Validity and responsiveness of the Daily- and Clinical visit-PROactive Physical Activity in COPD (D-PPAC and C-PPAC) instruments

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SUPPLEMENTARY MATERIAL

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METHODS (complete version)

Study Design and Subjects

We retrospectively pooled data from seven prospective randomised controlled trials testing the effect of pharmacological and non-pharmacological interventions in COPD patients from 17 countries in Europe and North America. Briefly, the ACTIVATE study (NCT02424344) evaluated the effects of aclidinium/formoterol on lung hyperinflation, exercise capacity and objective physical activity in GOLD II-III COPD patients, and used D-PPAC instrument daily during one week at baseline and at 8 weeks of follow-up[1]. The ATHENS study (NCT02437994) was an open label study conducted to assess pulmonary rehabilitation effectiveness on objective physical activity, exercise capacity and dyspnoea, and used C-PPAC instrument at baseline and at 12 weeks[2]. The EXOS study (ISRCTN:64759523) was an open label 3 arm study to assess the functional capacity of GOLD II-IV COPD patients following 6-9 weeks of pulmonary rehabilitation, inhaled bronchodilator (LAMA) therapy or placebo, and used D-PPAC instrument daily during one week at baseline[3]. MrPAPP study (NCT02158065) was a semi-automated tele coaching intervention designed to increase objective physical activity in COPD patients (all GOLD stages) after 12 weeks, and used both D-PPAC and C-PPAC instruments at baseline and at 12 weeks[4]. The PHYSACTO study (NCT02085161) evaluated the effects of tiotropium/olodaterol with/without exercise training on exercise capacity and objective physical activity in GOLD II-III COPD patients, and used D-PPAC instrument daily during one week at baseline and at 12 weeks[5]. The TRIGON-T9 (NCT02189577) 2-way crossover study was designed to demonstrate the superiority of glycopyrronium bromide vs. placebo over a 4-week treatment period in GOLD III-IV COPD patients, and used D-PPAC instrument daily during 14 days during the run-in period[6]. The URBAN TRAINING study

Garcia-Aymerich J, *et al. Thorax* 2021; 76:228–238. doi: 10.1136/thoraxjnl-2020-214554

(NCT01897298) assessed the long-term efficacy and effectiveness of a behavioural and community-based exercise intervention (Urban Training) to increase objective physical activity in patients with COPD (all GOLD stages), and used C-PPAC instrument at baseline and at 12 months[7]. Trials contributed differently to the evaluation of different measurement properties depending on when D-PPAC and C-PPAC were measured (Figure 1). Briefly, all studies contributed to reliability-internal consistency and validity analyses with their baseline data; TRIGON-T9 contributed to reliability-test-retest analysis with baseline and 14 days data; ACTIVATE (bronchodilator intervention) contributed to responsiveness with baseline and 8 weeks data; PHYSACTO (bronchodilator with behavioural physical activity intervention), MrPAPP (behavioural physical activity intervention) and ATHENS contributed to responsiveness with baseline and 12 weeks data; and URBAN TRAINING (behavioural physical activity intervention) contributed to the responsiveness analysis with baseline and 12 months data. All trials recruited patients with stable COPD defined by spirometry (according to the American Thoracic Society and European Respiratory Society (ATS/ERS) criteria)[8] and invited all patients to answer one of the PPAC questionnaires (except in MrPAPP that answered both D-PPAC and C-PPAC) and record physical activity data by wearing activity monitors. Table S1 below provides details on each trial's purpose, inclusion and exclusion criteria, design and intervention. The studies were approved by appropriate institutional review boards. Written informed consent was obtained from all patients.

Measures

D-PPAC and C-PPAC instruments require both questionnaire and activity monitor data. Patients completed D-PPAC and/or C-PPAC questionnaires, which had been previously developed using appropriate qualitative and quantitative research methods and culturally

sensitive translations[9] and a rigorous item reduction process[10] following current European Medicines Agency (EMA)[11] and US FDA[12] published standards. More details on the development and initial validation of the D-PPAC and C-PPAC instruments is described elsewhere[10]. In brief, the D-PPAC questionnaire consists of 7-items with a daily recall, and needs to be completed every evening for a week via an electronic handled device. The C-PPAC questionnaire has 12-items with a one-week recall, and is completed at the day of each study visit in an electronic handled device, a web-based system or using paper and pen. Patients also wore one of the activity monitors validated to be part of the PPAC instruments (DynaPort MoveMonitor, McRoberts B.V., The Netherlands; or Actigraph G3Tx, Actigraph, Pensacola, FL, United States) during waking time in one week at each study visit. Data from individuals was considered valid if they recorded more than 8 h of wearing time on at least 3 days (not necessarily consecutive) within 1 week. We calculated D-PPAC and C-PPAC scores by combining questionnaire items with two variables from activity monitors (steps/day and vector magnitude units (VMU)/min) if there was a minimum of 3 days of simultaneously collected monitoring and questionnaire items. Both for D-PPAC and C-PPAC, three scores are generated (amount of physical activity, difficulty with physical activity and total physical activity experience) ranging from 0 to 100, where higher numbers indicate a better score. For the D-PPAC instruments, we obtained scores for each day and calculated a weekly mean of D-PPAC amount, difficulty and total scores. For the C-PPAC instruments, only a weekly measure for each score was obtained. D-PPAC and C-PPAC items and scoring equivalences are reported below. For additional description of the study sample we also retrieved time in moderate-to-vigorous physical activity per day (>3 metabolic equivalents, MVPA) from the activity monitor. Lung function was evaluated by spirometry after reversibility testing and exercise capacity by six-minute walking distance (6MWD). Patients also completed the modified Medical Research

Council Dyspnoea scale (mMRC), the Chronic Respiratory Disease Questionnaire (CRQ), the Clinical COPD Questionnaire (CCQ) and/or the COPD Assessment Test (CAT). We also recorded demographics, smoking history and clinical data (medical and COPD histories) from patients and medical records. Finally, patients participating in follow-up visits also rated the global change of their physical activity experience in amount, difficulty and overall since baseline to follow-up on a 7-point Likert-type scale, ranging from 'much worse' to 'much better' (see below).

