**Physical activity patterns and clusters in 1001 patients with COPD**

Rafael Mesquita1,2,\*, Gabriele Spina3,4,\*, Fabio Pitta5, David Donaire-Gonzalez6,7, Brenda M. Deering8, Mehul S. Patel9, Katy E. Mitchell10, Jennifer Alison11,12, Arnoldus J. R. van Gestel13, Stefanie Zogg14, Philippe Gagnon15, Beatriz Abascal-Bolado16,17, Barbara Vagaggini18, Judith Garcia-Aymerich6,7,19, Sue C. Jenkins20, Elisabeth A. P. M. Romme21, Samantha S. C. Kon9, Paul S. Albert22, Benjamin Waschki23, Dinesh Shrikrishna9, Sally J. Singh10, Nicholas S. Hopkinson9, David Miedinger14, Roberto P. Benzo17, François Maltais15, Pierluigi Paggiaro18, Zoe J. McKeough11, Michael I. Polkey9, Kylie Hill20, William D-C. Man9, Christian F. Clarenbach13, Nidia A. Hernandes5, Daniela Savi24, Sally Wootton11, Karina C. Furlanetto5, Li W. Cindy Ng20, Anouk W. Vaes1, Christine Jenkins25, Peter R. Eastwood26, Diana Jarreta27, Anne Kirsten23, Dina Brooks28, David R. Hillman26, Thaís Sant’Anna5, Kenneth Meijer29, Selina Dürr14, Erica P. A. Rutten1, Malcolm Kohler13, Vanessa S. Probst5,30, Ruth Tal-Singer31, Esther Garcia Gil27, Albertus C. den Brinker4, Jörg D. Leuppi14, Peter M. A. Calverley22, Frank W. J. M. Smeenk21, Richard W. Costello8, Marco Gramm23, Roger Goldstein28, Miriam T. J. Groenen1, Helgo Magnussen23, Emiel F. M. Wouters1,2, Richard L. ZuWallack32, Oliver Amft3,33,†, Henrik Watz23,†, Martijn A. Spruit1,34,†.

\*Joint first authors

†Joint senior authors

**Affiliations:**

1Department of Research & Education, Center of expertise for chronic organ failure + (CIRO+), Horn, The Netherlands.

2Department of Respiratory Medicine, Maastricht University Medical Center+ (MUMC+), Maastricht, The Netherlands.

3Department of Signal Processing Systems, Technische Universiteit Eindhoven, Eindhoven, The Netherlands.

4Smart Sensing and Analysis Group, Philips Research, Eindhoven, The Netherlands.

5Laboratory of Research in Respiratory Physiotherapy, Department of Physiotherapy, State University of Londrina (UEL), Londrina, Brazil.

6Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain.

7CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain.

8Department of Respiratory Medicine, Beaumont Hospital, Dublin, Ireland.

9NIHR Respiratory Biomedical Research Unit, Royal Brompton & Harefield NHS Foundation Trust and Imperial College, London, United Kingdom.

10NIHR EM CLAHRC - Centre for Exercise and Rehabilitation Science, University Hospitals, Leicester, United Kingdom.

11Clinical and Rehabilitation Sciences, The University of Sydney, Sydney, NSW, Australia.

12Physiotherapy Department, Royal Prince Alfred Hospital, Sydney, NSW, Australia.

13Pulmonary Division, University Hospital of Zurich, Zurich, Switzerland.

14Medical University Clinic, Cantonal Hospital Baselland, Liestal and Medical Faculty, University of Basel, Basel, Switzerland.

15Centre de recherche, Institut Universitaire de cardiologie et de pneumologie de Québec, 2725 Chemin Ste-Foy Québec, Université Laval, Québec G1V 4G5, Canada.

16Division of Pulmonary, Hospital U. Marqués de Valdecilla, IFIMAV, Santander, Spain.

17Mindful Breathing Laboratory, Mayo Clinic, Rochester, MN, United States of America.

18Cardio-Thoracic and Vascular Department, University of Pisa, Pisa, Italy.

19Universitat Pompeu Fabra (UPF), Barcelona, Spain.

20School of Physiotherapy and Exercise Science, Curtin University, Perth, WA, Australia.

21Department of Respiratory Medicine, Catharina Hospital, Eindhoven, The Netherlands.

22School of Ageing and Chronic Disease, University Hospital Aintree, Liverpool, United Kingdom.

23Pulmonary Research Institute at LungClinic Grosshansdorf, Airway Research Center North, Member of the German Centre for Lung Research, Grosshansdorf, Germany.

24Department of Pediatrics and Pediatric Neurology, Cystic Fibrosis Center, Sapienza University of Rome, Rome, Italy.

25Woolcock Institute of Medical Research, The University of Sydney, Camperdown, NSW, Australia.

26Department of Pulmonary Physiology, Sir Charles Gairdner Hospital, Perth, WA, Australia.

27R&D Centre, Almirall, Barcelona, Spain.

28Respiratory Medicine, West Park Healthcare Centre and Faculty of Medicine, University of Toronto, Toronto, Canada.

29Department of Human Movement Science, Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands.

30Center for Research in Health Sciences, University North of Paraná (UNOPAR), Londrina, Brazil.

31GlaxoSmithKline R&D, King of Prussia, PA, United States of America.

