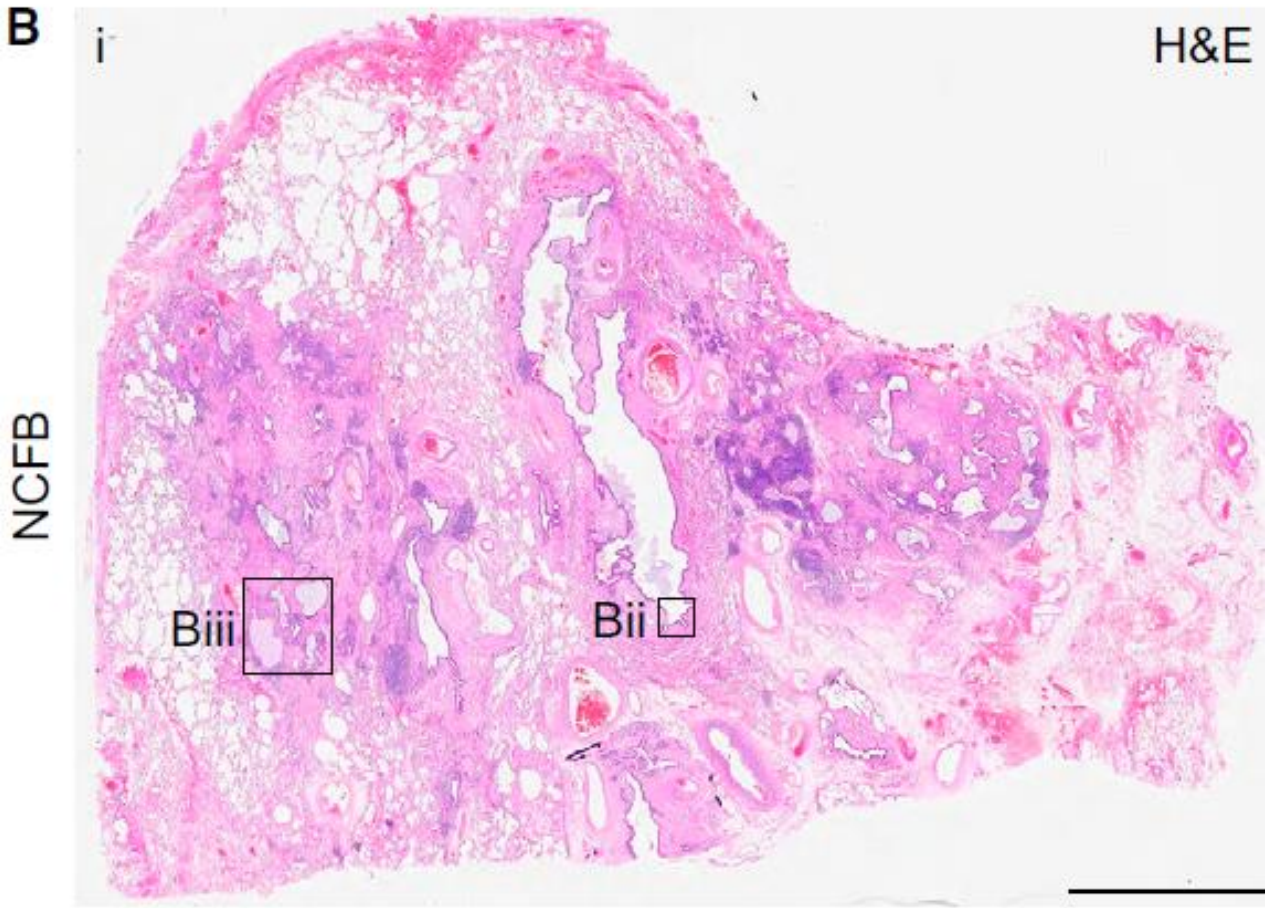
Takanori Asakura[1,4,5,6], Kenichi Okuda[1], Gang Chen[1], Hong Dang[1], Takafumi Kato[1], Yu Mikami[1], Stephen A. Schworer[1], Rodney C. Gilmore[1], Giorgia Radicioni[1], Padraig Hawkins[1], Selene Margarita Barbosa Cardenas[1], Minako Saito[1], Anne Marie Cawley[1], Gabriela De la Cruz[2], Michael Chua[1], Neil E. Alexis[3], Yohei Masugi[7], Peadar G. Noone[1], Carla M. P. Ribeiro[1], Mehmet Kesimer[1], Kenneth N. Olivier[1,9], Naoki Hasegawa[8], Scott H. Randell[1], Wanda K. O'Neal[1], and Richard C. Boucher[1]

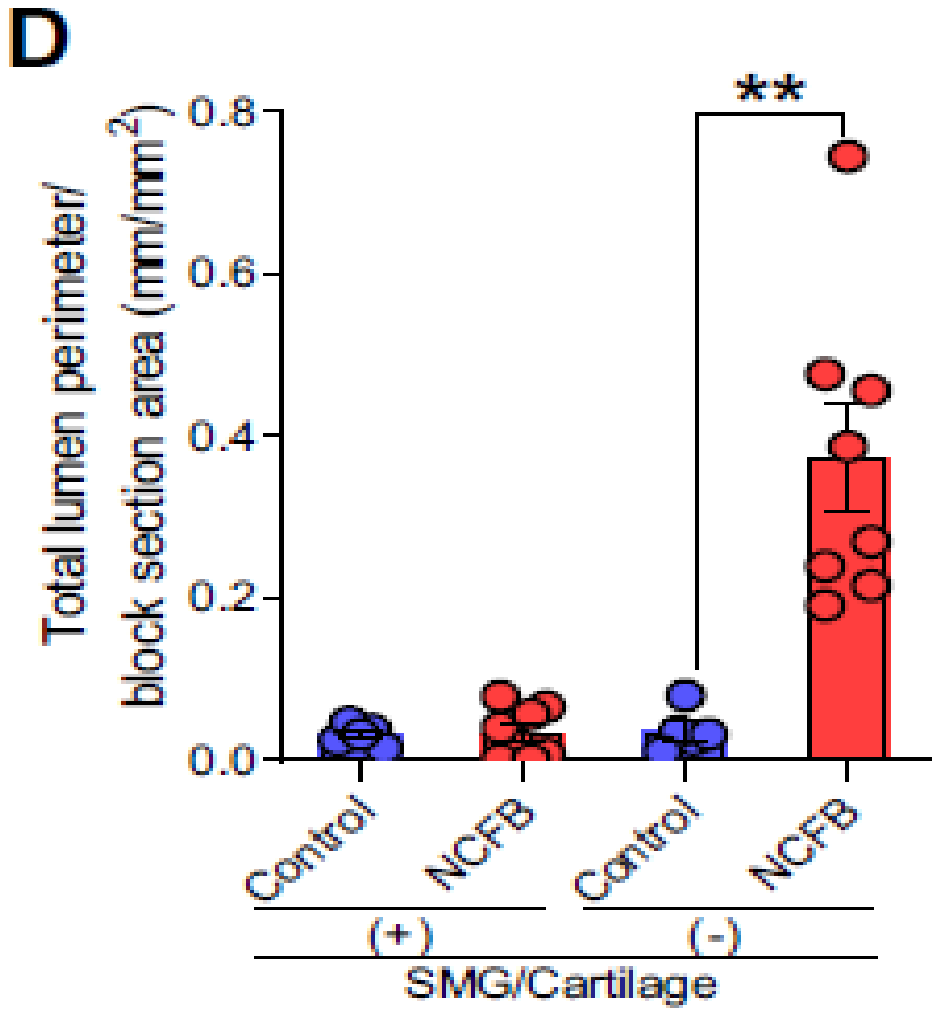
[1]Marsico Lung Institute/Cystic Fibrosis Research Center, [2]Pathology Services Core, Lineberger Comprehensive Cancer Center, and [3]Center for Environmental Medicine, Asthma, and Lung Biology, Division of Allergy and Immunology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; [4]Department of Clinical Medicine, Laboratory of Bioregulatory Medicine, Kitasato University School of Pharmacy, Tokyo, Japan; [5]Department of Respiratory Medicine, Kitasato University, Kitasato Institute Hospital, Tokyo, Japan; [6]Division of Pulmonary Medicine, Department of Medicine, [7]Department of Pathology, and [8]Department of Infectious Diseases, Keio University School of Medicine, Tokyo, Japan; and [9]Pulmonary Branch, National Heart, Lung, and Blood Institute, NIH, Bethesda, Maryland

- NCFB lungs from Japan were obtained from patients who underwent pulmonary resection for NCFB
- Control lungs: not suitable for transplantation because of size mismatch

Am J Respir Crit Care Med 2024; 209(4); 374-389

Airway Morphology (Bronchi vs Bronchiole)