Statistical Analysis

Using a two-sided α=0.05 and a power of 80%, we estimated that (i) 30 patients were required per stratum of sex, age, COPD severity, country and language in order to identify a statistically significant Cronbach's alpha ≥0.7 (for internal consistency), intraclass correlation ≥0.8 (for test-retest reliability) and correlations ≥0.5 (for convergent and discriminant validity), and that (ii) 23 patients were needed per group (in known-groups validity, responsiveness and ability to detect change) to detect a difference of minimum 10 points in PPAC scores between two groups equally sized assuming a standard deviation of 12 (based on own data). Calculations were done with the software GRANMO 7.10[13]. The analysis sets and statistical analysis plan were defined *a priori* based on study objectives. We used different study samples for the different measurement properties (Figure 1). All analyses were performed separately for D-PPAC and C-PPAC amount, difficulty and total scores.

Reliability was evaluated in terms of (i) internal consistency, by the Cronbach's alpha of D-PPAC daily scores and of C-PPAC scores, *a priori* defined as adequate: 0.7–0.9, in all subjects and stratified by sex, age group, COPD severity, country and language, and (ii) test-retest reproducibility, using intraclass correlation coefficients [ICC] and Bland-Altman plots

comparing the mean of D-PPAC scores from days 1-7 with the mean scores from days 8-14, *a priori* defined as adequate: ICC≥0.8; limit of agreement defined at the mean difference ± 2 standard deviations (SD). (Internal consistency of the total scores was not tested because total scores are calculated as the mean of amount and difficulty scores and not from a list of items). Convergent validity was explored by testing the Spearman correlations between D-PPAC and C-PPAC scores and related constructs, namely dyspnoea (mMRC), health-related quality of life (HRQoL) (CRQ, CCQ, CAT), exercise capacity (6MWD) and objective physical activity (MVPA). A matrix of expected correlations for each variable was built using bibliography at the time of analysis (see below in Table S2). Correlations with CCQ-total, 6MWD and MVPA were stratified by sex, age groups, COPD severity, country and language. We also tested the ability of the D-PPAC and C-PPAC scores to discriminate between groups *a priori* expected to have differences in physical activity experience (known-groups validity), using one-way ANOVA test and pairwise comparisons of means adjusting for multiple comparisons using Bonferroni correction: ATS/ERS COPD severity stages defined by spirometry (mild, moderate, severe and very-severe), groups defined by mMRC grades of dyspnoea (0, 1, 2, 3, and 4), and tertiles of 6MWD.

To quantify responsiveness (response to interventions and ability to detect change), we calculated the change (8 weeks, 12 weeks or 12 months minus baseline) and the standardised response mean (SRM, mean difference divided by SD of the difference) in (i) each intervention group, using each study separately (*a priori* expected significant differences ($p<0.05$) in the changes between groups and SRM>|0.5| in difficulty and total scores after bronchodilator and pulmonary rehabilitation interventions, and in amount and total scores after behavioural physical activity interventions, see below Table S3); (ii) groups defined by the self-reported global rating of change in physical activity experience, using a pooled dataset (*a priori*

expected significant differences (p<0.05) and SRM>|0.5| in PPAC scores between much worse/worse/slightly worse *vs* no change/slightly better, and better/much better *vs* no change/slightly better, see Table S3); and (iii) groups defined according to having had COPD exacerbations during follow-up, using a pooled dataset (*a priori* expected significant differences (p<0.05) and SRM>|0.5| in PPAC scores between those having any COPD exacerbation during follow-up *vs* none, see Table S3).

We established the MID by triangulation against the anchors 6MWD, CCQ and self-reported global rating of change in physical activity experience (only for the scores where the correlation between changes in scores and changes in anchor was >|0.3|)[14]. To provide insight on minimal detectable change (MDC), we calculated 0.5 of Cohen's effect size for D-PPAC and C-PPAC scores, and standard error of measurement (SEM) for D-PPAC scores. However, we did not aim to establish MDC because only one distribution-based estimate was available for C-PPAC. Analyses were performed using complete cases in STATA version 14 (StataCorp, College Station, TX, USA).

Table S1. Main characteristics of studies included in validation of D-PPAC and C-PPAC instruments.

Study name	**ACTIVATE**	**ATHENS**	**EXOS**	**MrPAPP**	**PHYSACTO**	**TRIGON-T9**	**URBAN TRAINING**
Sponsor	**AstraZeneca**	**Thorax Research Foundation**	**UK NHS Trust**	**KU Leuven**	**Boehringer Ingelheim**	**Chiesi Farmaceutici S.p.A.**	**ISGlobal**
CT number	NCT02424344	NCT02618746	ISRCTN 64759523	NCT02158065	NCT02085161	NCT02189577	NCT01897298
N included in PPAC validation	**229**	**52**	**22**	**330**	**282**	**87**	**313**
Key Inclusion criteria	GOLD II/III; Age ≥40 y; Current/ex-smokers; mMRC≥2; Willing to participate in a telecoaching program during four last weeks and to enhance their physical activity	All COPD patients entering pulmonary rehabilitation.	GOLD II-IV; MRC≥2; Age 40-85 years.	COPD of all stages.	GOLD II-III; Age >40 y; Current/ex-smokers.	FEV1<60% pred.; Age >40 y; Current/ex-smokers; Positive response to reversibility test defined as change in FEV1 ≥ 5%; BDI score ≤ 10; No exacerbations for at least 1 month.	Any COPD patient visiting a public primary care centre of five municipalities (Barcelona province); Age >45; clinical stability, defined as at least 4 weeks without antibiotics or oral corticosteroids.
Key exclusion criteria	Asthma; Hospitalized for acute exacerbation within 3 m prior to recruitment; Use of long-term oxygen therapy (≥ 15 hours/day); BMI≥40kg/m2; Evidence of clinically significant	Orthopaedic, neurological, and other musculoskeletal complaints that could impair normal movement patterns; Asthma; Hospital admission or COPD exacerbations	Co-morbidity that limits the ability to walk/ cycle (e.g. musculoskeletal, arthritic, or neurological disorders); Participation in rehabilitation over the last 12 months; Patients on long	Unable to increase physical activity; Asthma; Any complaints that impair normal biomechanical movement patterns, as judged by the investigator.	A limitation of exercise performance as a result of factors other than fatigue or excertional dyspnoea; A CI for exercise testing; Asthma; A completed rehabilitation	Asthma; Oxygen therapy for chronic hypoxia (at least 12 hours); Clinically significant cardiovascular condition.	Living >6 mths/year outside of the included municipalities; Mental disability; Comorbidity that could interfere with study tests; Severe psychiatric disease or severe

