COPD
-respiratory review of 2023

전남의대
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GOLD 2023 KEY CHANGES

Table 1.1 Proposed Taxonomy (Etiotypes) for COPD

Table 2.8 Use of CT in Stable COPD

Figure 3.2 Overview of Current and Proposed Surgical and Bronchoscopic Interventions for People with COPD

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- GOLD 2023 report

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- Tx
  - Blood eosinophil counts
  - HFNC for hypercapnic stable COPD
  - E_health, smartphone app for physical activity
- Px
  - Chest CT-assessed comorbidities

Chronic obstructive pulmonary disease in never-smokers: risk factors, pathogenesis, and implications for prevention and treatment

- *-Yang IA, Jenkins CR, Salvi SS.. Lancet Respir Med 2022; 10(5): 497-511.*

Large-scale studies of COPD prevalence in never-smokers (2009-)

	Setting (study name)	Never-smokers (n)	Definition of COPD	Prevalence of COPD in never-smokers	Prevalence of never-smokers among people with COPD
Zhou et al (2009)[7]	China (CESCOPD)	12 471	Post-bronchodilator FEV_1/FVC <0·7	5%	39%
Lamprecht et al (2011)[8]	14 countries (BOLD)	4291	Post-bronchodilator FEV_1/FVC <0·7	12%	28%
Hagsted et al (2012)[9]	Sweden (OLIN)	770	Post-bronchodilator FEV_1/FVC <0·7	7%	20%
Perez-Padilla et al (2012)[10]	Five Latin American cities (PLATINO)	2278	Post-bronchodilator FEV_1/FVC <0·7	4%	26%
Thomsen et al (2013)[11]	Denmark (Copenhagen General Population Study)	26 005	FEV_1/FVC <LLN	6%	22%
Smith et al (2014)[12]	China Kadoorie Biobank	317 000	Pre-bronchodilator FEV_1/FVC <0·7 and <LLN	4% (females); 5% (males)	Not measured
Tan et al (2015)[13]	Canada (CanCOLD)	2295	Pre-bronchodilator FEV_1/FVC <0·7 and <LLN	6%	29%
Lee et al (2016)[14]	Korea (KNHANES IV and V)	8984	Post-bronchodilator FEV_1/FVC <0·7	7%	31%
Terzikhan et al (2016)[15]	The Netherlands (Rotterdam Study)	4997	Post-bronchodilator FEV_1/FVC <0·7	6%	27% (females); 7% (males)
Wang et al (2018)[16]	China (China Pulmonary Health study)	36 429	Post-bronchodilator FEV_1/FVC <0·7	6%	51%

Clinical characteristics of COPD in never-smokers vs ever-smokers

	COPD in ever-smokers	COPD in never-smokers
Typical age of onset	>40 years	>30 years
Sex	More males than females affected	Males and females affected equally, or more females than males affected (especially in LMICs)
Symptoms	More cough and dyspnoea (relatively less sputum production)	More cough (relatively less dyspnoea and sputum production)
Respiratory exacerbations	Frequent (and potentially severe)	Frequent (and potentially severe)
Comorbidities	Prevalent	Generally less prevalent
Risk of lung cancer	High	High
Lung physiology	More severe airflow obstruction; greater increase in RV/TLC (hyperinflation); increase in airway resistance; less small airways obstruction; reduced DLCO	Milder airflow obstruction; increase in RV/TLC (hyperinflation); greater increase in airway resistance; more small airways obstruction; normal DLCO
FEV_1 decline	Can be rapid	Usually normal
Lung CT imaging	Less air trapping due to small airways obstruction; more emphysema	More air trapping due to small airways obstruction; less emphysema
Sputum inflammatory cells	Greater increase in neutrophils	Increase in neutrophils; relatively greater increase in eosinophils
Pharmacological responses	Long-acting bronchodilators favoured over inhaled corticosteroids in terms of safety and effectiveness, especially among those with predominant emphysema	Not known

mechanisms implicated in COPD in never-smokers

	Biomass smoke[37-39]	Asthma[40-42]	Occupational exposures[43]	Tuberculosis[44,45]	HIV[46-48]	Environmental tobacco smoke[49]	Impaired lung growth[50-52]
Pathways or pathology	Airway remodelling; oxidative stress; inflammation	Airway remodelling; bronchoconstriction; epithelial-to-mesenchymal transition	Inflammation	Tracheobronchial stenosis; small airway obstruction; bronchiolitis obliterans; matrix degradation	Altered immunity; respiratory infection; apoptosis; lung ageing	Inflammation; oxidative stress; epigenetics	Pathways and pathological features associated with various risk factors: maternal smoking; childhood respiratory infections and asthma; suboptimal nutrition; genetic factors
Cells, tissues, or structures involved	Bronchial epithelium; neutrophils; lymphocytes	Bronchial epithelium; smooth muscle; fibroblasts; goblet cells	Bronchial epithelium; monocytes; macrophages	Monocytes	Bronchial epithelium; $CD8^+$ lymphocytes; $CD4^+$ lymphocyte count	Bronchial epithelium; neutrophils; macrophages	Small airways and alveoli
Mediators	Cytokines; chemokines; MMP9, MMP12	Cytokines; TGF-β	Cytokines; adhesion molecules; pattern recognition receptors	Integrin αVβ3; MMP1, MMP10	MMP12; soluble CD14; reduced E-cadherin expression	Cytokines; p38 MAPK	Molecular and cellular responses to various in-utero and childhood exposures

A non-exhaustive list of potential mechanisms of action for risk factors for COPD in never-smokers identified in translational studies from the past 10 years. COPD=chronic obstructive pulmonary disease. MAPK=mitogen-activated protein kinase. MMP=matrix metalloproteinase. TGF-β=transforming growth factor-β.

Key messages

- About **half of all COPD cases** worldwide are due to **non-tobacco-related risk factors**.

- These factors include **air pollution, occupational exposures, poorly controlled asthma, environmental tobacco smoke, infectious diseases, and low socioeconomic status. Impaired lung growth** during childhood
- mechanisms for the **pathogenesis : inflammation, oxidative stress, airway remodelling, genetics etc.**

- relatively **mild chronic respiratory symptoms, little or no emphysema;** however, **exacerbations can still be frequent.**

- → In the **absence of research into optimal therapy for never smokers-COPD**

Accuracy of portable spirometers in the diagnosis of chronic obstructive pulmonary disease A meta-analysis.

- – *Zhou J, Li X, Wang X, Yu N, Wang W. NPJ Prim Care Respir Med 2022; 32(1): 15.*

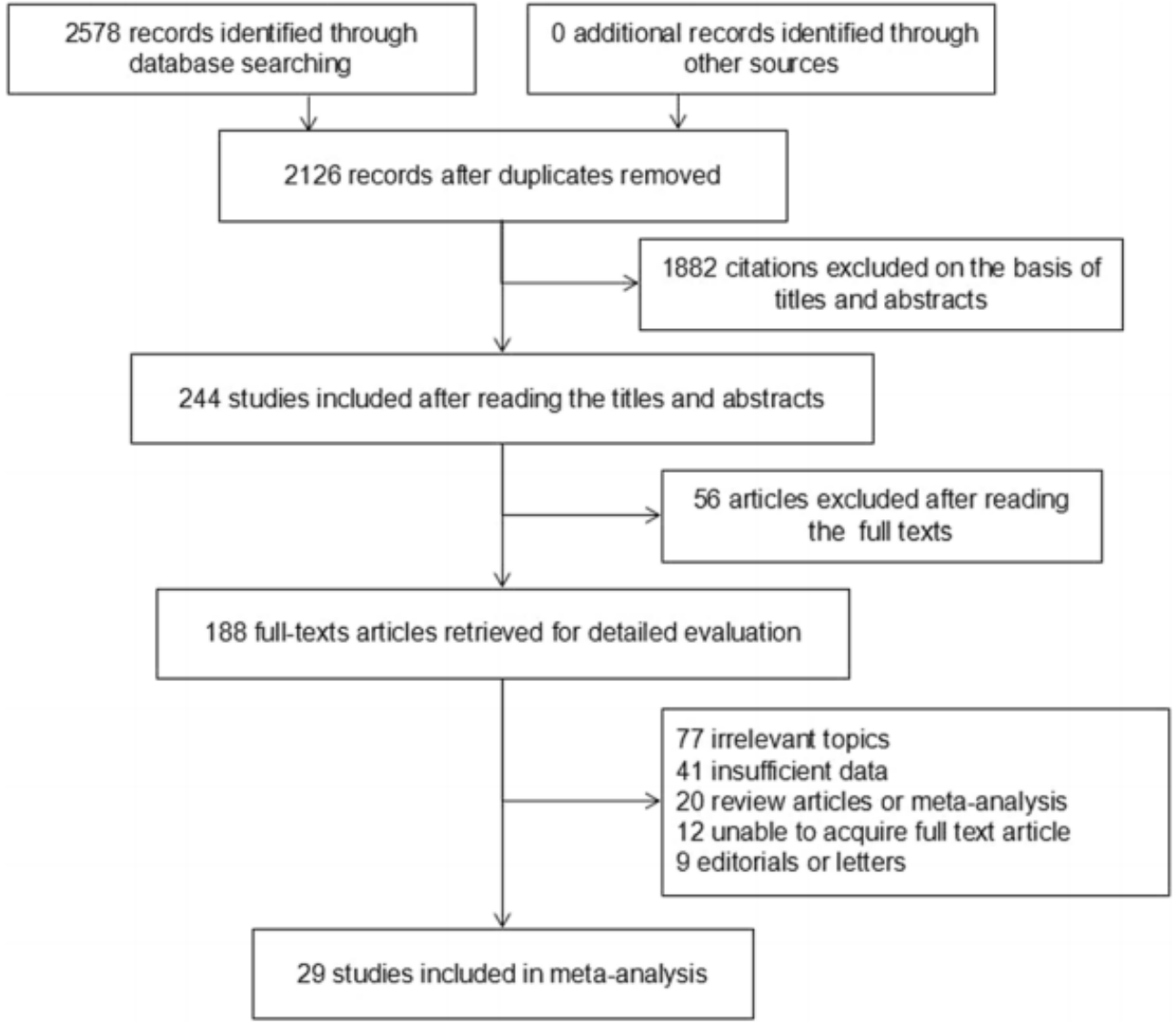


Fig. 1 Studies selection for meta-analysis. COPD chronic obstructive pulmonary disease.

Table 1. Characteristics of studies included in the meta-analysis.

