Physical activity is increased by a 12 week semi-automated telecoaching program in patients with COPD, a multicenter randomized controlled trial

Online data supplement

Methods

Sample size calculation

The sample size calculation prior to the study, based on previous interventions in the elderly or chronically ill patients (S1), resulted in a need of 253 patients in each arm (total of 506) for 90% power using an alpha level of 0.05 (2-sided). During the inclusion period this sample size calculation was revised because more recent data came available using similar interventions in patients with COPD. This calculation of sample size was based on repeated measurements in two groups (i.e. intervention and control group). The minimum difference in daily steps to be identified as statistically significant has been obtained from previous interventions to increase physical activity (PA) in a 3-months period in COPD patients, and ranges between 1334 steps.day^{-1} (S2) and 2984 steps.day^{-1} (S3) as the difference in intervention versus control group; to be conservative we used a value of 1500 in our sample size calculation. A previous review of the levels of physical activity in COPD patients has shown an SD in daily steps of around 3400 (S4), which has been used in the sample size calculation. Based on (i) unpublished data from the PROactive observational study (NCT01388218 S5) with COPD patients from the same geographical areas and of similar severity distribution to this study showing a correlation of 0.88 in steps between baseline and 6-weeks follow-up, and (ii) unpublished data from an intervention study in Belgium (NCT00948623 S6) with very severe COPD patients showing a correlation of 0.73 in steps between pre and post-intervention after adjusting for seasonality, a correlation between baseline and final daily steps of 0.75 was assumed for this study. Lastly a drop-out rate of 20% has been considered. Using these assumptions 68 patients are needed in each arm (total of 136) for 90% power using an alpha level of 0.05 (2-sided). Recruitment was subsequently stopped because we exceeded the sample size requirements.

Intervention

The 3 month intervention consisted of:

1) A 10-15 minutes semi-structured one-to-one interview with the investigator during visit 2 (V2) with the aim of discussing motivational factors and experienced barriers to become more active and exploring preferred and non-preferred activities and strategies to become more active. The patient created together with the investigator a plan with 3 concrete actions which could be used to increase the PA level. This action plan consisting of favorite activities was implemented in the semi-automated telecoaching.
2) A step counter (Fitbug Air©) providing direct feedback. This step counter, able to perform Bluetooth transmission to the company's smartphone application (Fitbug application), has a battery life of 4-6 months and an internal memory of 14 days, independent of wearing time. The step counter was worn at the waist during the whole study protocol, starting after randomization. Patients were asked to wear the step counter during waking hours.
3) Smartphone with Fitbug application and 'PROactive Linkcare' coaching application installed on it. The latter was developed for patients with COPD in this project and provided the semi-automated telecoaching and used data collated by the step counter and sent to the fitbug application. After 1 week of sufficient (at least 4 days) step counter data, the aim was to increase PA on a weekly basis using step count as an incentive. Patients' targets were revised every Sunday. On a daily basis patients were reminded at this target in the morning, which remained the same throughout the week. At the evening patients sent wirelessly their activity using the smartphone application and received feedback on their achievement by graphical representation together with an activity tip of the day, including educational messages (see Figure S1). At Sunday a weekly feedback was sent including proposals for being active based on the action plan, if the target was not reached. If the patient reached the target, the readiness for increase was questioned. Only if the patient agreed, an increase in target was initiated. In addition to this automated goal setting the investigator could agree on a 'manual goal' together with the patient. This manual goal setting was initiated if

the patient (1) decreased PA level very fast and the automatically calculated goal was still experienced as too high (e.g. exacerbation) or (2) increased his/her PA level during the coaching project to an experienced maximum (goal 'locked'). This manual goal setting was a rather rare situation where both patient and investigator agreed to change the automatically calculated targets.

4) Booklet containing home exercises, which were available in 3 difficulties. These exercises comprised general strengthening and stretching exercises for which patients did not need any equipment. Patients were reminded they could do these exercises on days the weather would prevent them to go out. The booklet was provided to the patients during V2.
5) Weekly group text messages sent by the study team providing tips for being active in the upcoming days, based on the local weather forecast.
6) Contacts initiated by the patients were not limited, contacts initiated by the investigator were standardized and only occurred in the following scenarios ('flagged patients') (Table S1). Investigators received an alert initiated by the system when patients had to be contacted.

Results

Characteristics of randomized patients

Patients in the usual care group (UCG) and intervention group (IG) were comparable at baseline, although the proportion of patients reporting osteo-articular comorbidities (p=0.04) and the number of exacerbations in the last 12 months tended to be slightly higher in the intervention group (p=0.06), see Table S2. There was a mean of 93±11 days between V2 and V3.