32Department of Pulmonary and Critical Care, Saint Francis Hospital and Medical Center, Hartford, CT, United States of America.

33ACTLab group, Chair of Sensor Technology, University Passau, Passau, Germany.

34REVAL - Rehabilitation Research Center, BIOMED - Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt University, Diepenbeek, Belgium.

**Correspondence:**

Rafael Mesquita, MSc, PT

Department of Research & Education, CIRO+, center of expertise for chronic organ failure+; Hornerheide 1, 6085 NM, Horn, The Netherlands; Telephone number: +31 475 587 645; Email: rafaelmesquita14@ymail.com

**"Take home" message**

Physical activity in patients with COPD needs to be clearly delineated when the aim is to promote physical activity.

**Running head:** Physical activity clusters in COPD.

**ABSTRACT**

Physical activity in patients with chronic obstructive pulmonary disease (COPD) is insufficiently understood. We aimed to describe physical activity measures and hourly patterns in patients with COPD after stratification for generic and COPD-specific characteristics; to compare these measures and patterns between patients and healthy subjects; and to identify clusters of patients based on physical activity measures.

1001 patients with COPD (age, 67 years; FEV1, 49% predicted) and 66 healthy subjects (age, 65 years; FEV1, 107% predicted) were studied cross-sectionally. Daily physical activity measures and physical activity hourly patterns (i.e., the graphic representation of the mean intensity per hour during a day) were analyzed based on data from a multi-sensor armband. Principal component analysis (PCA) and cluster analysis were applied to physical activity data to identify subgroups.

Age, body mass index (BMI), dyspnea grade and the ADO index (including age, dyspnea, and airflow obstruction) were associated with physical activity measures and hourly patterns in patients with COPD. Compared to matched healthy subjects, patients had lower intensities of physical activity across hourly patterns. Five clusters were identified based on 3 components from the PCA, which accounted for 60% of variance. Importantly, cluster 1 was characterized by higher BMI, lower FEV1, worse dyspnea and higher ADO index compared to other clusters (*P*<0.05 for all).

Daily physical activity measures and hourly patterns are heterogeneous in COPD. Subgroups of patients could be identified based on physical activity data. These findings may be useful for interventions aiming to promote physical activity in COPD.

**INTRODUCTION**

Patients with chronic obstructive pulmonary disease (COPD) undertake less physical activity compared to healthy individuals,([1](#_ENREF_1), [2](#_ENREF_2)) which is related to a higher risk of hospital (re-)admission and mortality.([3-5](#_ENREF_3)) Increase of physical activity in patients with COPD then becomes imperative, and indeed many treatment strategies have aimed this target (REFWatz2014). Nonetheless, the effect of these strategies on physical activity measures seems to be limited and/or insufficiently studied (REF15,31,35). Identifying groups with specific physical activity patterns may lead to more important improvements in physical activity. This can be achieved by the investigation of physical activity hourly patterns (REF11,12) and cluster analysis of physical activity measures (REF11,13).

([6-8](#_ENREF_6))([9](#_ENREF_9))([10](#_ENREF_10))

([11](#_ENREF_11), [12](#_ENREF_12))([11](#_ENREF_11), [13](#_ENREF_13)) Physical activity hourly patterns provide graphic representations of the temporal trends of physical activity intensities over the course of a day.([9](#_ENREF_9), [12](#_ENREF_12)) These data can reveal whether and to what extent physical activities are concentrated during certain periods of the day.([9](#_ENREF_9)) Cluster analysis may be useful to identify subgroups of patients with distinct physical activity characteristics.([14](#_ENREF_14)) It has been stressed that physical activity is a multi-dimensional construct that should be described by relevant constructs and measures besides its total amount (REF). Therefore, these approaches may provide a more comprehensive understanding of physical activity levels in patients with COPD.([8](#_ENREF_8), [15](#_ENREF_15), [16](#_ENREF_16))

To date, physical activity hourly patterns and cluster analysis of physical activity measures have not been investigated in patients with COPD. Therefore, we aimed i) to describe physical activity measures and physical activity hourly patterns in patients with COPD after stratification for generic and COPD-specific characteristics; ii) to compare physical activity measures and hourly patterns between patients with COPD and healthy subjects matched for gender, age and body mass index (BMI); and iii) to identify clusters of patients with COPD based on physical activity measures and the accompanying generic and COPD-specific characteristics, physical activity measures and physical activity hourly patterns.

**METHODS**

**Study design and participants**

In this multicenter, post-hoc, cross-sectional study, objectively assessed physical activity data from 10 countries (e.g., United Kingdom, Ireland, the Netherlands, Germany, Switzerland, Italy, Spain, the United States of America, Brazil, and Australia) were analysed. Published and/or unpublished physical activity data as assessed by the SenseWear Armband or SenseWear Mini Armband activity monitors (both from BodyMedia Inc., Pittsburgh, PA, USA) were considered for the current analyses. Subjects were included if they met the following inclusion criteria: COPD with a post-bronchodilator forced expiratory volume in the first 1 second (FEV1) / forced vital capacity (FVC) ratio <0.70,([17](#_ENREF_17)) stable condition (i.e., mainly no exacerbation in the previous four weeks), and complete data for age, gender, BMI and daily physical activity measures (see *Assessments* section). Centers from the Netherlands and the UK also provided data on healthy elderly subjects, who were then pairwise-matched (1:1) for gender, age and BMI with a subgroup of patients with COPD. Ethics Board approval was obtained from the local ethics committees, and written informed consent was provided by participants, except for the data from Italy (n=23), which was obtained as part of routine clinical assessments. The Italian data, however, was de-identified to protect patient information confidentiality. Please, see online supplement for details.