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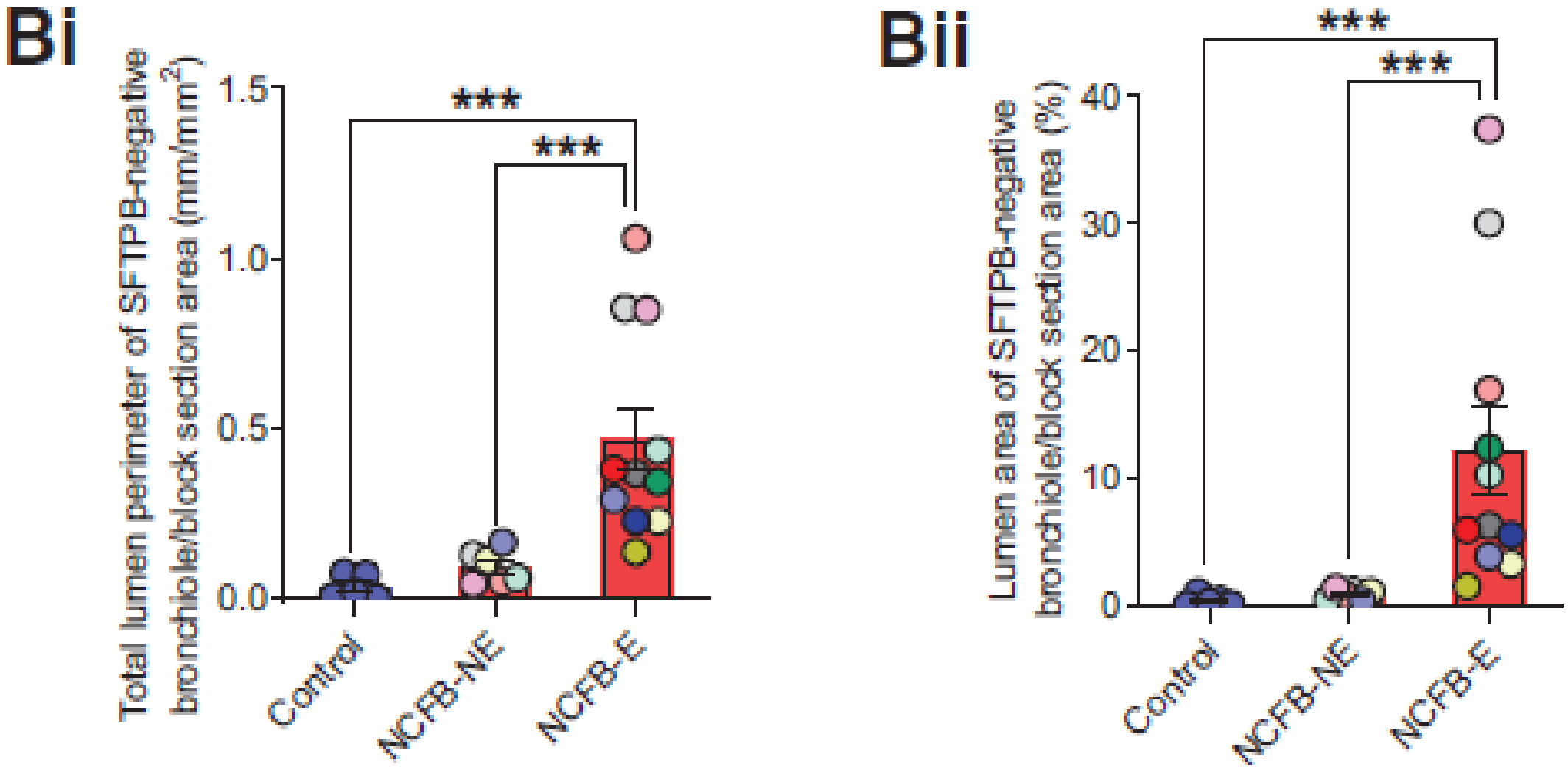
Characterization of Proximal Bronchioles (vs Distal)



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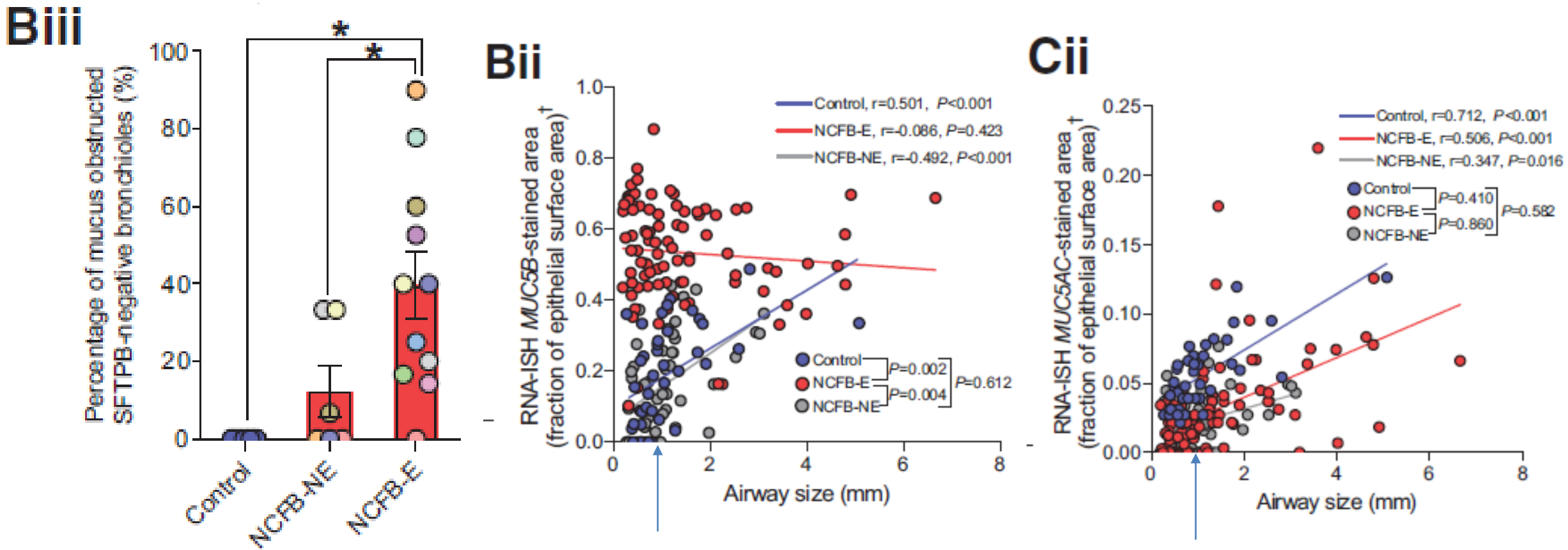
Exhibition of Mucus Obstruction



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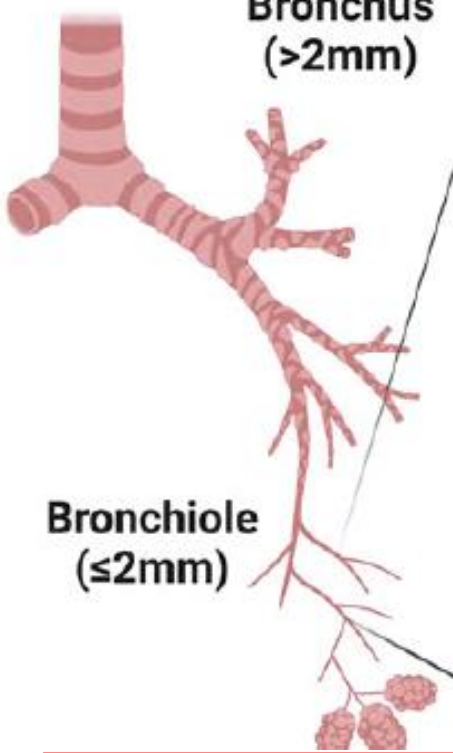
Geographic Summary

Morphologic/Gene Expression Analyses of Proximal and Distal Bronchioles



		Normal	NCFB (Non-ectatic)	NCFB (Bronchiolectasis)
Proximal Bronchiole	Ectasia	No Ectasia	No Ectasia	Ectasia
	MUC5B	Normal	Normal	Upregulated
	MUC5AC	Normal (Low)	Normal (Low)	Upregulated
	SFTPB	None	None	None
	SCGB3A2	None	None	None
Distal Bronchiole	Ectasia	No Ectasia	No Ectasia	No Ectasia
	MUC5B	Normal	Normal	Upregulated
	MUC5AC	Very Low	Very Low	Very Low
	SFTPB	High	High	Upregulated
	SCGB3A2	High	High	High

***Proximal (**vs. distal**) bronchiole-ectasis (**vs. bronchi-ectasis**)**

Am J Respir Crit Care Med 2024; 209(4); 374-389

Contents lists available at ScienceDirect

Respiratory Medicine

A comprehensive approach to lung function in bronchiectasis

Demographics, comorbidities and chronic treatment of the study population.

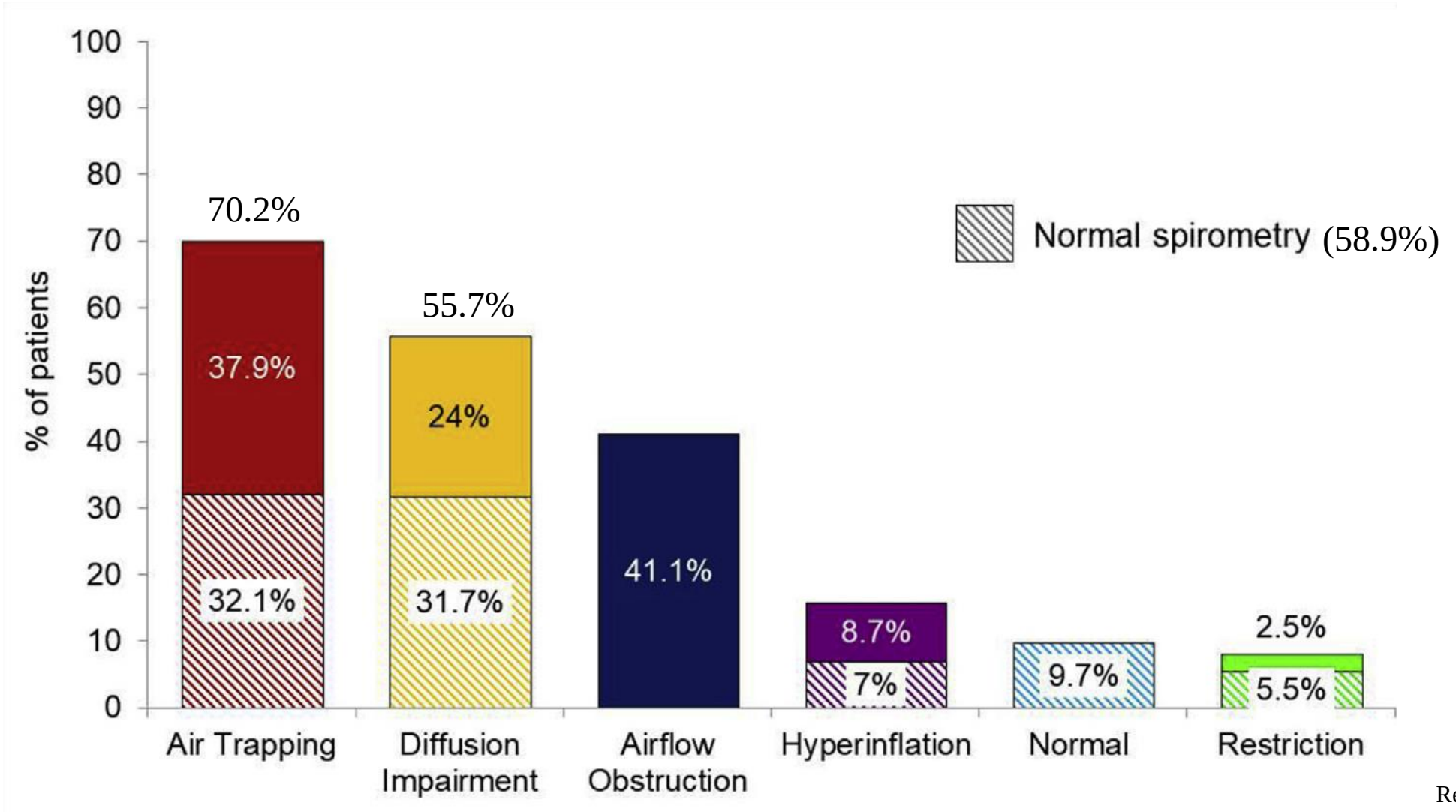
Variables	Study group
n.	187
Demographics	
Median (IQR) age, years	68 (59–73)
Either smokers or former smokers, n (%)	79 (42.2)
Comorbidity	
GERD, n (%)	39 (20.8)
COPD, n (%)	34* (16.6)
Asthma, n (%)	23* (12.3)
Connective tissue disease, n (%)	21 (11.2)
Myocardial infarction, n (%)	7 (3.7)
Peripheral vascular disease, n (%)	5 (2.7)
Moderate-severe liver disease, n (%)	5 (2.7)
Moderate-severe chronic kidney disease, n (%)	5 (2.7)
Congestive heart failure, n (%)	4 (2.1)
Mild liver disease, n (%)	2 (1.1)
Cerebrovascular accident, n (%)	1 (0.5)
Leukemia, n (%)	2 (1.1)
Treatment	
Macrolide, n (%)	14 (7.5)
Inhaled antibiotic treatment, n (%)	7 (3.7)
Chronic bronchodilator therapy	
LABA, n (%)	6 (3.2)
LAMA, n (%)	24 (12.8)
LABA/LAMA FDC or LAMA + LABA, n (%)	6 (3.2)
ICS, n (%)	6 (3.2)
LABA/ICS FDC	13 (10.5)
LABA/LAMA/ICS	33 (17.6)
Theophylline, n (%)	3 (1.6)