Characteristics of patients: completers vs. drop out

Patients who dropped out the study had a lower body mass index (BMI) (p<0.01), worse quadriceps force (p<0.01) and a higher COPD assessment test (CAT) score (p=0.02) compared to completers of the trial (Table S3).

Physical activity

A valid PA measurement was defined a priori as a minimum of 4 weekdays with at least 8 hours of wearing time, with weekend excluded from the analysis. If these specifications would lower the sample size significantly (defined as a 10% lower sample) compared to less strict definitions, a minimum number of days of 2 weekdays (still providing a reliable PA assessment) would be selected.

Physical activity has been measured by both the Dynaport Movemonitor and the Actigraph. The reason for this is that the present study is part of the clinical validation process of the PROactive instruments (S5). The PROactive instruments can be collected using either of these 2 accelerometers. Because of this, patients wore simultaneously both activity monitors. Although we collected data from 2 monitors we decided a priori to use the data from the Dynaport Movemonitor (DAM) in the analysis because this monitor provides all four PA outcomes (i.e. daily step count, time in at least moderate intense activity, walking time and movement intensity). We decided a prior that, if the Actigraph data would result in a significant higher sample in terms of valid PA measurement on both visits, we would opt to present data of 1) Actigraph for step count and time in at least moderate intense activity and 2) Dynaport Movemonitor for walking time and movement intensity.

Using the Actigraph, 77% (definition using 4 weekdays) versus 88% (definition using 2 weekdays) of the completers had valid PA data for both time points (DAM resulted in a representation of 70% vs. 82%). Because of this we opted to present the largest sample possible. Data based on the 2 weekdays definition are presented in the main manuscript (see below for parallel analyses with 4 days, providing similar results). Step count and time in at least moderate intense activity are presented based on Actigraph data, walking time and intensity during walking based on DAM.

Of the 318 completers, 38 patients (19 in each group) were not included in the physical activity analyses because they did not have a valid (at least 2 weekdays with 8 hours of wearing time) physical activity measurement (Actigraph) at baseline (n=15), during the final visit (n=22) or both (n=1). Patients excluded from the analysis had a lower FEV_1% predictive

compared to those included in the main analyses of the present paper ($p<0.01$), see Table S4.

Based on data obtained by the DAM, physical activity increased in the patients in the IG (71±35 to 77±45 minutes.day^{-1} walking; 1.83±0.27 to 1.89±0.34 m.s^{-2} intensity during walking) and decreased in the UCG (74±36 to 64±39 minutes.day^{-1} walking; 1.87±0.36 to 1.84±0.36 m.s^{-2} intensity during walking). IG patients had an increase over controls of mean [95%CI] 16.3 [9.5-23.2] min.day^{-1} time walking (22% from baseline, $p<0.0001$) and 0.084 [0.032-0.136] m.s^{-2} intensity during walking (5% from baseline, $p=0.002$).

Contacts with patients in the intervention group

The application driven contacts were a priori defined and standardized in the intervention description. Of all 'human driven' contacts (n=267), 72% was to discuss technical issues, 10% to discuss health issues and 18% to discuss physical activity (mainly discussing PA target). The total number of patients contacted, number of contacts per patient in the trial and total duration of contacts per patient in the trial are presented in Table S5.

Sensitivity analysis

A sensitivity analysis based on patients with at least 4 weekdays of valid PA data at baseline and 3 months was performed, representing 77% and 70% of the sample, respectively with Actigraph and DAM data. This analysis included 122 UCG and 122 IG patients with valid Actigraph measurements on both time points and 116 UCG and 108 IG by DAM. The 244 included patients wore the accelerometers for 4.8±0.4 weekdays with a wearing time of 819±114 minutes and 4.8±0.4 weekdays with a wearing time of 796±118 minutes, respectively during the baseline and final measurement (no differences between groups). Daylight during the baseline measurement of these patients (750±150 min) as well as changes in daylight (-171±158 min) were comparable between groups.

Intervention patients had an increase of mean [95%CI] 1546 [1008-2083] steps.day^{-1} and 11.1 [6.5-15.8] min.day^{-1} in at least moderate intense activity, as measured by Actigraph ($p\leq0.001$ for both) and 17.9[10.7-25.1] min.day^{-1} time walking ($p\leq0.001$) and 0.092[0.035-0.149] m.s^{-2} intensity during walking ($p=0.002$), as measured by DAM, more than controls.