Author and year	Country	Setting	Study designs	Portable spirometer	Test threshold of portable spirometers	Definition of airflow obstruction	Portable spirometers operator	Inclusion and exclusion criteria	Sample size (male)	Age (years, mean ±SD)
Chen G 2018[10]	China	1 tertiary hospital	randomized	IQ-spiro	Cut-off value unclear-FEV_1/FEV_6<0.74	post-FEV_1/FVC<0.70	Professional technician	Subjects who visited a tertiary hospital	159 (-)	55±14.7
Chen S 2021[37]	China	8 primary cares	cross-sectional study	COPD-6	Cut-off value unclear-FEV_1/FVC<0.77	post-FEV_1/FVC<0.70	Trained physician	Aged ≧ 40 years	1487 (-)	-
Dickens AP 2020[38]	UK	71 general practices	case-control	COPD-6	Cut-off value Pre-FEV_1/FEV_6<0.78	post-FEV_1/FVC<LLN	Trained research assistants	aged≧40, who either had previously clinically diagnosed COPD or had reported chronic respiratory symptoms.	544 (349)	69.6±9.1
Figueira Goncalves JM 2017[39]	Spain	1 tertiary hospital	cross-sectional observational study	COPD-6	Cut-off value Pre-FEV_1/FEV_6<0.75	pre-FEV_1/FVC<0.70	Professional technician	patients referred to laboratory for respiratory functional tests	233 (133)	59±15
Frith P 2011[40]	Australia	4 primary care practices	prospective, multicenter	PiKo-6	Cut-off value preFEV_1/FEV_6<0.75	post-FEV_1/FVC<0.70	Trained nurse or general practitioner (GP)	current or former smokers, aged > 50 years, no previous diagnosis of obstructive lung disease, and no treatment for obstructive lung disease in the past year.	204 (69)	61±8
Frith P 2011*[40]	Australia	4 primary care practices	prospective, multicenter	PiKo-6	Cut-off value Pre-FEV_1/FEV_6<0.75	post-FEV_1/FVC<0.70	Trained nurse or general practitioner (GP)	current and former smokers aged >50 years, a previous diagnosis of or treatment for asthma, and no previous diagnosis of COPD.	93 (54)	62±8.8
Hidalgo Sierra V 2018[41]	Spain	2 primary care centers*	-	PiKo-6	Cut-off value unclear-FEV_1/FEV_6≦0.70	post-FEV_1/FVC<0.70	Professional technician*	aged ≧40 years, a pack-year index (PYI)≧10, and typical symptoms, such as cough, expectoration and dyspnea, and with no previous diagnosis of COPD	155 (111)	63±14
Hwang YI 2021[42]	Korea	5 tertiary hospitals	-	COPD-6	Cut-off value pre-FEV_1/FEV_6<0.73	post-FEV_1/FVC<0.70	Professional technician	Aged ≧ 40 years; respiratory symptoms and PYI≧10 pack-years. Subjects who had a history of disease such as tuberculous sequalae, bronchiectasis, asthma, and lung cancer that might influence pulmonary function tests were excluded.	290 (-)	63.1 ± 11.0
Kim JK 2016[43]	Korea	9 primary clinics	prospective cohort study	COPD-6	Cut-off value preFEV_1/FEV_6≦0.77	post-FEV_1/FVC<0.70	primary care physicians	Subjects who visited a primary clinic complaining of respiratory symptoms and aged ≧40 years, PYI≧10 irrespective of their current smoking state and had no previous diagnosis of COPD. Patients with a history of disease that might have influenced spirometry results, such as tuberculosis-destroyed lungs, bronchiectasis, asthma, or lung cancer were excluded.	190 (-)	60.3±10.6
Kobayashi S 2017[44]	Japan	16 primary care clinics and 4 hospitals	prospective multi-center, observational study	Hi-Checker	Fixed value unclear-FEV_1/FEV_6≦0.75	post-FEV_1/FVC<0.70	primary care physicians	Patients > 40 years of age who received outpatient care for chronic disease at primary care clinics Patients with known chronic respiratory diseases, including asthma and COPD, and patients suffering from acute respiratory symptoms were excluded.	110 (91)	68.5±0.8

Table 1 continued

Author and year	Country	Setting	Study designs	Portable spirometer	Test threshold of portable spirometers	Definition of airflow obstruction	Portable spirometers operator	Inclusion and exclusion criteria	Sample size (male)	Age (years, mean ±SD)
Labor M 2016[9]	Croatia	26 general practitioners' office	prospective cohort study	COPD-6	Cut-off value unclear-FEV_1/FEV_6≦0.78	post-FEV_1/FVC<0.70	Trained GPs	written consent. aged 40–65 years with a smoking history of PYI≧2; with no previous diagnosis of COPD.	227 (112)	52.5±6.8
Li XF 2020[45]	China	1 district hospitals and ten primary care centers.	-	SP10BT	Cut-off value post-FEV_1/FVC<0.7 and FVC>80% pred	post-FEV_1/FVC<0.70 and FVC<80%pred	2 trained primary care physicians	aged > 40 years, typical symptoms such as chronic cough expectoration, or asthma, and risk factor exposure history	252 (182)	65.7±10.1
Lin CH 2021[46]	Taiwan, China	26 outpatient clinics	prospective multi-center,	Spirobank Smart	Cut-off value pre-FEV_1/FVC<0.74	post-FEV_1/FVC<0.70	trained nurses and physicians	Aged ≧ 40 years, PYI≧10 pack-years., with chronic respiratory disease and no previous diagnosis of COPD.	370 (349)	60.9±9.7
Llordes M 2017[47]	Spain	8 primary care centers	-	COPD-6	Cut-off value unclear-FEV_1/FEV_6≦0.78	post-FEV_1/FVC<0.70	Trained primary care physician, a nurse or a technician	Aged ≧ 40 years with a smoking history of PYI≧1; with no previous diagnosis of COPD and attended the primary care centers for any reason	407 (265)	57.4±8.9
Mahboub B 2014[22]	United Arab Emirates	5 primary cares, 2 large shopping malls and 1 industrial city	cross sectional study	PEF	Fixed value Pre-PEF<2.2L ($s*m^2$)	pre-FEV_1/FVC<0.70	Trained primary care physicians or nurses	Aged ≧ 40 years	525 (358)	49.6±4.1
Ng, S. C. 2017[48]	Malaysia	Medical Outpatient Department and health care clinics	cross-sectional study	COPD-6	Cut-off value post-FEV_1/FEV_6<0.75	post-FEV_1/FVC<0.70	Trained stuff	Aged ≧50 years; history of dyspnoea; history of chronic cough or chronic sputum production; history of exposure to risk factors; and any smoker even in the absence of above symptoms.	117(101)	67.38 ±11.58
Nishimura K 2011[49]	Japan	1 tertiary hospital	-	Hi-Checker	Cut-off value unclear-FEV_1/FEV_6<0.746	post-FEV_1/FVC<0.70	Professional technician	industrial workers who underwent annual health checks	312 (312)	55±9.4
Represas CR 2010[50]	Spain	1 tertiary hospital	prospective, descriptive transversal study	COPD-6	Cut-off value unclear-FEV_1/FEV_6<0.77	unclear-FEV_1/FVC<0.70	Professional technician	those who attended pulmonary function laboratory for functional respiratory tests	162 (95)	56±16
Represas-Represas C 2016[51]	Spain	8 primary care centers, 15 community pharmacies and 4 emergency services	prospective, multi-cohort study	COPD-6	Cut-off value preFEV_1/FEV_6<0.80	post-FEV_1/FVC<0.70	Trained primary care physicians or nurses	Aged ≧40 years, with a smoking history of PYI≧10, and symptoms suggestive of COPD. Individuals who had already been diagnosed with a respiratory disease were excluded.	362 (224)	55.4±9.9
Ronaldson SJ 2018[23]	UK	general practices	prospective case-finding stud	PEF	Fixed value Pre-PEF<80% pred	post-FEV_1/FVC<0.70 and FEV_1%<80%pred or FEV_1%>80% pred with at least 1 symptom	Trained nurses in primary care	aged≧35; current smokers, including those who had comorbidities, such as COPD or asthma	216 (109)	53.4±11.0
Ronaldson SJ 2018*[23]	UK	general practice	prospective case-finding stud	MS01 Micro spirometer	Fixed value FEV_1/FVC<0.7, FEV_1<80% pred, or FVC<80% pred	post-FEV_1/FVC<0.70 and FEV_1%<80%pred or FEV_1%>80% pred with at least 1 symptom	Trained nurses in primary care	aged≧35; current smokers, including those who had comorbidities, such as COPD or asthma	216 (109)	53.4±11.0

sensitivity and specificity of each screening test.

COPD-6

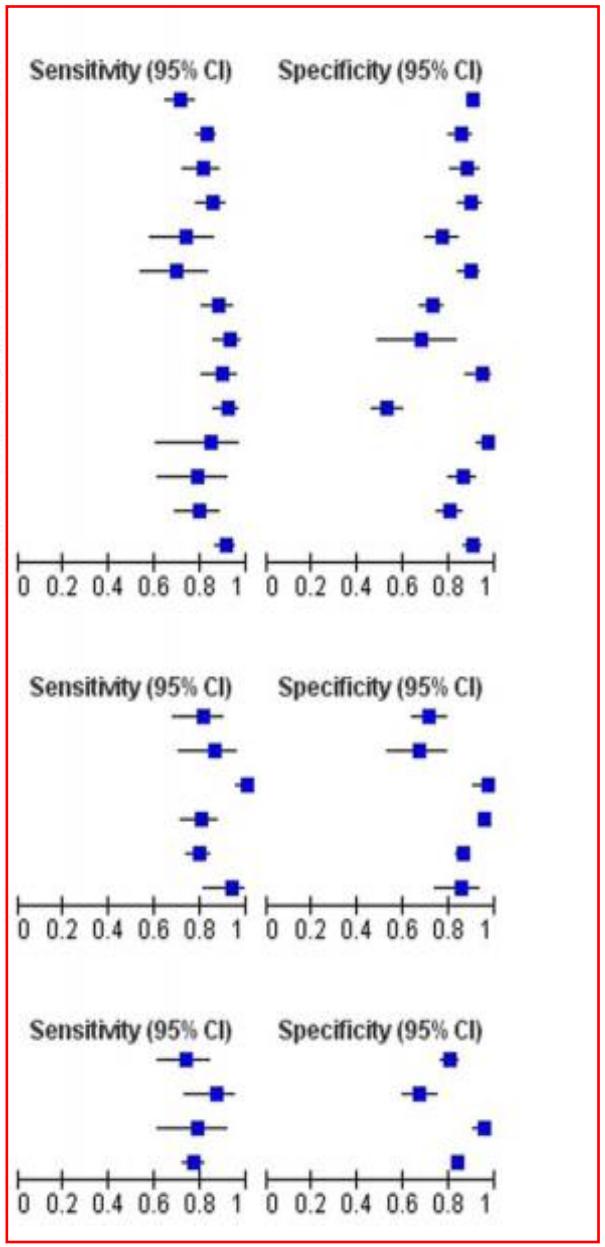
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chen S 2021	163	128	66	1130	0.71 [0.65, 0.77]	0.90 [0.88, 0.91]
Dickens AP 2020	279	31	58	176	0.83 [0.78, 0.87]	0.85 [0.79, 0.90]
Figueira Goncalves JM 2017	81	15	19	108	0.81 [0.72, 0.88]	0.88 [0.81, 0.93]
Hwang YI 2021	118	16	21	135	0.85 [0.78, 0.90]	0.89 [0.83, 0.94]
Kim JK 2016	33	33	12	112	0.73 [0.58, 0.85]	0.77 [0.70, 0.84]
Labor M 2016	30	20	13	164	0.70 [0.54, 0.83]	0.89 [0.84, 0.93]
Llordes M 2016	94	83	13	217	0.88 [0.80, 0.93]	0.72 [0.67, 0.77]
Ng, S. C. 2017	80	10	6	21	0.93 [0.85, 0.97]	0.68 [0.49, 0.83]
Represas CR 2010	68	5	8	81	0.89 [0.80, 0.95]	0.94 [0.87, 0.98]
Represas-Represas C 2016	105	117	9	131	0.92 [0.86, 0.96]	0.53 [0.46, 0.59]
Sami R 2020	16	3	3	100	0.84 [0.60, 0.97]	0.97 [0.92, 0.99]
Thorat YT 2017*	26	22	7	134	0.79 [0.61, 0.91]	0.86 [0.79, 0.91]
Thorn J 2012	61	45	16	183	0.79 [0.68, 0.88]	0.80 [0.74, 0.85]
Wang XY 2012	180	27	18	250	0.91 [0.86, 0.95]	0.90 [0.86, 0.93]

PiKo-6

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Frith P 2011	46	42	11	105	0.81 [0.68, 0.90]	0.71 [0.63, 0.79]
Frith P 2011*	31	19	5	38	0.86 [0.71, 0.95]	0.67 [0.53, 0.79]
Hidalgo Sierra V 2018	82	2	0	71	1.00 [0.96, 1.00]	0.97 [0.90, 1.00]
Sichletidis L 2011	89	49	22	918	0.80 [0.72, 0.87]	0.95 [0.93, 0.96]
Toda R 2009	216	69	56	427	0.79 [0.74, 0.84]	0.86 [0.83, 0.89]
van den Bemt L 2014	41	9	3	51	0.93 [0.81, 0.99]	0.85 [0.73, 0.93]

PEF

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mahboub B 2014	50	91	18	366	0.74 [0.61, 0.83]	0.80 [0.76, 0.84]
Ronaldson SJ 2018	39	56	6	115	0.87 [0.73, 0.95]	0.67 [0.60, 0.74]
Thorat YT 2017	26	8	7	148	0.79 [0.61, 0.91]	0.95 [0.90, 0.98]
Tian J 2012	265	492	80	2542	0.77 [0.72, 0.81]	0.84 [0.82, 0.85]



