Synergistic Action of Pulmonary Rehabilitation with Bronchodilator

전남의대
김유일

NON-PHARMACOLOGIC MANAGEMENT OF COPD

PATIENT GROUP	ESSENTIAL	RECOMMENDED	DEPENDING ON LOCAL GUIDELINES
A	Smoking Cessation (can include pharmacologic treatment)	Physical Activity	Flu Vaccination Pneumococcal Vaccination
B-D	Smoking Cessation (can include pharmacologic treatment) Pulmonary Rehabilitation	Physical Activity	Flu Vaccination Pneumococcal Vaccination

TABLE 4.8

Non-pharmacological treatment

Exercise training

- A meta-analysis of RCTs found that **exercise training alone, or with the add ition of activity counseling**, significantly **improved physical activity** levels i n COPD patients.
- A combination of constant load or interval training with strength training p rovides better outcomes than either method alone.
- Where possible, endurance exercise training to 60-80% of the symptom-li mited maximum work or heart rate is preferred, or to a Borg-rated dyspne a or fatigue score of 4 to 6 (moderate to severe).
- Exercise training can be **enhanced by optimizing bronchodilators,** since bo th LAMA and LABA have shown **reduced resting and dynamic hyperinflatio n.**

비약물적 치료 : 호흡재활

- 육체적 활동으로 인한 일반적인 이점과 심혈관계 질환에 미치는 이점을 고려하여 COPD 환자에서 매일 육체적인 활동을 하도록 권장

- 호흡재활의 목적은 증상을 완화시키고, 삶의 질을 향상시키며, 일상생활에서 신체적, 정서적인 참여를 확대

운동능력의 향상
호흡곤란 감소
건강과 관련된 삶의 질의 향상
병원 입원 횟수와 입원기간의 감소
COPD와 관련된 불안과 우울증의 감소
상지근력과 지구력 훈련으로 상지기능 호전
재활치료의 효과가 치료 후에도 지속
생존율 증가
일반적인 운동훈련과 병행하였을 때 호흡근육 훈련이 효과적
급성악화로 입원 후 회복을 향상
지속성베타2-항진제 효과증대

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Improvement of physical activity in chronic obstructive pulmonary disease by pulmonary rehabilitation and pharmacological treatment

- -TakanobuShioya[a,n], SusumuSato[b], MasahiroIwakura[a,c], HitomiTakahashi[c], YoshinoTerui[a], SachikoUemura[a], MasahiroSatake[a]

-Respiratory investigation56(2018) 292–306

Introduction

- Physical activity (PA)
  - related to reduced morbidity and mortality in chronic obstructive pulmonary disease (COPD).

- effects of PR and pharmacological treatment on PA in COPD patients.

- 32 studies evaluating the effects of PR
- 11 studies examining the effects of pharmacological treatment on PA.

Effects of pulmonary rehabilitation on physical activity in COPD

Author (year)	Number of PTs, & Severity	Intervention Program	Accelerometer	Results	Exercise capacity
Steele (2003)[36]	41 pts	PR 8 wk, hospital,	triaxial	PA not changed	NA
	moderate-very severe	2 sessions/wk	RT3		
Coronado (2003)[37]	15 pts	PR 3 wk, inpatient,	uniaxial	PA not changed	○
	mild-very severe	6-7 sessions/wk	ADXL05		
Sewell (2005)[38]	180 pts, (90 vs 90)	PR 7 wk	activity monitor	PA improved	○
	FEV1 0.9L	2 sessions/wk	Z80-32k		
Mercken (2005)[39]	11 pts	PR 8 wk	uniaxial	PA improved	○
	moderate-very severe	5 sessions/wk	AM 100		
de Block (2006)[40]	10 pts	PR/Counseling 9 wk	pendulum	PA improved	NA
	mild-very severe	3 sessions/wk	Yamax Digiwalker SW200	no enhance	
	11 pts	PR 9 wk	pendulum	PA improved	NA
	moderate-very severe	3 sessions/wk	Yamax Digiwalker SW200		
Pitta (2008)[41]	41 pts	PR 12-24 wk	triaxial	PA improved	○
	severe	2-3 sessions/wk	Dynaport Activity Monitor		
Walker (2008)[42]	24 pts	PR 8 wk	triaxial	PA improved	○
	moderate-very severe	3 sessions (1 supervised)/wk	Dynaport Activity Monitor		
Dallas (2009)[43]	54 pts	PR 6-12 wk	pedometer	PA not changed	○
	severe	2-3 sessions/wk	NL-2000		
Breyer (2011)[44]	30 pts	Nordic walk training 12 wk	triaxial	PA improved	○
	moderate-very severe	3 sessions/wk	Dynaport Activity Monitor		
Mador (2011)[45]	24 pts	PR 8 wk	triaxial	PA not changed	○
	moderate-severe	3 sessions/wk	RT3		
Effing (2011)[46]	74 pts	COPE-active; 24 wk	pendulum	PA improved	○
	moderate-very severe	Self-management 3 sessions/wk 1 unsupervised excise/wk	Yamax Digiwalker SW200		

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Using pedometers to monitor walking activity in outcome assessment for pulmonary rehabilitation

MI Dallas[1], C McCusker[2], MC Haggerty[3], CL Rochester[4,5] and R ZuWallack[6], for the Northeast Pulmonary Rehabilitation Consortium

Table 1. Patient characteristics, $N = 45$

Age (years)	69 ± 8
Male/female	21/24
BMI (kg/m^2)	27 ± 5
FEV_1, % predicted	45 ± 18
6MWT distance (m)	355 ± 90
Using supplemental oxygen (*n*)	21
MRC score (1–5)	3.0 ± 1.3
CRQ total score	90 ± 22

Data shown represent mean ± standard deviation.
BMI, body mass index; FEV_1, forced expiratory volume in 1 second; 6MWT, 6-min walk test; MRC, Medical Research Council; CRQ, Chronic Respiratory Disease Questionnaire.

Table 2. Changes in outcome variables after versus before PR, $N = 45$

	Mean pre-PR ± SD	Mean post-PR ± SD	Mean change ± SD	p value (for change)
Pedometer counts per hour	207 ± 139	240 ± 153	33 ± 149	.14
6MWT distance (m)	355 ± 90	410 ± 94	49 ± 59	<.0001
MRC dyspnea (units)	3.0 ± 1.3	2.7 ± 1.1	−0.64 ± 0.96	.003
CRQ total score (units)	90 ± 22	100.3 ± 16.3	10 ± 18	.0007

Data shown represent mean ± standard deviation.

PR, pulmonary rehabilitation; 6MWT, 6-min walk test; MRC, Medical Research Council; CRQ, Chronic Respiratory Disease Questionnaire.

Conclusions

- A standard pedometer worn at the waist did not detect changes in lower extremity activity following PR.
- This negative finding occurred despite demonstrated improvements in dyspnea, exercise tolerance and quality of life measures.

- Although pedometers are inexpensive and easy to use, they may not be sensitive enough to be used routinely as an outcome measure for PR.

Can Individualized Rehabilitation Improve Functional Independence in Elderly Patients With COPD?