39% Of patients in the intervention group vs 11% of control patients ($p<0.001$) increased PA with by least 1000 steps from baseline (OR [95%CI] for increase 4.83 [2.48-9.41] IG vs UCG).

Reference List

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S5 Gimeno-Santos E, Raste Y, Demeyer H, Louvaris Z, de Jong C, Rabinovich RA, Hopkinson NS, Polkey MI, Vogiatzis I, Tabberer M, Dobbels F, Ivanoff N, de Boer WI, Van der Molen T, Kulich K, Serra I, Basagana X, Troosters T, Puhan MA, Karlsson N, Garcia-Aymerich J, The PROactive instruments to measure physical activity in patients with chronic obstructive pulmonary disease. Eur Respir J 2015; 46:988-1000.

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Figures

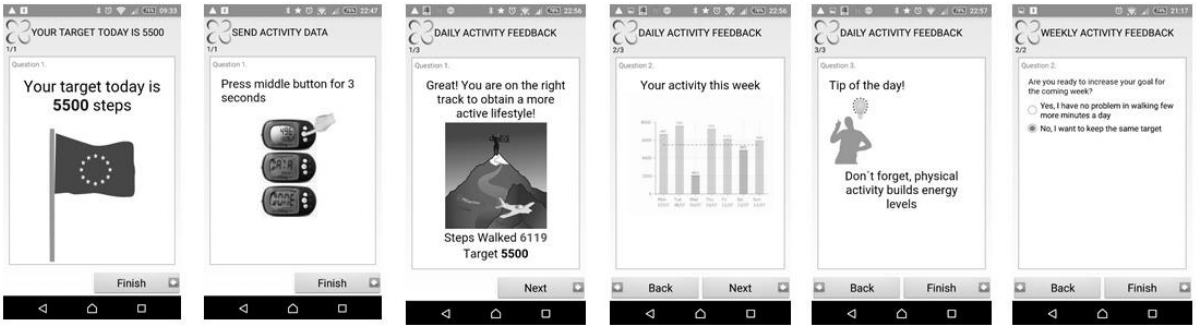

Figure S1: Screenshots of the PROactive Linkcare application; 1) Display of the goal in the morning, 2) Instructions how to send PA data by bluetooth in the evening, 3-5) Daily feedback received after sending PA data in the evening, 6) questioning readiness to increase if patient reached the weekly goal (Sunday).

Tables

Scenario ('flag')	Action of investigator
Patient did not send PA data for 2 consecutive days	Text message
Patient did not achieve the proposed target for 2 consecutive weeks	Phone call
Patient was not willing to increase target for 2 consecutive weeks	Phone call
Patient was not compliant (data sent for at least 4 days) 2 consecutive weeks	Phone call

Table S1: Standardized contacts initiated by the investigator

Variable	UCG n=172	IG n=171
Exacerbation history	1.13 ± 1.81	1.61 ± 2.71
Pack year (year)	58.1 ± 38.6	51.0 ± 31.3
COPD diagnosis (years)	7.6 ± 5.9	7.5 ± 6.2
Center of inclusion*		
Athens	43 (25)	43 (25)
Edinburgh	20 (12)	21 (12)
Leuven	40 (23)	42 (25)
London	26 (15)	27 (16)
Groningen	19 (11)	15 (9)
Zurich	24 (14)	23 (13)
GOLD*		
I	30 (17)	22 (13)
II	71 (41)	70 (41)
III	53 (31)	58 (34)
IV	18 (11)	21 (12)
Comorbidity*		
Diabetes	11 (6)	17 (10)
Cancer	6 (3)	5 (3)
Cardiovascular	31 (18)	36 (21)
Hypertension	39 (23)	42 (25)
Osteo-articular	25 (15)	40 (23)
Asthma	1 (1)	1 (1)
Marital status*		
Married or co-habiting	112 (65)	117 (68)
Single	17 (10)	18 (11)
Widow	17 (10)	10 (6)
Divorced or separated	26 (15)	26 (15)
Education*		
Primary school	27 (16)	14 (8)
Secondary school	88 (51)	96 (56)
Further education	49 (29)	51 (30)
Post graduate	7 (4)	10 (6)
Work status*		
Employed	20 (12)	27 (16)
Unemployed	20 (12)	14 (8)
Retired	132 (76)	130 (76)
Respiratory medication*		
No	22 (13)	13 (8)
SAB	77 (45)	85 (50)
LABA	96 (56)	103 (60)
LAAC	107 (62)	115 (67)
ICS	89 (52)	93 (54)
Theophylline	10 (6)	10 (6)
mucolytics	11 (6)	16 (9)