- N=187, 2 centers in Italy
- Spirometry, DLco, Body plethysmography

- Air trapping: RV> 120%
- Hyperinflation: TLC> 120%

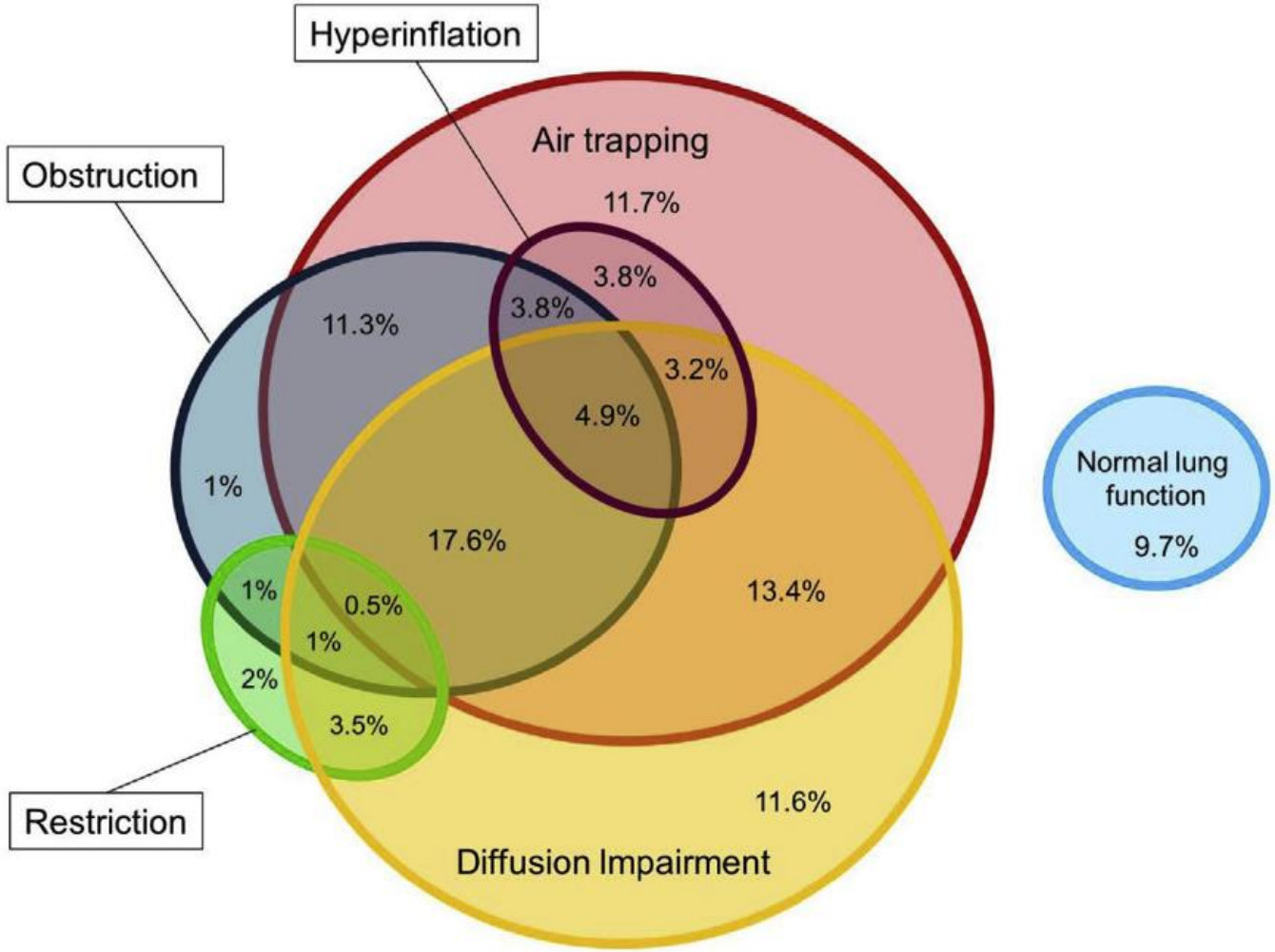
Respir Med 2018; 145; 120-129

Lung Function in Bronchiectasis



Respir Med 2018; 145; 120-129

Overlap of parameters



Respir Med 2018; 145; 120-129

Taylor & Francis
Taylor & Francis Group

COPD: Journal of Chronic Obstructive Pulmonary Disease

Outcome in Adult Bronchiectasis

Table 2. Demographics/co-morbidities of 101 patients

Period of follow-up (years)	8.0 ± 4.9 (mean ± SD)
Age (years)	54 ± 14 (mean ± SD)
Sex ratio of group	33 male 68 female
Ex-smokers	20 patients
HRCT score	33 ± 21 (mean ± SD)
Co-morbidities	
Asthma	11 patients
COPD	5 patients
Ischemic heart disease	9 patients
Hypertension	12 patients
Cerebrovascular disease	3 patients
Esophageal reflux	7 patients
Rheumatoid arthritis	2 patients

*excluded current-smoker

COPD 2005; 21; 27-34

Symptom Changes during Follow-up

Table 3. Symptoms; initial assessment and follow-up review

	Initial review (n = 101 patients)	Follow-up (n = 101 patients)	*p*
Symptoms			
Productive cough	98%	93%	
Daily sputum	69%	72%	
Rhinosinusitis	72%	79%	
Hemoptysis	31%	21%	
Hospitalization	24%	32%	
Fatigue	69%	79%	
Daily sputum (mls)	32 ± 29 mls	47 ± 34 mls	$p < 0.05$
MRC dyspnoea score	1.9 ± 1.1	2.8 ± 1.3	$p < 0.05$
Signs			
Crackles	86%	63%	
Wheeze	6%	12%	
Clubbing	1%	1%	

COPD 2005; 21; 27-34

Lung Function Trajectory in Bronchiectasis

Table 4. Spirometry; initial assessment and follow-up review

Spirometry	Initial review (n = 101 patients)	Follow-up (n = 101 patients)
FEV_1		
Litres (mean and SD)	1.87 ± 0.68	1.49 ± 0.64
% predicted (mean and SD)	72.2 ± 25.0	61.2 ± 24.3
FVC		
Litres (mean and SD)	2.79 ± 0.92	2.38 ± 0.79
% predicted (mean and SD)	86.1 ± 21.8	76.4 ± 21.4
FEV_1/FVC		
	67.0	63.7
BD effect > 15% (patients)	24	22

*FEV1 decline of 48ml/yr

COPD 2005; 21; 27-34

International Journal of COPD

Dovepress

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ORIGINAL RESEARCH

Effects of long-term bronchodilators in bronchiectasis patients with airflow limitation based on bronchodilator response at baseline

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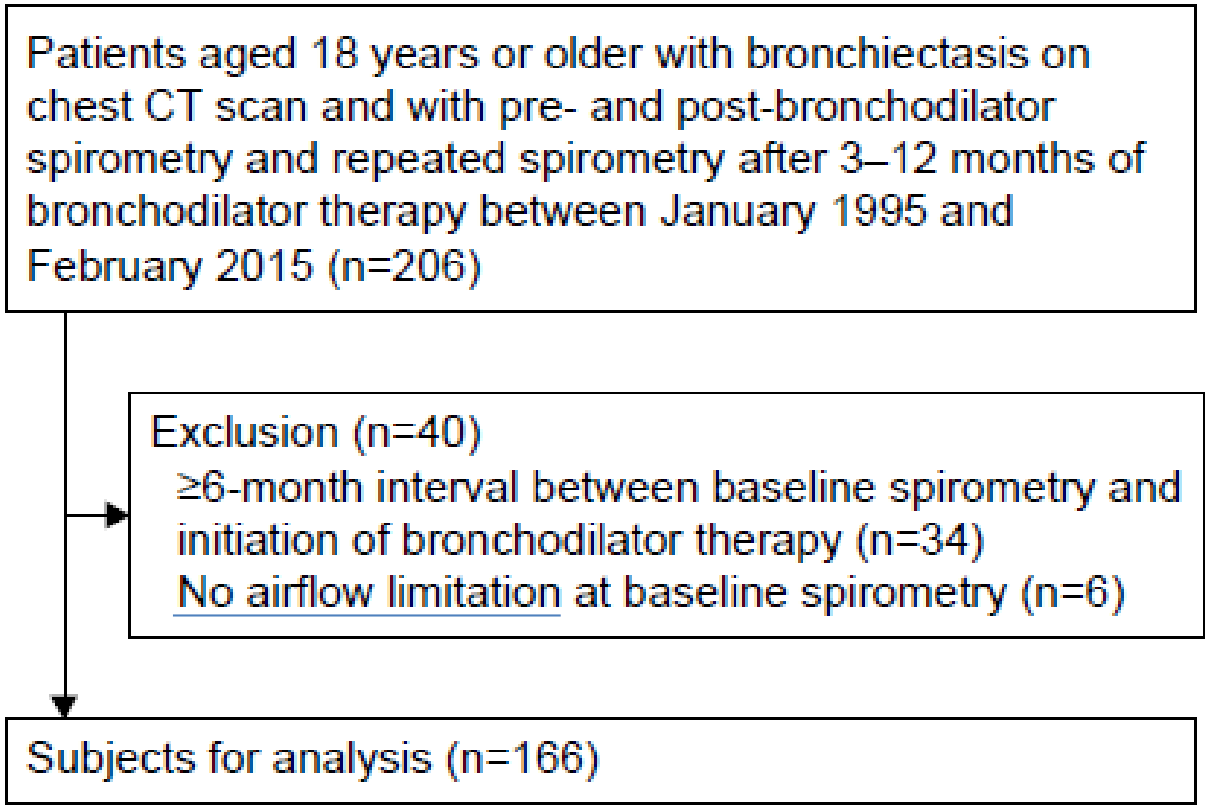