**Assessments**

Demographics, anthropometrics, lung function, and clinical data were assessed. In order to investigate their association with physical activity measures and hourly patterns, these outcomes were stratified according to established criteria or by the median split method (see online supplement). Disease severity was assessed by Global Initiative for Chronic Obstructive Lung Disease (GOLD) grades (1 to 4),([18](#_ENREF_18)) GOLD groups (A to D),([17](#_ENREF_17)) and age, dyspnea, and airflow obstruction ADO index,([19](#_ENREF_19)) which predicts COPD mortality. Moreover, the SenseWear Armband or SenseWear Mini Armband activity monitors were used to assess physical activity. These devices have showed their validity in field studies,([20](#_ENREF_20), [21](#_ENREF_21)) and in laboratory studies.([22](#_ENREF_22), [23](#_ENREF_23)) Physical activity intensities were classified based on the thresholds proposed by the American College of Sports Medicine (ACSM):([24](#_ENREF_24)) very light intensity, <2.0 metabolic equivalents of task (METs); light intensity, 2.0 to 2.9 METs; and moderate-to-vigorous intensity, ≥3.0 METs.

A minimum of 4 days (2 weekdays + Saturday + Sunday) was considered acceptable,([6](#_ENREF_6)) with the device being used for ≥22 hours·day-1.([2](#_ENREF_2)) Since physical activity measures during the week and the weekend are known to be different,([6](#_ENREF_6)) only recordings during waking hours of weekdays were considered for the cluster analysis. Details on the selection of waking hour recordings can be found online. The PA measures represent the average of all valid weekdays. Weekend days were used only for the presentation of daily physical activity hourly patterns, which consist of a graphic representation of the intensity of physical activity per hour during the course of a day.([9](#_ENREF_9), [11](#_ENREF_11), [12](#_ENREF_12)) For the clustering of patients, a set of relevant variables were generated after stratifying averages of physical activity measures according to different criteria (i.e., intensity, duration, period of the day, frequency and quantity, or the combination of these criteria; Table E1, online supplement).

**Statistical Analyses**

Continuous variables were expressed as median (interquartile range), as most variables presented non-normal distribution. Categorical variables were expressed as absolute and/or relative frequency. Mann-Whitney U test or Kruskal-Wallis test (post hoc Dunn) was used for comparing continuous variables, while the chi-square test was used for categorical variables. Spearman coefficient was used to investigate correlations, when appropriate. *P*<0.05 was considered significant and all statistical analyses were performed using SPSS 17.0 (SPSS, Chicago, Illinois, USA) or GraphPad Prism 5 (GraphPad Software, La Jolla, California, USA). Details about sample size calculation can be found online.

Cluster analysis was adopted to identify subgroups with distinct physical activity profiles. Firstly, Principal Component Analysis (PCA) was used to reduce the high-dimensional feature set (180 dimensions) to a lower subspace useful for data visualization (3 dimensions), not by discarding some of these variables but by computing 3 principal components that maximize the variance of the data in the subspace. The features were first standardized using z-scores. Secondly, a k-means clustering algorithm with automatic selection of the number of clusters was applied to the 3 dimensional principal components space to separate the subjects into groups with distinct characteristics. The algorithm selects the number of clusters in a way that the corresponding clustering results are the most stable under small perturbations of the input dataset.([25](#_ENREF_25)) The normalized mean over pairwise clustering distances was used as an instability measure.([25](#_ENREF_25)) Feature extraction, PCA and cluster analysis were performed using Matlab R2012b (Mathworks Inc., USA).

**RESULTS**

**General characteristics**

In total, 1001 patients with COPD were analyzed (Table 1). The number of subjects recruited from each country can be found online in Table E2. The majority of patients were men, had a normal-to-overweight BMI and a moderate-to-severe degree of airflow limitation, were categorized to GOLD group D, and only a small proportion used LTOT.

**Table 1** General characteristics of patients with COPD (n=1001)

|  |  |
| --- | --- |
| **Characteristic** | **Value** |
| Age, years | 67 (61 – 72) |
| Male, % | 65 |
| Body weight, kg | 74 (62 – 87) |
| Height, m | 1.70 (1.63 – 1.75) |
| BMI, kg·m-2 | 25.8 (22.5 – 29.6) |
| BMI classification  Underweight, %  Normal weight, %  Overweight, %  Obese, % | 7  37  34  22 |
| mMRC dyspnea grade\* | 2 (1 – 3) |
| Long-term oxygen therapy, %† | 10 |
| FEV1, L | 1.31 (0.91 – 1.79) |
| FEV1, % predicted | 49 (34 – 64) |
| FEV1/FVC, % | 45 (35 – 56) |
| DLCO, % predicted‡ | 51 (37 – 67) |
| ADO index\* | 4 (3 – 5) |
| GOLD 2007 classification 1 / 2 / 3 / 4, % | 9 / 40 / 34 / 17 |
| GOLD 2011 classification A / B / C / D, %\* | 29 / 16 / 17 / 38 |

Data expressed as absolute/relative frequency, or median (interquartile range). BMI: body mass index; mMRC: modified Medical Research Council; FEV1: forced expiratory volume in the first second; FVC: forced vital capacity; DLCO: diffusion capacity of the lung for carbon monoxide; ADO: age dyspnea obstruction index; GOLD: Global Initiative for Chronic Obstructive Lung Disease. \*Data available for 868 subjects; †Data available for 707 subjects; ‡Data available for 505 subjects.