-Sewell, Louise; Singh, Sally; Williams, Johanna; Collier, Rachael; Morgan, Michael

-Chest. 128(3):1194-1200, September 2005.

Table 2—*Subject Characteristics

Characteristics	GEP Group	ITEP Group
No.	90	90
Age, yr	69.34 ± 8.73	67.33 ± 8.41
FEV_1, L	0.93 ± 0.39	0.97 ± 0.45
Men/women, ratio	60:30	51:39
LTOT	14	8
Current smokers	21	14

*Values given as mean ± SD or No., unless otherwise indicated.
LTOT = long-term oxygen therapy.

DESIGN:
Prospective randomized, controlled trial.
SETTING:
7-week general exercise program ([GEP] n = 90) or an individually targeted exercise program ([ITEP] n = 90).

Figure 2 . Percentage change in activity monitor counts.

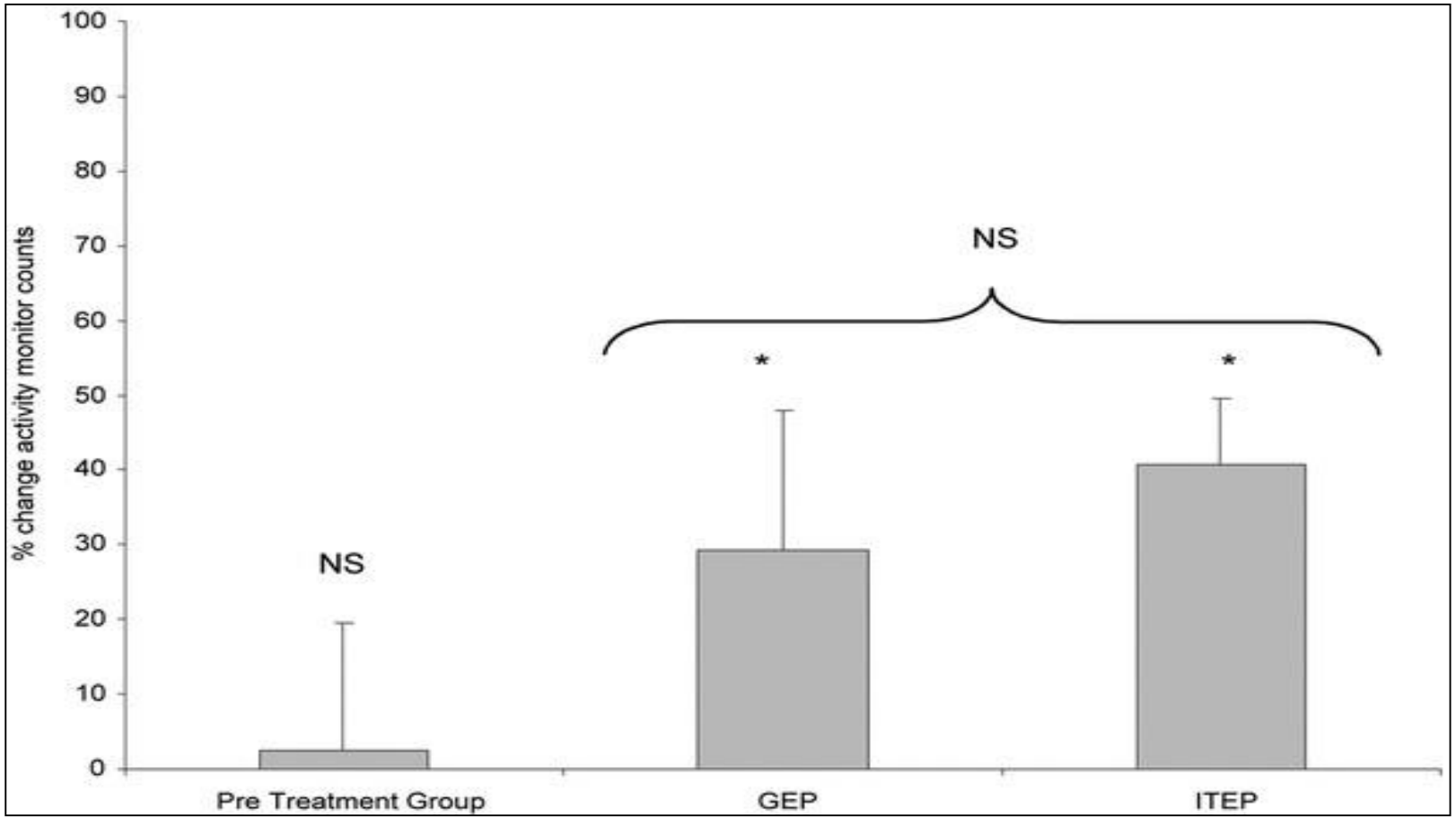


Table 3—*Prerehabilitation and Mean Change Results for Measures of Self-Reported Domestic Function, Health Status, and Exercise Performance**

Variables	GEP Group			ITEP Group		
	Pre-PR	Mean Change (95% CI)	p Value	Pre-PR	Mean Change (95% CI)	p Value
COPM performance	3.53 ± 1.17	1.71 (1.37–2.05)	0.0001†	3.96 ± 1.35	1.46 (1.05–1.87)	0.0001†
COPM satisfaction	2.91 ± 1.41	2.27 (1.74–2.81	0.0001†	3.18 ± 1.69	2.04 (1.56–2.52)	0.0001†
ISWT, m	154.83 ± 92.01	81.72 (63.83–99.62)	0.0001‡	198.62 ± 119.48	85.52 (67.62–103.42)	0.0001‡
ESWT, s	238.16 ± 169.54	511.21 (417–604.58)	0.0001‡	262.42 ± 197.76	435.39 (344.60–526.17)	0.0001‡
CRQ-SR						
Dyspnea	2.48 ± 1.05	0.89 (0.55–1.23)	0.0001†	2.45 ± 0.94	0.62 (0.26–0.97)	0.001†
Fatigue	3.08 ± 1.06	0.83 (0.52–1.14)	0.0001†	3.48 ± 1.28	0.53 (0.18–0.88)	0.004†
Emotion	4.00 ± 1.39	0.60 (0.26–0.93)	0.001†	4.25 ± 1.26	0.62 (0.33–0.92)	0.0001†
Mastery	3.88 ± 1.31	0.79 (0.47–1.10)	0.0001†	4.24 ± 1.43	0.66 (0.28–1.04)	0.002†

*Values given as mean ± SD or No., unless otherwise indicated. ESWT = endurance shuttle walking test; CRQ-SR = chronic respiratory questionnaire—self-reported.

†p Value on difference between week 1 and week 7 from Wilcoxon signed rank test.

‡p Value on difference between week 1 and week 7 from paired *t* test.

