

RESEARCH ARTICLE

Determinants of study completion and response to a 12-month behavioral physical activity intervention in chronic obstructive pulmonary disease: A cohort study

Maria Koreny^{1,2,3}, Heleen Demeyer^{4,5}, Ane Arbillaga-Etxarri⁶, Elena Gimeno-Santos^{7,8}, Anael Barberan-Garcia^{7,8,9}, Marta Benet^{1,2,3}, Eva Balcells^{2,9,10}, Eulàlia Borrell¹¹, Alicia Marin^{9,12,13}, Diego A. Rodríguez Chiaradía^{2,9,10}, Pere Vall-Casas¹⁴, Jordi Vilaró¹⁵, Robert Rodríguez-Roisin⁸, Judith Garcia-Aymerich^{1,2,3*}



1 ISGlobal, Barcelona, Spain, **2** Pompeu Fabra University (UPF), Barcelona, Spain, **3** CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain, **4** Department of Rehabilitation Sciences, KU Leuven -University of Leuven, Leuven, Belgium, **5** Department of Respiratory Diseases, University Hospitals KU Leuven, Leuven, Belgium, **6** Physical Activity and Sports Sciences, Faculty of Psychology and Education, University of Deusto, Donostia-San Sebastián, Spain, **7** Respiratory Clinic Institute, Hospital Clinic of Barcelona, Barcelona, Spain, **8** August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain, **9** CIBER Enfermedades Respiratorias (CIBERES), Madrid, Spain, **10** Pneumology Department, Institut Hospital del Mar d'Investigacions Mèdiques (IMIM), Hospital del Mar, Barcelona, Spain, **11** Sant Roc Primary Health Care Centre, Institut Català de la Salut (ICS), Badalona, Spain, **12** Department of Pulmonary Medicine, Hospital Universitari Germans Trias i Pujol, Badalona, Spain, **13** Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, Spain, **14** Universitat Internacional de Catalunya (UIC), Barcelona, Spain, **15** Global Research on Wellbeing (GRoW), Blanquerna Health Sciences School, Ramon Llull University, Barcelona, Spain

* judith.garcia@isglobal.org

OPEN ACCESS

Citation: Koreny M, Demeyer H, Arbillaga-Etxarri A, Gimeno-Santos E, Barberan-Garcia A, Benet M, et al. (2019) Determinants of study completion and response to a 12-month behavioral physical activity intervention in chronic obstructive pulmonary disease: A cohort study. *PLoS ONE* 14(5): e0217157. <https://doi.org/10.1371/journal.pone.0217157>

Editor: Davor Plavec, Srebrnjak Children's Hospital, CROATIA

Received: November 30, 2018

Accepted: May 2, 2019

Published: May 20, 2019

Copyright: © 2019 Koreny et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: Data contain potentially identifying variables. For example, built environment variables together with sociodemographics and clinical conditions could allow identification of patients in some geographic areas. Therefore, data cannot be made publicly available according to the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal

Abstract

Objectives

Physical activity is key to improve the prognosis of chronic obstructive pulmonary disease (COPD). To help to tailor future interventions we aimed to identify the baseline characteristics of COPD patients which predict 12-month completion and response to a behavioral physical activity intervention.

Methods

This is a 12-month cohort study of the intervention arm of the Urban Training randomized controlled trial (NCT01897298), an intervention proven to be efficacious to increase physical activity. We considered baseline sociodemographic, interpersonal, environmental, clinical and psychological characteristics as potential determinants of completion and response. We defined completion as attending the 12-month study visit. Among completers, we defined response as increasing physical activity ≥ 1100 steps/day from baseline to 12 months, measured by accelerometer. We estimated the factors independently for completion and response using multivariable logistic regression models.

data and on the free movement of such data. The corresponding author and the Coordination and Research Management Office of the Projects Unit (research.management@isglobal.org) could provide, upon request, individual participant data that underlie some of the results reported in this article (except variables that may allow identification of patients), after applying necessary measures to guarantee that no individual is identified or identifiable.

Funding: HD is the recipient of a joint ERS/SEPAR Fellowship (LTRF 2015) (Sociedad Española De Neumología Y Cirugía Torácica (Separ) www.separ.es) and is a post-doctoral research fellow of the FWO-Flanders (Fonds voor Wetenschappelijk Onderzoek – Vlaanderen <https://www.fwo.be/en>). The Urban TrainingTM study (NCT01897298) was funded by grants from Fondo de Investigación Sanitaria, Instituto de Salud Carlos III (ISCIII, PI11/01283 and PI14/0419) (Fondo de Investigación Sanitaria, Instituto de Salud Carlos III <http://www.isciii.es>), integrated into Plan Estatal I+D+I 2013-2016 and co-funded by ISCIII-Subdirección General de Evaluación y Fomento de la Investigación and Fondo Europeo de Desarrollo Regional (FEDER); Sociedad Española de Neumología y Cirugía Torácica (SEPAR, 147/2011 and 201/2011), Societat Catalana de Pneumologia (Ajuts al millor projecte en fisioteràpia respiratòria 2013). ISGlobal is a member of the CERCA Program, Generalitat de Catalunya (El programa de centres de recerca de Catalunya <http://cerca.cat/>). Anaël Barberan-Garcia had personal funding from AGAUR 2014-SGR-661, Catalan Government (Agencia de Gestió de Ayudas Universitaries y de Investigación <http://agaur.gencat.cat/es>). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: I have read the journal's policy and the authors of this manuscript have the following competing interests: MK: The work was selected for an ERS Grant for Best Abstract in Physiotherapy supported by POWERbreathe. RRR: reports grants and personal fees from Almirall, personal fees from AstraZeneca, personal fees from Boehringer Ingelheim, personal fees from Ferrer Group, grants and personal fees from Menarini, personal fees from Mylan, personal fees from Novartis, personal fees from Pearl Therapeutics, personal fees from Takeda, and personal fees from TEVA during the conduct of the study. He was member of the GOLD Board of Directors (2014-17) and of the Scientific Committee (2014). JGA: JGA's institution has received consulting and lecture fees from

Results

Of a total of 202 patients (m (SD) 69 (9) years, 84% male), 132 (65%) completed the study. Among those, 37 (28%) qualified as responders. Higher numbers of baseline steps/day (OR [95% CI] 1.11 [1.02–1.21] per increase of 1000 steps, $p < 0.05$) and living with a partner (2.77 [1.41–5.48], $p < 0.01$) were related to a higher probability of completion while more neighborhood vulnerability (0.70 [0.57–0.86] per increase of 0.1 units in urban vulnerability index, $p < 0.01$) was related to a lower probability. Among the completers, working (3.14 [1.05–9.33], $p < 0.05$) and having an endocrino-metabolic disease (4.36 [1.49–12.80], $p < 0.01$) were related to a higher probability of response while unwillingness to follow the intervention (0.21 [0.05–0.98], $p < 0.05$) was related to a lower probability.

Conclusions

This study found that 12-month completion of a behavioral physical activity intervention was generally determined by previous physical activity habits as well as interpersonal and environmental physical activity facilitators while response was related to diverse factors thought to modify the individual motivation to change to an active lifestyle.

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide [1]. Over the last decades, physical activity has been increasingly recognized as a key factor for COPD for two main reasons. First, higher levels of physical activity practice in daily life have been consistently related to improved prognosis in COPD, specifically to reductions in exacerbations and mortality [2]. Second, in comparison with healthy peers, COPD patients exhibit reduced levels of physical activity already in the early stages [3] and across all other airflow limitation severity stages [4]. As a result, the guidelines for the prevention and management of COPD developed by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 include physical activity as a non-pharmacological therapeutic approach that all COPD patients should receive [5].