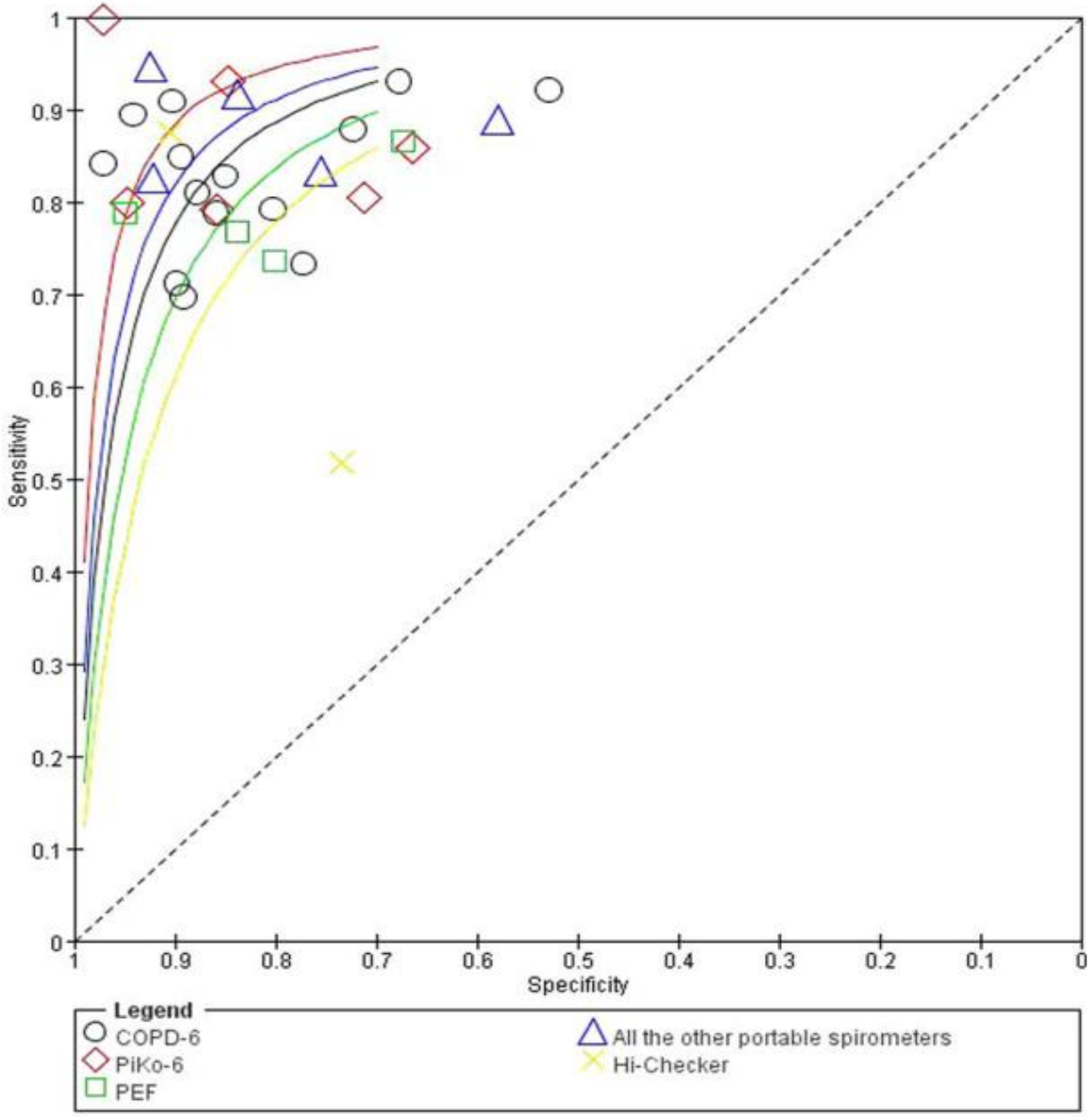


Fig. 7 The SROC of portable spirometers classified by type. All the other portable spirometers including IQ-spiro, SP10BT, Medikro SpiroStar, MS01 Micro spirometer and Spirobank Smart.

Key messages

- **Portable spirometers has been approved for diagnosing chronic obstructive pulmonary disease (COPD).**

- **Thirty one studies** were included in the meta-analysis. The pooled **sensitivity, specificity**, **AUC of the SROC of portable spirometers** were **0.85 (0.81–0.88), 0.85 (0.81–0.88),** and **0.91 (0.89–0.94), respectively.**
- Among the three commonly used types of portable spirometers, **the accuracy of PIKO-6 (0.95), COPD-6 (0.91) and PEF (0.82).**

- In addition, portable **spirometry performed by professional technicians in tertiary hospitals was more accurate** than for those conducted by trained technicians in primary care facilities and communities ($P < 0.05$).
- **Standardized training** of instrument operators should be considered to achieve reliable results.

- Portable spirometers are characterized by **user-friendly, patient-friendly, inexpensive**, and portable, making them **suitable for primary care use** and providing a feasible pathway for early diagnosis of COPD.

국내 COPD환자 폐기능검사 시행률

[그림 10] 종별 폐기능검사

-2020년(7차) 만성폐쇄성폐질환적정성 평가 보고서

Blood Eosinophils and Chronic Obstructive Pulmonary Disease: A Global Initiative for Chronic Obstructive Lung Disease Science Committee 2022 Review.

-Singh D, Agusti A, Martinez FJ, et al. Am J Respir Crit Care Med 2022; 206(1): 17-24.

Table 1. Global Initiative for Chronic Obstructive Lung Disease 2022 Report: Key Evidence and Recommendations for Blood Eosinophil Counts in Chronic Obstructive Pulmonary Disease

Prediction of ICS benefits
The use of BEC to predict ICS effects should be combined with exacerbation risk (using exacerbation history).
The relationship between BEC and ICS effects is continuous; no/small effects are observed at lower BEC, with increasing effects at higher BEC.
Less than 100 cells/μl and ⩾300 cells/μl are estimates, not precise cutoff values, to identify individuals with the lowest and greatest (respectively) likelihood of ICS benefit.
T2 inflammation
Higher BEC are associated with increased lung eosinophil numbers and higher concentrations of T2 inflammation markers in the airways.
The differences in T2 inflammation can explain the differential ICS response according to BEC.
COPD vs. control subjects
A subset of patients with COPD has BEC above those found in control subjects.
Microbiome
Lower BEC are associated with a greater presence of proteobacteria, notably *Haemophilus*, and increased bacterial infections and pneumonia.
Future risk of exacerbations/disease progression
In younger individuals without COPD, higher BEC are associated with an increased risk of FEV_1 decline and the development of COPD.
BEC cannot be used as a standalone biomarker of future risk without considering exacerbation risk and ICS use.

Definition of abbreviations: BEC = blood eosinophil counts; COPD = chronic obstructive pulmonary disease; ICS = inhaled corticosteroid; T2 = type-2.

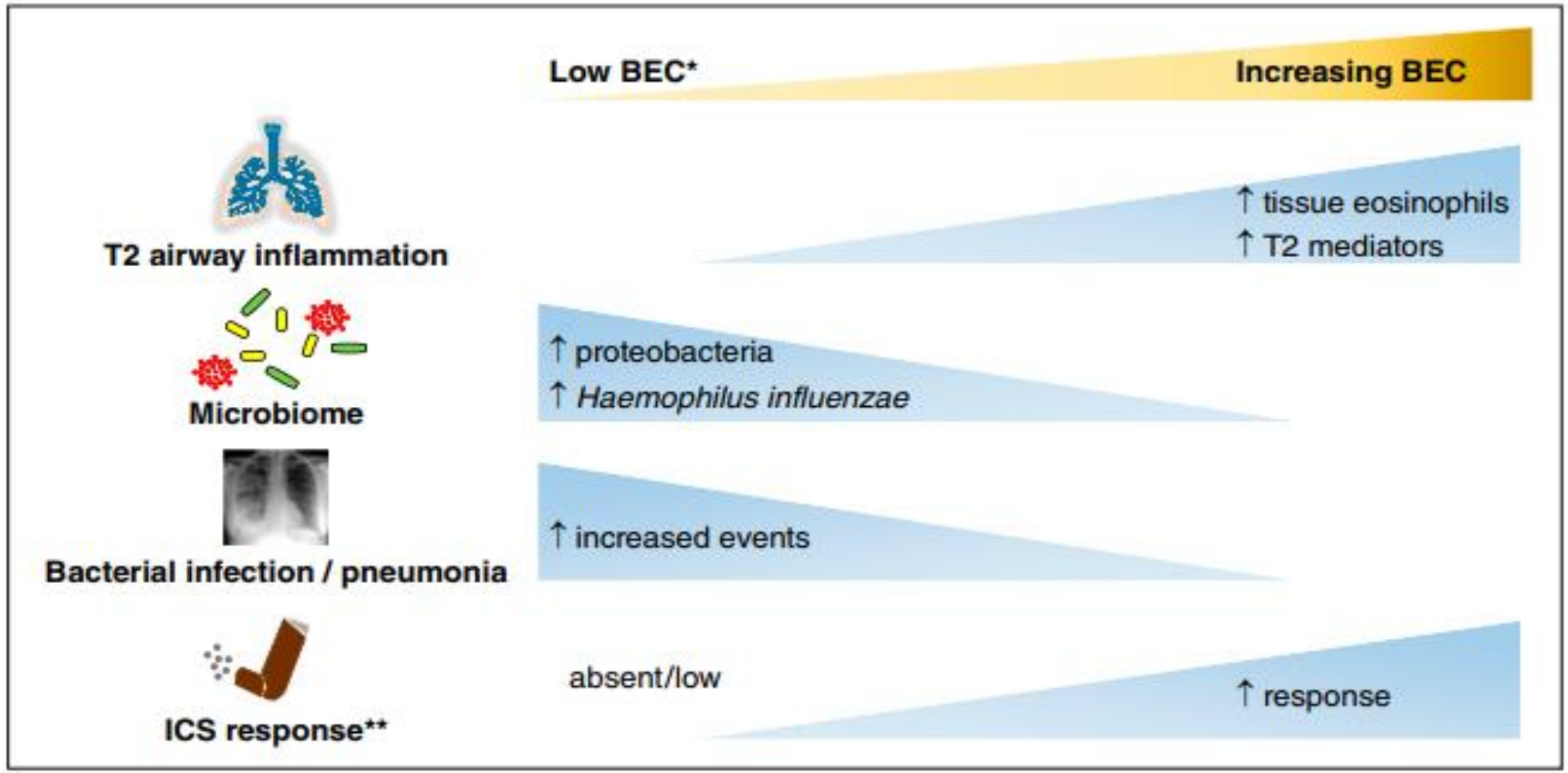


Figure 1. The relationships between blood eosinophil counts (BEC) and type-2 (T2) inflammation, microbiome, bacterial infection/pneumonia episodes, and ICS response (exacerbation prevention). ICS = inhaled corticosteroid. *<100 cells/μL. **In patients with chronic obstructive pulmonary disease who have increased exacerbation risk.

→ " U-shaped" future risk of exacerbation

Factors to Consider when Initiating ICS Treatment

Figure 3.1

Factors to consider when adding ICS to long-acting bronchodilators:

(note the scenario is different when considering ICS withdrawal)

STRONGLY FAVORS USE	History of hospitalization(s) for exacerbations of COPD[#]
	≥ 2 moderate exacerbations of COPD per year[#]
	Blood eosinophils ≥ 300 cells/µL
	History of, or concomitant asthma
FAVORS USE	1 moderate exacerbation of COPD per year[#]
	Blood eosinophils 100 to < 300 cells/µL
AGAINST USE	Repeated pneumonia events
	Blood eosinophils < 100 cells/µL
	History of mycobacterial infection

[#]despite appropriate long-acting bronchodilator maintenance therapy (see Table 3.4 and Figure 4.3 for recommendations);
*note that blood eosinophils should be seen as a continuum; quoted values represent approximate cut-points; eosinophil counts are likely to fluctuate.