	respiratory and/or cardiovascular conditions; Pulmonary rehabilitation during at least 3 months prior to the screening	within the previous 4 weeks; Not on an optimal pharmacotherapy.	term oxygen therapy; Patients requiring oxygen therapy during the course of an exercise test (i.e. de-saturation documented <85%).		program in the 6 wks prior to screening, or currently in a rehabilitation program.		comorbidity limiting survival at one year.
Design	Double-blind, randomised, parallel group, placebo controlled, multicentre and multinational clinical trial	Randomised controlled trial open labelled	Randomised controlled trial cross over 2 groups (only baseline data used in PPAC validation)	Randomised controlled trial open labelled	Randomised controlled trial placebo controlled parallel groups	Randomised controlled trial double blind placebo controlled 2 way cross over study	Multicentre randomised controlled trial, blinded to outcome assessment
Intervention	Aclidinium bromide+ formoterol DPI FDC vs. Placebo; All patients take part in a coaching program.	Rehabilitation programme vs. placebo	n.a.	Telecoaching vs. Usual care program	Olodaterol + tiotropium vs. tiotropium vs. Behavioural modification; All supervised exercise training	Glycopyrrolate bromide (CHF 5259) *vs*. placebo	Urban training (behavioural intervention + unsupervised walking intervention) vs. Usual care
Phase	Ph4	n.a.	n.a.	n.a.	Ph3	Ph2b	n.a.
D-PPAC	Exploratory endpoint		Primary endpoint	Key 2nd endpoint	Key 2nd endpoint	Exploratory endpoint	
C-PPAC		Primary endpoint		Key 2nd endpoint			Exploratory endpoint
Activity Monitor(s) used in PPAC validation	Dynaport	Dynaport	ActiGraph	Dynaport	Dynaport	Dynaport	Dynaport

Length of study as used in PPAC validation	8 weeks	12 weeks	Baseline	12 weeks	12 weeks	2 weeks	12 months
Countries of recruitment	Canada, Germany, Hungary, Spain	Greece	UK	UK, Netherlands, Greece, Germany, Switzerland	Australia, Austria, Belgium, Canada, Denmark, Germany, New Zealand, Poland, Portugal, UK, USA	Bulgaria, Germany, Poland, UK	Spain

PROactive Physical Activity in COPD (PPAC) instruments

The PROactive Physical Activity in COPD (PPAC) instruments are **reproduced below** to help understanding the main manuscript but **CAN NOT** be used without a licensing agreement.

License to use D-PPAC and C-PPAC can be requested from the PROactive team, and will include a commitment to use and score the instruments as outlined in the Users Guide. This will guarantee that the estimates of PPAC scores are valid and reliable, and will increase interpretablibility across studies.

Only **approved translations** may be used. If new languages are required, the translation process must be agreed with the PROactive team who can provide a translation guidance document and perform developer review. All new translations and associated certification will be provided to the PROactive team as part of the licensing agreement, to maintain the integrity of the instruments.

The **User's Guide**, available from PROactive team, includes all details about context of use, development and validation process, instruments description, procedures to administer the questionnaire, procedures to use (and process data of) the activity monitors, data aggregation between questionnaires and activity monitors, scoring, and translations available.

Garcia-Aymerich J, *et al. Thorax* 2021; 76:228–238. doi: 10.1136/thoraxjnl-2020-214554

DAILY PROACTIVE PHYSICAL ACTIVITY IN COPD: D-PPAC

INSTRUCTIONS TO PATIENTS DAY 1:

Patients with chronic lung disease like you often report that they have problems during physical activity. By physical activity, we mean all activities that require movement of your body. Examples are household activities, walking, going to work, or getting dressed. However, please consider all activities you do, and not only these examples. We would like to know how you experienced your physical activity since you woke up TODAY.

Please complete this questionnaire in the evening before going to bed. Please select the box next to the response that best applies to you TODAY.

There are no wrong answers. We very much value your response.

INSTRUCTIONS FOR SUBSEQUENT DAYS:

We would like to know how you experienced your physical activity since you woke up TODAY. Please complete this questionnaire in the evening before going to bed. Please select the box next to the response that best applies to you TODAY.