Recent efforts have succeeded in designing and testing interventions that increased physical activity in COPD patients either at short [6–8] or long-term [9]. However, research is still scarce and there are no clear guidelines on how, when, where or to whom such interventions should be provided [10]. A critical issue is to ensure that a relevant proportion of patients completes the intervention period and responds to the intervention (e.g. with an increase in the targeted outcome above a critical threshold). Unfortunately, research of this kind in physical activity and COPD is scarce. To our knowledge, four studies have assessed factors that affect completion and/or response to a physical activity intervention in COPD in *post hoc* or secondary analyses. Altenburg et al showed that only patients with baseline physical activity $< 10,000$ steps/day maintained a significant long-term effect at 15 months of a 12-week physical activity counselling program [11]. Moy et al found that, among a large number of clinical factors, only age was associated with changes in steps/day at 4 months of an internet-mediated, pedometer-based exercise intervention [12]. Demeyer et al reported that the magnitude of the response to a 12-week semiautomated telecoaching program was higher in patients who exhibited at baseline lower dyspnea scores, better exercise capacity and who suffered from mild-to-moderate COPD [8]. This research also found that study completion was associated with higher body mass index (BMI), higher isometric quadriceps force and a better health status [8]. Finally,

AstraZeneca (not related to this study); she has received lecture fees from Esteve and Chiesi (not related to this study). HD, AAE, EGS, ABG, MB, EBa, EBo, AM, DAR, PVC and JV declare that they have no competing interests. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

Kantorowski et al recently found that lower baseline physical activity, social support, lack of depression or oxygen use, and recruitment in spring were significant predictors of a positive change (≥ 1 step/day) in physical activity after a 12-week pedometer and website intervention (vs pedometer only) [13]. Overall, these studies seem to suggest that lower baseline physical activity and better functional performance relate to a better response and completion.

An important characteristic of the mentioned trials is that they were limited to COPD patients with reduced functional exercise capacity (median 6-min walking distance (6MWD) test ≈ 450 m [8,11] or below [13]) and/or low baseline physical activity [8,11–13]. Therefore, their results on completion and response to physical activity interventions may not be transferable to other patients. Another shortcoming in previous studies is that they mostly focused on characteristic features of COPD to predict completion and/or response. These characteristics do not reflect the complex interplay of factors affecting physical activity as described by the ecological framework [14].

According to the World Health Organization (WHO) strategy for chronic medical conditions, the outcomes of health promotion and secondary prevention interventions strongly depend on the involvement of patients and their families [15]. Thus, the deployment at the population level of interventions originally assessed at clinical trial level requires a proper assessment of the determinants of completion and response using a broad approach and involving patients across all severity levels as typically found in the community setting.

The aim of our study was to identify which sociodemographic, interpersonal, environmental, clinical, and psychological baseline characteristics were associated with 12-month completion and response to a behavioral physical activity intervention in COPD patients, using data from the intervention arm of the randomized controlled Urban Training trial (NCT01897298) mostly involving COPD patients from primary care. This intervention has previously been reported to be efficacious to increase physical activity in the per protocol population but ineffective in the full population [9], which prompts the need to identify the profile of future completers and/or responders. Ideally, the present results will help to improve clinical guidance on how to tailor behavioral physical activity interventions in COPD patients.

Methods

Design and subjects

We performed a cohort study of 12-month follow-up of the intervention group participating in the Urban Training trial behavioral physical activity intervention in COPD patients. This was a prospective, multicenter, parallel-group, randomized controlled trial, registered at clinicaltrials.gov (NCT01897298) and previously described in detail [9]. In brief, the Urban Training trial recruited 407 patients with a diagnosis of COPD according to the American Thoracic Society and European Respiratory Society (ATS/ERS) recommendations (post-bronchodilator forced expiratory volume in the first second (FEV₁) to forced vital capacity (FVC) ratio < 0.70) [16] from 33 primary care and 5 tertiary hospitals of five Catalan seaside municipalities between October 2013 and January 2016 and randomized them to the intervention or usual care group. For the present study we included only patients in the intervention arm ($n = 202$).

The Urban Training trial was approved by the Ethics Committees of all participating institutions (Comitè Ètic d'Investigació Clínica Parc de Salut MAR 2011/4291/I, Comitè Ètic d'Investigació Clínica de l'IDIAP Jordi Gol i Gurina P11/116, Comitè Ètic d'Investigació Clínica de l'Hospital Universitari de Bellvitge PR197/11, Comitè Ètic d'Investigació Clínica de l'Hospital Universitari Germans Trias i Pujol AC-12-004, Comitè Ètic d'Investigació Clínica de l'Hospital Clínic de Barcelona 2011/7061, Comitè Ètic d'Investigació Clínica de l'Hospital de Mataró November 23rd, 2011) and all participants provided written informed consent.

Intervention

The Urban Training intervention included six elements aiming to elicit a behavioral change and to maintain it during the 12 months of the study: (1) a [motivational interview](#) [17], following a stage-matched approach [18], with up to four short motivational phone calls during the subsequent 12 months; (2) instructions to walk at least one of the previously validated [19] [Urban Training walking trails](#) per day, at least 5 days per week on the appropriate intensity trail with tailored increase of volume and/or intensity over 12 months; (3) a [pedometer](#) and a [personalised calendar](#) to monitor and note their physical activity and keep motivation; (4) the [project website](#) [20] and [phone text messages](#) every 2 weeks with educational or motivational messages and the European Lung Foundation information [brochure](#) [21]; (5) a [guided walking group](#) once per month; and (6) a [support phone number](#) available during the 12-month study period.

Procedures

Full details on study procedures and quality control have been reported previously [9,22]. Briefly, we obtained at baseline the following data from all patients using standardized procedures: (i) [sociodemographic variables](#): age, sex, smoking and socioeconomic status; (ii) [interpersonal variables](#): living with a partner (vs single, widowed or divorced), grandparenting and working status (working full-time or part-time vs unemployed, housework or retired); (iii) [environmental variables](#): urban vulnerability index, a measure of socioeconomic status at the census tract level (median area of 0.26 km²) that combines demographic, economic, residential and subjective indicators, and ranges from 0 (lowest) to 1 (highest level of neighborhood vulnerability) [23], and season of recruitment; (iv) [clinical variables](#): forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) by forced spirometry after bronchodilator, functional exercise capacity measured by the 6-min walking distance (6MWD) test, the modified Medical Research Council dyspnea scale (mMRC), the number of severe COPD exacerbations (defined as requiring a visit to the emergency room or hospital admission) in the 12 months prior to recruitment and during follow-up, body mass index (BMI) and fat free mass index (FFMI) by physical examination and bioelectrical impedance, physician diagnosed comorbidities categorized according to the International Classification of Diseases, Tenth Revision ICD-10 (C00 to D48 for Neoplasm; E00 to E90 for Endocrine, nutritional and metabolic diseases; E10 to E14 for Diabetes mellitus; I00 to I99 for Cardiovascular diseases; I10 to I15 for Hypertension) and physical activity variables: steps/day and time spent on moderate to vigorous physical activity (>3 METs [metabolic equivalents of task(s)] measured by the Dyna-port accelerometer (McRoberts BV, The Hague, The Netherlands) previously validated for COPD [24,25], defining a valid physical activity measurement as a minimum of 3 days with at least 8 h of wearing time within waking hours [26], and physical activity experience (total and amount and difficulty domains) by the Clinical-PROactive Physical Activity (C-PPAC) tool [27]; and (v) [psychological variables](#): the Hospital Anxiety and Depression scale (HADS), unwillingness to follow the physical activity intervention (i.e. patients who '*spontaneously reported at baseline that they were unwilling to follow any of the instructions*' [9]), stage of change [17,18] and self-efficacy (from 0 to 10).