Adapted from & reproduced with permission of the © ERS 2019: *European Respiratory Journal 52 (6) 1801219; DOI: 10.1183/13993003.01219-2018 Published 13 December 2018*

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Key messages

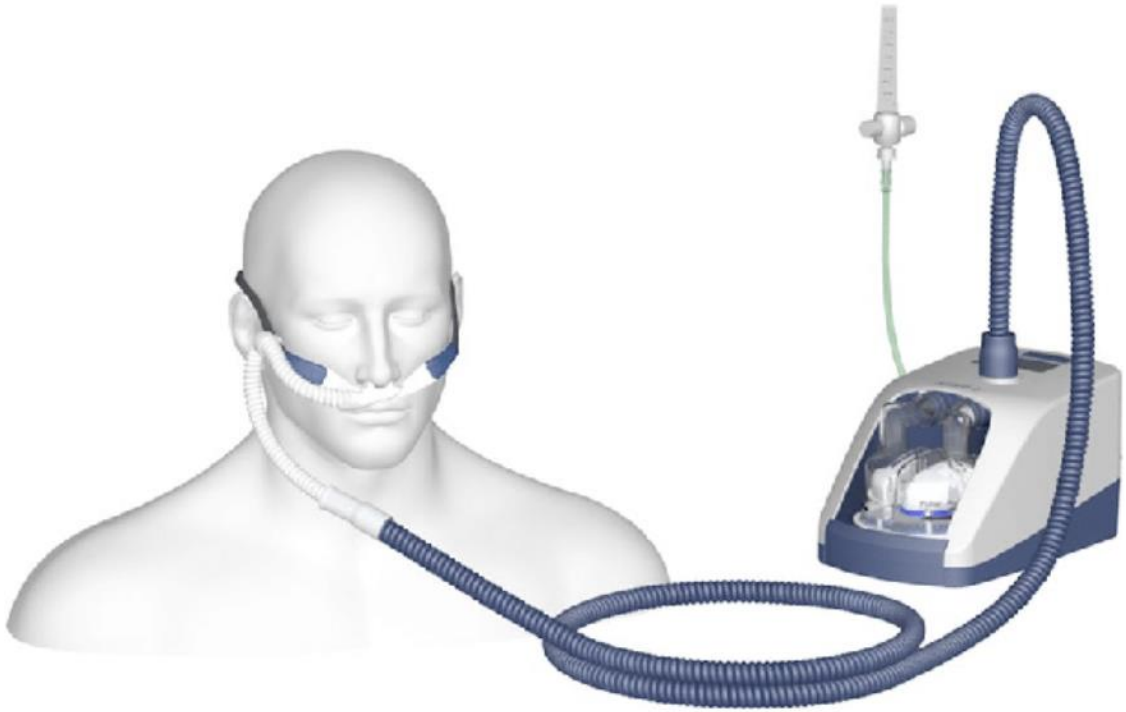
- blood eosinophil counts (BEC)
  - T2 inflammation, microbiome, exacerbation risk

- COPD subtype/endotype by BEC

→ precision medicine strategies

Home High-Flow Nasal Cannula Oxygen Therapy for Stable Hypercapnic COPD: A Randomized Trial

- *Nagata K, Horie T, Chohnabayashi N, et al.. Am J Respir Crit Care Med 2022.*



Airvo 2 high-flow system (Fisher & Paikel Healthcare). The high flow (up to 60 l/min) is generated by a turbine and the system can be used at home.

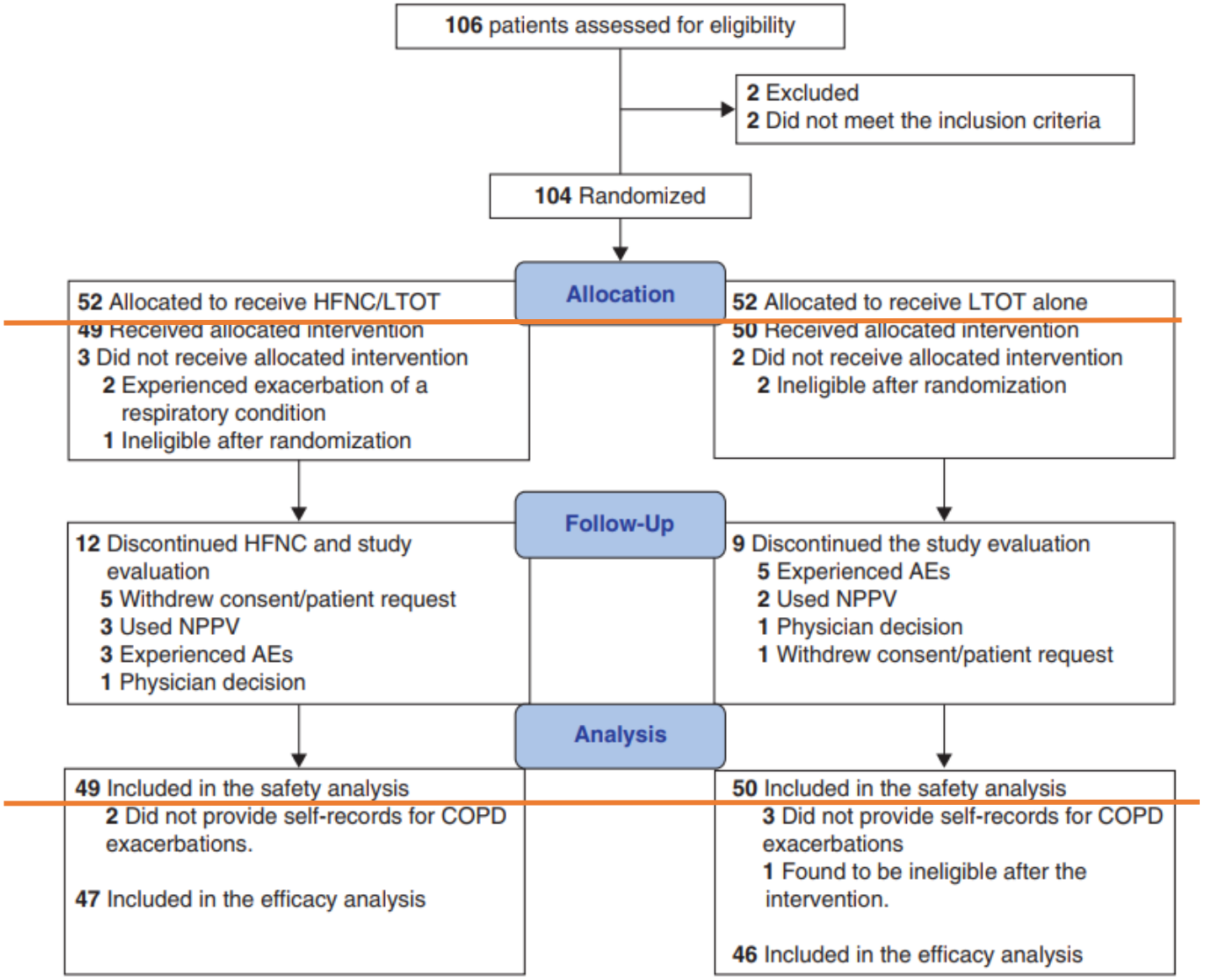


Figure 1. Flow diagram of participant inclusion and exclusion. AE = adverse event; COPD = chronic obstructive pulmonary disease; HFNC = high-flow nasal cannula oxygen therapy; LTOT = long-term oxygen therapy; NPPV = noninvasive positive pressure ventilation.

: COPD_GOLD 2-4

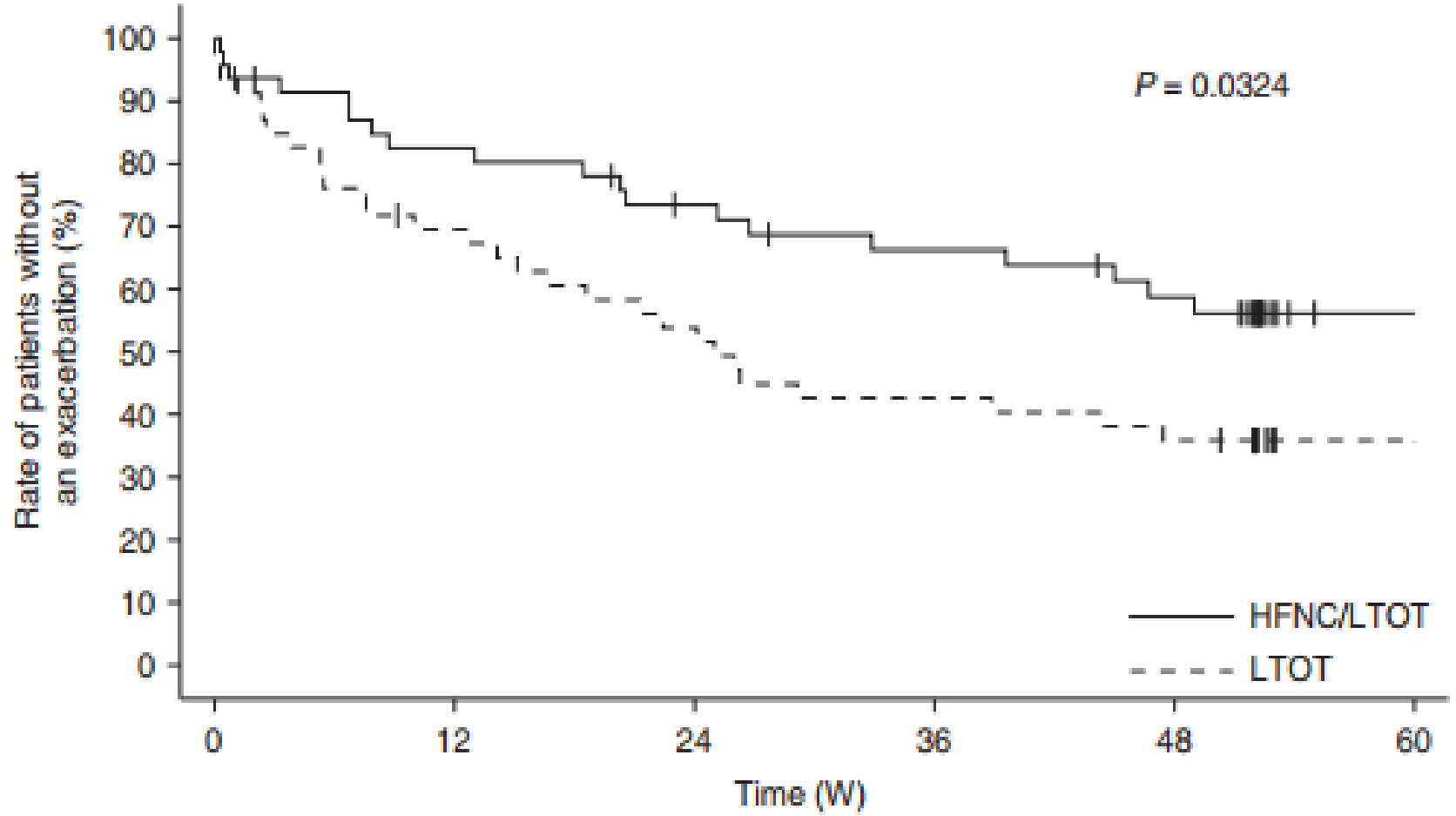
→ LTOT &
hypercapnia ($PaCO_2$ > 45mmHg)
In 42 Japanese hospital

→ **52 weeks f/u**
: exacerbation, survival, SGRQ

Table 1. Patient Demographic Data, Smoking Status, Global Initiative for Chronic Obstructive Lung Disease Stage, and Prescribed Drugs