**Daily physical activity measures and physical activity hourly patterns**

The median number of valid days was 6 (6 – 6) days, resulting in a total of 6074 valid physical activity days, of which 4049 (67%) were weekdays. Table 2 presents the daily physical activity measures during the weekdays. The smallest amount of time and lowest energy expenditure (EE) were spent in moderate-to-vigorous intensity. At this intensity, patients spent a median of 6 (0 – 22) min·day-1 in bouts of ≥10 minutes and 38 (17 – 79) min·day-1 in bouts of ≥2 minutes. The time in bouts of ≥10 minutes is actually lower than 10 minutes as a consequence of the averaging process, since not all days had bouts of at least 10 minutes. Figure 1 presents the daily physical activity hourly patterns of the patients. A similar pattern can be observed between weekdays (Figure 1A) and weekend days (Figure 1B), and in both analyses the peak of intensity occurred before midday.

**Table 2** Daily physical activity measures during weekdays in patients with COPD

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **General physical activity** | | | |
| **Physical activity measure** | Very light intensity | Light intensity | | Moderate-to-vigorous intensity |
| Time, min∙day-1  Before midday  After midday  Total | 283 (236 – 347)  514 (449 – 577)  803 (710 – 901) | 49 (31 – 74)†  88 (53 – 123)†  142 (92 – 194)† | | 21 (10 – 42)†,‡  27 (13 – 59)†,‡  52 (26 – 99)†,‡ |
| EE, METs-min∙day-1  Before midday  After midday  Total | 364 (274 – 502)  668 (521 – 858)  1032 (822 – 1327) | 154 (95 - 263)†  273 (167 – 413)†  435 (291 – 655)† | | 110 (46 – 232)†,‡  147 (65 – 310)†,‡  267 (132 – 550)†,‡ |
|  | Bouts of physical activity | | | |
| Physical activity measure | Very light intensity | | Light intensity | Moderate-to-vigorous intensity |
| Time, min∙day-1\*  ≥2-minute  Before midday  After midday  Total  ≥10-minute  Before midday  After midday  Total | 273 (225 – 338)  503 (435 – 569)  781 (683 – 884)  215 (167 – 284)  436 (352 – 526)  657 (539 – 780) | | 37 (22 – 59)†  67 (37 – 97)†  107 (65 – 156)†  3 (0 – 8)†  4 (0 – 14)†  7 (0 – 22)† | 15 (6 – 34)†,‡  20 (8 – 47)†,‡  38 (17 – 79)†,‡  2 (0 – 11)†  3 (0 – 13)†,‡  6 (0 – 22)† |
| Frequency, bouts∙day-1\*  ≥2-minute  Before midday  After midday  Total  ≥10-minute  Before midday  After midday  Total | 21 (17 – 25)  27 (21 – 34)  48 (39 – 58)  7 (6 – 9)  11 (9 – 13)  18 (16 – 21) | | 11 (7 – 16)†  19 (11 – 26)†  31 (20 – 41)†  0 (0 – 1)†  0 (0 – 1)†  1 (0 – 2)† | 4 (2 – 8)†,‡  5 (2 – 10)†,‡  10 (5 – 17)†,‡  0 (0 – 1)†  0 (0 – 1)†  1 (0 – 2)† |
| Average duration, min∙bout-1\*  ≥2-minute  Before midday  After midday  Total  ≥10-minute  Before midday  After midday  Total | 13 (10 – 17)  18 (13 – 27)  16 (12 – 21)  29 (24 – 36)  37 (29 – 50)  34 (28 – 43) | | 3 (3 – 4)†  3 (3 – 4)†  3 (3 – 4)†  10 (0 – 13)†  11 (0 – 13)†  12 (0 – 14)† | 4 (3 – 5)†,‡  4 (3 – 5)†,‡  4 (3 – 5)†,‡  10 (0 – 15)†,‡  11 (0 – 15)†  13 (0 – 16)†,‡ |
| EE, METs-min∙day-1\*  ≥2-minute  Before midday  After midday  Total  ≥10-minute  Before midday  After midday  Total | 347 (261 – 490)  648 (501 – 845)  1000 (783 – 1298)  273 (193 – 411)  572 (410 – 783)  847 (626 – 1168) | | 118 (67 – 205)†  211 (119 – 335)†  340 (204 – 523)†  6 (0 – 26)†  14 (0 – 47)†  26 (0 – 77)† | 86 (29 – 187)†,‡  106 (41 – 255)†,‡  205 (86 – 436)†,‡  9 (0 – 61)†,‡  12 (0 – 69)†  36 (0 – 132)† |

Data expressed as median (interquartile range). EE: energy expenditure; MET: metabolic equivalent of task. \*The time, frequency and EE in bouts of physical activity were averaged out over the total number of valid days, while the duration of bouts of physical activity was averaged out over the total number of bouts available. †*P*<0.05 vs very light intensity; ‡*P*<0.05 vs light intensity.