Study outcomes

We defined study completion as participation in the final visit (12 months after the baseline visit). Among patients who completed the study, we defined intervention response as a positive change in mean daily step count between baseline (visit 2) and 12 months (visit 4) equal or higher than the minimal important difference (MID) [28]. Steps MID in COPD has been estimated to

range between 600 and 1100 steps/day [28]; therefore we used a cut-off of ≥ 1100 vs < 1100 steps/day for the main analysis and ≥ 600 vs < 600 steps/day for the secondary analysis.

Statistical analysis

The available sample size ($n = 202$) was fixed by the primary objectives of the Urban Training study, therefore we calculated the statistical power to answer the current research question. Calculations were performed for a difference in age, FEV₁, FVC, 6MWD, and steps/day at baseline and resulted in a range of statistical power between 93% to 98% for study completion and 79% to 90% for response, using unpaired t-test ($p < 0.05$) and assuming a relation of loss-to follow-up to completion and responders to non-responders of 1:2.

We assessed the presence and patterns of missing data. Due to the small proportion of missings ($< 5\%$ of total data), main analysis was conducted using a complete case strategy and we reported missing data in the Table footnotes. As a sensitivity analysis, to account for the possibility of bias due to missing data, we used multiple imputation (20 imputed datasets) with the method of chained equations [29] assuming the missing-at-random hypothesis (i.e., missingness conditional on measured patients' characteristics [30]). We repeated bivariable and multivariable analysis using the imputed datasets.

To analyze determinants of study completion and response to intervention, we first compared the individual's characteristics (sociodemographic, interpersonal, environmental, clinical and psychological) at baseline between patients lost to follow-up and completers, and between non-responders and responders using unpaired Student's t-test, Wilcoxon rank-sum, Chi square or Fisher's tests, depending on the variable distribution. Second, we built two multivariable logistic regression models (one for study completion and one for response to the intervention) including as exposures all variables that exhibited a p -value < 0.2 in the bivariable analysis between lost to follow-up and completers, and non-responders and responders, respectively. Model building combined step-forward and backward algorithms, and covariates were included in the final model if: (i) they related to both the exposure and the outcome in bivariable analysis; (ii) they modified ($> 10\%$ change in regression coefficient) the estimates of the remaining variables in the multivariable models; or, (iii) there was consistent evidence in the literature of their association with the outcome [31]. To exclude overfitting, we applied the least absolute shrinkage and selection operator (LASSO) approach. We tested goodness of fit of the final models by means of the Hosmer-Lemeshow test, identification of influential observations, and estimation of the specification error. Finally, we tested the discrimination and accuracy to predict the outcome of the final models by calculating the area under the receiver operating characteristic curve (AUROC) and the Brier score, respectively.

We conducted several secondary analyses. First, we used 600 steps (lower limit of steps MID) as a cut-off to define response to the intervention both in bivariable and multivariable analyses. Second, we repeated the final multivariable model for response: (1) including severe acute exacerbations of COPD during follow-up in the multivariable models to test the possibility that this variable affected the risk of being a non-responder; and (2) using time in moderate to vigorous physical activity (categorized according to its median value) instead of steps to define response to the intervention.

All analyses were conducted with Stata 12.0 (StataCorp, College Station, TX, USA).

Results

Patient characteristics

Patient characteristics are shown in [Table 1](#). Patients had a mean (SD) age of 69 (9) years and were mostly male (84%) and living with a partner (72%). Only 14% were active workers and

71% had low socioeconomic status. Patients were mainly in the earlier stages of COPD with a mean FEV₁ 56% of predicted and a mean 6MWD of 487m; 29% of patients had an mMRC dyspnea score ≥ 2 , 9% of patients had a severe COPD exacerbation within the previous year and only 6% were participating in a pulmonary rehabilitation program at study inclusion. Patients had a large prevalence of endocrino-metabolic and cardiovascular chronic comorbid conditions and walked more than 7000 steps per day on average. At baseline, 26 patients (13%) reported unwillingness to follow the intervention, 50% of patients were in later phases of stage of change (action, maintaining and finalizing), and self-efficacy was high (median 8 on a scale from 0 to 10).

Determinants of study completion

After 12 months, 70 patients (35%) were lost to follow-up and 132 patients (65%) completed the study (completers) (Fig 1).

Of the broad range of variables assessed at baseline, physical activity levels, marital status, neighborhood vulnerability, unwillingness to follow the intervention and baseline 6MWD were significantly different between patients lost to follow-up and completers (Table 1). In the mutually adjusted logistic regression model, being physically more active (OR [95% CI] 1.11 [1.02–1.21] per increase of 1000 steps, $p = 0.012$) and living with a partner (2.77 [1.41–5.48], $p = 0.003$) were independently related to a higher probability of completion while more neighborhood vulnerability (0.70 [0.57–0.86] per increase of 0.1 units in urban vulnerability index, $p = 0.001$) was related to a lower probability (Table 2).

Determinants of intervention response

Among patients who completed the study, 37 patients (28%) qualified as responders using as threshold 1100 steps/day (Fig 1). The change in steps/day between baseline and 12 months was heterogeneous and ranged between less than minus 10,000 and more than plus 10,000 steps/day following a normal distribution (mean (SD) -67 (3648) steps/day) (Fig 2).

Active working, diagnosis of an endocrino-metabolic disease, unwillingness to follow the physical activity intervention, and FVC at baseline were related to the response to the intervention on bivariable analysis (Table 3).

After mutual adjustment in a multivariable model, being an active worker (3.14 [1.05–9.33], $p = 0.040$) and having an endocrino-metabolic disease (4.36 [1.49–12.80], $p = 0.007$) were independently related to a higher probability of response while unwillingness to follow the intervention (0.21 [0.05–0.098], $p = 0.047$) was related to a lower probability (Table 4).

Models fitting and additional analyses

The LASSO approach confirmed that final models of determinants of completion and response (Tables 2 and 4) were not overadjusted. Goodness of fit tests did not reveal any abnormality. Final models indicated good discrimination, as per AUROC of 0.73 for study completion and 0.71 for intervention response, and accuracy with Brier scores lower than 0.2 in both models. All secondary and sensitivity analyses provided very similar results (Tables A-H in S1 File).

Discussion

This study about the determinants of 12-month completion and response to a behavioral physical activity intervention in COPD patients has found that: (1) being more physically active and living with a partner were positively associated with study completion while living in more

Table 1. Variables related to 12-month completion in COPD patients participating in a behavioral physical activity intervention.