Table S2 : Baseline characteristics; UCG= usual care group, IG = intervention group; data are expressed as mean±SD or n(%)*; n = number of patients; Exacerbation history = total number of exacerbations during the last 12 months, COPD diagnosis = Years of being diagnosed with COPD, education = Highest education, SAB= Short acting bronchodilators , LABA= Long acting beta-adrenoceptor agonist, LAAC= Long acting anticholinergics, ICS= Inhalation corticosteroids. Education was missing in 1 patient

Variable	Completers n=318	Drop out n=25
Age (y)	66 ± 8	69 ± 9
BMI ($kg.m^{-2}$)	26.5 ± 5.1	23.9 ± 3.5
FEV1 ($\%_{pred}$)	55 ± 20	62 ± 24
6MWD (m)	446 ± 106	413 ± 100
QF (kg)	31.7 ± 10.3	25.2 ± 6.9
Exacerbation history (n)	1.36 ± 2.34	1.58 ± 1.98
CAT score (points)	13.6 ± 7.4	17.1 ± 7.7
mMRC (0/1/2/3/4)*	49 (15)/139 (44)/85 (27)/39 (12)/6 (2)	3(12)/7 (28)/10 (40)/3 (12)/2 (8)
Step count ($steps.day^{-1}$)	4945 ± 2832	4079 ± 2653
MPA ($min.day^{-1}$)	22.4 ± 24.3	15.9 ± 18.5
Any comorbidity*	177 (56)	16 (64)
Osteo-articular*	62 (20)	3 (12)

Table S3: **Baseline characteristics of completers and patients who dropped out the study**; data are expressed as mean±SD or n (%)*; n = number of patients; BMI = body mass index, 6MWD = six minute walk distance, QF = quadriceps force, Exacerbation history = total number of exacerbations during the last 12 months, CAT = COPD assessment test, mMRC = modified Medical research council, MPA = time in at least moderate intense activity; Physical activity data based on 302 completers and 25 patients who dropped out (Actigraph data).

Variable	Valid PA data n=280	Unvalid PA data n=38
Randomization (UCG/IG)	140 (50) / 140 (50)	19 (50) / 19 (50)
Age (y)	66 ± 8	67 ± 8
BMI ($kg.m^{-2}$)	26.6 ± 5.2	25.3 ± 4.7
FEV_1 ($\%_{pred}$)	56 ± 21	47 ± 17
6MWD (m)	448 ± 105	429 ± 119
QF (kg)	31.8 ± 10.6	31.4 ± 8.6
Exacerbation history (n)	1.28 ± 2.28	1.92 ± 2.69
CAT score (points)	13.4 ± 7.3	14.8 ± 8.1
mMRC (0/1/2/3/4)*	45 (16)/121 (43)/75 (27)/34 (12)/5 (2)	4 (11)/18 (47)/10 (26)/5 (13)/1 (3)
Any comorbidity*	153 (55)	24 (63)
Osteo-articular*	55 (20)	7 (18)

Table S4: Baseline characteristics of completers with and without valid physical activity data (Actigraph); data are expressed as mean±SD or n(%)*;n =number of patients; UCG =usual care group, IG = intervention group; BMI= body mass index, 6MWD = six minute walk distance, QF = quadriceps force, CAT = COPD assessment test, mMRC= modified Medical research council

Reason of contact	%	Patients (n)	Number of contacts (n)	Time consumption (minutes)
Application driven				
Patient did not send PA data for 2 consecutive days	38	106	1 (0-22)	10 (0-190)
Patient was not compliant (data sent for at least 4 days) 2 consecutive weeks	16	59	0 (0-9)	0 (0-70)
Patient did not achieve the proposed target for 2 consecutive weeks	30	103	1 (0-9)	5 (0-95)
Patient was not willing to increase target for 2 consecutive weeks	16	51	0 (0-7)	0 (0-45)
Human driven				
Technical issue	72	68	0 (0-12)	0 (0-240)
Health issue	10	21	0 (0-4)	0 (0-75)
Physical activity	18	25	0 (0-4)	0 (0-50)

Table S5: Contacts with patients in the intervention group; % = percentage of contacts of respectively application and human driven contacts, N=number of patients, number of contacts= number of contacts per patient in the trial, data expressed as median (range), time consumption= total time of contact per patient in the trial, data expressed as median (range)