***Stratification for generic and COPD-specific characteristics***

Patients of older age, female gender, LTOT users, lower DLCO, higher mMRC dyspnea grade, higher BMI, higher ADO index, higher GOLD grade and patients from GOLD group D spent the smallest amount of time and lowest EE in moderate-to-vigorous intensity (Tables E3-E11, online supplement). Daily physical activity hourly patterns after stratification for the abovementioned characteristics are presented in figures 2 and E1 (online supplement), showing a noticeable influence of age, BMI, mMRC dyspnea grades, and ADO index scores. The influence of GOLD grades or GOLD groups on these patterns was small. Indeed, a significant but weak positive association existed between FEV1 (% predicted) and the time in activities of moderate-to-vigorous intensity (*r*s=0.20, *P*<0.0001; Figure 3).

***Patients with COPD versus healthy subjects***

Table 3 presents the characteristics and daily physical activity measures in moderate-to-vigorous intensity of 66 healthy subjects and a subgroup of 66 patients with COPD, pairwise-matched for gender, age and BMI. As expected, subjects with COPD had worse lung function, higher mMRC dyspnea grade and worse physical activity measures compared to healthy subjects. The comparison of daily physical activity measures in very light and light intensities can be found in Table E12 (online supplement). Patients with COPD spent more time in very light intensity than healthy subjects, but there was no difference for the time in light intensity. Figure 4 presents the daily physical activity hourly patterns. In general, healthy subjects performed their activities at higher intensities compared to patients with COPD, and this difference was more pronounced during weekdays.

**Table 3** General characteristics and daily physical activity measures in moderate-to-vigorous intensity of healthy subjects and matched patients with COPD

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic/Physical activity measure** | **Healthy subjects** | **Matched patients with COPD** | ***P*-value** |
| General characteristics  N | 66 | 66 |  |
| Age, yrs | 65 (61 – 70) | 65 (61 – 70) | 1.00 |
| Male, % | 45 | 45 | 1.00 |
| BMI, kg·m-2 | 25.3 (22.9 – 28.1) | 24.9 (22.4 – 27.9) | 0.65 |
| FEV1, % predicted | 107 (97 – 117) | 43 (29 – 63) | <0.0001 |
| FEV1/FVC, % | 78 (75 – 82) | 42 (32 – 54) | <0.0001 |
| mMRC dyspnea grade, points\* | 0 (0 – 0) | 2 (1 – 3) | <0.0001 |
| Physical activity measures in moderate-to-vigorous intensity  Time, min∙day-1 | 101 (57 – 163) | 47 (30 – 95) | <0.0001 |
| EE, METs-min∙day-1 | 461 (271 – 797) | 213 (123 – 435) | <0.0001 |
| Time in ≥2-min bouts, min∙day-1 | 82 (38 – 138) | 37 (15 – 83) | <0.0001 |
| Time in ≥10-min bouts, min∙day-1 | 29 (10 – 73) | 6 (0 – 20) | <0.0001 |
| Frequency of ≥2-min bouts, bouts∙day-1 | 17 (10 – 25) | 9 (5 – 17) | <0.0001 |
| Frequency of ≥10-min bouts, bouts∙day-1 | 2 (1 – 4) | 0 (0 – 1) | <0.0001 |
| Average duration of ≥2-min bouts, min∙bout-1 | 5 (4 – 7) | 4 (3 – 5) | <0.0001 |
| Average duration of ≥10-min bouts, min∙bout-1 | 16 (13 – 21) | 12 (0 – 14) | <0.0001 |
| EE in ≥2-min bouts, METs-min∙day-1 | 362 (212 – 712) | 164 (65 – 376) | <0.0001 |
| EE in ≥10-min bouts, METs-min∙day-1 | 107 (47 – 417) | 23 (0 – 121) | <0.0001 |

Data expressed as absolute/relative frequency, or median (interquartile range). See Tables 1 and 2 for definition of abbreviations. \*Data available for 48 healthy subjects and 59 patients with COPD.

**Cluster analysis of daily PA measures in 1001 patients with COPD**

The PCA identified 3 components, which accounted for 60% of the total variance (first component, 34%; second component, 17%; third component, 9%). The most relevant features of each principal component are described in the online supplement. Cluster analysis, performed on the 3 principal components, identified five distinct clusters (Figure 5; see online supplement for a 3-dimensional video of Figure 5). Table 4 presents the characteristics and physical activity measures of these groups. Cluster 1 (n=216, 22%) was characterized by higher BMI, more dyspnea, higher ADO index, more time and EE in very light intensity, and less time and EE in light and moderate-to-vigorous intensities compared to other clusters. This cluster also had worse lung function compared to clusters 3 and 4, and a higher proportion of GOLD D patients. Cluster 2 (n=415, 41%) had the largest sample size with the most similar general characteristics and physical activity measures to the total sample. Cluster 2 also had more dyspnea and a higher ADO index than clusters 3 and 5. Similarly to cluster 1, this cluster spent more time and EE in very light intensity, and less time and EE in moderate-to-vigorous intensity than other clusters. Cluster 3 (n=184, 18%) exhibited a higher FEV1 than cluster 2 and a higher FEV1/FVC ratio than clusters 1 and 2, while cluster 4 (n=165, 17%) was younger than clusters 1 and 2 and had a lower BMI compared to cluster 2. Moreover, cluster 3 spent more time and EE in light intensity and less time and EE in moderate-to-vigorous intensity than clusters 4 and 5, while cluster 4 spent more time in light intensity compared to cluster 5. Cluster 5 (n=21, 2%) had the smallest sample size (n=21) and was characterized by less time in very light intensity and more time in moderate-to-vigorous intensity compared to other clusters. Figure 6 presents the daily physical activity hourly patterns of the clusters. In all clusters the peak of intensity during the day occurred before midday, and in general, weekdays and weekend days presented a similar pattern, especially in more inactive clusters.