CONCLUSIONS

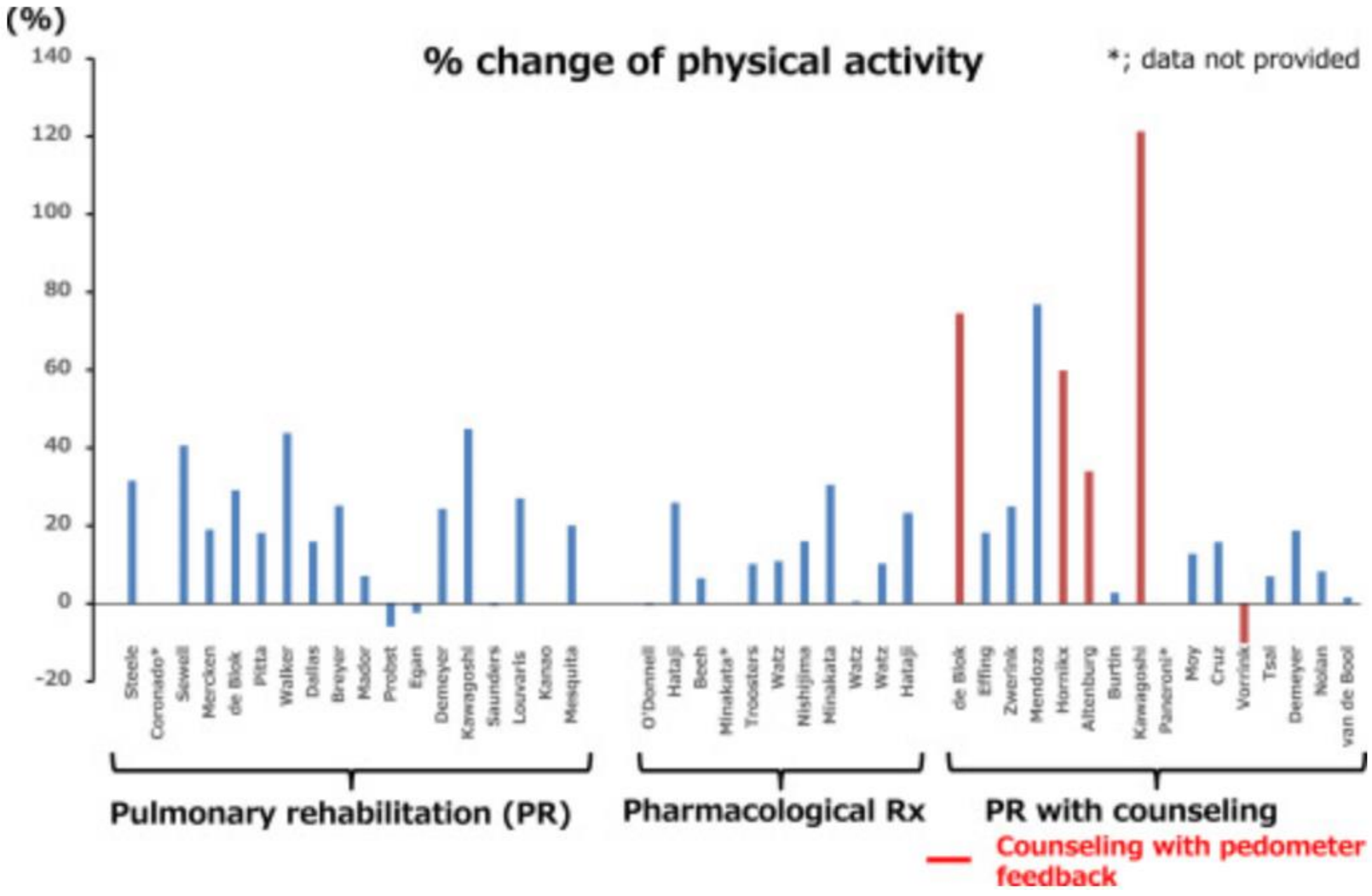
- Pulmonary rehabilitation improves domestic function and physical activity.

- This study also demonstrates that general exercise training is as effective as individually targeted training.

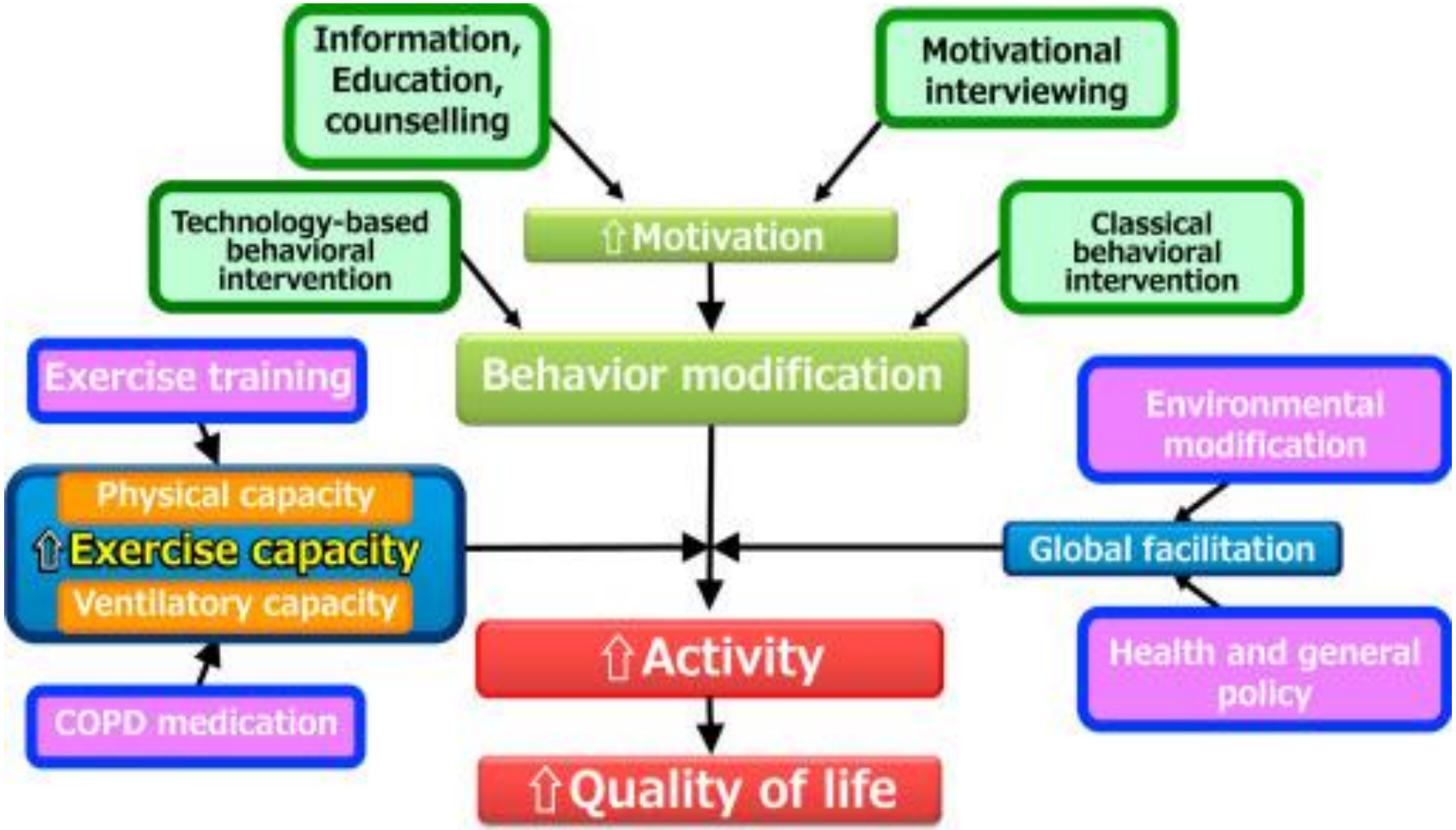
- **Effects of pharmacological treatment on physical activity in COPD**