	Difficulty score	Amount score
How much walking did you do outside today?		
☐ None at all		0
☐ A little bit (up to 10 minutes in total)		1
☐ Some (up to 30 minutes in total)		2
☐ A lot (up to 1 hour in total)		3
☐ A great deal (more than 1 hour in total)		4
How many chores did you do outside the house today? Some examples are gardening, taking the rubbish out, or doing small errands.		
☐ None at all		0
☐ A few		1
☐ Some		2
☐ A lot		3
☐ A large amount		4
How much difficulty did you have getting dressed today?		
☐ None at all	4	
☐ A little bit	3	
☐ Some	2	
☐ A lot	1	
☐ A great deal	0	
How often did you avoid doing activities because of your lung problems today?		
☐ Not at all	4	
☐ Rarely	3	
☐ Sometimes	2	
☐ Frequently	1	
☐ All the time	0	

How breathless were you in general during your activities today?				
☐ Not at all			4	
☐ A little bit			3	
☐ Moderately			2	
☐ Very			1	
☐ Extremely			0	
How tired were you in general during your activities today?				
☐ Not at all			4	
☐ A little bit			3	
☐ Moderately			2	
☐ Very			1	
☐ Extremely			0	
How often did you have to take breaks during your physical activities today?				
☐ Not at all			4	
☐ Rarely			3	
☐ Sometimes			2	
☐ Frequently			1	
☐ All the time			0	
Daily steps:	Measured by Actigraph	Measured by Dynaport		
	<1000	<1900		0
(please adhere to Users	1001-3000	1901-3700		1
Guide procedures)	3001-5000	3701-5500		2
	5001-7000	5501-7300		3
	>7000	>7300		4
Daily VMU/min:	Measured by Actigraph	Measured by Dynaport		
	<100	<50		0
(please adhere to Users	101-200	51-110		1
Guide procedures)	201-300	111-190		2
	301-400	191-270		3
	401-600	271-440		4
	>600	>440		5

	Difficulty raw score	**Amount raw score**
Sum above:		

	Difficulty score	**Amount score**
See equivalences raw-Rasch:		

Total score (average of amount and difficulty)

Table of equivalences between D-PPAC raw scores and D-PPAC 0-100 Rasch scaled scores:

Difficulty score				**Amount score**			
raw	***Rasch 0-100***	**raw**	***Rasch 0-100***	**raw**	***Rasch 0-100***	**raw**	***Rasch 0-100***
0	*0*	11	*56*	0	*0*	11	*57*
1	*10*	12	*59*	1	*10*	12	*61*
2	*20*	13	*62*	2	*19*	13	*65*
3	*26*	14	*65*	3	*25*	14	*71*
4	*32*	15	*68*	4	*31*	15	*80*
5	*36*	16	*72*	5	*35*	16	*90*
6	*40*	17	*77*	6	*39*	17	*100*
7	*43*	18	*84*	7	*43*		
8	*46*	19	*92*	8	*47*		
9	*49*	20	*100*	9	*50*		
10	*52*			10	*54*		

CLINICAL VISIT PROACTIVE PHYSICAL ACTIVITY IN COPD: C-PPAC

INSTRUCTIONS TO PATIENTS:

Patients with chronic lung disease like you often report that they have problems during physical activity. By physical activity, we mean all activities that require movement of your body. Examples are household activities, walking, going to work, or getting dressed. However, please consider all activities you do, and not only these examples. We would like to know how you experienced your physical activity IN THE PAST 7 DAYS.

Please select the box next to the response that best applies to you IN THE PAST 7 DAYS.

There are no wrong answers. We very much value your response.

	Difficulty score	Amount score
In the past 7 days, how much walking did you do outside?		
☐ None at all		0
☐ A little bit (about 10 minutes every day)		1
☐ Some (about 30 minutes every day)		2
☐ A lot (about 1 hour every day)		3
☐ A great deal (more than 1 hour every day)		3*
In the past 7 days, how many chores did you do outside the house? Some examples are gardening, taking the rubbish out, or doing small errands.		
☐ None at all		0
☐ A few		1
☐ Some		2
☐ A lot		3
☐ A large amount		4
In the past 7 days, how much difficulty did you have getting dressed?		
☐ None at all	4	
☐ A little bit	3	
☐ Some	2	
☐ A lot	1	
☐ A great deal	0	
In the past 7 days, how much difficulty did you have getting out and about?		
☐ None at all	4	
☐ A little bit	3	
☐ Some	2	
☐ A lot	1	
☐ A great deal	0	
In the past 7 days, how often did you avoid doing activities because of your lung problems?		
☐ Not at all	4	
☐ Rarely	3	
☐ Sometimes	2	
☐ Frequently	1	
☐ All the time	0	
In the past 7 days, how breathless were you in general during your activities?		
☐ Not at all	4	
☐ A little bit	3	
☐ Moderately	2	

☐ Very			1	
☐ Extremely			0	
In the past 7 days, how often did you lack physical strength to do things because of your lung problems?				
☐ Not at all			4	
☐ Rarely			3	
☐ Sometimes			2	
☐ Frequently			1	
☐ All the time			0	
In the past 7 days, how tired were you in general during your activities?				
☐ Not at all			4	
☐ A little bit			3	
☐ Moderately			2	
☐ Very			1	
☐ Extremely			0	
In the past 7 days, how often did you have to take breaks during your physical activities?				
☐ Not at all			4	
☐ Rarely			3	
☐ Sometimes			2	
☐ Frequently			1	
☐ All the time			0	
In the past 7 days, how breathless were you when walking on level ground indoors and outdoors?				
☐ Not at all			4	
☐ A little bit			3	
☐ Moderately			2	
☐ Very			1	
☐ Extremely			0	
In the past 7 days, how much time did you need to recover from your physical activities?				
☐ None at all			4	
☐ A little bit			3	
☐ Some			2	
☐ A lot			1	
☐ A great deal			0	
In the past 7 days, did you need to consider your lung problems when you planned your activities because of your lung problems? Examples are a trip out, an appointment or expecting visitors.				
☐ No			4	
☐ A little bit			3	
☐ Sometimes			2	
☐ A lot			1	
☐ A great deal			0	
Weekly mean steps of daily value: *(please adhere to Users Guide procedures)*	Measured by Actigraph	Measured by Dynaport		
	<1300	<1500		0
	1301-2200	1501-2500		1
	2201-4000	2501-4500		2
	4001-5700	4501-6500		3
	>5700	>6500		4

Weekly mean VMU/min of daily value: *(please adhere to Users Guide procedures)*	Measured by Actigraph	Measured by Dynaport		
	≤180	≤60		0
	181-260	61-130		1
	261-350	131-210		2
	351-490	211-370		3
	>490	>370		4
			Difficulty raw score	**Amount raw score**
		Sum above:		
			Difficulty score	**Amount score**
		See equivalences raw-Rasch:		
			Total score (average of amount and difficulty)	

* This is not a mistake. The last category should be scored 3.