**Table 4** General characteristics and daily physical activity measures of clusters of patients with COPD

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Characteristic/Physical activity measure** | **Cluster 1**  **(very long very light intensity/very short moderate-to-vigorous intensity)** | **Cluster 2**  **(very long very light intensity/ short moderate-to-vigorous intensity)** | **Cluster 3**  **(long very light intensity/short moderate-to-vigorous intensity)** | **Cluster 4**  **(long very light intensity/long moderate-to-vigorous intensity)** | **Cluster 5**  **(intermediate very light intensity/very long moderate-to-vigorous intensity)** | ***P*-value** |
| General characteristics  N | 216 | 415 | 184 | 165 | 21 |  |
| Age, yrs | 68 (62 – 74) | 67 (61 – 72) | 67 (60 – 72) | 63 (58 – 70)†,‡ | 63 (56 – 68) | <0.0001 |
| Male, % | 67 | 67 | 51 | 76 | 67 | 0.32 |
| BMI, kg·m-2 | 30.4 (26.5 – 34.7) | 25.7 (22.6 – 29.0)† | 24.9 (22.2 – 27.4)† | 23.1 (20.3 – 26.8)†,‡ | 22.5 (18.3 – 30.9)† | <0.0001 |
| FEV1, % predicted | 44 (32 – 58) | 48 (34 – 61) | 57 (41 – 71)†,‡ | 50 (36 – 68)† | 51 (39 – 70) | <0.0001 |
| FEV1/FVC, % | 43 (34 – 55) | 44 (34 – 55) | 50 (38 – 61)†,‡ | 47 (36 – 57) | 49 (38 – 64) | 0.002 |
| mMRC dyspnea grade, points\* | 2 (1 – 3) | 2 (1 – 3)† | 1 (1 – 2)†,‡ | 1 (0 – 3)† | 1 (0 – 2)†,‡ | <0.0001 |
| ADO index\* | 5 (3 – 6) | 4 (3 – 5)† | 4 (3 – 5)†,‡ | 4 (3 – 5)† | 3 (2 – 4)†,‡ | <0.0001 |
| GOLD 2007 classification 1 / 2 / 3 / 4, % | 4 / 34 / 43 / 19 | 8 / 38 / 35 / 19 | 18 / 46 / 23 / 13 | 9 / 42 / 31 / 18 | 10 / 43 / 33 / 14 | 0.17 |
| GOLD 2011 classification A / B / C / D, %\* | 18 / 19 / 16 / 47 | 28 / 15 / 17 / 40 | 44 / 16 / 16 / 24 | 31 / 13 / 20 / 36 | 44 / 6 / 28 / 22 | 0.02 |
| Physical activity measures in very light intensity  Time, min∙day-1 | 955 (904 – 1042) | 823 (768 – 879)† | 706 (641 – 769)†,‡ | 675 (604 – 735)†,‡ | 516 (456 – 621)†,‡,§ | <0.0001 |
| EE, METs-min∙day-1 | 1356 (1165 – 1730) | 1022 (854 - 1222)† | 855 (729 – 1118)†,‡ | 789 (692 – 1019)†,‡ | 853 (661 – 1884)† | <0.0001 |
| Time in ≥2-min bouts, min∙day-1 | 946 (894 – 1033) | 802 (746 – 858)† | 682 (611 – 744)†,‡ | 647 (573 – 707)†,‡ | 480 (428 – 591)†,‡,§ | <0.0001 |
| Time in ≥10-min bouts, min∙day-1 | 890 (815 – 968) | 680 (622 – 745)† | 534 (452 – 601)†,‡ | 490 (415 – 561)†,‡ | 340 (254 – 444)†,‡,§ | <0.0001 |
| Frequency of ≥2-min bouts, bouts∙day-1 | 33 (26 – 39) | 50 (42 – 57)† | 54 (48 – 61)†,‡ | 54 (47 – 65)†,‡ | 46 (43 – 59)† | <0.0001 |
| Frequency of ≥10-min bouts, bouts∙day-1 | 17 (14 – 20) | 20 (17 – 22)† | 18 (16 – 20)†,‡ | 17 (15 – 20)‡ | 12 (11 – 16)†,‡,§,ǁ | <0.0001 |
| Average duration of ≥2-min bouts, min∙bout-1 | 29 (23 – 36) | 16 (14 – 19)† | 12 (10 – 15)†,‡ | 11 (10 – 14)†,‡ | 10 (8 – 13)†,‡ | <0.0001 |
| Average duration of ≥10-min bouts, min∙bout-1 | 53 (43 – 65) | 35 (30 – 41)† | 29 (25 – 34)†,‡ | 27 (24 – 32)†,‡ | 26 (22 – 32)†,‡ | <0.0001 |
| EE in ≥2-min bouts, METs-min∙day-1 | 1344 (1145 – 1709) | 988 (827 – 1186)† | 810 (687 – 1074)†,‡ | 748 (650 – 976)†,‡ | 832 (606 – 1730)† | <0.0001 |