Intern J of COPD 2016; 11; 2757-2764

Responder vs. Poor Responder

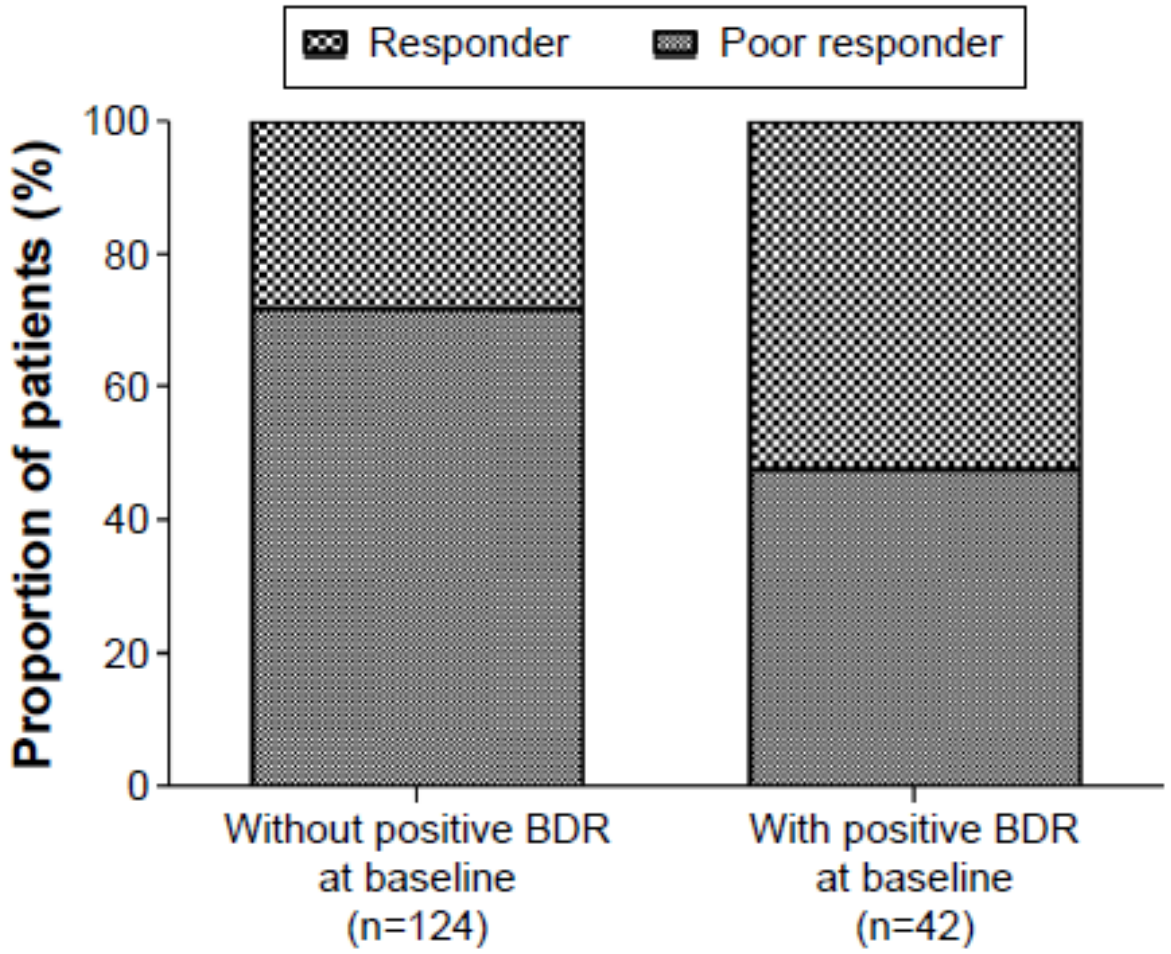
Characteristics	Total (n=166)	Poor responders (n=109)	Responders (n=57)	*P*-value
Age, years	64 (56–70)	62 (54–70)	64 (59–70)	0.202
Sex, male	113 (68.1)	68 (62.4)	45 (78.9)	0.03
Current smoker or ex-smoker	93/162 (57.4)	54/106 (50.9)	39/56 (69.6)	0.022
Body mass index, kg/m^2	22.8 (20.7–25.4)	22.7 (20.5–25.2)	23.6 (21.3–25.7)	0.24
Body mass index ≥25 kg/m^2	51 (30.7)	30 (27.5)	21 (36.8)	0.217
Previous pulmonary tuberculosis	74 (44.6)	51 (46.8)	23 (40.4)	0.428
Coexisting pulmonary comorbidities				
Bronchial asthma	28 (16.9)	16 (14.7)	12 (21.1)	0.298
NTM lung disease	13 (7.8)	11 (10.1)	2 (3.5)	0.222
Chronic aspergillosis	5 (3)	2 (1.8)	3 (5.3)	0.34
Extrapulmonary comorbidities				
Hypertension	51 (30.7)	33 (30.3)	18 (31.6)	0.863
Malignant disease	23 (13.9)	13 (11.9)	10 (17.5)	0.32
Diabetes mellitus	21 (12.7)	14 (12.8)	7 (12.3)	0.917
Chronic kidney disease	7 (4.2)	4 (3.7)	3 (5.3)	0.692
Cerebrovascular disease	7 (4.2)	3 (2.8)	4 (7)	0.234
Baseline pulmonary function test				
FVC, L	2.8 (2.1–3.3)	2.6 (2.1–3.4)	2.9 (2.3–3.2)	0.526
FVC, % predicted	70.5 (60.0–80.0)	73.0 (60.5–80.5)	69.0 (60.0–77.5)	0.276
FEV_1, L	1.4 (1.1–1.8)	1.5 (1.1–1.9)	1.4 (1.1–1.7)	0.288
FEV_1, % predicted	50.0 (39.0–61.0)	51.0 (39.5–63.0)	46.0 (38.0–55.5)	0.065
FEV_1/FVC, %	53.7 (45.6–60.9)	55 (47–62.4)	50.5 (43.5–58)	0.011
Positive bronchodilator response	42 (25.3)	20 (18.3)	22 (38.6)	0.004

*Responders (34.3%): FEV1 values improved at least 12% and 200 mL from baseline FEV1 following 3–12 months of bronchodilator therapy

Intern J of COPD 2016; 11; 2757-2764

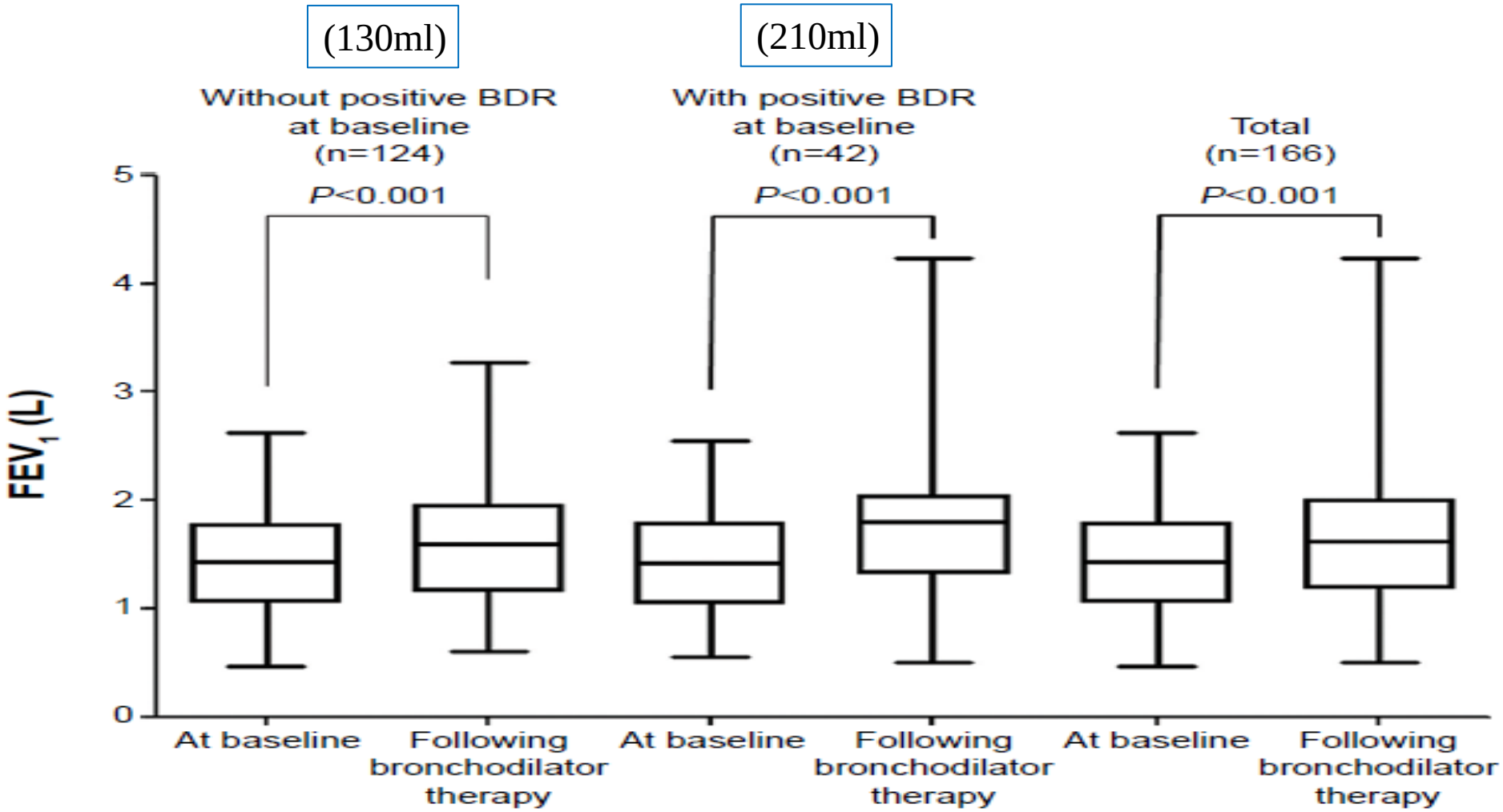
BDR at baseline and Response to LABD

Responder: 28.2% vs 52.4%, *P*=0.004



Intern J of COPD 2016; 11; 2757-2764

Change of FEV1



Intern J of COPD 2016; 11; 2757-2764

Study Proposal to Pharmaceutical Company

ISS

Investigator Supported Study

Personal opinion

Difficulties to get Research Fund

Our **Areas of Interest** within Respiratory are outlined below. For greater detail on exact study areas, please visit our portal.