Author (year)	Number of PTs, & Severity	Intervention Program	Accelerometer	Results	Exercise capacity
O'Donnell (2011)[69]	89 pts moderate-severe	8 wk Indacaterol vs Placebo	biaxial SenseWear	PA not changed	○
Hataji (2013)[70]	23 pts mild-very severe	8 wk Indacaterol no control	uniaxial LifeCoder	PA improved	○
Beeh (2014)[71]	112 pts moderate-severe	3 wk Aclidinium cross-over	biaxial SenseWear	PA improved	○
Minakata (2014)[72]	8 pts mild-severe	8 wk Turobuterol no control	triaxial Actimarker	PA not changed	×
Troosters (2014)[73]	238 pts moderate	24 wk Tiotropium vs Placebo	biaxial SenseWear	PA not changed	NA
Watz (2014)[74]	120 pts moderate	3 wk Indacaterol cross-over	biaxial SenseWear	PA improved	NA
Nishijima (2015)[75]	18 pts moderate-severe	12 wk Indacaterol no control	uniaxial LifeCorder	PA improved	NA
Minakata (2015)[76]	21 pts mild-very severe	4 wk *various LABD* no control	triaxial Actimarker	PA improved	○
Watz (2016)[77]	194 pts moderate-severe	3 wk Indacaterol/Glycopyrronium cross-over	biaxial SenseWear	PA improved	NA
Watz (2017)[78]	134 pts moderate-severe	8 wk Formoterol/Aclidinium (4wk Behavior intervention) vs Placebo	triaxial Dynaport MoveMonitor	PA improved	○
Hataji (2017)[79]	20 pts moderate-severe	4 wk Tiotropium/Oldaterol no control	uniaxial Lifecorder	PA improved	○

Percentage changes of physical activity from baseline



A putative model to improve physical activity levels in COPD



Summary

- **Findings in both categories were inconsistent.**
  - **19 studies showed a positive effect with PR whereas 13 showed no effect.**
  - **8 studies showed a positive effect, while 3 revealed no effect from pharmacological intervention.**

- **Both interventions increase exercise capacity without a consistent effect on PA**
- **→ counseling with behavioral changes may be necessary**

- **Changing PA behavior in COPD**
  - **interdisciplinary approach involving specialists in respiratory medicine, rehabilitation, social, and behavioral sciences.**

- **Future research**
  - **interaction of pharmacological and non-pharmacological interventions.**

-Respiratory investigation56(2018) 292-306

Open Access Protocol

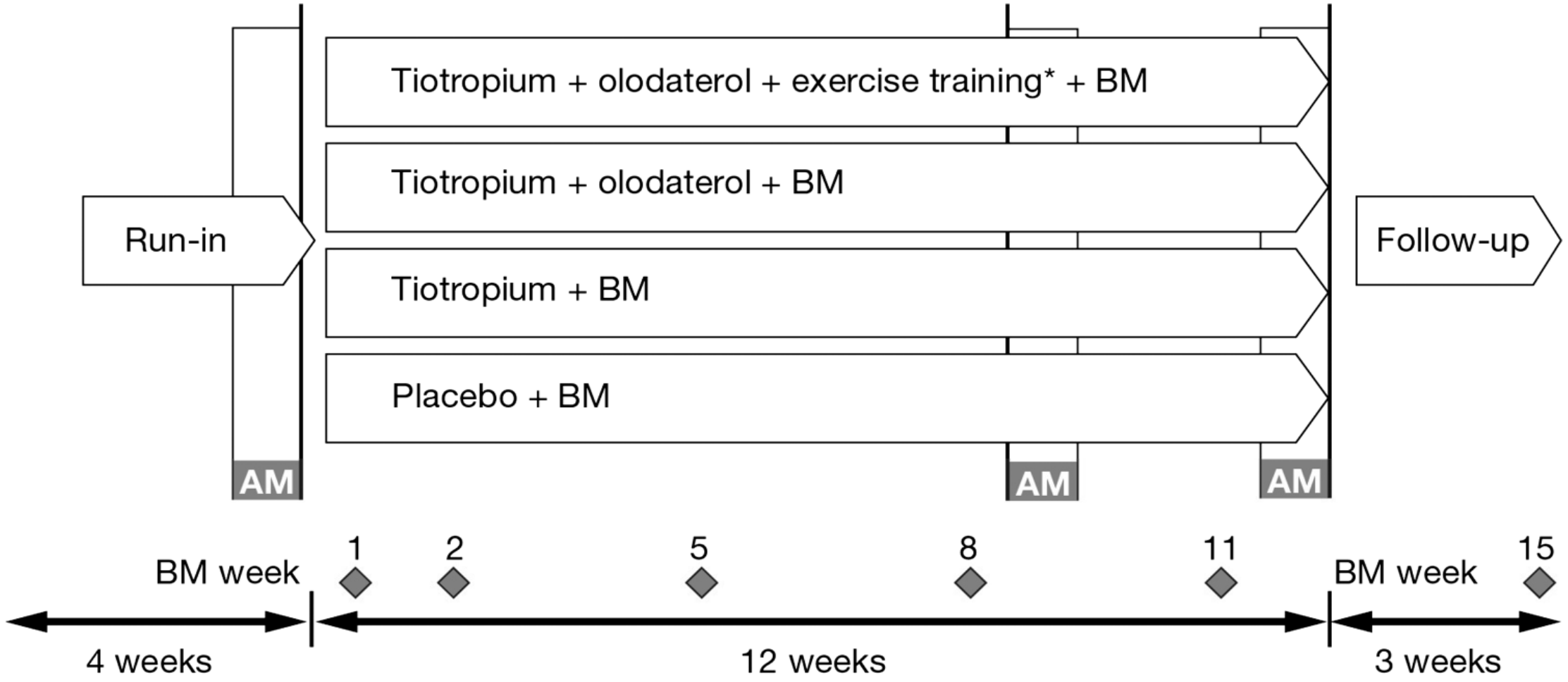
BMJ Open

Enhancing exercise tolerance and physical activity in COPD with combined pharmacological and non-pharmacological interventions: PHYSACTO randomised, placebo-controlled study design

Thierry Troosters,[1] Jean Bourbeau,[2] François Maltais,[3] Nancy Leidy,[4] Damijan Erzen,[5] Dorothy De Sousa,[6] Lawrence Korducki,[7] Alan Hamilton[6]

- Troosters T, et al. BMJ Open 2016

PHYSACTO trial design



- PHYSACTO trial design. *Eight weeks only. AM, activity monitoring, 1 week; BM, behaviour modification at weeks 1,2, 5, 8, 11 and 15.