| EE in ≥10-min bouts, METs-min∙day-1 | 1257 (1068 – 1632) | 836 (693 – 1050)† | 628 (516 – 862)†,‡ | 589 (467 – 779)†,‡ | 704 (420 – 1185)† | <0.0001 |
| Physical activity measures in light intensity  Time, min∙day-1 | 57 (35 – 79) | 139 (113 – 167)† | 245 (208 – 282)†,‡ | 167 (134 – 209)†,‡,§ | 121 (87 – 163)†,§,ǁ | <0.0001 |
| EE, METs-min∙day-1 | 196 (121 – 305) | 408 (320 – 517)† | 725 (591 – 958)†,‡ | 526 (366 – 735)†,‡,§ | 416 (227 – 1093)†,§ | <0.0001 |
| Time in ≥2-min bouts, min∙day-1 | 38 (19 – 56) | 105 (85 – 130)† | 205 (175 – 244)†,‡ | 126 (97 – 161)†,‡,§ | 79 (50 – 120)†,§,ǁ | <0.0001 |
| Time in ≥10-min bouts, min∙day-1 | 0 (0 – 3) | 8 (3 – 16)† | 46 (32 – 65)†,‡ | 8 (3 – 16)†,§ | 0 (0 – 4)‡,§,ǁ | <0.0001 |
| Frequency of ≥2-min bouts, bouts∙day-1 | 13 (7 – 17) | 30 (24 – 36)† | 49 (40 – 56)†,‡ | 37 (31 – 46)†,‡,§ | 28 (20 – 37)†,§,ǁ | <0.0001 |
| Frequency of ≥10-min bouts, bouts∙day-1 | 0 (0 – 0) | 1 (0 – 1)† | 3 (2 – 5)†,‡ | 1 (0 – 1)†,§ | 0 (0 – 0)‡,§ | <0.0001 |
| Average duration of ≥2-min bouts, min∙bout-1 | 3 (3 – 3) | 3 (3 – 4)† | 4 (4 – 5)†,‡ | 3 (3 – 4)†,§ | 3 (3 – 3)‡,§,ǁ | <0.0001 |
| Average duration of ≥10-min bouts, min∙bout-1 | 0 (0 – 11) | 12 (11 – 13)† | 14 (13 – 15)†,‡ | 12 (10 – 14)†,§ | 0 (0 – 11)‡,§,ǁ | <0.0001 |
| EE in ≥2-min bouts, METs-min∙day-1 | 131 (68 – 215) | 317 (241 – 408)† | 620 (510 – 801)†,‡ | 390 (263 – 586)†,‡,§ | 307 (159 – 748)†,§ | <0.0001 |
| EE in ≥10-min bouts, METs-min∙day-1 | 0 (0 – 12) | 26 (10 – 54)† | 155 (99 – 240)†,‡ | 26 (8 – 54)†,§ | 0 (0 – 19)‡,§,ǁ | <0.0001 |
| Physical activity measures in moderate-to-vigorous intensity  Time, min∙day-1 | 15 (7 – 27) | 48 (30 – 70)† | 68 (43 – 96)†,‡ | 166 (136 – 219)†,‡,§ | 361 (332 – 458)†,‡,§ | <0.0001 |
| EE, METs-min∙day-1 | 90 (40 – 192) | 235 (138 – 349)† | 327 (198 – 527)†,‡ | 805 (616 – 1134)†,‡,§ | 2693 (1694 – 5886)†,‡,§ | <0.0001 |
| Time in ≥2-min bouts, min∙day-1 | 9 (4 – 19) | 36 (20 – 54)† | 51 (29 – 72)†,‡ | 145 (118 – 190)†,‡,§ | 336 (293 – 433)†,‡,§ | <0.0001 |
| Time in ≥10-min bouts, min∙day-1 | 0 (0 – 3) | 5 (0 – 14)† | 9 (3 – 18)†,‡ | 60 (38 – 91)†,‡,§ | 209 (161 – 317)†,‡,§ | <0.0001 |
| Frequency of ≥2-min bouts, bouts∙day-1 | 3 (1 – 5) | 9 (6 – 13)† | 13 (8 – 17)†,‡ | 26 (20 – 33)†,‡,§ | 41 (35 – 52)†,‡,§ | <0.0001 |
| Frequency of ≥10-min bouts, bouts∙day-1 | 0 (0 – 0) | 0 (0 – 1)† | 1 (0 – 1)†,‡ | 3 (2 – 5)†,‡,§ | 10 (8 – 13)†,‡,§ | <0.0001 |
| Average duration of ≥2-min bouts, min∙bout-1 | 3 (2 – 4) | 4 (3 – 5)† | 4 (3 – 5)† | 6 (5 – 7)†,‡,§ | 8 (7 – 11)†,‡,§ | <0.0001 |
| Average duration of ≥10-min bouts, min∙bout-1 | 0 (0 – 11) | 12 (0 – 14)† | 13 (10 – 16)†,‡ | 17 (15 – 21)†,‡,§ | 20 (17 – 25)†,‡,§ | <0.0001 |
| EE in ≥2-min bouts, METs-min∙day-1 | 56 (20 – 123) | 173 (92 – 280)† | 251 (146 – 392)†,‡ | 704 (544 – 992)†,‡,§ | 2583 (1589 – 5348)†,‡,§ | <0.0001 |
| EE in ≥10-min bouts, METs-min∙day-1 | 0 (0 – 20) | 25 (0 – 70)† | 47 (13 – 105)†,‡ | 300 (171 – 513)†,‡,§ | 1635 (1102 – 2590)†,‡,§ | <0.0001 |