Severe asthma, Mepolizumab

- Severe asthma / COPD
- Nasal polyps / EGPA
- Disease mechanism

COPD

- Advancing disease understanding
- Patient centric outcome measures
- Advancing precision medicine

Asthma

Inhaled delivery systems

- Inhaled Delivery System
- Connected Inhaler

	Proposals Received from IC LOCs	Proposal Submitted for Global Review	Proposal with Scientific Approval	Fully Funded by Global
Australia	18	11	7	5
Canada	10	8	5	4
Japan	5	4	4	3
Korea	5	3	1	1
New Zealand	1	0	0	0
Total	39	26	17	13

Oct 2019

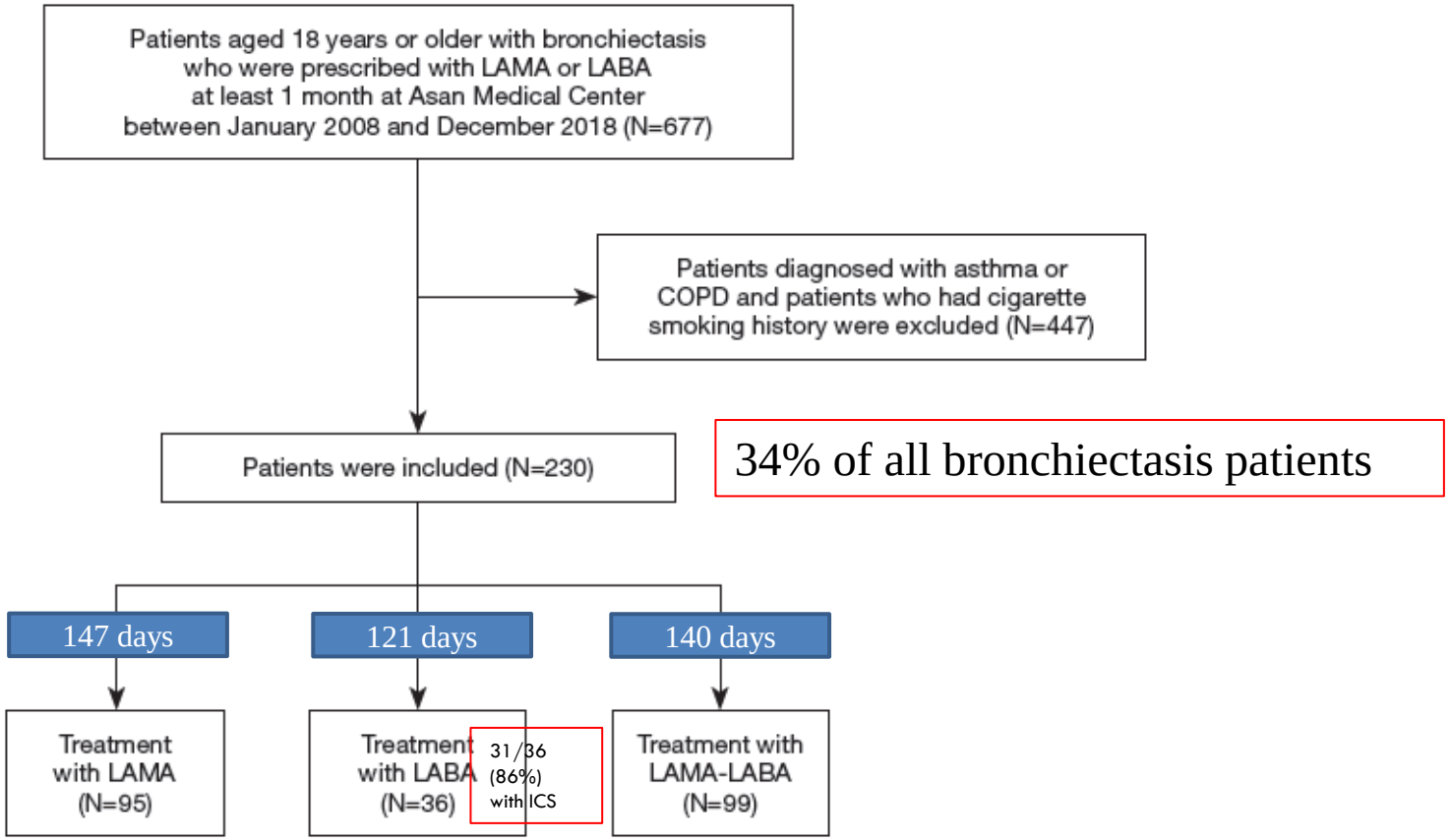
Personal opinion

Original Article

Effects of treatment with long-acting muscarinic antagonists (LAMA) and long-acting beta-agonists (LABA) on lung function improvement in patients with bronchiectasis: an observational study

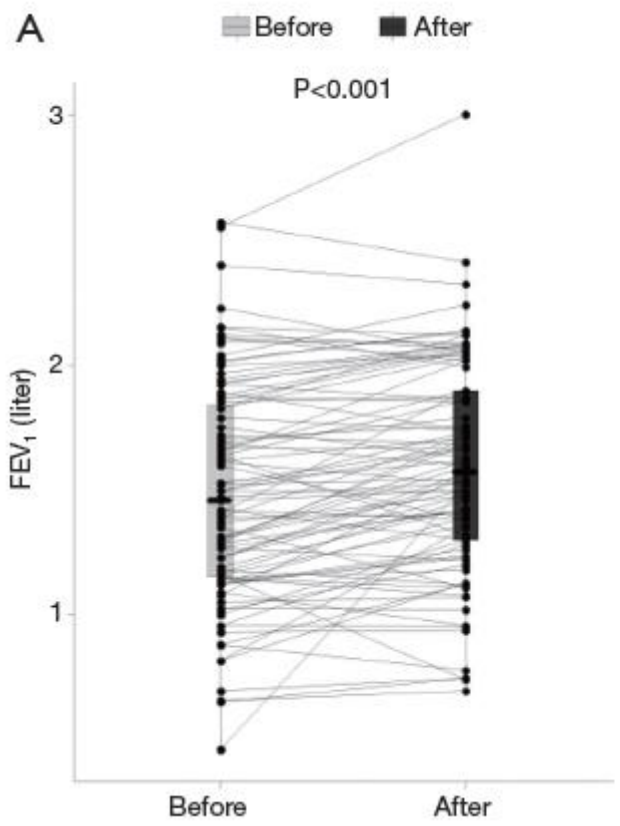
Su Yeon Lee, Jae Seung Lee, Sei Won Lee, Yeon-Mok Oh

Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

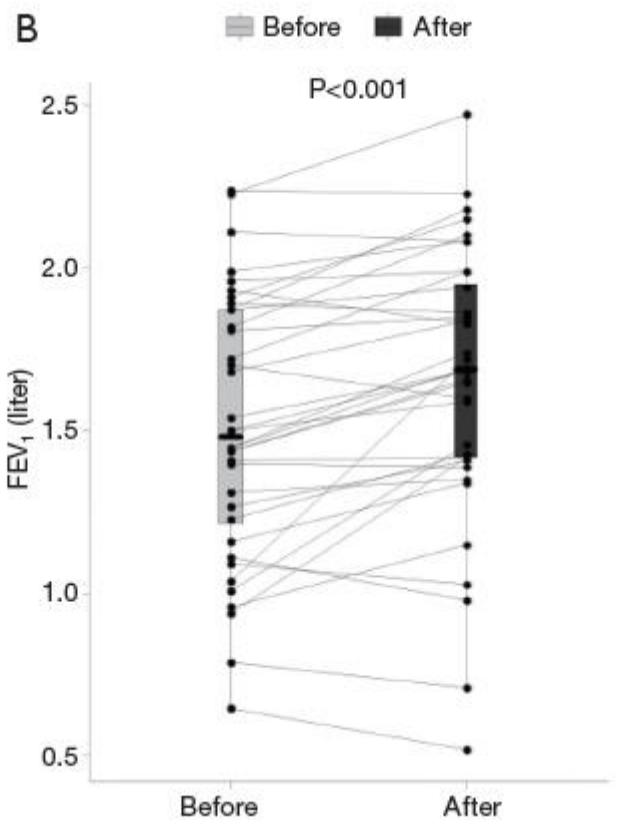


J Thorac Dis 2021; 13(1); 169-177

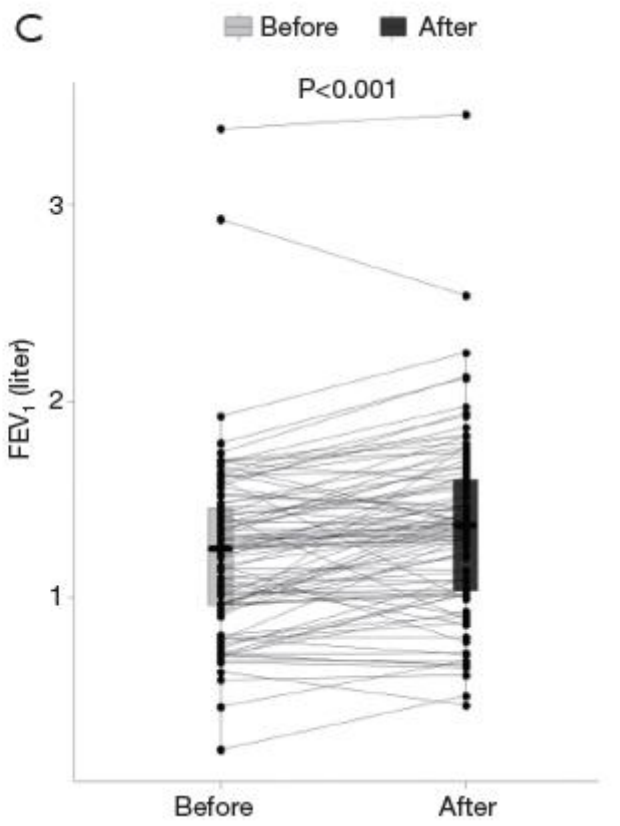
Changes of FEV1 after LABD Use



102ml in LAMA group



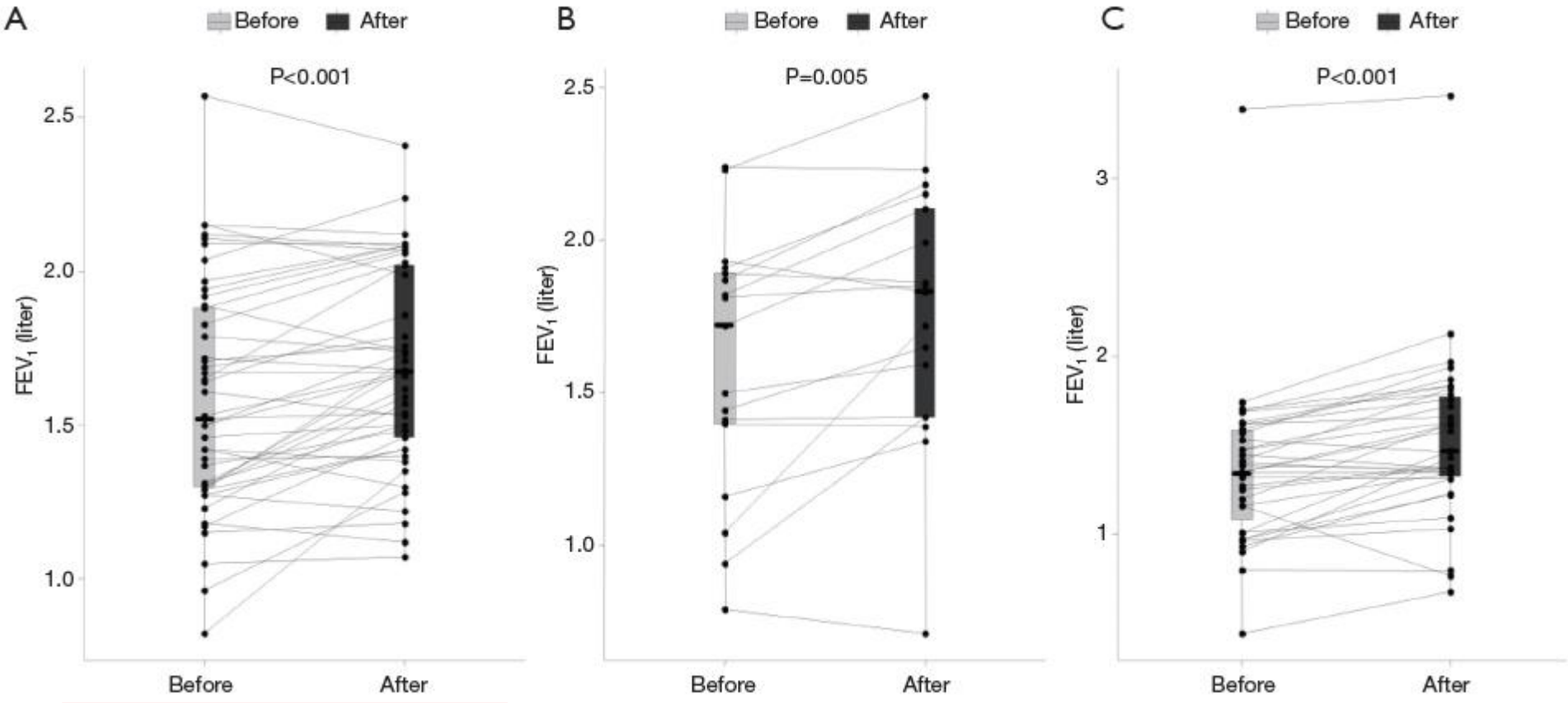
133ml in LABA group



122ml in LAMA/LABA group

Changes of FEV1, without concurrent medication

Figure 3 Changes in FEV_1 in patients without concurrent treatments after treatment with LAMA (N=45) (A), LABA (N=17) (B), or LAMA-LABA (N=35) (C). FEV_1, forced expiratory volume in 1 second; LAMA, long-acting muscarinic antagonist; LABA, long-acting beta-agonists.

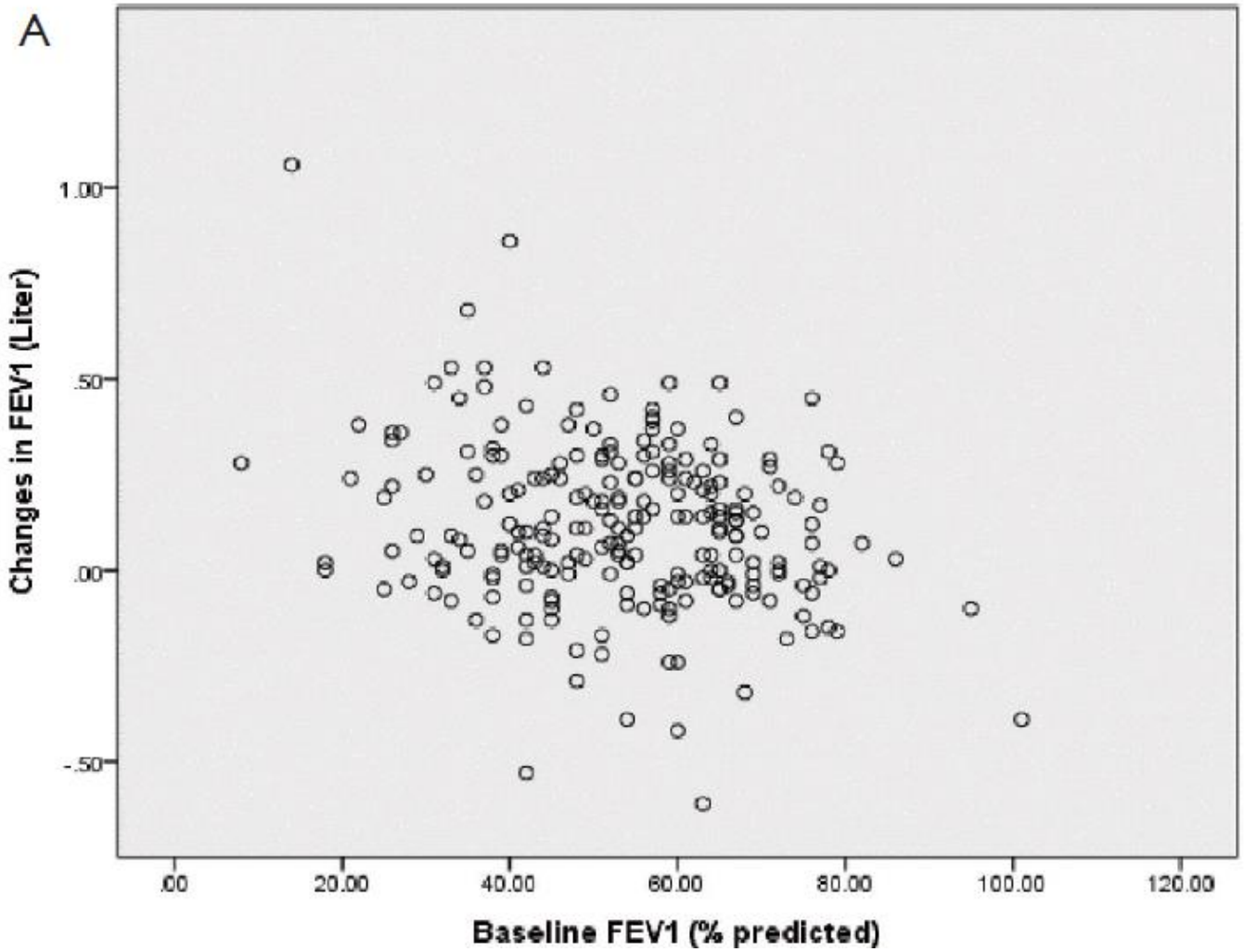


107ml in LAMA group

165ml in LABA group

165ml in LAMA/LABA group

Greater bronchodilation in case of poorer lung function

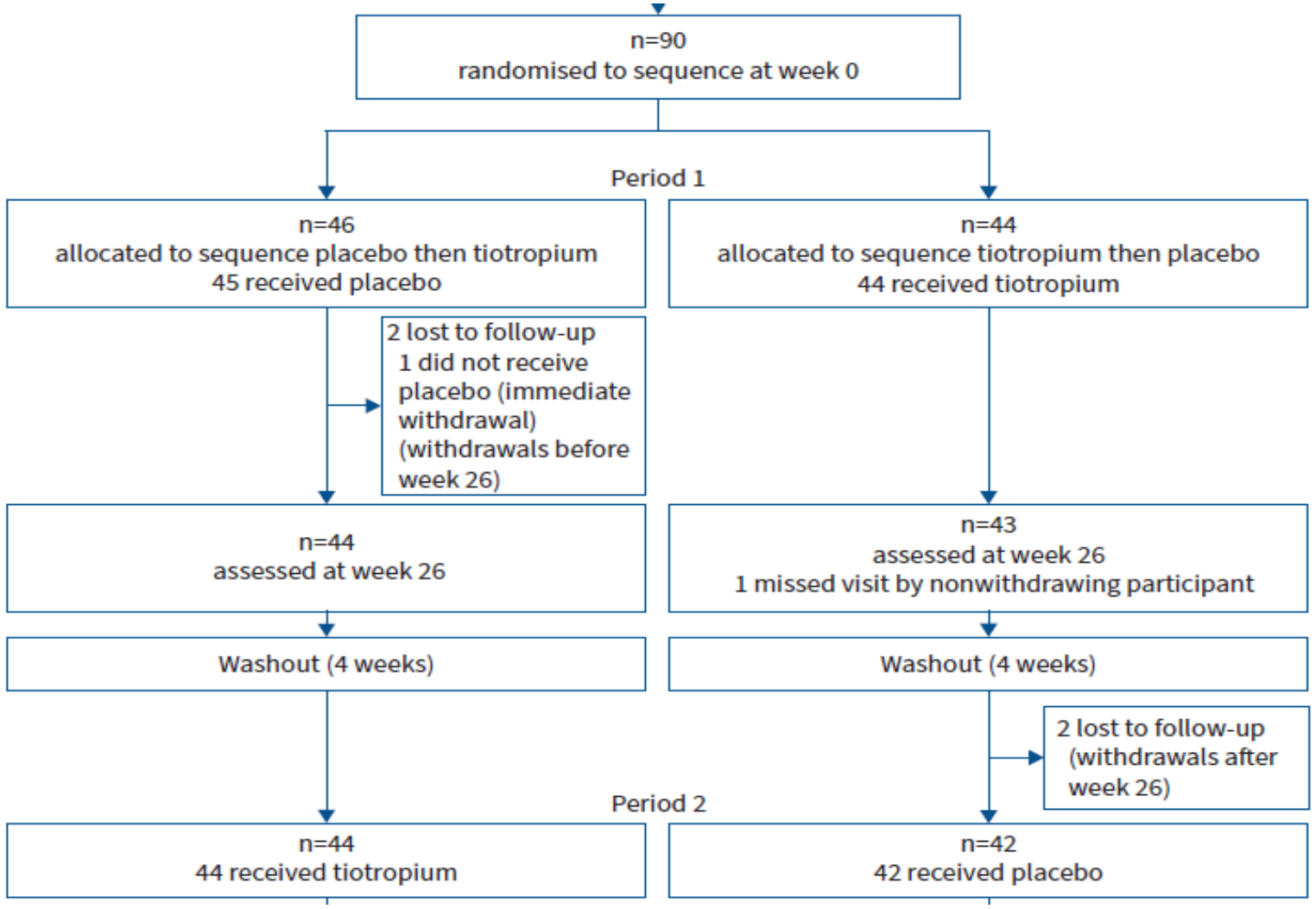


N = 230

R = -0.242, $p < 0.001$

J Thorac Dis 2021; 13(1); 169-177

Tiotropium treatment for bronchiectasis: a randomised, placebo-controlled, crossover trial