Table of equivalences between C-PPAC raw scores and C-PPAC 0-100 Rasch scaled scores:

Difficulty score				**Amount score**	
raw	***Rasch 0-100***	**raw**	***Rasch 0-100***	**raw**	***Rasch 0-100***
0	*0*	21	*60*	0	*0*
1	*8*	22	*61*	1	*13*
2	*15*	23	*63*	2	*25*
3	*20*	24	*65*	3	*33*
4	*24*	25	*66*	4	*39*
5	*28*	26	*68*	5	*45*
6	*31*	27	*70*	6	*50*
7	*34*	28	*72*	7	*54*
8	*36*	29	*73*	8	*59*
9	*38*	30	*75*	9	*63*
10	*40*	31	*77*	10	*67*
11	*42*	32	*79*	11	*72*
12	*44*	33	*81*	12	*77*
13	*46*	34	*83*	13	*83*
14	*48*	35	*86*	14	*91*
15	*50*	36	*89*	15	*100*
16	*51*	37	*92*		
17	*53*	38	*94*		
18	*55*	39	*97*		
19	*56*	40	*100*		
20	*58*				

Global rating of change in physical activity experience

Instruction: This question should be used immediately before the patient completes other visit specific questionnaires. The investigator is to read out the question and response options to the patient. The patient's response should be noted in the e-CRF.

Rating of change; overall concept

The comparison to the time at which the patient answered the global rating of severity question (study start/randomisation) should be emphasised and the patient asked to think about the last week.

Compared to the start of the study –mention day and month-, how would you describe your experience with physical activity in the past week? *(please select one answer)*:
☐ Much worse
☐ Worse
☐ Slightly worse
☐ No change
☐ Slightly better
☐ Better
☐ Much better

Rating of change; amount domain

The comparison to the time at which the patient answered the global rating of severity question (study start/ randomisation) should be emphasised and the patient asked to think about the last week.

Compared to the start of the study –mention day and month-, how physically active have you been in the last week? *(amount) (please select one answer)*:
☐ Much less active
☐ Less active
☐ A little less active
☐ No change
☐ A little more active
☐ More active
☐ Much more active

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Rating of change; difficulty domain

The comparison to the time at which the patient answered the global rating of severity question (study start/ randomisation) should be emphasised and the patient asked to think about the last week.

Compared to the start of the study, how difficult was it to conduct your physical activity in the last week was: *(difficulty) (please select one answer)*:
☐ Much more difficult ☐ More difficult ☐ A little more difficult ☐ No change ☐ A little easier ☐ More easy ☐ Much more easy

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Table S2. Matrix of *a priori* hypothesised correlations of D-PPAC and C-PPAC scores with dyspnea, health-related quality of life, exercise capacity and objective physical activity level (convergent validity)

	Amount	Difficulty	Total
mMRC	-0.5 to -0.8	-0.3 to -0.5	-0.4 to -0.7
CRQ Dyspnea	0 to 0.3	0.5 to 0.8	0 to 0.6
CRQ Fatigue	0 to 0.3	0.5 to 0.8	0 to 0.6
CRQ Emotional	0 to 0.3	0.5 to 0.8	0 to 0.6
CRQ Mastery	0 to 0.3	0.5 to 0.8	0 to 0.6
CCQ Symptoms	0 to 0.3	-0.5 to -0.8	0 to -0.6
CCQ Functional	-0.3 to -0.5	-0.5 to -0.8	0 to -0.7
CCQ Mental	0 to -0.3	-0.5 to -0.8	0 to -0.6
CCQ Total	-0.3 to -0.5	-0.5 to -0.8	0 to -0.7
CAT Total	0 to -0.3	-0.5 to -0.8	0 to -0.6
6MWD	0.3 to 0.5	0.5 to 0.8	0.3 to 0.7
MVPA	0.5 to 0.8	0 to 0.3	0 to 0.7

Table S3. *A priori* hypothesised statistically significant differences (p<0.05) in the changes between groups and/or SRM>|0.5| (responsiveness).

	Amount	Difficulty	Total
Interventions			
Bronchodilator interventions			
ACTIVATE		X	X
PHYSACTO		X	X
Pulmonary rehabilitation interventions			
ATHENS		X	X
Behavioural physical activity interventions			
MrPAPP	X		X
URBAN TRAINING	X		X
Self-reported global rating of change			
Change in physical activity experience overall	X	X	X
Change in difficulty with physical activity		X	X
Change in amount of physical activity	X		X
COPD exacerbations during follow-up	X	X	X

Table S4. Baseline demographic and clinical characteristics of COPD patients included in the validation of D-PPAC and C-PPAC instruments, by study