Trial end points and safety assessments

Table 2 Trial end points and safety assessments

	End point	Time
Primary end point	Endurance time during ESWT to symptom limitation at 85% of VO_2 peak	Week 8
Secondary end point	Average daily walking time measured by activity monitor	Week prior to week 12 visit
Secondary end point	Average daily walking intensity measured by activity monitor	Week prior to week 12 visit
Secondary end point	Perceived ease/difficulty with daily activities assessed by FPI-SF	Week 12
Secondary end point	Endurance time during ESWT to symptom limitation at 85% of VO_2 peak	Week 12
Secondary end point	1 h postdose FEV_1	Week 8
Secondary end point	1 h postdose forced vital capacity	Week 8
Secondary end point	Resting inspiratory capacity measured at 1.5 h postdose	Week 8
Further efficacy end point	PROactive daily difficulties domain and amount domain scores	Week 12/weeks 8, 12
Further efficacy end point	Distance measured during 6MWT	Weeks 8, 12
Further efficacy end point	Intensity of breathing discomfort during 6MWT: pre-exercise, during exercise and at end-exercise	Weeks 8, 12
Further efficacy end point	Intensity of breathing discomfort during ESWT: pre-exercise, during exercise and at end-exercise	Weeks 8, 12
Further efficacy end point	Average number of steps per day measured by the activity monitor	Week preceding week 9 visit, week preceding week 12 visit
Further efficacy end point	Health status measured by SGRQ	Weeks 9, 12
Safety assessments	Heart rate and blood pressure in conjunction with spirometry	Weeks 1, 8, 12
Safety assessments	Heart rate, oxygen saturation and blood pressure in conjunction with exercise testing	Weeks 8, 12
Safety assessments	All adverse events (including physical examination) until end of study	Throughout
Other outcomes	A multivariate regression analysis of the following factors that may affect activity: motivation, self-efficacy, cognitive function, depression, anxiety, baseline level of activity, 6MWT distance, BMI, sex, age, waist circumference, rescue medication use, and external and internal barriers (eg, environmental/seasonal, social, economic)	

6MWT, 6 min walk test; BMI, body mass index; ESWT, endurance shuttle walk test; FEV_1, forced expiratory volume in 1 s; FPI-SF, Functional Performance Inventory—Short Form; SGRQ, St George's Respiratory Questionnaire; VO_2 peak, predicted maximum oxygen consumption.

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Effect of Bronchodilation, Exercise Training, and Behavior Modification on Symptoms and Physical Activity in Chronic Obstructive Pulmonary Disease

Thierry Troosters[1,2], François Maltais[3], Nancy Leidy[4], Kim L. Lavoie[5,6], Maria Sedeno[7], Wim Janssens[8,9], Judith Garcia-Aymerich[10], Damijan Erzen[11], Dorothy De Sousa[12], Lawrence Korducki[13], Alan Hamilton[12], and Jean Bourbeau[7]

Am J Respir Crit Care Med. 2018 Oct 15

Overview of the Self-Management Behavior Modification Program

Week	Session Type	Assessment and Education	Questionnaires
1	Induction; individual	Assessment of current level of PA Assessment of readiness and motivation Goal setting Pedometer technique	PA Outcome Expectancies PCS (PA) TSRQ (PA)
2	Group session 1	COPD disease education Benefits of PA Readiness and motivation Goal setting with pedometer	Stage of change (PA) Motivation Self-efficacy
5	Group session 2	Readiness and motivation Follow-up on goals Breathing and energy-conservation techniques	PA Outcome Expectancies PCS (PA) TSRQ (PA)
8	Group session 3	Readiness and motivation Follow-up on goals Stress-management techniques	Stage of change (PA) Motivation Self-efficacy
11	Group session 4	Readiness and motivation Follow-up on goals Healthy life habits	PA Outcome Expectancies PCS (PA) TSRQ (PA)
15	Follow-up; individual	Readiness and motivation Follow-up on goals	Stage of change (PA) Motivation Self-efficacy

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; PA = physical activity; PCS = Perceived Competence Scale; TRSQ = Treatment Self-Regulation Questionnaire.
Adapted by permission from Reference 20.

Endpoint Classification of Improvements in Lung Function and Exercise Tolerance

Concept of Interest	Endpoint	SMBM	Tiotropium	Tiotropium/Olodaterol	ExT
Lung function	FEV_1 FVC IC		✓	✓✓	
Exercise tolerance	EET during ESWT 6MWT		✓	✓	✓✓
Physical activity (amount)	Steps per day Daily walking time	✓		[✓]	[✓]
Physical activity (intensity)	Daily walking intensity	✓			✓
Activity-related difficulty	FPI-SF		(✓)	(✓)	(✓)
Physical activity experience	D-PPAC (amount and difficulty domains)	(A)	(D)	(D)	(D)

Definition of abbreviations: 6MWT = 6-minute-walk test; A = activity; COPD = chronic obstructive pulmonary disease; D = difficulty; D-PPAC = daily version of the PROactive Physical Activity in COPD; EET = exercise endurance time; ESWT = endurance shuttle walk test; ExT = exercise training; FPI-SF = Functional Performance Inventory Short Form; IC = inspiratory capacity; SMBM = self-management behavior modification.
Checks show where direct action of an intervention is anticipated, and a double check means a greater effect is expected than a single check. Parentheses indicate hypothetical relations, as these are novel endpoints; brackets indicate mixed results in the literature.

Baseline Characteristics, by Treatment Group (Full Analysis Set)

	SMBM + Placebo (*n* = 65)	SMBM + Tiotropium (*n* = 67)	SMBM + Tiotropium/Olodaterol (*n* = 72)	SMBM + Tiotropium/Olodaterol + ExT (*n* = 70)
Male	46 (70.8)	51 (76.1)	45 (62.5)	42 (60.0)
Age, yr	64.2 ± 6.5	65.4 ± 6.3	64.9 ± 6.9	64.7 ± 6.5
Body mass index, kg/m^2	28.6 ± 4.8	27.3 ± 4.6	27.1 ± 4.9	27.8 ± 5.6
Smoking history				
Ex-smoker	41 (63.1)	45 (67.2)	45 (62.5)	44 (62.9)
Current smoker	24 (36.9)	22 (32.8)	27 (37.5)	26 (37.1)
Medication use				
ICS	30 (46.2)	34 (50.7)	36 (50.0)	32 (45.7)
LABA	41 (63.1)	41 (61.2)	45 (62.5)	38 (54.3)
LAMA	45 (69.2)	41 (61.2)	42 (58.3)	51 (72.9)
Post-bronchodilator FEV_1 at screening, L	1.64 ± 0.57	1.63 ± 0.44	1.63 ± 0.42	1.53 ± 0.50
% predicted normal	56 ± 14	57 ± 13	59 ± 11	57 ± 13
Change from prebronchodilator, L	0.20 ± 0.14	0.20 ± 0.16	0.22 ± 0.15	0.18 ± 0.15
FEV_1/FVC	49.5 ± 10.6	49.9 ± 10.6	50.4 ± 10.2	48.9 ± 9.9
GOLD stage				
1 (≥80%)	2 (3.1)	0 (0.0)	0 (0.0)	0 (0.0)
2 (50% to <80%)	41 (63.1)	47 (70.1)	55 (76.4)	49 (70.0)
3 (30% to <50%)	22 (33.8)	20 (29.9)	17 (23.6)	21 (30.0)
EET during ESWT, s	272 ± 173	288 ± 183	309 ± 196	318 ± 224
EET during ESWT, s, geometric mean ± SE	227 ± 17	240 ± 18	254 ± 19	250 ± 21
Distance covered during 6MWT, m	453 ± 100	461 ± 89	458 ± 103	449 ± 91