	All patients	Lost to follow-up	Completers	p-value
	n = 202*	n = 70	n = 132	
Sociodemographic				
Age (years), m (SD)	68.8 (9.2)	69.9 (9.3)	68.3 (9.1)	0.229
Sex: male, n (%)	170 (84)	56 (80)	114 (86)	0.239
Smoking status, current, n (%)	56 (28)	22 (31)	34 (26)	0.392
Socioeconomic status, IIIM-IV-V, n (%)	143 (71)	50 (71)	93 (71)	0.948
Interpersonal				
Living with a partner**, n (%)	145 (72)	41 (59)	104 (79)	0.004
Grandparenting, n (%)	68 (34)	21 (31)	47 (36)	0.481
Active workers, n (%)	28 (14)	9 (13)	19 (14)	0.764
Environmental				
Urban vulnerability index (from 0 -lowest to 1 -highest), m (SD)	0.64 (0.17)	0.69 (0.16)	0.61 (0.17)	0.003
Recruitment season				
Spring, n (%)	46 (23)	13 (19)	33 (25)	0.305
Summer, n (%)	22 (11)	11 (16)	11 (8)	
Fall, n (%)	73 (36)	27 (38)	46 (35)	
Winter, n (%)	61 (30)	19 (27)	42 (32)	
Clinical				
FEV ₁ (% pred), m (SD)	56.4 (17.1)	57.2 (17.9)	55.9 (16.7)	0.616
FVC (% pred), m (SD)	77.3 (16.8)	76.9 (16.8)	77.5 (16.9)	0.817
6MWD (m), m (SD)	487 (98)	464 (102)	498 (95)	0.018
Moderate to very severe dyspnea (mMRC ≥2), n (%)	58 (29)	22 (31)	36 (27)	0.534
Any severe [†] COPD exacerbation in previous 12 months, n (%)	17 (9)	7 (11)	10 (8)	0.591
Any severe [†] COPD exacerbation during follow-up, n (%)	22 (17)	-	22 (17)	-
BMI (kg/m ²), m (SD)	28.5 (5.0)	28.6 (5.1)	28.4 (4.9)	0.812
FFML, m (SD)	19.6 (3.2)	19.6 (3.5)	19.6 (3.0)	0.978
Neoplasm [†] , n (%)	24 (12)	5 (8)	19 (15)	0.248
Endocrine, nutritional and metabolic diseases [†] , n (%)	131 (67)	42 (64)	89 (68)	0.546
Diabetes mellitus [†] , n (%)	61 (31)	17 (26)	44 (34)	0.262
Cardiovascular disease [†] , n (%)	124 (63)	43 (65)	81 (62)	0.649
Hypertension [†] , n (%)	94 (48)	33 (50)	61 (47)	0.649
Steps/day, m (SD)	7488 (4234)	6395 (3315)	8069 (4554)	0.007
Time in moderate to vigorous physical activity (>3 METs; h/day), med (P25-P75)	1.7 (1.2–2.2)	1.6 (1.1–2.0)	1.7 (1.3–2.4)	0.058
Intensity during physical activities (m/s ²), m (SD)	1.029 (0.265)	0.970 (0.229)	1.060 (0.279)	0.020
C-PPAC amount, med (P25-P75)	77 (67–83)	72 (65–83)	77 (67–83)	0.223
C-PPAC difficulty, med (P25-P75)	83 (72–94)	81 (69–94)	86 (75–94)	0.562
C-PPAC score, med (P25-P75)	78 (70–86)	78 (67–84)	78 (72–86)	0.265
Psychological				
Anxiety (HAD-A), m (SD)	5.4 (4.2)	5.6 (4.6)	5.3 (4.0)	0.637
Depression (HAD-D), m (SD)	3.6 (3.7)	3.3 (4.1)	3.8 (3.4)	0.449
Unwillingness to follow the intervention, n (%)	26 (13)	2 (3)	24 (18)	0.002
Stage of change: action, maintaining, finalizing [§] , n (%)	80 (50)	22 (41)	58 (55)	0.095

(Continued)

Table 1. (Continued)

	All patients	Lost to follow-up	Completers	p-value
	n = 202*	n = 70	n = 132	
Self-efficacy [‡] (0 to 10), med (P25-P75)	8 (7–10)	9 (7–10)	8 (7–10)	0.920

Data are presented as n (%), mean (SD) or median (P25-P75). FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; 6MWD: 6-min walking distance; mMRC: modified Medical Research Council; BMI: body mass index; FFMI: fat free mass index; MET: metabolic equivalent of task; C-PPAC: Clinical visit—PROactive Physical Activity in COPD; HAD-A: Hospital Anxiety and Depression scale- Anxiety; HAD-D: Hospital Anxiety and Depression scale- Depression.

** Living with a partner vs single, widowed or divorced.

[‡] A COPD exacerbation was considered severe if the patient required admission to the hospital or the emergency department.

[†] ICD10 codes: C00 to D48 for Neoplasm; E00 to E90 for Endocrine, nutritional and metabolic diseases; E10 to E14 for Diabetes mellitus; I00 to I99 for Cardiovascular diseases; I10 to I15 for Hypertension.

[§] Stage of change: action, maintaining, finalizing vs pre-contemplation, contemplation, preparation.

[‡] Self-efficacy: Sure to go out for a walk every day (0 not sure- 10 completely sure).

* Some variables had missing values. Number of missings for 12-month completion: 1 in socioeconomic status, 1 in marital status, 3 in grandparenting, 3 in urban vulnerability index, 7 for severe COPD exacerbation in previous 12 months, 16 for FFMI, 5 for neoplasm, 5 for endocrine, nutritional and metabolic diseases, 5 for diabetes mellitus, 5 for any cardiovascular disease, 5 for hypertension, 57 for C-PPAC, 1 in depression, 42 in stage of change, 14 in self-efficacy.

<https://doi.org/10.1371/journal.pone.0217157.t001>

vulnerable neighborhoods was negatively associated; (2) active working and endocrino-metabolic comorbidities were positively associated with intervention response while unwillingness to follow the intervention was negatively associated; (3) most clinical and functional

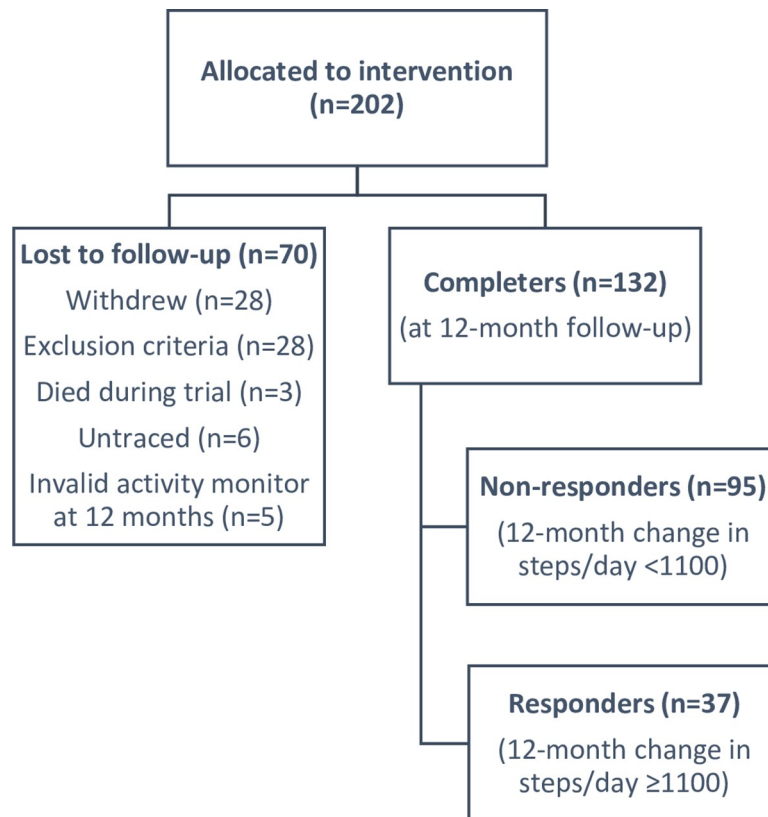


Fig 1. Flow of participants through the study.

<https://doi.org/10.1371/journal.pone.0217157.g001>

Table 2. Adjusted predictive factors of 12-month completion of a behavioral physical activity intervention in 202 COPD patients.

	OR (95% CI)	p-value
Steps/day (per increase of 1000 steps)	1.11 (1.02–1.21)	0.012
Living with a partner (vs single/ widowed/ divorced)	2.77 (1.41–5.48)	0.003
Urban vulnerability index (per increase of 0.1 units)	0.70 (0.57–0.86)	0.001

OR: odds ratio; CI: confidence interval.