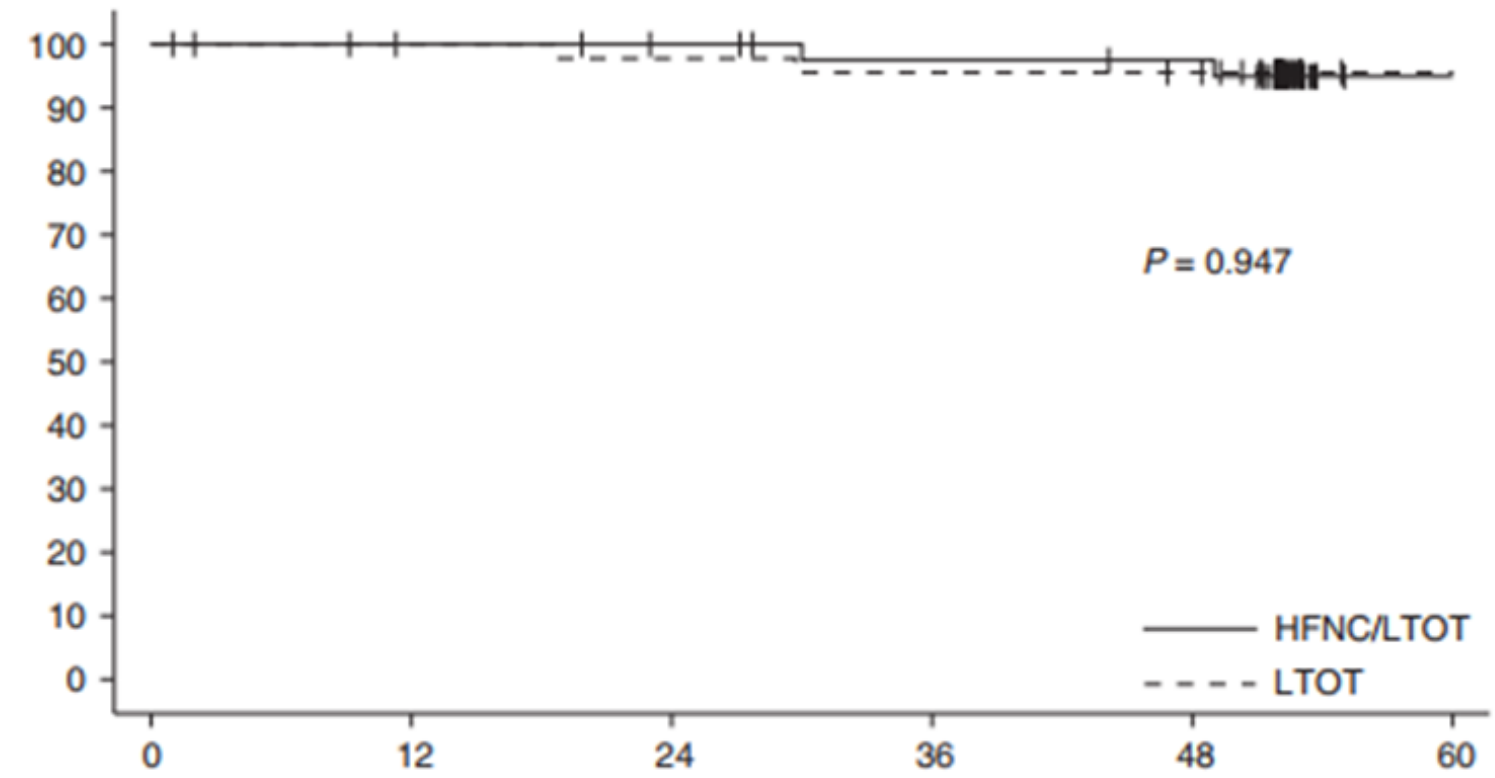
Characteristic	HFNC/LTOT, *n* (%)	LTOT, *n* (%)
Sex		
Male	44 (89.8)	44 (88.0)
Female	5 (10.2)	6 (12.0)
Age, yr		
Mean	72.9	75.16
SD	7.43	6.67
BMI, kg/m^2		
Mean	20.21	20.38
SD	3.57	3.64
Smoking history		
Current	0 (0.0)	2 (4.0)
Past	48 (98.0)	48 (96.0)
Never	1 (2.0)	0 (0.0)
Cigarettes per day, *n*		
Mean	31.67	30
SD	14.7	13.85
Yr		
Mean	39.63	39.84
SD	11.17	9.35
GOLD stage		
2	1 (2.0)	4 (8.0)
3	10 (20.4)	11 (22.0)
4	38 (77.6)	35 (70.0)
LAMA*		
N	1 (2.0)	7 (14.0)
Y	48 (98.0)	43 (86.0)
LABA*		
N	2 (4.1)	4 (8.0)
Y	47 (95.9)	46 (92.0)
Inhaled steroids*		
N	22 (44.9)	19 (38.0)
Y	27 (55.1)	31 (62.0)
Arterial blood gas		
pH		
Mean	7.38	7.39
SD	0.02	0.02
Pa_{CO_2}		
Mean	51.38	50.50
SD	4.96	5.03
Pa_{O_2}		
Mean	80.37	84.10
SD	21.75	21.85
Pulmonary function		
FEV_1		
Mean	0.64	0.66
SD	0.22	0.19
Percent predicted FEV_1		
Mean	25.59	27.08
SD	8.40	8.94
FEV_1/FVC		
Mean	32.65	32.53
SD	8.86	10.14

A Time to first moderate/severe COPD exacerbation

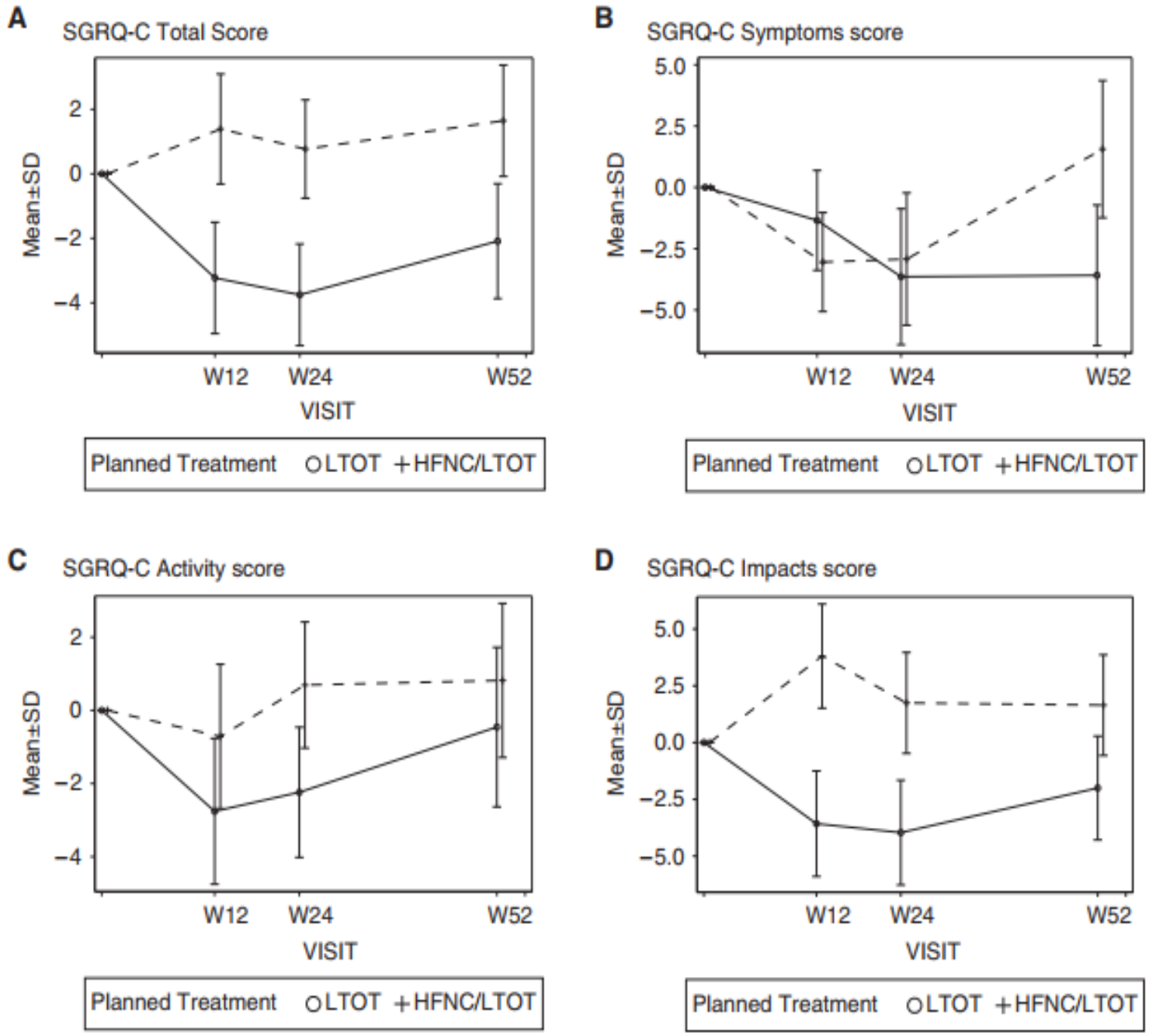


No. of patients at risk						
HFNC/LTOT	47	37	31	27	23	0
LTOT	46	31	24	19	16	0

B Time to death by all causes: overall survival



No. of patients at risk						
HFNC/LTOT	47	44	42	39	38	0
LTOT	46	45	44	43	42	0


A
SGRQ-C Total Score
Mean±SD
2
0
−2
−4
W12
W24
W52
VISIT
Planned Treatment ○LTOT +HFNC/LTOT
B
SGRQ-C Symptoms score
Mean±SD
5.0
2.5
0.0
−2.5
−5.0
W12
W24
W52
VISIT
Planned Treatment ○LTOT +HFNC/LTOT
C
SGRQ-C Activity score
Mean±SD
2
0
−2
−4
W12
W24
W52
VISIT
Planned Treatment ○LTOT +HFNC/LTOT
D
SGRQ-C Impacts score
Mean±SD
5.0
2.5
0.0
−2.5
−5.0
W12
W24
W52
VISIT
Planned Treatment ○LTOT +HFNC/LTOT

Key messages

- **The first randomized clinical trial** to evaluate the number of severe or moderate exacerbations in patients with stable **hypercapnic COPD** who were randomly administered either long-term oxygen therapy alone or long-term oxygen therapy plus **high-flow nasal cannula oxygen therapy for 52 weeks**.
- Our study revealed that treatment with domiciliary high-flow nasal cannula oxygen therapy **reduced the number of exacerbations** and SGRQ

- **HFNC use may be a reasonable therapeutic option for hypercapnic patients with COPD.**

Using a smartphone application maintains physical activity following pulmonary rehabilitation in patients with COPD: a randomised controlled trial.