Definition of abbreviations: 6MWT = 6-minute-walk test; EET = exercise endurance time; ESWT = endurance shuttle walk test; ExT = exercise training; GOLD = Global Initiative for Chronic Obstructive Lung Disease; ICS = inhaled corticosteroid; LABA = long-acting β_2-agonist; LAMA = long-acting muscarinic antagonist; SMBM = self-management behavior modification.
Data presented as *n* (%) or mean ± SD unless otherwise noted.

Geometric mean exercise endurance time (EET)

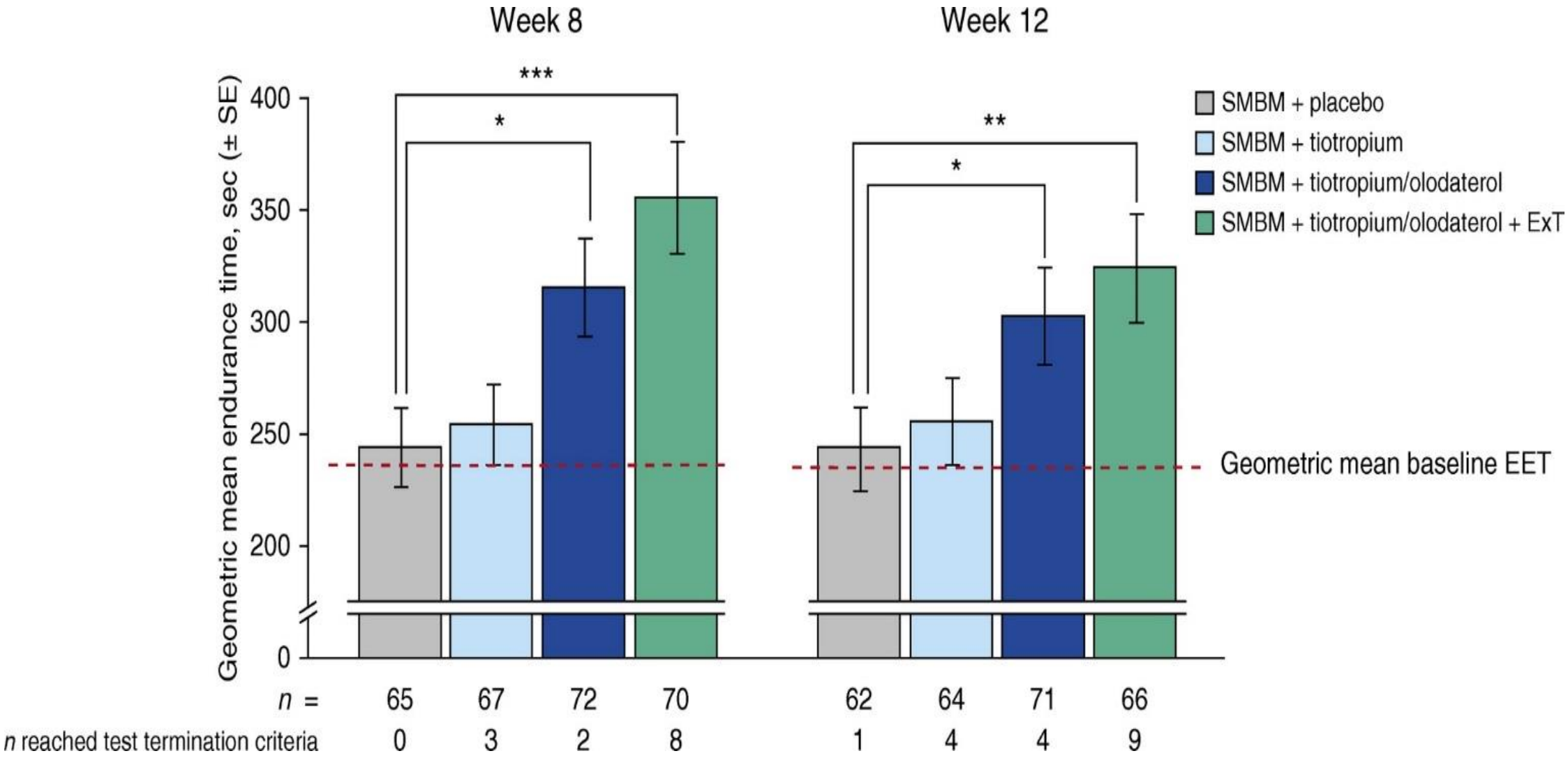

Figure 2. Geometric mean exercise endurance time (EET) during endurance shuttle walk test at Weeks 8 and 12 (full analysis set). Geometric mean results reported as primary analysis based on log10-transformed data. Exercise training (ExT) was stopped after 8 weeks in the SMBM plus tiotropium/olodaterol plus ExT arm; all treatment arms continued study medication until Week 12. Geometric mean baseline EET: 242.73 ± 9.42 seconds (Week 8); 241.96 ± 9.36 seconds (Week 12). Test termination time limit was 20 minutes. Results for change from baseline are provided in Figure E1. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.
SMBM = self-management behavior modification.

Adjusted Mean (SE) Change from Baseline in Key Variables

	Time (*wk*)	SMBM + Placebo (*n* = 65)*	SMBM + Tiotropium (*n* = 67)*	SMBM + Tiotropium/Olodaterol (*n* = 72)*	SMBM + Tiotropium/Olodaterol + ExT (*n* = 70)*
FEV_1, L	Δ8	0.00 ± 0.03	**0.18 ± 0.03**†	**0.36 ± 0.03**†	**0.33 ± 0.03**†
	Δ12	0.01 ± 0.03	**0.19 ± 0.03**†	**0.33 ± 0.03**†	**0.29 ± 0.03**†
EET, s, arithmetic mean‡	Δ8§	23 ± 30	47 ± 30	104 ± 29†	**172 ± 29**†
	Δ12	31 ± 30	62 ± 29†	91 ± 28†	**146 ± 29**†
Steps per day	Δ9	922 ± 325†	676 ± 325	1,147 ± 320†	594 ± 314
	Δ12	1,098 ± 325†	**153 ± 318**	1,394 ± 310†	557 ± 318
CRQ-SAS dysp	Δ9	0.17 ± 0.10	0.36 ± 0.10†	**0.50 ± 0.10**†	0.45 ± 0.10†
	Δ12	0.24 ± 0.10†	0.35 ± 0.10†	**0.59 ± 0.10**†	**0.71 ± 0.10**†
D-PPAC total	Δ9	3.10 ± 0.90†	5.13 ± 0.94†	5.48 ± 0.93†	5.19 ± 0.90†
	Δ12	1.65 ± 0.96	3.61 ± 0.99†	**5.76 ± 0.96**†	**5.31 ± 0.93**†

Definition of abbreviations: CRQ-SAS dysp = dyspnea domain of the CRQ questionnaire; D-PPAC total = daily PROactive physical activity total score; EET = exercise endurance time; ExT = exercise training; SMBM = self-management behavior modification.