<https://doi.org/10.1371/journal.pone.0217157.t002>

characteristics of COPD previously reported to be relevant for physical activity and specifically interventions' completion or response were not associated with these outcomes in our sample population; and (4) predictors of study completion were different from predictors of intervention response.

Determinants of study completion

Our study shows that patients who were more physically active at baseline were more likely to complete the study. We hypothesize that physically active patients already had established a habit around regular physical activity, which acted as a facilitator for participation so that these patients were willing and able to complete the study. Indeed, continuation of an active lifestyle from the past has been reported as a reason to be physically active in an earlier mixed-methods study which combined qualitative and quantitative approaches [32]. Thus, while some intervention studies have excluded more active patients, our results support the inclusion of all COPD patients, even those already considerably active at baseline, in line with the GOLD strategy to promote physical activity for all patients [5].

Living with a partner or in a less vulnerable neighborhood were further predictors of study completion. The role of interpersonal factors such as social support from family, or environmental factors (e.g. 'seeing others active' or 'neighborhood walkability'), has been recognized within the ecological model of the determinants of physical activity in the general population [14] and is increasingly studied in COPD patients. Being in a supportive relationship was associated with higher levels of physical activity in COPD patients [22,33]. Qualitative studies on barriers to pulmonary rehabilitation have linked living alone to a lack of support, increased challenges to participate, and reduced motivation [34,35]. We anticipate that both living with a partner and living in a less vulnerable neighborhood may facilitate study completion through mechanisms such as social support, behavioral modeling and walkable access to public open spaces [14], thereby lowering mental and physical barriers.

Determinants of intervention response

Being an active worker was related to a higher likelihood of response to the Urban Training intervention. This finding was surprising since one might expect that working actively might hinder a response to the intervention for time constraints. Lack of time has been acknowledged as a barrier to physical activity in the general [36] and in the COPD population [37] and working is often used as excuse not to exercise. Several hypotheses might explain this unexpected association. First, active workers were younger (mean age 59 vs 70 years in our sample, $p < 0.001$), which could have increased their capacities to engage in the intervention. However, in our study age was not related with response (Table 3). Second, patients who kept working despite their COPD, may have had better overall health conditions than those who were retired (which was supported by higher exercise capacity in this group, median 6MWD 540 vs 508, $p = 0.139$). However, our data does not support a role for exercise capacity in response to the

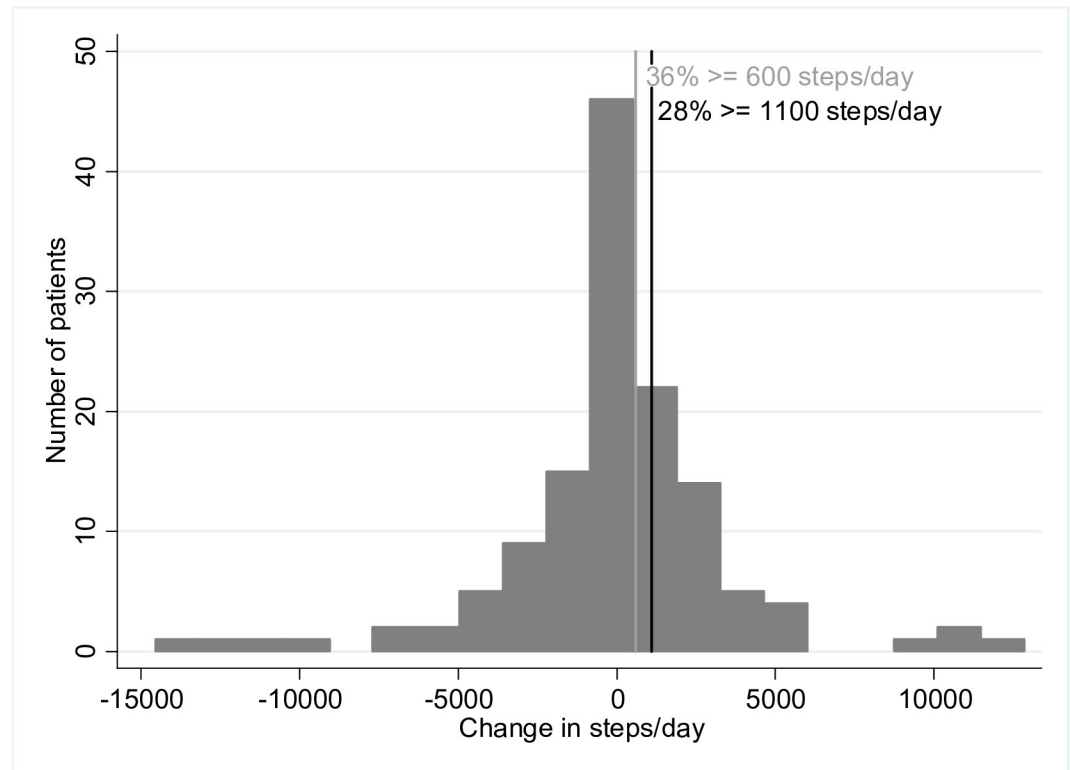


Fig 2. Change in steps/day between baseline and 12-month follow-up after a behavioral physical activity intervention.

<https://doi.org/10.1371/journal.pone.0217157.g002>

intervention (Table 3). We speculate that active workers may have a more active attitude and higher social support (by work colleagues) to engage in an intervention. They also may have experienced more opportunities to integrate a new physical activity habit into daily life routine and change to a more active life style e.g. switching the commuting mode from private car to walking.

Diagnosis of an endocrino-metabolic comorbidity was also significantly associated with higher likelihood of intervention response, which could seem counterintuitive if patients with concomitant diseases have a poorer health status. In the previous study by Demeyer et al the response to the telecoaching intervention was similar in patients with more than two comorbidities compared to none or one comorbidity [8]. Unfortunately, specific comorbidities were not investigated in that study which precludes direct comparison. Similarly, in the previous study by Moy the number of comorbidities did not predict a change in steps/day at 4 months [12]. Akin to our results, metabolic disease has been reported as an independent predictor for higher response to pulmonary rehabilitation in COPD patients [38]. In our specific sample, endocrino-metabolic comorbidity included mostly a physician diagnosis of diabetes, overweight/obesity and/or hyperlipidemia. However, the small number of cases combined with the high variability in the outcome (response to the intervention) preclude the analysis of the individual effect of each chronic condition. We speculate that the diagnosis of some comorbidities prior to our intervention may have led to the recommendation of increased physical activity in the past. Raised awareness and sensitivity to the topic may in turn have motivated response to the Urban Training intervention.

Spontaneously expressed unwillingness to follow the intervention instructions at baseline was inversely related to the likelihood of response. This is in line with the Urban Training

Table 3. Variables related to 12-month response in COPD patients participating in a behavioral physical activity intervention.