- -*Spielmanns M, Gloeckl R, Jarosch I, et al. Thorax 2022.*

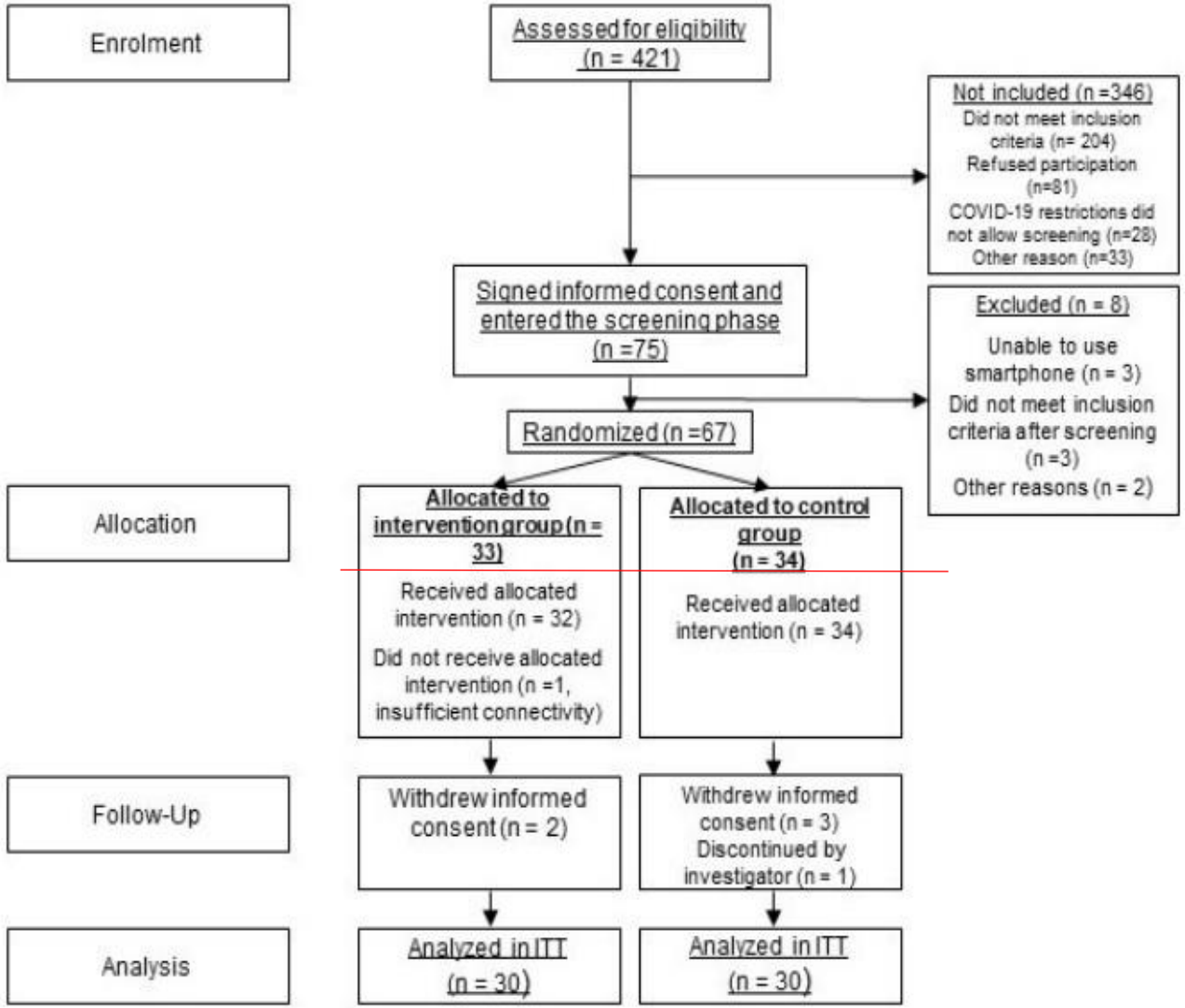
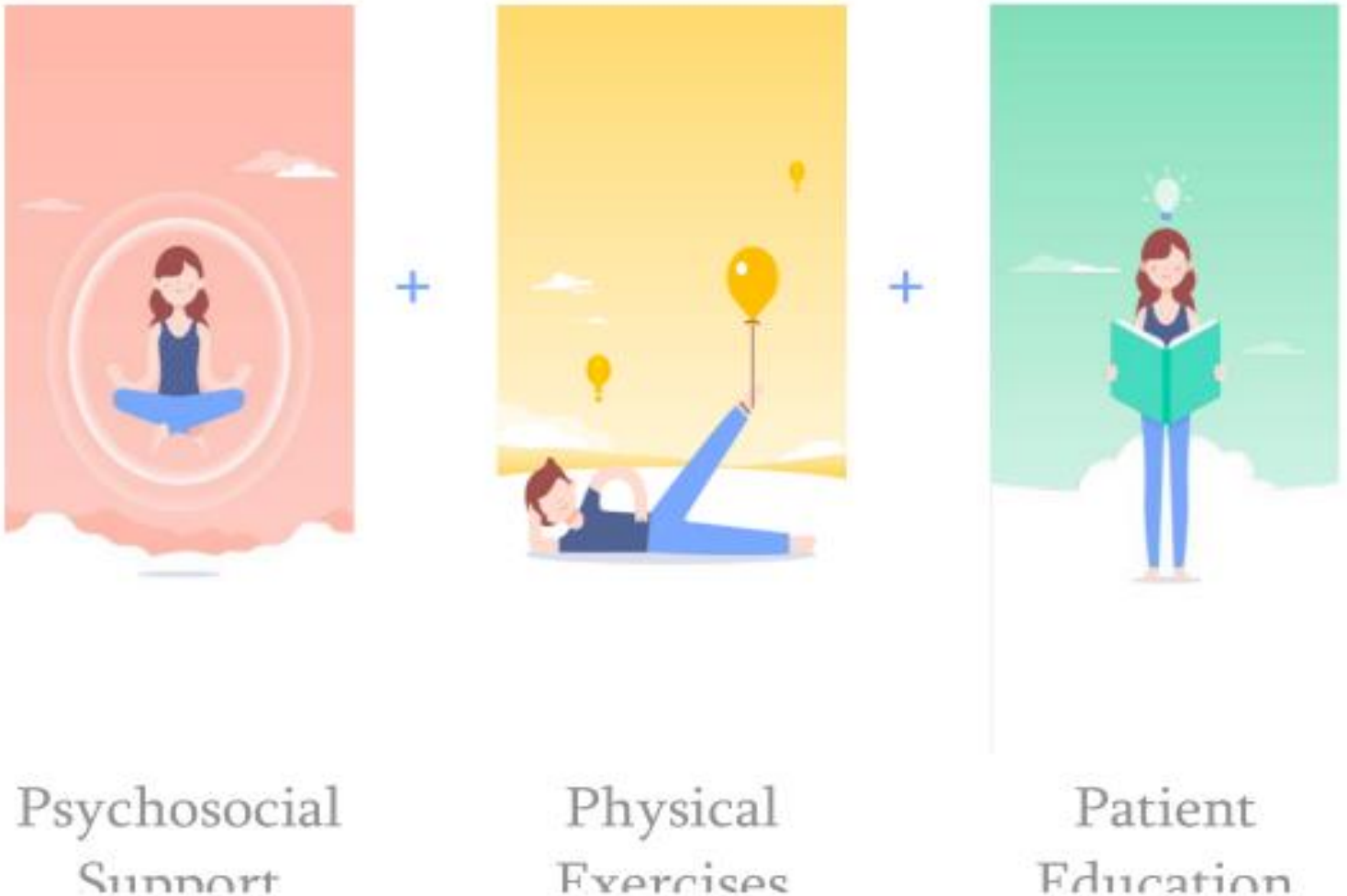


Figure 1 Consolidated Standards of Reporting Trials diagram. ITT, intention to treat.

- COPD GOLD 2-4
- PR inpatient program for 3wks in 2 hospitals
- → PR using smartphone App. for 6mo

Figure S7: Contents of the KAIA COPD App



Outcomes after 6mo

: physical activity (PA)
: CAT, CRQ
: HADS (hospital anxiety, depression scale)

Table 1 Demographic characteristics of the study population

Characteristics	Overall n=67	IG n=33	CG n=34
Age (years), mean (SD)	64.3 (7.7)	66.1 (6.8)	62.7 (8.2)
Sex (female), n (%)	33 (49.3)	16 (48.5)	17 (50.0)
BMI (kg/m^2), mean (SD)	24.4 (5.1)	25.0 (4.7)	23.8 (5.6)
Current smoker, n (%)	8 (11.9)	3 (9.1)	5 (14.7)
Smoking in the past, n (%)	58 (86.6)	30 (90.9)	28 (82.4)
Never smoker, n (%)	1 (1.5)	0 (0.0)	1 (2.9)
Exacerbation in the last 12 months, n (%)	53 (79.1)	29 (87.9)	24 (70.6)
Number of exacerbations treated as outpatient in the past 12 months, mean (SD)	1.19 (1.14)	1.19 (1.33)	1.19 (0.87)
Number of exacerbations treated as inpatient in the past 12 months, mean (SD)	1.08 (1.23)	1.21 (1.50)	0.91 (0.79)
Long-term oxygen therapy, n (%)	40 (59.7)	18 (54.5)	22 (64.7)
FEV_1 (L) (mean (SD))	1.27 (0.50)	1.31 (0.53)	1.23 (0.46)
FEV_1% predicted (mean (SD))	44.0 (16.2)	45.5 (14.5)	42.6 (17.8)
FEV_1% FVC, mean (SD)	0.52 (0.14)	0.54 (0.14)	0.50 (0.15)
FVC% predicted, mean (SD)	64.8 (18.4)	63.9 (17.9)	65.7 (19.2)
CAT (points), mean (SD)	16.3 (7.09)	16.5 (7.2)	16.0 (7.1)
GOLD stage II, n (%)	20 (29.9)	10 (30.3)	10 (29.4)
GOLD stage III, n (%)	29 (43.3)	17 (51.5)	12 (35.3)
GOLD stage IV, n (%)	18 (26.9)	6 (18.2)	12 (35.3)

BMI, body mass index; CAT, COPD Assessment Test; CG, control group; FEV_1, forced expiratory volume in 1 s ; FVC, forced vital capacity; GOLD, Global Initiative for Obstructive Lung Disease; IG, intervention group;

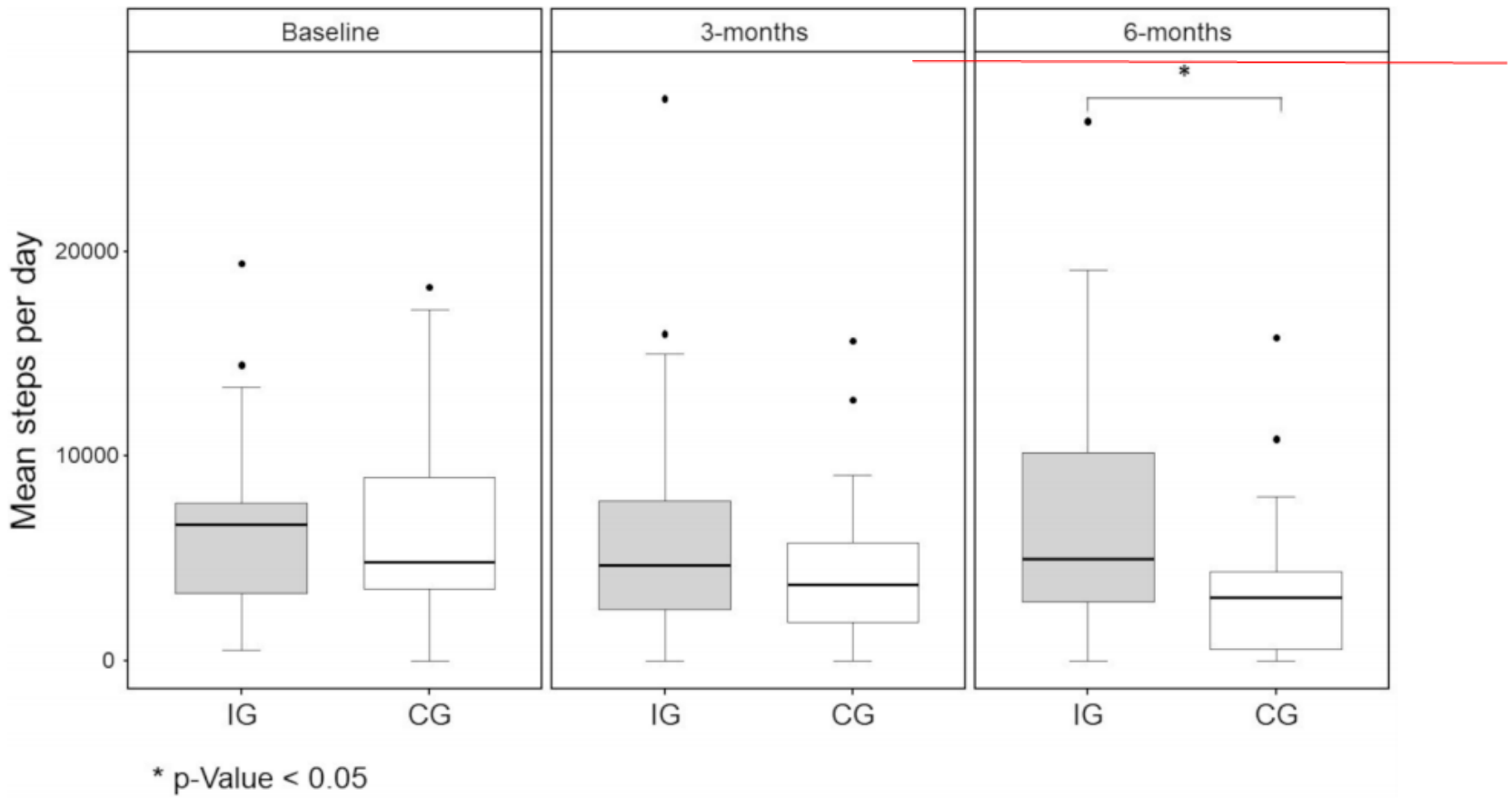


Figure 3 Steps per day at baseline and 3 and 6 months for the IG and the CG. P value obtained from the Mann-Whitney U test. CG, control group; IG, intervention group. *P<0.05.