	D-PPAC dataset n = 950					C-PPAC dataset n = 651		
	ACTIVATE	**EXOS**	**MrPAPP**	**PHYSACTO**	**TRIGON-T9**	**ATHENS**	**MrPAPP**	**URBAN TRAINING**
	m (SD) / n (%)	m (SD) / n (%)	m (SD) / n (%)	m (SD) / n (%)	m (SD) / n (%)	m (SD) / n (%)	m (SD) / n (%)	m (SD) / n (%)
n	229	22	330	282	87	52	286	313
Age (years)	62.5 (7.7)	64.5 (7.1)	66.4 (8.0)	64.7 (6.6)	62.2 (8.1)	67.1 (8.8)	66.9 (8.0)	68.6 (8.9)
Gender: male	135 (59)	17 (77)	209 (63)	184 (65)	52 (60)	42 (81)	183 (64)	261 (83)
Working status: employed	n.a.	3 (14)	45 (14)	n.a.	n.a.	6 (12)	35 (12)	38 (13)
Current smoker	143 (62)	3 (14)	85 (26)	107 (38)	56 (64)	10 (19)	74 (26)	73 (23)
BMI (kg/m^2)	27.1 (5.0)	26.0 (5.7)	26.4 (5.0)	27.6 (4.9)	27.0 (6.0)	27.3 (5.1)	26.3 (5.0)	28.3 (5.1)
Any cardiovascular disease	n.a.	3 (14)	62 (19)	95 (34)	18 (21)	n.a.	61 (21)	194 (63)
Diabetes	36 (16)	5 (23)	27 (8)	23 (8)	0 (0)	n.a.	25 (9)	87 (28)
Musculoskeletal disorders	n.a.	3 (14)	65 (20)	122 (43)	3 (3)	n.a.	58 (20)	37 (12)
FEV_1 (% predicted)	60.7 (10.7)	46 (20)	57 (22)	48 (13)	48 (12)	51 (20)	57 (22)	57 (18)
ATS/ERS stages:								
I - mild ($FEV_1 \geq 80\%$)	0 (0)	0 (0)	53 (16)	1 (0)	1 (1)	4 (8)	45 (16)	31 (10)
II - Moderate ($FEV_1 < 80\%$ and $\geq 50\%$)	181 (79)	8 (36)	136 (41)	123 (44)	41 (47)	23 (44)	119 (41)	166 (53)
III - Severe ($FEV_1 < 50\%$ and $\geq 30\%$	47 (21)	9 (41)	104 (32)	139 (49)	40 (46)	21 (40)	91 (32)	90 (29)
IV - very severe ($FEV_1 < 30\%$)	0 (0)	5 (23)	37 (11)	19 (7)	5 (6)	4 (8)	31 (11)	26 (8)
FVC (% predicted)	100 (17)	83 (14)	92 (23)	104 (20)	80 (14)	79 (19)	92 (23)	77 (17)
FEV_1/FVC (%)	50 (9)	43 (14)	49 (15)	47 (10)	48 (13)	48 (14)	49 (16)	54 (12)
6MWD (m)	n.a.	315 (105)	443 (105)	452 (100)	n.a.	400 (113)	445 (107)	487 (94)
Dyspnea (mMRC 0-4)	2.1 (0.3)	2.0 (0.8)	1.4 (1.0)	1.3 (0.9)	n.a.	2.3 (1.0)	1.5 (1.0)	1.2 (0.9)
Any COPD exacerbations last 12 m	61 (27)	19 (86)	167 (51)	21 (7)	n.a.	46 (89)	138 (48)	139 (46)

Any COPD exacerbations requiring admissions last 12 m	n.a.	3 (14)	50 (15)	13 (5)	n.a.	23 (44)	42 (15)	17 (6)
CRQ dyspnea (1-7)	n.a.	2.8 (1.1)	n.a.	5.3 (1.2)	n.a.	2.3 (0.7)	n.a.	n.a.
CRQ fatigue (1-7)	n.a.	4.1 (0.9)	n.a.	4.6 (1.2)	n.a.	1.7 (0.5)	n.a.	n.a.
CRQ emotional (1-7)	n.a.	4.8 (1.1)	n.a.	5.2 (1.1)	n.a.	3.4 (1.1)	n.a.	n.a.
CRQ mastery (1-7)	n.a.	4.7 (1.4)	n.a.	5.4 (1.2)	n.a.	2.0 (0.6)	n.a.	n.a.
CCQ symptoms (0-6)	n.a.	n.a.	1.9 (1.1)	n.a.	n.a.	n.a.	1.9 (1.0)	1.6 (1.1)
CCQ functional (0-6)	n.a.	n.a.	1.8 (1.3)	n.a.	n.a.	n.a.	1.8 (1.2)	1.3 (1.1)
CCQ mental (0-6)	n.a.	n.a.	1.4 (1.4)	n.a.	n.a.	n.a.	1.4 (1.4)	1.3 (1.4)
CCQ total (0-6)	n.a.	n.a.	1.8 (1.0)	n.a.	n.a.	2.1 (1.2)	1.8 (1.0)	1.4 (0.9)
CAT (0-40)	n.a.	20 (6)	n.a.	n.a.	n.a.	16.7 (8.2)	n.a.	12.3 (6.9)
Steps per day (n/day)	5982 (3915)	4500 (2347)	5786 (3700)	5697 (3760)	5230 (3878)	4246 (3014)	5627 (3457)	7673 (4247)
VMU/min	437 (256)	426 (243)	394 (294)	434 (306)	492 (282)	397 (194)	417 (331)	472 (324)
Time in moderate-to-vigorous physical activity (min/day)	94 (52)	13 (17)	89 (47)	92 (50)	88 (53)	n.a.	88 (43)	107 (50)
PPAC-amount (0-100)	57 (14)	48 (13)	52 (13)	54 (13)	59 (14)	63 (17)	68 (15)	73 (16)
PPAC-difficulty (0-100)	70 (14)	63 (12)	71 (15)	71 (14)	63 (12)	70 (17)	75 (13)	82 (15)
PPAC-total (0-100)	63 (10)	55 (8)	62 (11)	62 (10)	61 (9)	66 (14)	71 (11)	78 (12)

n.a. Variable not available in a specific study. BMI: body mass index; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; 6MWD: 6-minute walking distance; mMRC: modified medical research council dyspnea scale; CRQ: chronic respiratory questionnaire; CCQ: clinical chronic obstructive pulmonary disease questionnaire; CAT: chronic obstructive pulmonary disease assessment test; VMU: vector magnitude unit; PPAC: PROactive physical activity in COPD.