	Non-responders (12-month change in steps/day <1100)	Responders (12-month change in steps/day ≥1100)	p-value
	n = 95*	n = 37*	
Sociodemographic			
Age (years), m (SD)	69.2 (8.7)	66.0 (9.7)	0.075
Sex: male, n (%)	85 (89)	29 (78)	0.095
Smoking status, current, n (%)	24 (25)	10 (27)	0.835
Socioeconomic status, I-III-IV-V, n (%)	66 (70)	27 (73)	0.754
Interpersonal			
Living with a partner**, n (%)	75 (79)	29 (78)	0.943
Grandparenting, n (%)	38 (40)	9 (24)	0.084
Active workers, n (%)	10 (11)	9 (24)	0.043
Environmental			
Urban vulnerability index (from 0 -lowest to 1 -highest), m (SD)	0.60 (0.18)	0.63 (0.15)	0.494
Recruitment season			
Spring, n (%)	24 (25)	9 (24)	0.921
Summer, n (%)	9 (9)	2 (6)	
Fall, n (%)	33 (35)	13 (35)	
Winter, n (%)	29 (31)	13 (35)	
Clinical			
FEV ₁ (% pred), m (SD)	54.3 (16.4)	60.1 (17.1)	0.074
FVC (% pred), m (SD)	75.7 (16.3)	82.2 (17.9)	0.048
6MWD (m), m (SD)	493 (97)	512 (90)	0.299
Moderate to very severe dyspnea (mMRC ≥2), n (%)	27 (28)	9 (24)	0.635
Any severe [†] COPD exacerbation in previous 12 months, n (%)	9 (10)	1 (3)	0.282
Any severe [†] COPD exacerbation during follow-up, n (%)	13 (14)	9 (26)	0.123
BMI (kg/m ²), m (SD)	28.4 (5.3)	28.4 (4.1)	0.998
FFMI, m (SD)	19.6 (3.3)	19.4 (2.4)	0.690
Neoplasm [†] , n (%)	14 (15)	5 (14)	0.902
Endocrine, nutritional and metabolic diseases [†] , n (%)	58 (61)	31 (86)	0.006
Diabetes mellitus [†] , n (%)	31 (33)	13 (36)	0.707
Cardiovascular disease [†] , n (%)	58 (61)	23 (64)	0.765
Hypertension [†] , n (%)	41 (43)	20 (56)	0.204
Steps/day, m (SD)	8241 (4824)	7625 (3794)	0.487
Time in moderate to vigorous physical activity (>3 METs; h/day), med (P25-P75)	1.7 (1-3-2.4)	1.8 (1.2-2.4)	0.933
Intensity during physical activities (m/s ²), m (SD)	1.09 (0.31)	1.05 (0.27)	0.431
C-PPAC amount, med (P25-P75)	77 (67-83)	77 (70-91)	0.238
C-PPAC difficulty, med (P25-P75)	86 (75-94)	85 (73-94)	0.908
C-PPAC score, med (P25-P75)	78 (73-86)	83 (68-89)	0.423
Psychological			
Anxiety (HAD-A), m (SD)	5.3 (4.2)	5.4 (3.7)	0.861
Depression (HAD-D), m (SD)	3.8 (3.5)	3.6 (3.3)	0.810
Unwillingness to follow the intervention, n (%)	22 (23)	2 (5)	0.022
Stage of change: action, maintaining, finalizing [§] , n (%)	44 (56)	14 (50)	0.559

(Continued)

Table 3. (Continued)

	Non-responders (12-month change in steps/day <1100)	Responders (12-month change in steps/day ≥1100)	p-value
	n = 95*	n = 37*	
Self-efficacy [‡] (0 to 10), med (P25-P75)	8 (7–10)	8 (6–10)	0.755

Data are presented as n (%), mean (SD) or median (P25-P75). FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; 6MWD: 6-min walking distance; mMRC: modified Medical Research Council; BMI: body mass index; FFMI: fat free mass index; MET: metabolic equivalent of task; C-PPAC: Clinical visit—PROactive Physical Activity in COPD; HAD-A: Hospital Anxiety and Depression scale- Anxiety; HAD-D: Hospital Anxiety and Depression scale- Depression.

** Living with a partner vs single, widowed or divorced.

[‡] A COPD exacerbation was considered severe if the patient required admission to the hospital or the emergency department.

[†] ICD10 codes: C00 to D48 for Neoplasm; E00 to E90 for Endocrine, nutritional and metabolic diseases; E10 to E14 for Diabetes mellitus; I00 to I99 for Cardiovascular diseases; I10 to I15 for Hypertension.

[§] Stage of change: action, maintaining, finalizing vs pre-contemplation, contemplation, preparation.

^{*} Self-efficacy: Sure to go out for a walk every day (0 not sure- 10 completely sure).

* Some variables had missing values. Number of missings for 12-month response: 1 in socioeconomic status, 1 in grandparenting, 1 in urban vulnerability index, 2 for severe COPD exacerbation in previous 12 months, 5 for severe COPD exacerbation during follow-up, 12 for FFMI, 1 for neoplasm, 1 for endocrine, nutritional and metabolic diseases, 1 for diabetes mellitus, 1 for any cardiovascular disease, 1 for hypertension, 35 for C-PPAC, 1 in depression, 26 in stage of change, 8 in self-efficacy.

<https://doi.org/10.1371/journal.pone.0217157.t003>

principal paper which observed the intervention to be efficacious to increase physical activity in the *per protocol* population but ineffective in the full population [9]. It also underlines clearly the important role of motivation and a positive mindset towards the physical activity intervention, which have been established previously as important factors for physical activity in qualitative and mixed-methods cross-sectional studies with COPD patients [32,37,39]. Unfortunately, our study did not collect quantitative data on motivation. However, it could be argued that both being an active worker and having a diagnosis of endocrino-metabolic comorbidities essentially also reflect the importance of motivation.

There was a number of variables we had expected to be associated with the intervention response, based on the results of previous studies [8,11,13], on research on physical activity and COPD [2] and on clinical experience. These variables included markers of COPD severity (FEV₁, COPD exacerbations, dyspnea or exercise capacity), psychological factors (depression, anxiety or self-efficacy), the season of inclusion, or the baseline levels of physical activity. Whether their lack of association with intervention response may be due to the fact that other studies recruited patients in more advanced stages of disease needs to be confirmed in further clinical trials.

Implications

Our study has implications for future research, clinical management and public health and policies. First, the response to the Urban Training intervention (defined as an increase of

Table 4. Adjusted predictive factors of 12-month response to a behavioral physical activity intervention in 132 COPD patients.

	OR (95% CI)	p-value
Active workers	3.14 (1.05–9.33)	0.040
Endocrine, nutritional and metabolic diseases [†]	4.36 (1.49–12.80)	0.007
Unwillingness to follow the intervention	0.21 (0.05–0.98)	0.047

OR: odds ratio; CI: confidence interval.

[†] ICD10 codes: E00 to E90 for endocrine, nutritional and metabolic diseases.

<https://doi.org/10.1371/journal.pone.0217157.t004>

≥ 1100 steps/day after 12 months, according to previously published MID [28]) has been low with 28% which is in line with the telecoaching intervention which observed a 36% response (defined as an increase of > 1000 steps/day) [8]. This reinforces the need to understand which patients would benefit most from the available resources. Second, we may consider excluding patients who reject participation at baseline to contain health service costs and maximize effectiveness, and consider alternative strategies for these patients. Third, physical activity interventions should neither exclude patients with certain chronic conditions nor actively working patients but rather pay special attention to these individuals since they may be particularly motivated and thus respond better. Fourth, the role of baseline levels of physical activity to include or exclude COPD patients into physical activity interventions should be cautiously considered, since existing literature is still unclear and no patient should be left without an intervention potentially efficacious for him/her. Finally, we suggest that screening for interpersonal and environmental factors may help to decide which patients are more likely to succeed in long-term physical activity interventions.

Strengths and limitations

A major strength of our study lies within the fact that the Urban Training intervention was administered to COPD patients from hospital and primary care settings. The findings therefore reflect more closely than previous studies (based on hospitals or rehabilitation settings only) what can be expected when deploying a physical activity intervention at the population level. Moreover, the study design allowed us to assess the determinants of a long-term effect. These are more likely to be the determinants of a real behavior change as compared to the short-term effects shown in literature. Finally, the broad number of variables included in our study reflect well the various domains of the determinants of physical activity within the ecological framework [14].