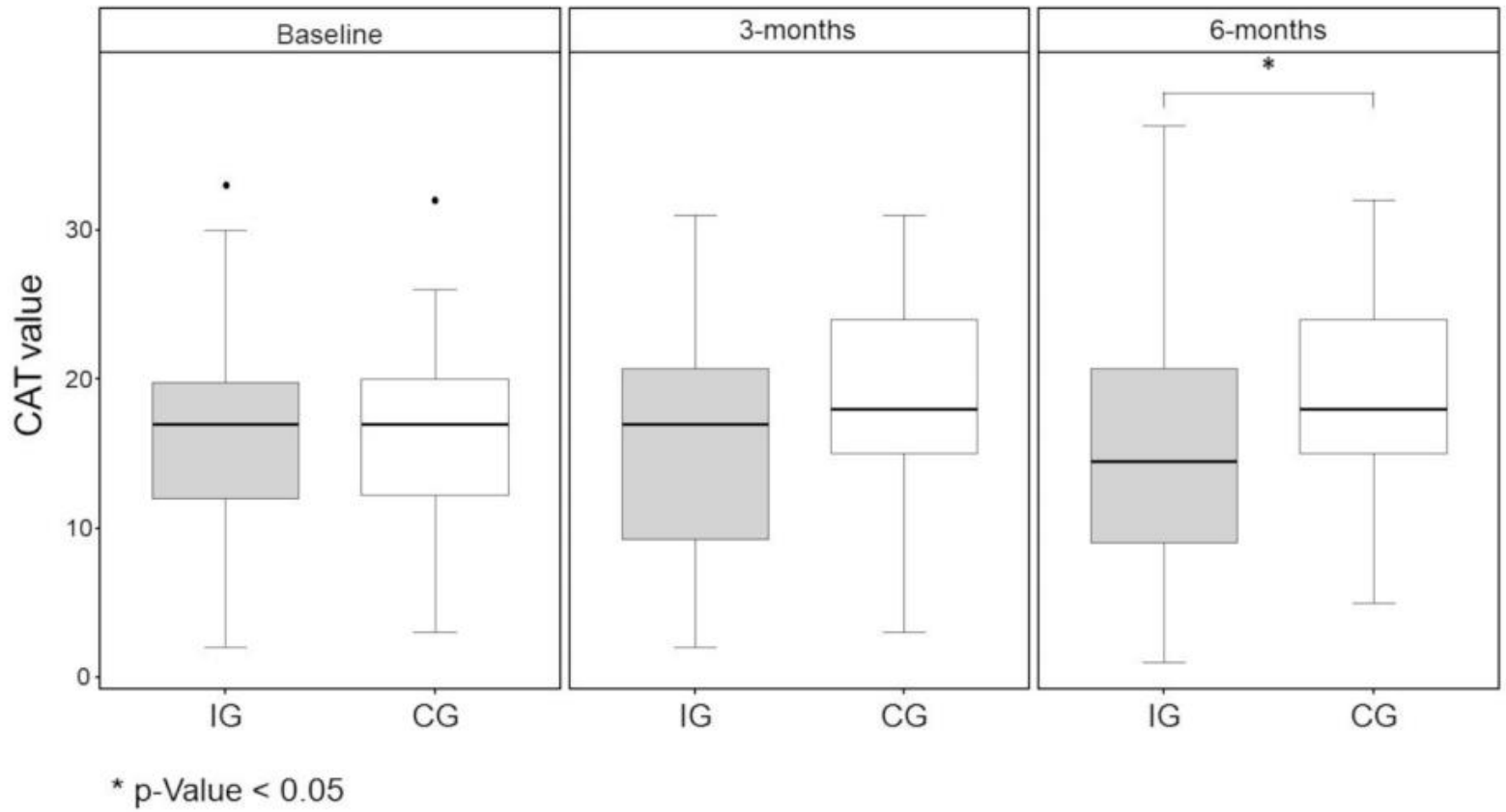


Figure 4 Results of the CAT for the IG and the CG. P value was obtained from the t-test. CAT, COPD Assessment Test; CG, control group; IG, intervention group. *P<0.05.

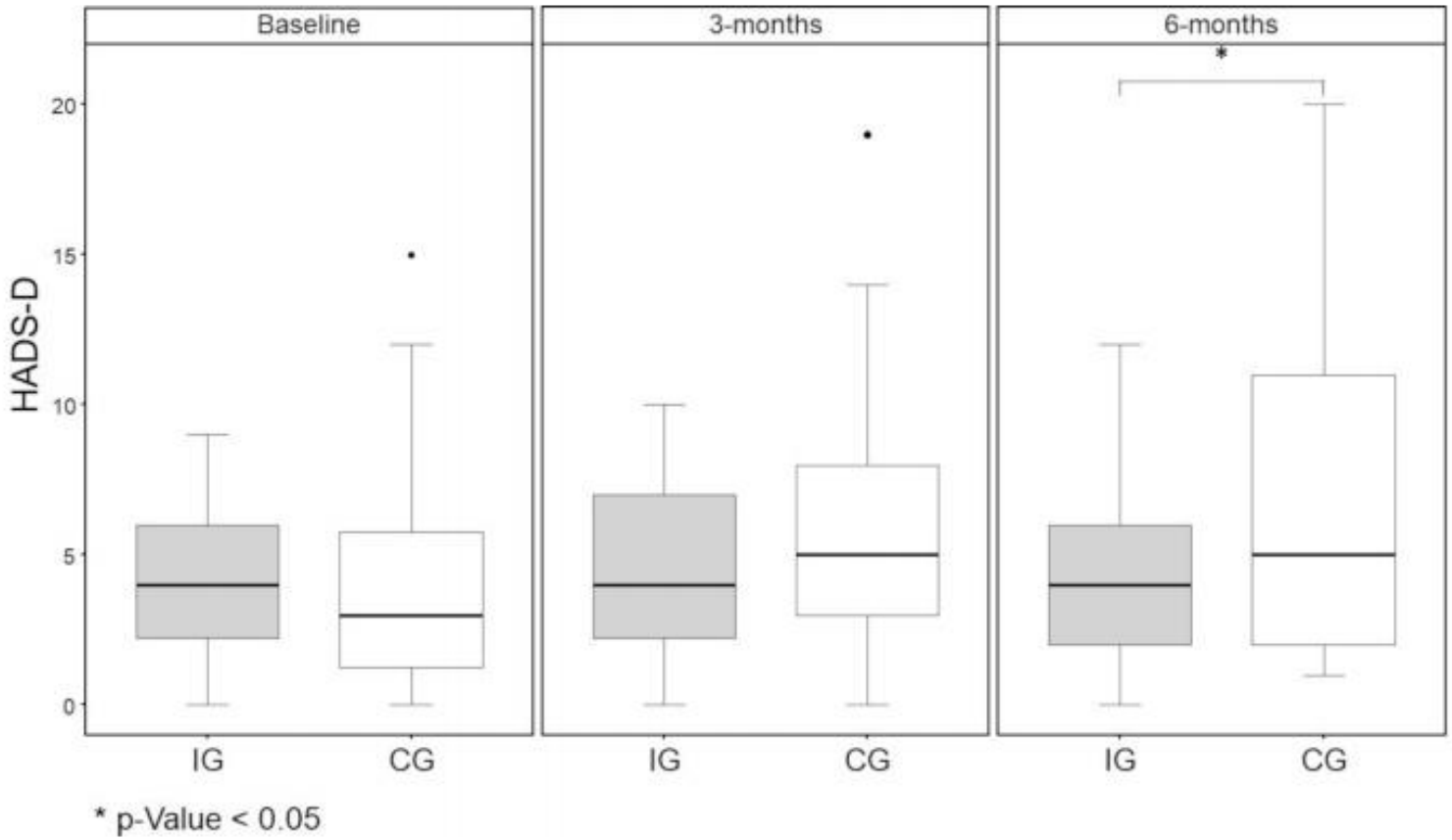


Figure 5 Results of the HADS-D for the IG and the CG. P value was obtained from the t-test. CG, control group; HADS-D, Hospital Anxiety and Depression Scale–Depression Subscale; IG, intervention group. *P<0.05.

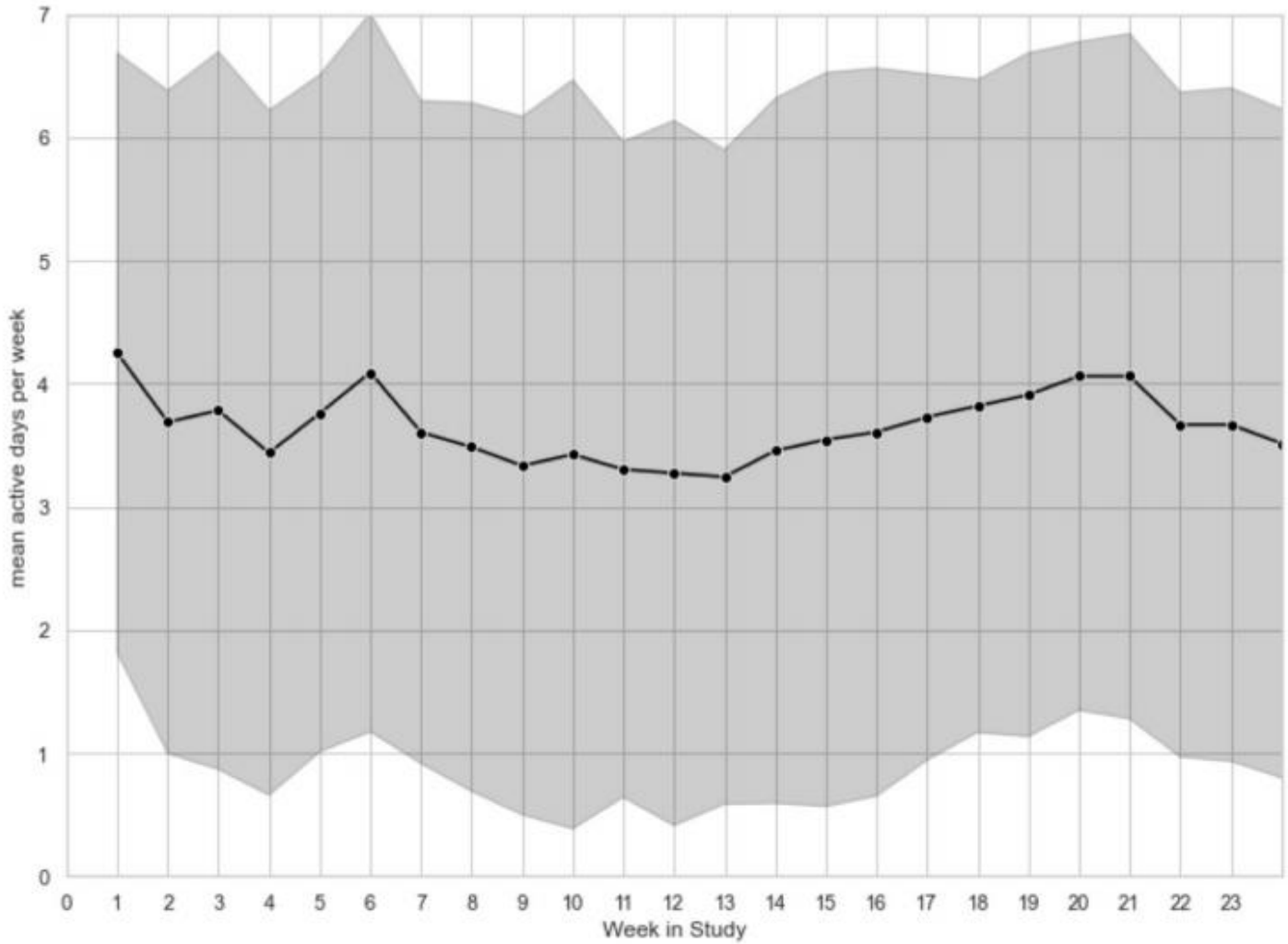


Figure 7 Usage rates per week during the observational period. Mean values are indicated by the black line and dots; SDs are indicated by grey bars.

Key messages

- **Regular use of the contents of the smartphone application** (app) Kaia COPD app not only **maintained PA** in patients with COPD after rehabilitation but also **improved symptoms**.
- **Widespread use of eHealth** has the potential to **close the long-known gap in postrehabilitation.**

- Limitations : small sample size, two center study, only smartphone users etc.

Chest CT-assessed comorbidities and all-cause mortality risk in COPD patients in the BODE cohort.