*3 Centers in New zealand

-BE pts. with airflow limitation
- >20 pack-years
- ≥1 exacerbation

-1st end-point: rate of event-based exacerbations during each 6-month period
-2nd outcomes: FEV1, time to first exacerbation, health-related quality of life (as measured by SGRQ, LCQ and CAT)

Eur Respir J 2022; 2102184

Baseline characteristics

	Sequence A: placebo–tiotropium (n=46)	Sequence B: tiotropium–placebo (n=44)
Male	22 (48)	12 (27)
Age (years)	59.3±13.0	62.0±11.3
Smoking status		
Current/ex-smoker	21 (46)	16 (37)
Smoking history (pack-years)#	6.0±5.7	6.0±5.3
Asthma	11 (24)	11 (25)
Medical conditions (n)	3.8±2.4	4.0±2.1
Body mass index ($kg \cdot m^{-2}$)	28.3±7.7	28.8±9.8
Ethnic origin		
European	29 (63)	25 (57)
Pasifika	6 (13)	7 (16)
Māori	8 (17)	10 (23)
Other	3 (7)	2 (5)
Exacerbations in past year (n)	2.4±1.4	3.2±1.6
Spirometry		
Pre-bronchodilator		
FEV_1 (L)	1.78±0.53	1.67±0.45
FEV_1 (% pred)	59.4±14.2	64.2±17.2
FVC (L)	3.02±0.83	2.82±0.67
FVC (% pred)	75.3±15.1	81.6±16.9
Post-bronchodilator		
FEV_1 (L)	1.88±0.55	1.76±0.50
FEV_1 (% pred)	63.1±14.4	68.3±18.6
FVC (L)	3.06±0.83	2.87±0.72
FVC (% pred)	77.5±14.9	84.2±16.5

Eur Respir J 2022; 2102184

Baseline characteristics

Respiratory drugs		
Any	33 (72)	29 (66)
Inhaled anticholinergic		
Short- or long-acting	0 (0)	0 (0)
Inhaled β_2-agonists		
Short-acting, alone	9 (17)	4 (7)
Long-acting, alone	0 (0)	0 (0)
ICS		
Alone	2 (4)	5 (11)
Mucolytic agent	5 (11)	1 (2)
Leukotriene receptor antagonist	0 (0)	0 (0)
Combination inhalers		
LABA/ICS	5 (11)	1 (2)
LABA combined with ICS in two separate inhalers	20 (43)	17 (39)
Aetiology		
Idiopathic	36 (78)	31 (70)
Inflammatory bowel disease	3 (7)	2 (5)
Pink disease (infantile mercury exposure)	0 (0)	1 (2)

No difference in exacerbation rate

Primary outcome

The annual rate of exacerbations was 2.17 per patient under tiotropium treatment and 2.27 per patient under placebo (rate ratio 0.96, 95% CI 0.72–1.27; p=0.77).

Eur Respir J 2022; 2102184

Lung function changes

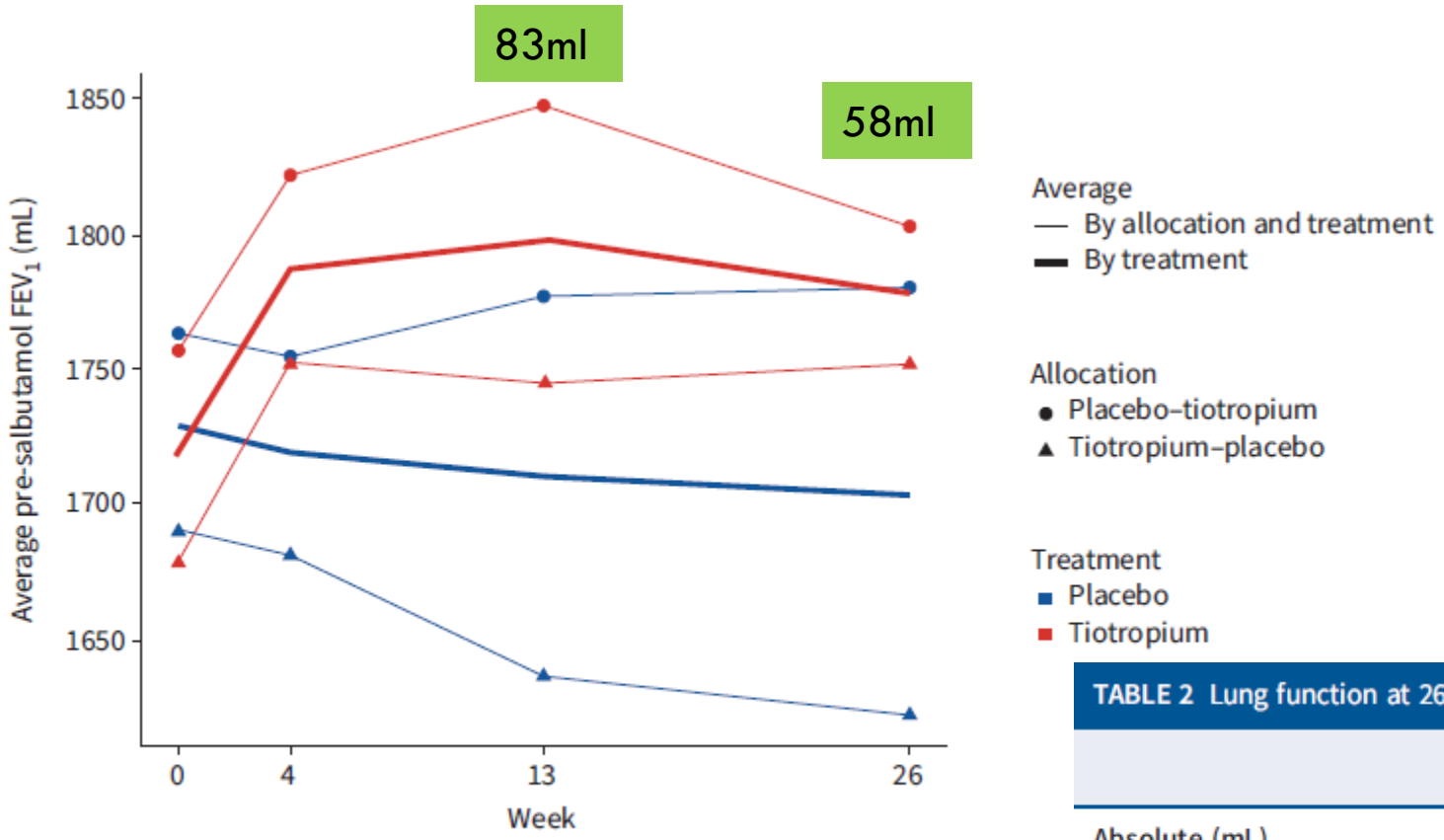


FIGURE 2 Pre-bronchodilator (salbutamol) forced expiratory volume in 1 s

TABLE 2 Lung function at 26 weeks

	Placebo[#]	Tiotropium[#]	Mean difference (95% CI)[¶]	p-value
Absolute (mL)				
Pre-BD FEV_1	1704±528	1778±526	58 (23–92)	0.002
Post-BD FEV_1	1798±555	1871±574	56 (17–92)	0.005
Pre-BD FVC	2880±805	2956±767	78 (25–131)	0.004
Post-BD FVC	2974±827	3011±785	34 (−22–90)	0.24

Eur Respir J 2022; 2102184

Other secondary outcomes

TABLE 3 Secondary outcome measures at 26 weeks

	Placebo	Tiotropium	Difference in change adjusted for period (95% CI)	p-value
Exacerbation duration (days)	19.6±14.6[#]	21.7±16.9[#]	2.4 (−1.5–6.2)	0.49
Time to first exacerbation (days)	104 (80–136)[¶]	74 (50–156)[¶]	1.00 (0.68–1.46)[+]	0.98
6MWT (m)	522±91	526±79	−0.3 (−8.0–7.3)	0.93
SGRQ domain score				
Symptoms	45.5±232.3	46.0±23.1	0.7 (−3.5–4.8)	0.31
Activity	34.7±22.8	33.5±20.9	−0.9 (−3.7–2.0)	0.54
Impacts	23.1±16.5	24.0±16.3	0.5 (−2.1–3.0)	0.72
Total	30.0±17.2	30.5±16.4	0.3 (−2.0–2.6)	0.81
LCQ domain score				
Physical	5.21±1.08	5.08±1.19	−0.12 (−0.34–0.10)	0.28
Psychological	5.34±1.47	5.29±1.50	−0.09 (−0.37–0.18)	0.50
Social	5.41±1.36	5.33±1.41	−0.12 (−0.37–0.13)	0.35
Total	16.0±3.8	15.7±3.9	−0.33 (−1.01,0.35)	0.34
CAT score	14.7±6.9	14.6±7.6	−0.17 (−1.47–1.14)	0.80