Variables are ordered from lung function to exercise tolerance, physical activity, symptoms in daily life, and activity experience. FEV_1 is post-dose FEV_1. Bold font indicates a response significantly different from SMBM.

*Full analysis set; number analyzed varies slightly by endpoint and time point.

†$P < 0.05$ compared with baseline.

‡We have expressed the arithmetic mean EET in this table for consistency with change from baseline for the other measurements, rather than the geometric mean as per the primary endpoint.

§Primary endpoint.

Adjusted mean Chronic Respiratory Questionnaire–Self Administered Standardized (CRQ-SAS) dyspnea domain

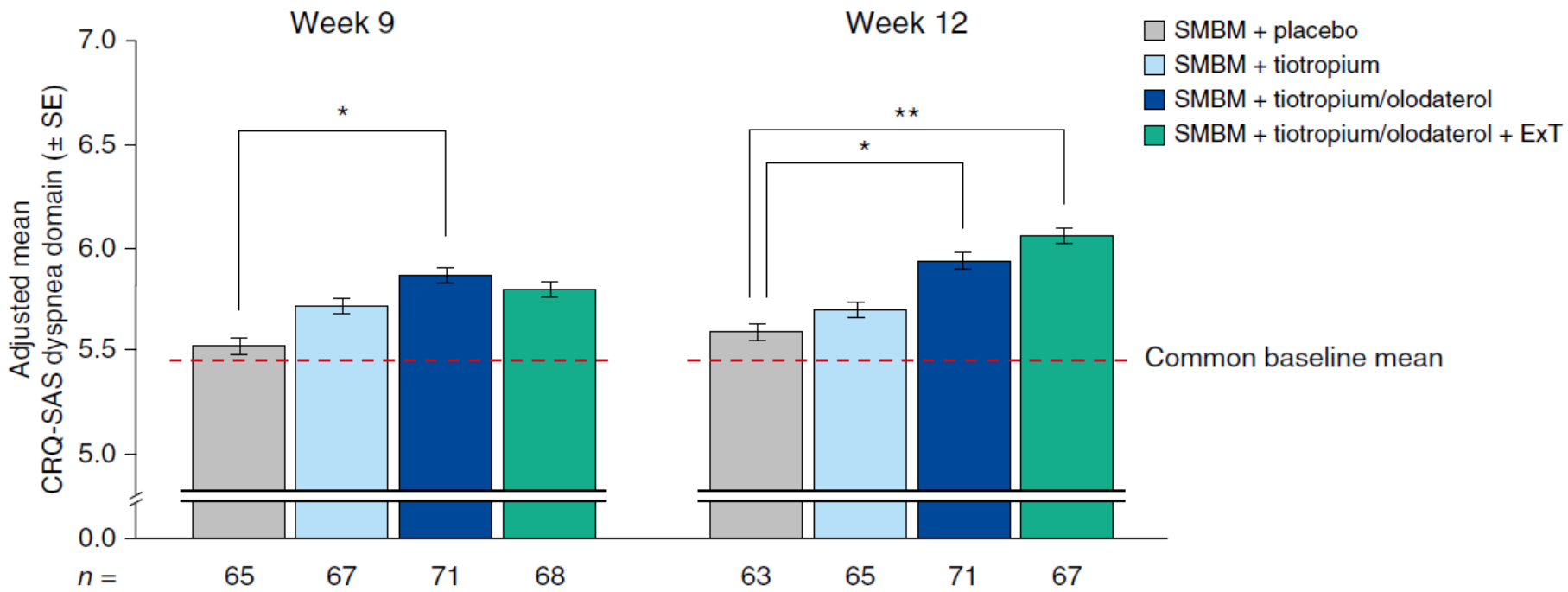

Figure 4. Adjusted mean Chronic Respiratory Questionnaire–Self Administered Standardized (CRQ-SAS) dyspnea domain at Weeks 9 and 12 (full analysis set). A positive change in the CRQ-SAS dyspnea domain score means less dyspnea experienced by the patient. Common baseline mean: 5.36 ± 0.07 (Week 9); 5.35 ± 0.07 (Week 12). Results for change from baseline are provided in Figure E3. *$P < 0.05$; **$P < 0.01$. ExT = exercise training; SMBM = self-management behavior modification.