- *Ezponda A, Casanova C, Divo M, et al. Respirology 2022; 27(4): 286-93.*

TABLE 1 Demographic characteristics and functional data of participants at baseline ($n = 379$)

Variables	
Age in years, median (IQR)	66 (59–72)
Male sex, *n* (%)	297 (78.4%)
Pack-years, median (IQR)	50 (36–75)
Current smoker, *n* (%)	136 (37.3)
BMI kg/m^2, median (IQR)	27 (23.7–30.1)
BSA (kg/m^2), mean (SD)	1.9 (0.3)
FEV_1/FVC (%), median (IQR)	55 (44–63)
FEV_1 %, mean (SD)	64.4 (21.9)
FVC %, mean (SD)	93.6 (22.4)
TLC %, median (IQR)	107 (96–116)
DLCO %, mean (SD)	62.1 (46.8)
6MWD (m), median (IQR)	480 (403–545)
MMRC, median (IQR)	1 (0–2)
BODE, median (IQR)	1 (0–2)
Spirometric GOLD stages (%)	I (36.2) II (47.9) III (13.3) IV (2.7)
Exacerbations in the previous year, median (IQR)	0 (0–1)
Exacerbations in the previous year, yes (%)	97 (37.9)
Charlson index, median (IQR)	1 (0–2)

Abbreviations: 6MWD, 6-min walking distance; BODE, BMI, Obstruction, Dyspnoea and Exercise capacity, GOLD Global Initiative for Obstructive Lung Disease; BSA, body surface area; DLCO, diffusion capacity for carbon monoxide; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; IQR, interquartile range; mMRC, modified Medical Research Council; TLC total lung capacity.

BODE cohort
: 2012-15 mild to moderate COPD without malignancy
: f/u until 2021 (about 6yr)

TABLE 2 Prevalence of the different CT-assessed comorbidities

Morbidity detected	% of patients
Emphysema	62.7
Bronchiectasis	33.9
ILA	9.2
CAC	79.8
PAE (≥30 mm)	15.6
Ascending aorta enlargement	16
Hiatal hernia	24.2
Liver steatosis	23.4
Osteoporosis	25.7
Low PsD	15.8

Abbreviations: CAC, coronary artery calcification; CT, computed tomography; ILA, interstitial lung abnormalities; PAE, pulmonary artery enlargement; PsD, Psoas density.

TABLE 3 Contribution of chest CT to the diagnosis of comorbidities

Morbidity	Clinically diagnosed	Radiologically detected	*p*-value
Emphysema, %	34.4	62.7	0.011
Bronchiectasis, %	25.9	33.9	<0.001
ILA, %	4.2	9.2	<0.001
CAC, %	15.6	79.8	<0.001
PAE (≥30 mm), %	9	15.6	<0.001
Ascending aorta enlargement, %	7.1	16	<0.001
Hiatal hernia, %	21.6	24.2	<0.001
Liver steatosis, %	15	23.4	0.018
Osteoporosis, %	12.9	25.7	0.039
Muscle weakness versus low PsD, %	0.3	15.8	0.021

Abbreviations: CAC, coronary artery calcification; CT, computed tomography; ILA, interstitial lung abnormalities; PAE, pulmonary artery enlargement; PsD, Psoas density.

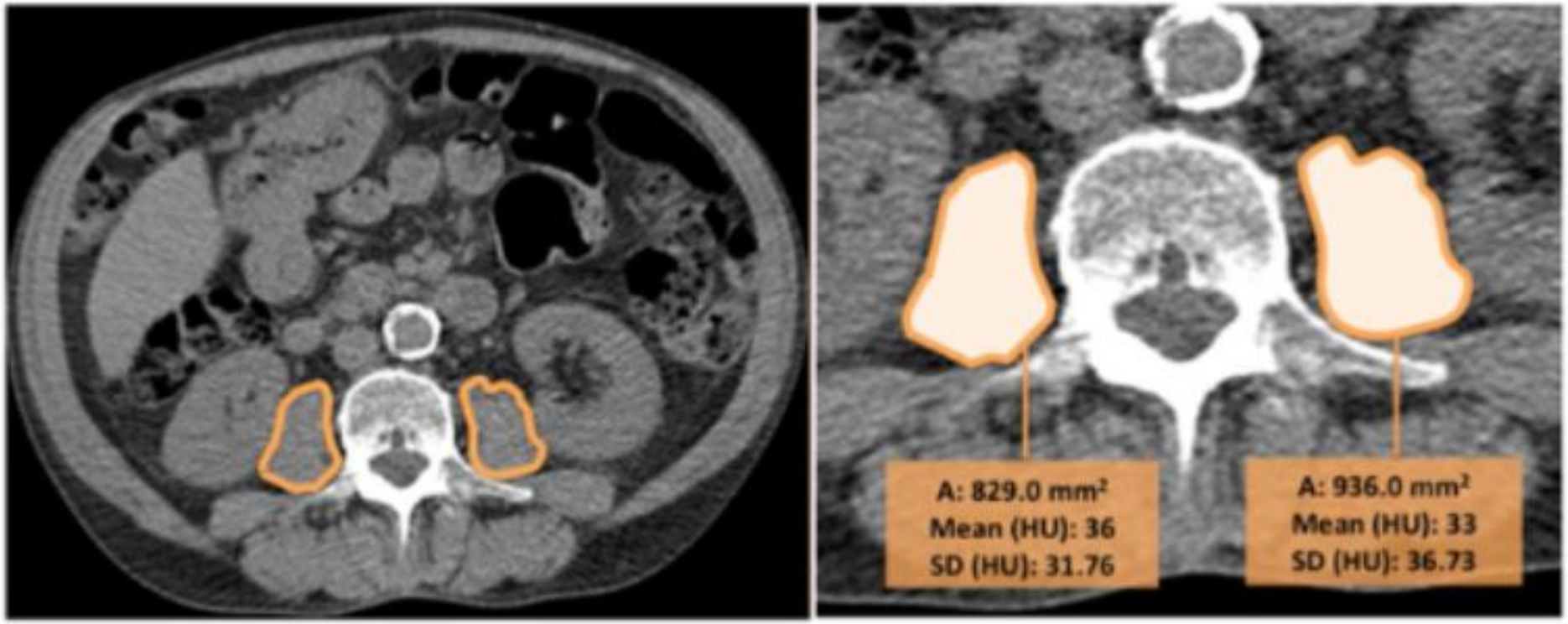


Fig. 1. This is one example showing how the psoas measurement was performed in a participant from the COPD group. A region of interest (ROI) was manually traced involving all the psoas muscle. No special imaging post-processing was required.

- Psoas Muscle Density Evaluated by ChestCT and Long-Term Mortality in COPD Patients. ArchivosdeBronconeumología (2021)

TABLE 4 Multivariate analysis exploring the CT-determined comorbidities and risk of all-cause mortality

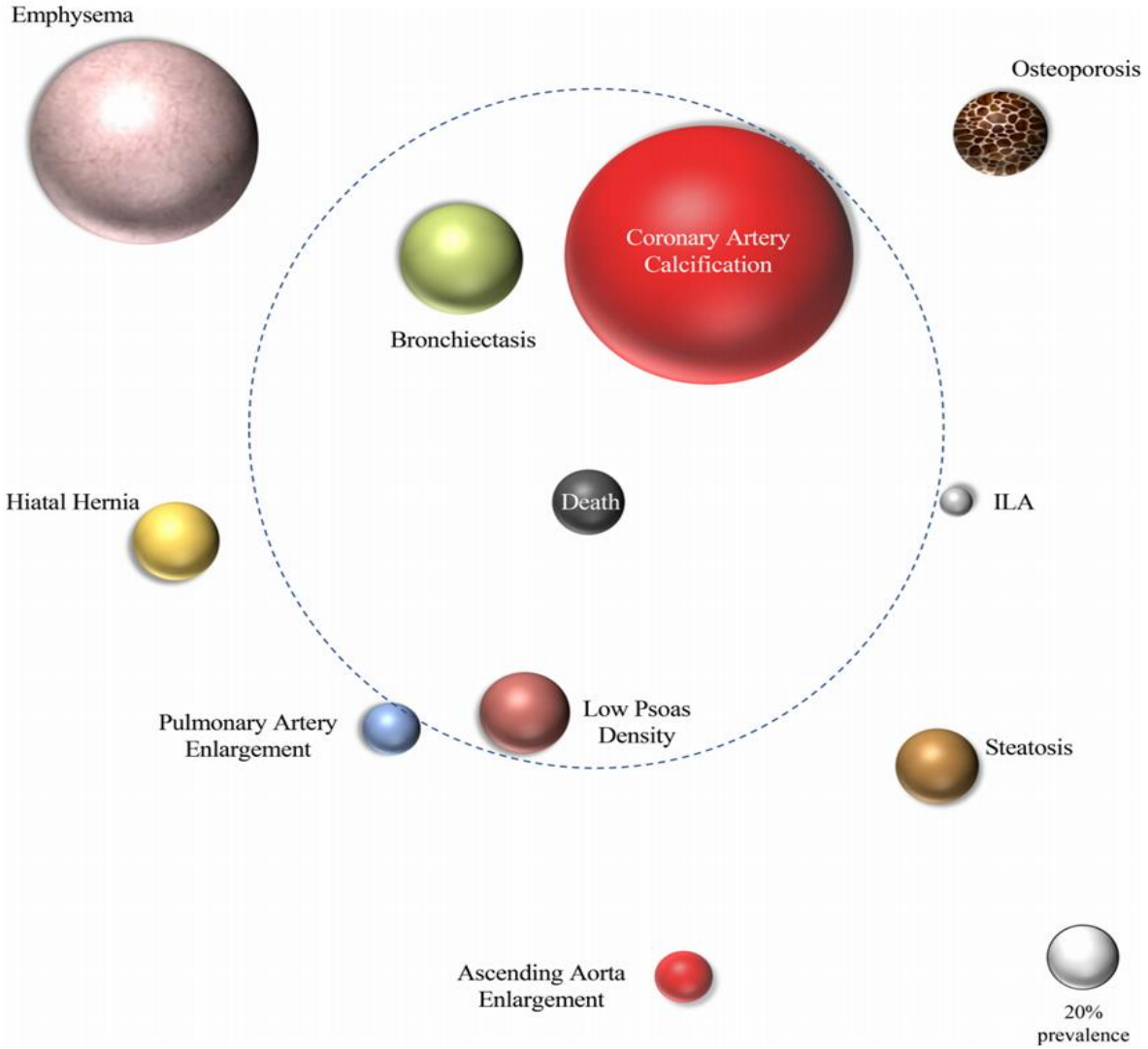
Variables	HR (95% CI)	*p*-value
Emphysema (yes vs. no)	1.06 (0.53–2.14)	0.89
Bronchiectasis (yes vs. no)	**2.12 (1.05–4.26)**	**0.036**
ILA (yes vs. no)	1.93 (0.79–4.74)	0.151
CAC (low risk vs. high risk)	**2.09 (1.03–4.26)**	**0.042**
PAE (≥30 mm)	1.98 (0.69–5.73)	0.21
Ascending aorta enlargement (yes vs. no)	1.18 (0.48–2.90)	0.724
Hiatus hernia (yes vs. no)	1.53 (0.69–3.36)	0.269
Liver steatosis (yes vs. no)	1.39 (0.66–2.94)	0.392
Osteoporosis by CT (yes vs. no)	1.09 (0.44–2.68)	0.864
Low PsD (yes vs. no)	**2.61 (1.23–5.57)**	**0.013**

Note: Adjusted for age, sex, BMI, pack-year history and FEV_1.

Abbreviations: CAC, coronary artery calcification; CT, computed tomography; FEV_1, forced expiratory volume in 1 s; HR, hazard ratio; ILA, interstitial lung abnormalities; PAE, pulmonary artery enlargement; PsD, Psoas density.

Computed tomography (CT)-comorbidome

: an orbital bubble chart showing the prevalence of the 10 CT-assessed comorbidities and the strength of their association with all-cause mortality



Key messages

- This study of COPD patients shows that **systematic detection of 10 CT-diagnosed comorbidities**, most of which were not detected before CT.
- **Coronary artery calcification, emphysema and bronchiectasis were the most prevalent** comorbidities (79.8%, 62.7% and 33.9%, respectively). All were underdiagnosed before CT.
- **Coronary artery calcium, bronchiectasis and low psoas muscle density** were independently associated with **all-cause mortality** and helped define the '**CT-comorbidome'.**

- ***As many of the comorbidities are treatable***, their systematic evaluation is of practical use for clinicians and patients alike. Whether this approach can result in **better outcomes** needs to be tested.

Summary

- Risk factors, pathogenesis in never smoker
  - air pollution, occupational exposures, asthma, infection, impaired lung growth etc. → less Sx, but frequent exacerbation (+), Tx (?)
- Diagnosis
  - Accuracy of portable spirometer
- Tx
  - Blood eosinophil counts
  - HFNC for hypercapnic stable COPD
  - E_health, smartphone app for physical activity
- Px
  - Chest CT-assessed comorbidities
    : Coronary artery calcium, bronchiectasis, low psoas muscle density → mortality(+)