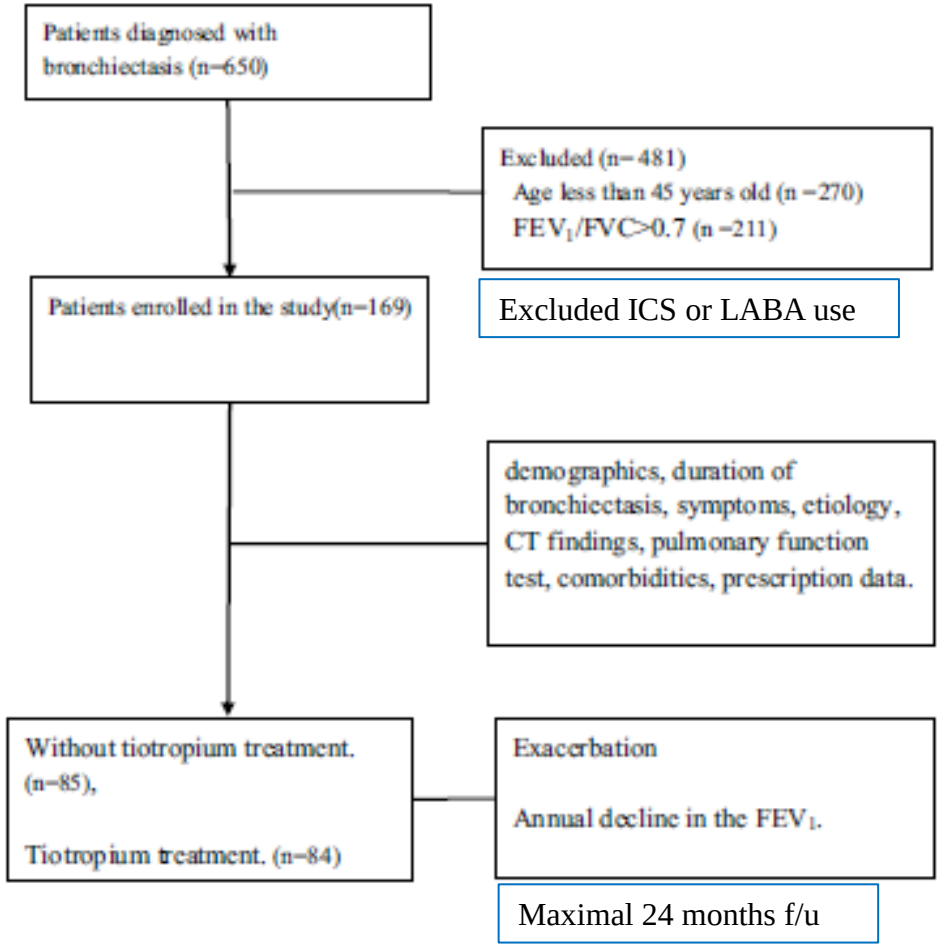
Eur Respir J 2022; 2102184

Lung (2023) 201:9–15
https://doi.org/10.1007/s00408-023-00597-8

BRONCHIECTASIS

Tiotropium in Patients with Bronchiectasis: A Prospective Cohort Study

Zu-Liang Shi[1] · Hong-Ying Zhang[2] · Hai-Bo Peng[1] · Zhong-Ming Zhu[2]



Characteristic	Tiotropium Group 84	Without Tiotropium Group 85	*P* Value
Age	64.3±7.5	65.4±8.3	0.37
Male sex—no. (%)	48 (56)	52 (61)	0.77
Body mass index	20.5±5.8	22.4±6.1	0.04
BMI<18.5	27 (32.14%)	20 (23.5%)	0.1
Duration of bronchiectasis (years)	9.3±5.7	10.4±6.5	0.26
Previous medication for respiratory disease	25 (29.8)	27 (31.8)	0.94
After bronchodilator use FEV_1 -liters	1.35±0.57	1.85±0.54	$p<0.001$
FEV_1% of predicted value	52.7±14.2	64.6±12.9	$p<0.001$
After bronchodilator use FVC—liters	2.33±1.24	2.56±1.13	0.21
FVC predicted	65.3±14.8	68.1±13.9	0.21
FEV_1/FVC	0.57±0.23	0.61±0.25	0.28
positive bronchodilator response percentage	17 (20.2)	14 (16.4)	0.69
mMRC dyspnea scale score>2	40 (47.1)	28 (32.9)	$p<0.001$
lung lobe>2	49 (58.3)	35 (42.2)	$p<0.001$
FEV_1% predicted<50	44 (52.4%)	30 (35.3%)	$p<0.001$

Annual decline of lung function

Annual decline, Tio vs control group

Characteristic	Tiotropium Group 84	Without Tiotropium Group 85	*P* Value
FEV_1 After bronchodilator use	27.08 ± 7.54	42.9 ± 5.98	$p < 0.001$
FVC After bronchodilator use	49.7 ± 9.87	52.9 ± 14.79	0.101

BDR(+) vs BDR(-) in Tio group

Variable	Positive broncho-dilator response 17(20.2%)	Without positive bron-chodilator response 67(79.8%)	*P* Value
FEV_1 (ml) After broncho-dilator use	24.56 ± 6.77	29.85 ± 7.94	0.01
FVC (ml) After broncho-dilator use	46.67 ± 9.98	49.73 ± 8.49	0.20

Lung 2023; 201; 9-15

Moderate exacerbation

Variable	Crude RR (95% CI)	*P* Value	Adjusted RR (95% CI)	*P* Value
Tiotropium treatment	0.894 (0.755–0.992)	0.038	0.618 (0.493–0.774)	$p < 0.001$
Body mass index < 18.5	–	–	1.525 (1.256–1.851)	$p < 0.001$
mMRC dyspnea scale score > 2	–	–	1.005 (0.816–1.239)	0.961
Lung lobe > 2	–	–	1.391 (1.123–1.721)	0.002
FEV1% predicted < 50	–	–	1.219 (0.988–0.1.504)	0.064

*Modified Poisson regression analysis of Tio associated with exacerbation

*Of the 169 patients, 143 (84.6%) experienced at last one moderate exacerbations (65 in the tiotropium group and 78 in the no-tiotropium group) during the **12 months** follow- up period.

Lung 2023; 201; 9-15

Severe exacerbation

Characteristic	Tiotropium Group 84	Without Tio-tropium Group 85	*P* Value
No. of patients with at last one severe exacer-bation	42 (50%)	59 (69.4%)	0.012
Time to first severe exacerbation (months)	18.14 ± 6.03	12.22 ± 6.98	$p < 0.001$

*Of the 169 patients, 101 (59.8%) experienced (42 in the tiotropium group vs 59 in the no-tiotropium group) at last one severe exacerbation that required hospitalization during the **2-year** follow-up period.

Lung 2023; 201; 9-15

Lung (2023) 201:5–7
https://doi.org/10.1007/s00408-023-00600-2

EDITORIAL

Bronchodilators in bronchiectasis: we urgently need more trials

Miguel Ángel Martínez-García[1,2,3]

Bronchodilators in bronchiectasis: there is light but it is still too dim

Mario Cazzola[1], Miguel Ángel Martínez-García[2,3] and Maria Gabriella Matera[4]

[1]Unit of Respiratory Medicine, Dept of Experimental Medicine, University of Rome "Tor Vergata", Rome, Italy. [2]Respiratory Dept, Polytechnic and University La Fe Hospital, Valencia, Spain. [3]Centro de Investigación Biomédica en Red (CIBERES), Instituto de Salud Carlos III, Madrid, Spain. [4]Unit of Pharmacology, Dept of Experimental Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy.

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Necessary Study in the Future

- LABD effective group
  - -(Low FEV1)
  - -(BDR positive)
  - -New biomarkers, specific phenotype
- LAMA or LABA or Dual-BD
- Triple-BD (ICS effect)

- LABD effect in BE patients without airflow obstruction

BMJ Open

Dual bronchodilators in Bronchiectasis study (DIBS): protocol for a pragmatic, multicentre, placebo-controlled, three-arm, double-blinded, randomised controlled trial studying bronchodilators in preventing exacerbations of bronchiectasis

Miranda Morton ,[1] Nina Wilson ,[2] Tara Marie Homer,[3] Laura Simms,[1] Alison Steel,[1] Rebecca Maier,[1] James Wason ,[2] Laura Ternent,[3] Alaa Abouhajar,[1] Maria Allen,[4] Richard Joyce,[1] Victoria Hildreth,[1] Rachel Lakey,[1] Svetlana Cherlin,[2] Adam Walker,[4] Graham Devereux,[5] James D Chalmers,[6] Adam T Hill,[7] Charles Haworth,[8] John R Hurst ,[9] Anthony De Soyza[2,4]

Dual vs Triple vs Placebo (2:2:1 ratio)

Inhaler	Contents of each dose delivered	Name of equivalent commercially available product
Dual therapy (LAMA/LABA)	▶ 55 µg umeclidinium ▶ 22 µg vilanterol	Anoro Ellipta dry powder inhaler
Triple therapy (ICS/LAMA/LABA)	▶ 92 µg fluticasone furoate ▶ 55 µg umeclidinium ▶ 22 µg vilanterol	Trelegy Ellipta dry powder inhaler
Placebo	▶ Placebo	Matched placebo dry powder inhaler

History of two or more exacerbations in any 12 month period in the preceding 2 years requiring antibiotics and/or steroids.

Evidence of airflow limitation with an forced expiratory volume in 1 s/forced vital capacity (FEV_1/FVC) ratio less than 0.7 and/or daily mucus expectoration.

*The primary outcome is the number of protocol defined exacerbations requiring treatment with antibiotics during the 12 month treatment period.

*Randomisation is stratified by two variables: BSI score (BSI score of 0–8 or 9+) and by baseline ICS use

KMBARC registry

Allergy Asthma Immunol Res. 2023 Jan;15(1):83-93
https://doi.org/10.4168/aair.2023.15.1.83
pISSN 2092-7355·eISSN 2092-7363

Allergy, Asthma & Immunology Research AAIR

Original Article

Impacts of Asthma in Patients With Bronchiectasis: Findings From the KMBARC Registry

Seong Mi Moon,[1†] Hayoung Choi,[2,3†] Hyung Koo Kang,[4] Sei Won Lee,[5] Yun Su Sim,[2] Hye Yun Park,[6] Yong-Soo Kwon,[7] Sang-Heon Kim,[8] Yeon-Mok Oh,[5] Hyun Lee [8*]

울산대병원	COPD가 동반된 기관지확장증 환자에서 기관지확장증 subtype (cylindrical, varicose, cystic)에 따른 흡입제 효과 비교 분석: ICS containing bronchodilator vs. Bronchodilator
춘천성심병원	COPD가 동반한 기관지확장증 환자의 임상적 특성

Summary

- Bronchiectasis is an important airway Dz. and commonly overlaps with COPD or asthma
- Use of LABD is recommended according to ROSE criteria (***R***adiology, ***O***bstruction, ***S***ymptom, ***E***xposure)
- LABD is commonly used without coexisting COPD or asthma
- Proximal (vs. distal) bronchiole-ectasis (vs. bronchi-ectasis)
- Pulmonary function in bronchiectasis

  (Air-trapping, diffusion impairment, and rapid FEV1 decline)
- Evidences are increasing but, still lacking

감사합니다

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