Adjusted mean Functional Performance Inventory Short Form (FPI-SF) total score

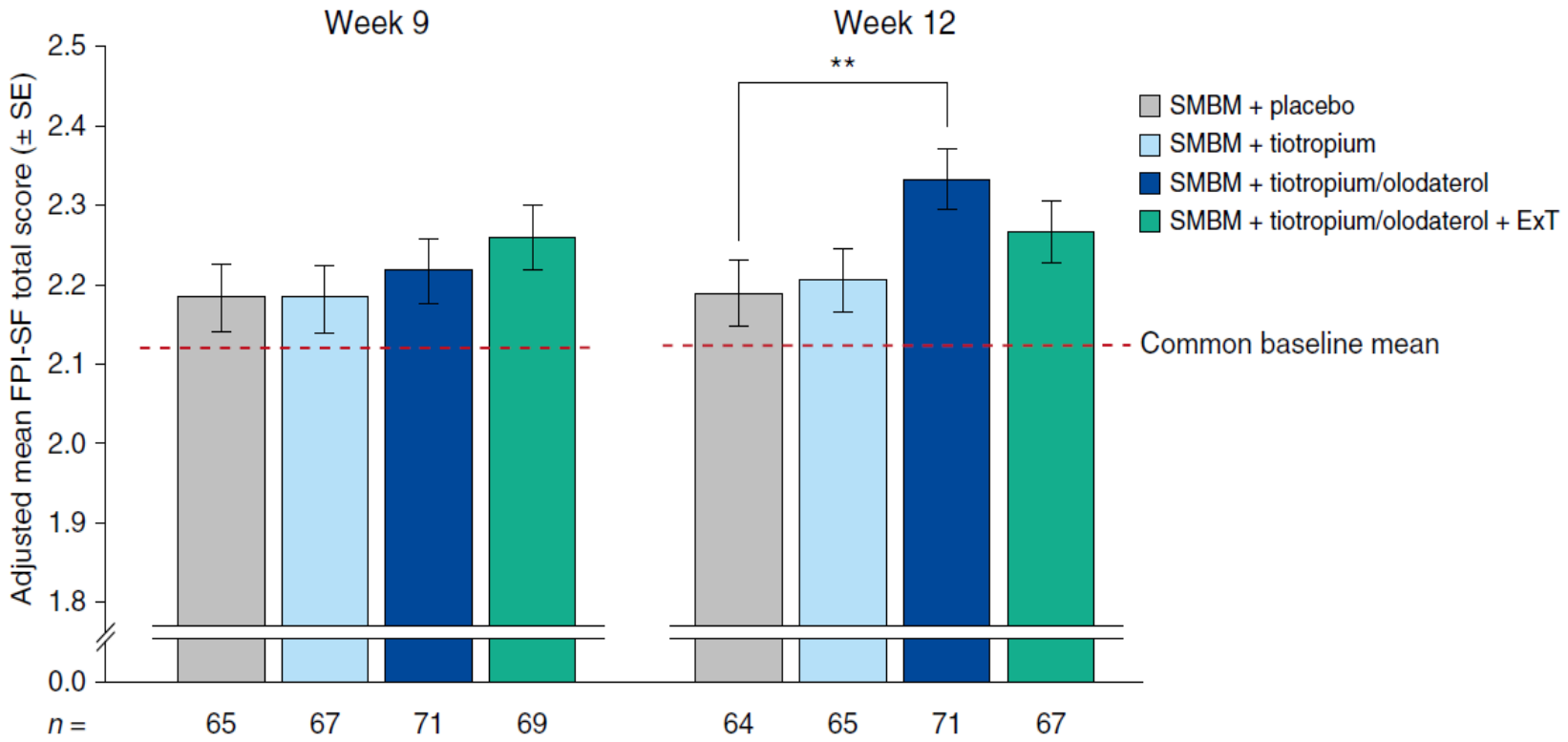

Figure 5. Adjusted mean Functional Performance Inventory Short Form (FPI-SF) total score at Week 9 and Week 12 (full analysis set). A positive change in FPI-SF total score means less difficulty for the patient. Common baseline mean: 2.124 ± 0.029 (Week 9); 2.126 ± 0.030 (Week 12). Results for change from baseline are provided in Figure E4. $^{**}P < 0.01$. ExT = exercise training; SMBM = self-management behavior modification.

Adjusted mean daily version of the PROactive Physical Activity

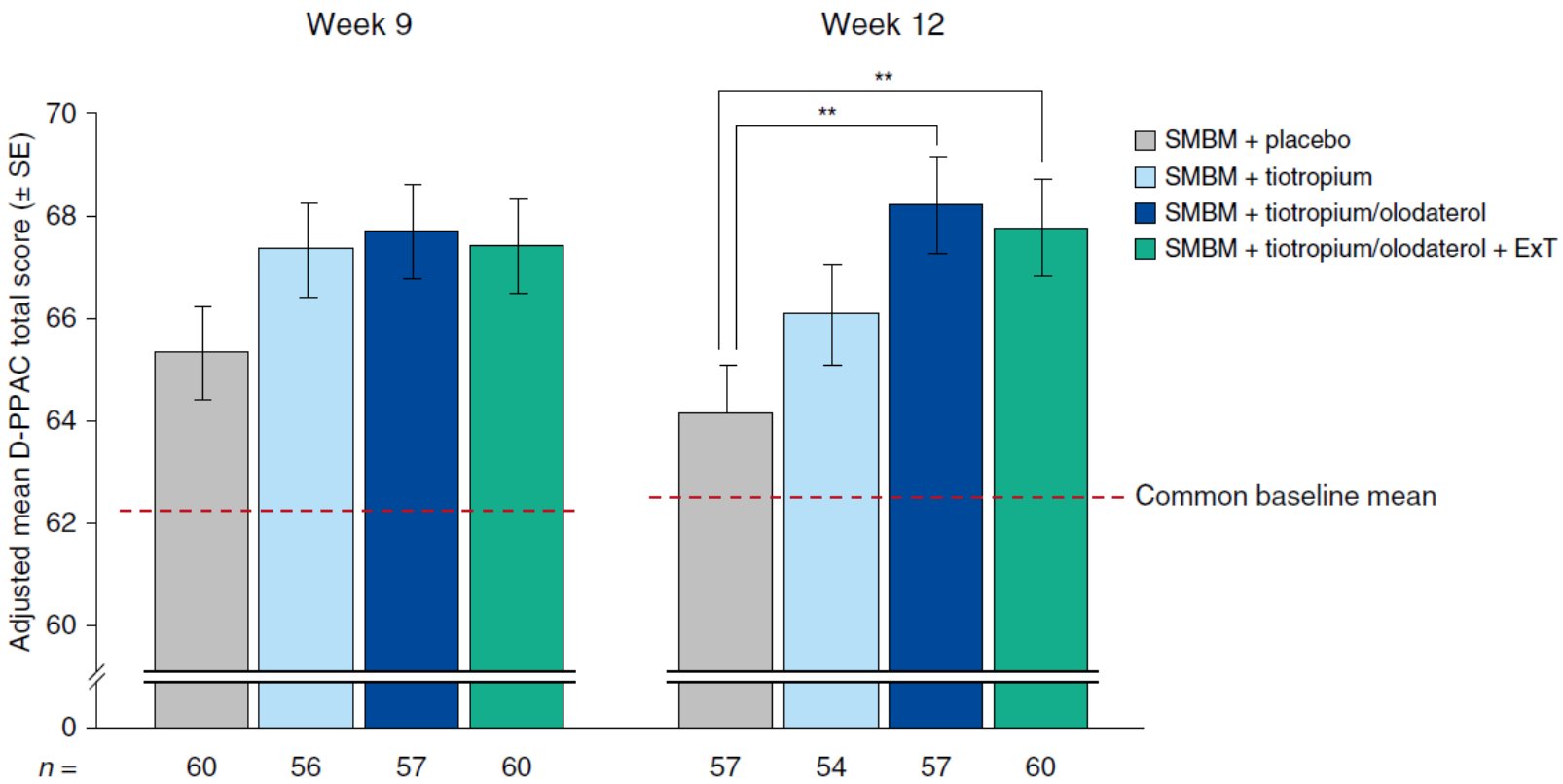

Figure 6. Adjusted mean daily version of the PROactive Physical Activity in Chronic Obstructive Pulmonary Disease (D-PPAC) average total score at Weeks 9 and 12 (full analysis set). A positive change in D-PPAC average total score means a better physical activity experience for the patient. Common baseline mean: 62.20 ± 0.66 (Week 9); 62.45 ± 0.68 (Week 12). Results for change from baseline are provided in Figure E5. $^{**}P < 0.01$. ExT = exercise training; SMBM = self-management behavior modification.

Conclusions

- **Exercise-tolerance improvements require physiologic improvements in lung function, muscle function, or both, as demonstrated with treatment including bronchodilators with or without ExT.**

- **SMBM seems to play an important role in the improvement of objectively measured PA, even in the absence of improvements in exercise capacity.**

- **Improvements in PA experience and dyspnea symptoms**
  - **best served by the addition of dual bronchodilation and ExT to the SMBM program**

Summary

- **Physical activity by pulmonary rehabilitation or medical Tx**
- PHYSACTO trial design
- PHYSACTO trial Results
  - Synergistic Action of Pulmonary Rehabilitation with Bronchodilator


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