Garcia-Aymerich J, *et al. Thorax* 2021; 76:228–238. doi: 10.1136/thoraxjnl-2020-214554

Table S5. Countries and languages of COPD patients included in the validation of D-PPAC and C-PPAC instruments.

	D-PPAC dataset n=950	C-PPAC dataset n=651
	n (%)	n (%)
Country		
Australia	25 (3%)	
Austria	7 (1%)	
Belgium	119 (13%)	81 (12%)
Bulgaria	13 (1%)	
Canada	43 (5%)	
Denmark	17 (2%)	
Germany	336 (35%)	
Greece	82 (9%)	127 (20%)
Hungria	5 (1%)	
Netherlands	34 (4%)	19 (3%)
New Zealand	10 (1%)	
Poland	48 (5%)	
Portugal	5 (1%)	
Spain	15 (2%)	313 (48%)
Switzerland	45 (5%)	38 (6%)
UK	122 (13%)	73 (11%)
USA	24 (3%)	
Language		
Bulgarian	13 (1%)	
Danish	17 (2%)	
Dutch/Flemish	153 (16%)	100 (15%)
English	194 (20%)	73 (11%)
French	30 (3%)	
German	388 (41%)	38 (6%)
Greek	82 (9%)	127 (20%)
Hungarian	5 (1%)	
Polish	48 (5%)	
Portuguese	5 (1%)	
Spanish	15 (2%)	313 (48%)

Garcia-Aymerich J, *et al. Thorax* 2021; 76:228–238. doi: 10.1136/thoraxjnl-2020-214554

Table S6. Cronbach's alpha of D-PPAC and C-PPAC amount and difficulty scores (reliability, internal consistency).

D-PPAC			C-PPAC		
n ranging between 983 and 2075*	**Amount**	**Difficulty**	**n=651**	**Amount**	**Difficulty**
Day 1	0.79	0.84			
Day 2	0.77	0.87			
Day 3	0.78	0.87			
Day 4	0.78	0.88	Week 1	0.72	0.92
Day 5	0.81	0.89			
Day 6	0.78	0.88			
Day 7	0.77	0.89			

* N day 1=2075, n day 2=1764, n day 3=1758, n day 4=1714, n day 5=1645, n day 6=1454, n day 7=983

Table S7. Intraclass correlation coefficient (ICC) of week 1 mean vs week 2 mean of D-PPAC scores (reliability, test-retest reproducibility).

n=168	**Amount** ICC (95% CI)	**Difficulty** ICC (95% CI)	**Total** ICC (95% CI)
Week 1 vs week 2	0.84 (0.76-0.89)	0.86 (0.79-0.91)	0.87 (0.81-0.91)

Figure S1. Bland Altman plots (mean week 1 *vs* mean week 2) of D-PPAC amount, difficulty and total scores (test-retest reproducibility).

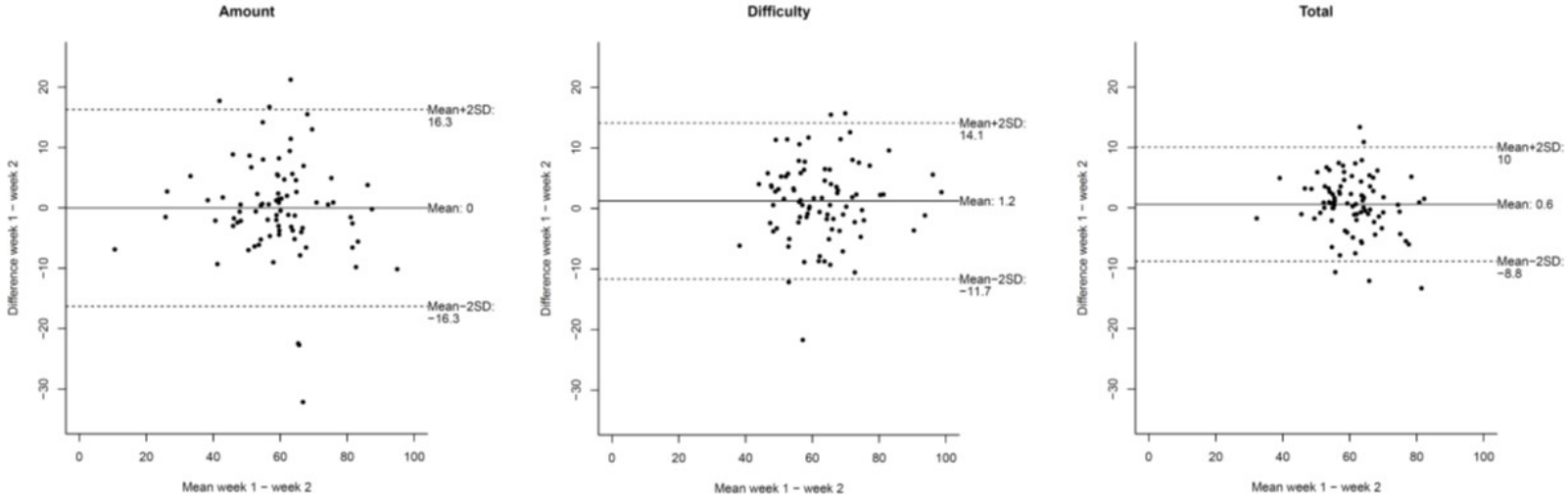

Table S8. Distribution of D-PPAC and C-PPAC scores according to COPD airflow severity groups, dyspnoea groups and exercise capacity groups (known-groups validity).