As potential limitation we have to acknowledge the small sample size that did not allow testing the potential association of some rare factors (e.g. less frequent comorbidities) with completion or response. Although we included a broad range of variables, some variables related to physical activity limitation in COPD patients such as reduced muscle strength or impaired lung volumes were missing. Finally, our study population reflects the behavior of a population from a specific geographic area (i.e. 'elderly inhabitants of Mediterranean cities' [9]) and included a large proportion of patients with relatively mild-to-moderate stages of disease. Thus, further research is needed to identify determinants of completion and response in patients from other regions or medical settings, as is usually done prior to deployment of any intervention.

Conclusions

Among a broad range of potential predictors of 12-month completion or response to a behavioral physical activity intervention, this study found that completion was generally determined by previous physical activity habits as well as interpersonal and environmental physical activity facilitators while response was related to diverse factors thought to modify the individual motivation to change to an active lifestyle. These results support a look beyond the traditional clinical and functional variables and the consideration of psychological, interpersonal and environmental factors related to habits and motivation to optimize the outcome of physical activity interventions in COPD.

Supporting information

S1 File. Supporting information.
(PDF)

Acknowledgments

The Urban Training Study Group: ISGlobal, Barcelona: Ane Arbillaga-Etxarri, Marta Benet, Anna Delgado, Judith Garcia-Aymerich, Elena Gimeno-Santos, Jaume Torrent-Pallicer; FCS Blanquerna, Universitat Ramon Llull, Barcelona: Jordi Vilaró; Servei de Pneumologia, Hospital Clínic de Barcelona, Barcelona: Anael Barberan-Garcia, Robert Rodriguez-Roisin; Hospital del Mar, Institut Hospital del Mar d'Investigacions Mèdiques (IMIM), Barcelona: Eva Balcells, Diego A Rodríguez Chiaradía; Hospital Universitari Germans Trias i Pujol, Badalona: Alicia Marín; Hospital de Mataró, Consorci Sanitari del Maresme, Mataró: Pilar Ortega; Hospital de Viladecans, Viladecans: Nuria Celorrio; Institut Universitari d'Investigació en Atenció Primària Jordi Gol (IDIAP Jordi Gol): Mónica Mon teagudo, Nuria Montellà, Laura Muñoz, Pere Toran; Centre d'Atenció Primària Viladecans 2, Institut Català de la Salut, Viladecans: Pere Simonet; Centre d'Atenció Primària Passeig de Sant Joan, Institut Català de la Salut, Barcelona: Carme Jané, Carlos Martín-Cantera; Centre d'Atenció Primària Sant Roc, Institut Català de la Salut, Badalona: Eulàlia Borrell; Universitat Internacional de Catalunya (UIC), Barcelona: Pere Vall-Casas.

Author Contributions

Conceptualization: Maria Koreny, Heleen Demeyer, Ane Arbillaga-Etxarri, Elena Gimeno-Santos, Anael Barberan-Garcia, Marta Benet, Eva Balcells, Eulàlia Borrell, Alicia Marin, Diego A. Rodríguez Chiaradía, Pere Vall-Casas, Jordi Vilaró, Robert Rodríguez-Roisin, Judith Garcia-Aymerich.

Formal analysis: Maria Koreny, Marta Benet, Judith Garcia-Aymerich.

Writing – original draft: Maria Koreny, Judith Garcia-Aymerich.

Writing – review & editing: Maria Koreny, Heleen Demeyer, Ane Arbillaga-Etxarri, Elena Gimeno-Santos, Anael Barberan-Garcia, Marta Benet, Eva Balcells, Eulàlia Borrell, Alicia Marin, Diego A. Rodríguez Chiaradía, Pere Vall-Casas, Jordi Vilaró, Robert Rodríguez-Roisin, Judith Garcia-Aymerich.

References

1. Soriano JB, Abajobir AA, Abate KH, Abera SF, Agrawal A, Ahmed MB, et al. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Respir Med*. 2017; 5(9):691–706. [https://doi.org/10.1016/S2213-2600\(17\)30293-X](https://doi.org/10.1016/S2213-2600(17)30293-X) PMID: 28822787
2. Gimeno-Santos E, Frei A, Steurer-Stey C, De Batlle J, Rabinovich RA, Raste Y, et al. Determinants and outcomes of physical activity in patients with COPD: a systematic review on behalf of PROactive consortium. *Thorax*. 2014; 69(8):731–9. <https://doi.org/10.1136/thoraxjnl-2013-204763> PMID: 24558112
3. Van Remoortel H, Hornikx M, Demeyer H, Langer D, Burtin C, Decramer M, et al. Daily physical activity in subjects with newly diagnosed COPD. *Thorax*. 2013 Oct; 68(10):962–3. <https://doi.org/10.1136/thoraxjnl-2013-203534> PMID: 23604460
4. Waschki B, Kirsten AM, Holz O, Mueller K-C, Schaper M, Sack A-L, et al. Disease Progression and Changes in Physical Activity in Patients with Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med*. 2015; 192(3):295–306. <https://doi.org/10.1164/rccm.201501-0081OC> PMID: 26020495
5. From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 [Internet]. 2017 [cited 2018 Oct 19]. Available from: <http://www.goldcopd.org/>
6. Mendoza L, Horta P, Espinoza J, Aguilera M, Balmaceda N, Castro A, et al. Pedometers to enhance physical activity in COPD: a randomised controlled trial. *Eur Respir J*. 2015; 45:347–54. <https://doi.org/10.1183/09031936.00084514> PMID: 25261324