	D-PPAC						C-PPAC					
	Amount		Difficulty		Total		Amount		Difficulty		Total	
	m (SD)	*p-value**	m (SD)	*p-value**	m (SD)	*p-value**	m (SD)	*p-value**	m (SD)	*p-value**	m (SD)	*p-value**
ATS/ERS stages												
Mild	55 (12)	--	76 (14)	--	65 (10)	--	75 (13)	--	82 (14)	--	79 (11)	--
Moderate	56 (14)	*to mild: >0.999*	72 (14)	*to mild: 0.211*	64 (10)	*to mild: >0.999*	73 (14)	*to mild: >0.999*	82 (13)	*to mild: >0.999*	77 (11)	*to mild: >0.999*
Severe	54 (13)	*to mild: >0.999* *to moderate: 0.038*	68 (14)	*to mild: 0.001* *to moderate: 0.005*	61 (10)	*to mild: 0.014* *to moderate: <0.001*	67 (15)	*to mild: <0.001* *to moderate: <0.001*	74 (15)	*to mild: <0.001* *to moderate: <0.001*	71 (12)	*to mild: <0.001* *to moderate: <0.001*
Very severe	43 (12)	*to mild: <0.001* *to moderate: <0.001* *to severe: <0.001* *<0.001*	63 (13)	*to mild: <0.001* *to moderate: <0.001* *to severe: 0.014* *<0.001*	53 (10)	*to mild: <0.001* *to moderate: <0.001* *to severe: <0.001* *<0.001*	59 (20)	*to mild: <0.001* *to moderate: <0.001* *to severe: <0.001* *<0.001*	66 (16)	*to mild: <0.001* *to moderate: <0.001* *to severe: 0.002* *<0.001*	62 (15)	*to mild: <0.001* *to moderate: <0.001* *to severe: <0.001* *<0.001*

Dyspnoea (mMRC)												
0	58 (14)	--	82 (13)	--	70 (10)	--	78 (14)	--	92 (8)	--	85 (8)	--
1	55 (12)	*to 0: 0.573*	74 (12)	*to 0: <0.001*	65 (8)	*to 0: <0.001*	74 (13)	*to 0: 0.143*	82 (11)	*to 0: <0.001*	78 (9)	*to 0: <0.001*
2	54 (14)	*to 0: 0.042* *to 1: >0.999*	68 (13)	*to 0: <0.001* *to 1: <0.001*	61 (10)	*to 0: <0.001* *to 1: <0.001*	66 (15)	*to 0: <0.001* *to 1: <0.001*	70 (12)	*to 0: <0.001* *to 1: <0.001*	68 (9)	*to 0: <0.001* *to 1: <0.001*
3	46 (14)	*to 0: <0.001* *to 1: <0.001* *to 2: <0.001*	62 (14)	*to 0: <0.001* *to 1: <0.001* *to 2: 0.006*	54 (10)	*to 0: <0.001* *to 1: <0.001* *to 2: <0.001*	59 (17)	*to 0: <0.001* *to 1: <0.001* *to 2: 0.003*	64 (16)	*to 0: <0.001* *to 1: <0.001* *to 2: 0.004*	62 (13)	*to 0: <0.001* *to 1: <0.001* *to 2: <0.001*
4	39 (10)	*to 0: <0.001* *to 1: 0.003* *to 2: 0.007* *to 3: >0.999* *<0.001*	55 (9)	*to 0: <0.001* *to 1: <0.001* *to 2: 0.020* *to 3: 0.831* *<0.001*	47 (6)	*to 0: <0.001* *to 1: <0.001* *to 2: <0.001* *to 3: 0.220* *<0.001*	52 (16)	*to 0: <0.001* *to 1: <0.001* *to 2: 0.002* *to 3: 0.707* *<0.001*	56 (11)	*to 0: <0.001* *to 1: <0.001* *to 2: <0.001* *to 3: 0.090* *<0.001*	54 (9)	*to 0: <0.001* *to 1: <0.001* *to 2: <0.001* *to 3: 0.037* *<0.001*
6MWD (m)												
1st tertile	46 (13)	--	65 (14)	--	55 (10)	--	59 (15)	--	69 (15)	--	64 (12)	--
2nd tertile	54 (12)	*to 1st tertile: <0.001*	71 (13)	*to 1st tertile: <0.001*	62 (9)	*to 1st tertile: <0.001*	74 (12)	*to 1st tertile: <0.001*	78 (13)	*to 1st tertile: <0.001*	76 (10)	*to 1st tertile: <0.001*
3rd tertile	58 (12)	*to 1st tertile: <0.001* *to 2nd tertile: 0.001* *<0.001*	78 (14)	*to 1st tertile: <0.001* *to 2nd tertile: <0.001* *<0.001*	68 (9)	*to 1st tertile: <0.001* *to 2nd tertile: <0.001* *<0.001*	77 (12)	*to 1st tertile: <0.001* *to 2nd tertile: 0.049* *<0.001*	86 (12)	*to 1st tertile: <0.001* *to 2nd tertile: <0.001* *<0.001*	82 (9)	*to 1st tertile: <0.001* *to 2nd tertile: <0.001* *<0.001*

* Comparison between groups from the pairwise comparisons of means adjusting for multiple comparisons using Bonferroni correction, and overall comparison from one-way ANOVA.

Table S9. Correlations* of changes in D-PPAC and C-PPAC amount, difficulty and total scores with changes in potential anchors.

	D-PPAC			C-PPAC		
	Change in amount score	**Change in difficulty score**	**Change in total score**	**Change in amount score**	**Change in difficulty score**	**Change in total score**
Change 6MWD	0.14	0.18	0.20	0.16	0.16	0.22
Change total CCQ	-0.11	**-0.32**	**-0.34**	-0.20	**-0.46**	**-0.39**
Global rating change: overall	**0.31**	0.25	**0.37**	**0.35**	0.18	**0.35**
Global rating change: difficulty	**0.31**	**0.32**	**0.42**	**0.32**	0.26	**0.37**
Global rating change: amount	**0.40**	0.24	**0.43**	**0.32**	0.16	**0.31**

* Correlation coefficients are in bold when >|0.3|; these anchors were used to estimate MID (Table 4 in main text).

Garcia-Aymerich J, *et al. Thorax* 2021; 76:228–238. doi: 10.1136/thoraxjnl-2020-214554

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