7. Moy ML, Martinez CH, Kadri R, Roman P, Holleman RG, Myra Kim H, et al. Long-Term Effects of an Internet-Mediated Pedometer-Based Walking Program for Chronic Obstructive Pulmonary Disease: Randomized Controlled Trial. *J Med Internet Res*. 2016; 18(8):e215. <https://doi.org/10.2196/jmir.5622> PMID: 27502583
8. Demeyer H, Louvaris Z, Frei A, Rabinovich RA, De Jong C, Gimeno-Santos E, et al. Physical activity is increased by a 12-week semiautomated telecoaching programme in patients with COPD: a multicentre randomised controlled trial. *Thorax*. 2017; 72:415–23. <https://doi.org/10.1136/thoraxjnl-2016-209026> PMID: 28137918
9. Arbillaga-Etxarri A, Gimeno-Santos E, Barberan-Garcia A, Balcells E, Benet M, Borrell E, et al. Long-term efficacy and effectiveness of a behavioural and community-based exercise intervention (Urban Training) to increase physical activity in patients with COPD: a randomised controlled trial. *Eur Respir J*. 2018; 52:1800063. <https://doi.org/10.1183/13993003.00063-2018> PMID: 30166322
10. Garcia-Aymerich J. Research Needs on Physical Activity and Chronic Obstructive Pulmonary Disease: Bridging the Gap between Knowledge and Behaviour. *BRN Rev*. 2015; 1:92–104.
11. Altenburg WA, Ten Hacken NHT, Bossenbroek L, Kerstjens HAM, De Greef MHG, Wempe JB. Short- and long-term effects of a physical activity counselling programme in COPD: A randomized controlled trial. *Respir Med*. 2015; 109:112–21. <https://doi.org/10.1016/j.rmed.2014.10.020> PMID: 25499548
12. Moy ML, Collins RJ, Martinez CH, Kadri R, Roman P, Holleman RG, et al. An Internet-Mediated Pedometer-Based Program Improves Health-Related Quality-of-Life Domains and Daily Step Counts in COPD. A Randomized Controlled Trial. *Chest*. 2015; 148(1):128–37. <https://doi.org/10.1378/chest.14-1466> PMID: 25811395
13. Kantorowski A, Wan ES, Homsy D, Kadri R, Richardson CR, Moy ML. Determinants and outcomes of change in physical activity in COPD. *ERJ Open Res*. 2018; 4:00054–2018. <https://doi.org/10.1183/23120541.00054-2018> PMID: 30083551
14. Bauman AE, Reis RS, Sallis JF, Wells JC, F Loos RJ, Martin BW, et al. Correlates of physical activity: why are some people physically active and others not? *Lancet*. 2012; 380:258–71. [https://doi.org/10.1016/S0140-6736\(12\)60735-1](https://doi.org/10.1016/S0140-6736(12)60735-1) PMID: 22818938
15. WHO. Innovative Care for Chronic Conditions: Building Blocks for Action. 2002.
16. Celli BR, Macnee W, Agusti A, Anzueto A, Berg B, Buist AS, et al. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*. 2004; 23:932–46. PMID: 15219010
17. Miller WR, Rollnick S. Motivational interviewing: preparing people for change. 2nd ed. New York: Guilford Press; 2002.
18. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. *Am J Health Promot*. 1997; 12(1):38–48. <https://doi.org/10.4278/0890-1171-12.1.38> PMID: 10170434
19. Arbillaga-Etxarri A, Torrent-Pallicer J, Gimeno-Santos E, Barberan-Garcia A, Delgado A, Balcells E, et al. Validation of Walking Trails for the Urban Training™ of Chronic Obstructive Pulmonary Disease Patients. Zulueta JJ, editor. *PLoS One*. 2016 Jan 14; 11(1):e0146705. <https://doi.org/10.1371/journal.pone.0146705> PMID: 26766184
20. Projecte Entrenament Urbà [Internet]. [cited 2018 Oct 20]. Available from: <http://www.entrenament-urba.cat/>
21. European Lung Foundation—ELF. Factsheets. Living an active life with COPD. [Internet]. [cited 2018 Oct 20]. Available from: <http://www.europeanlung.org/assets/files/en/publications/living-an-active-life-with-copd-en.pdf>
22. Arbillaga-Etxarri A, Gimeno-Santos E, Barberan-Garcia A, Benet M, Borrell E, Dadvand P, et al. Socio-environmental correlates of physical activity in patients with chronic obstructive pulmonary disease (COPD). *Thorax*. 2017; 0:1–7.
23. Atlas de la Vulnerabilidad Urbana. Ministerio de Fomento. Gobierno de España. [Internet]. [cited 2018 Oct 20]. Available from: www.fomento.gob.es/MFOM/LANG_CASTELLANO/DIRECCIONES_GENERALES/ARQ_VIVIENDA/SUELO_Y_POLITICAS/OBSERVATORIO/Atlas_Vulnerabilidad_Urbana/%0D
24. Rabinovich RA, Louvaris Z, Raste Y, Langer D, Van Remoortel H, Giavedoni S, et al. Validity of physical activity monitors during daily life in patients with COPD. *Eur Respir J*. 2013 Nov 1; 42(5):1205–15. <https://doi.org/10.1183/09031936.00134312> PMID: 23397303
25. Van Remoortel H, Raste Y, Louvaris Z, Giavedoni S, Burtin C, Langer D, et al. Validity of six activity monitors in chronic obstructive pulmonary disease: a comparison with indirect calorimetry. *PLoS One*. 2012 Jan; 7(6):e39198. <https://doi.org/10.1371/journal.pone.0039198> PMID: 22745715

26. Demeyer H, Burtin C, Van Remoortel H, Hornikx M, Langer D, Decramer M, et al. Standardizing the analysis of physical activity in patients with COPD following a pulmonary rehabilitation program. *Chest*. 2014 Aug; 146(2):318–27. <https://doi.org/10.1378/chest.13-1968> PMID: 24603844
27. Gimeno-Santos E, Raste Y, Demeyer H, Louvaris Z, De Jong C, Rabinovich RA, et al. The PROactive instruments to measure physical activity in patients with chronic obstructive pulmonary disease. *Eur Respir J*. 2015; 46:988–1000. <https://doi.org/10.1183/09031936.00183014> PMID: 26022965
28. Demeyer H, Burtin C, Hornikx M, Camillo CA, Van Remoortel H, Langer D, et al. The Minimal Important Difference in Physical Activity in Patients with COPD. *PLoS One*. 2016; 11(4):e0154587. <https://doi.org/10.1371/journal.pone.0154587> PMID: 27124297
29. Donders ART, Van Der Heijden GJMG, Stijnen T, Moons KGM. Review: A gentle introduction to imputation of missing values. *J Clin Epidemiol*. 2006; 59:1087–91. <https://doi.org/10.1016/j.jclinepi.2006.01.014> PMID: 16980149
30. van Buuren S, Boshuizen HC, Knook DL. Multiple imputation of missing blood pressure covariates in survival analysis. *Stat Med*. 1999; 18(6):681–94. PMID: 10204197
31. Hosmer DW, Lemeshow S, Sturdivant RX. *Applied logistic regression*. 3rd ed. Hoboken, New Jersey: John Wiley & Sons; 2013.
32. Hartman JE, ten Hacken NHT, Boezen HM, de Greef MHG. Self-efficacy for physical activity and insight into its benefits are modifiable factors associated with physical activity in people with COPD: A mixed-methods study. *J Physiother*. 2013; 59(2):117–24. [https://doi.org/10.1016/S1836-9553\(13\)70164-4](https://doi.org/10.1016/S1836-9553(13)70164-4) PMID: 23663797
33. Mesquita R, Nakken N, A Janssen DJ, A van den Bogaart EH, L Delbressine JM, N Essers JM, et al. Activity Levels and Exercise Motivation in Patients With COPD and Their Resident Loved Ones. *Chest*. 2017; 151(5):1028–38. <https://doi.org/10.1016/j.chest.2016.12.021> PMID: 28087303
34. Keating A, Lee A, Holland AE. What prevents people with chronic obstructive pulmonary disease from attending pulmonary rehabilitation? A systematic review. *Chron Respir Dis*. 2011; 8(2):89–99. <https://doi.org/10.1177/1479972310393756> PMID: 21596892
35. Arnold E, Bruton A, Ellis-Hill C. Adherence to pulmonary rehabilitation: A qualitative study. *Respir Med*. 2006; 100:1716–23. <https://doi.org/10.1016/j.rmed.2006.02.007> PMID: 16554147
36. Centers for Disease Control and Prevention. Overcoming Barriers to Physical Activity [Internet]. [cited 2018 Oct 20]. Available from: <http://www.cdc.gov/physicalactivity/everyone/getactive/barriers.html>
37. Kosteli M-C, Heneghan NR, Roskell C, Williams SE, Adab P, Dickens AP, et al. Barriers and enablers of physical activity engagement for patients with COPD in primary care. *Int J Chron Obstruct Pulmon Dis*. 2017; 12:1019–31. <https://doi.org/10.2147/COPD.S119806> PMID: 28405162
38. Walsh JR, McKeough ZJ, Morris NR, Chang AT, Yerkovich ST, Seale HE, et al. Metabolic Disease and Participant Age Are Independent Predictors of Response to Pulmonary Rehabilitation. *J Cardiopulm Rehabil Prev*. 2013; 33(4):249–56. <https://doi.org/10.1097/HCR.0b013e31829501b7> PMID: 23748375
39. Thorpe O, Saravana K, Johnston K. Barriers to and enablers of physical activity in patients with COPD following a hospital admission: a qualitative study. *Int J COPD*. 2014; 2014(9):115–28.