Data expressed as absolute/relative frequency, or median (interquartile range). See Tables 1 and 2 for definition of abbreviations. \*Data available for 198 subjects in Cluster 1, 367 subjects in Cluster 2, 159 subjects in Cluster 3, 126 subjects in Cluster 4, and 18 subjects in Cluster 5; †*P*<0.05 vs Cluster 1; ‡*P*<0.05 vs Cluster 2; §*P*<0.05 vs Cluster 3; ǁ*P*<0.05 vs Cluster.

**DISCUSSION**

The present study provides the first detailed analyses of objectively measured physical activity in a large, multinational sample of 1001 patients with COPD. The principal findings were that daily physical activity measures and hourly patterns vary considerably after stratification for generic and COPD-specific characteristics; and that patients with COPD exhibit physical activity hourly patterns at lower intensities in comparison with healthy subjects. Furthermore, patients with COPD can be clustered based on daily physical activity measures, with 5 clusters being identified, each with distinct physical activity measures and hourly patterns.

**Daily physical activity measures and physical activity hourly patterns in COPD**

Our results clearly show that physical activity is a heterogeneous outcome in patients with COPD, corroborating previous findings.(26, 27) Distinct daily physical activity measures were found after stratification for most generic and COPD-specific characteristics investigated in our study (Table E3-E11). Interestingly, comparable time in very light and moderate-to-vigorous intensities was found between GOLD groups A and C, and B and D (Table E11). This suggests that symptoms of dyspnea, which discriminates between groups A/C and B/D, are better associated with physical activity measures than the degree of airflow limitation, which discriminates between groups A/B and C/D. Nonetheless, the influence of the GOLD 2011 classification on physical activity hourly patterns was less evident. In fact, only age, BMI, mMRC dyspnea grade, and ADO index scores seemed to associate with physical activity hourly patterns (Figures 2 and E1). Previous studies have showed interesting associations between generic characteristics and steps per day (REFGimeno-Santos). On the other hand, other studies have questioned the accuracy of these data (REF). For this reason these data were not included in the current analysis.

Patients with COPD are physically less active compared to healthy subjects.(1, 2) The present study is the first to confirm this finding after a pairwise matching for gender, age and BMI. Moreover, patients with COPD performed their activities at a lower intensity compared with healthy subjects (Figure 4), and this difference was more evident during weekdays. To our knowledge, this study is the first large study to show that patients with COPD not only spend less time in moderate-to-vigorous intensity, but also more time in very light intensity, which can be considered a surrogate of sedentary time (i.e., activities between 1.0-1.5 METs).(28) Reducing the time in very light intensity without necessarily increasing the time in moderate-to-vigorous intensity may be an important strategy for achieving health benefits in patients with COPD.([3](#_ENREF_3))

**Clusters of patients with COPD based on daily PA measures**

The present study is the first to cluster patients with COPD based on daily physical activity measures. Indeed, five clusters were identified, each with distinct physical activity measures and hourly patterns. One very active cluster and one very inactive cluster were identified, but clusters in intermediate categories were also observed.

Only a few studies have used objectively measured physical activity data solely for clustering subjects. In 10-to-12-year-old children, De Bourdeaudhuij and colleagues (29) were able to identify a cluster with a mixed arrangement of physical activity (i.e., less time in moderate-to-vigorous intensity + less sedentary time). In our study, we also found a cluster with resembling characteristics (i.e., cluster 4, long very light intensity/long moderate-to-vigorous intensity), confirming that activities of moderate-to-vigorous intensity and sedentary activities are not two sides of one continuum.(29) On the other hand, more inactive clusters were also observed (clusters 1, 2 and 3). In middle-aged Chinese adults, Lee et al ([11](#_ENREF_11)) observed that male subjects from the least active cluster presented higher body fat percentage and older age than those from the active group. In our study, patients from cluster 1 had older age, lower FEV1, higher BMI, worse dyspnea and higher ADO index than other clusters. Based on their characteristics, patients from this cluster may have a worse prognosis, but no follow-up data is available to confirm this hypothesis.

**Strengths and methodological consideration**

Our sample is by far the largest and most diverse sample of patients with COPD with objectively assessed physical activity data ever studied. This allowed detailed analyses of daily physical activity, even identifying clusters of patients with COPD with similar physical activity measures, a true novelty within the COPD literature. Physical activity hourly patterns were also investigated for the first time in a large-scale study in COPD, another important advance. All these analyses were only possible due to the use of objective methods of physical activity, another strength of our study.

Some methodological considerations need to be taken into account. First, selection and information biases might be present, as parts of the data were collected with different purposes. Nevertheless, having patients from different studies and countries allowed us to have a more diverse sample, which may enhance the external validity of our findings. Second, the clusters identified in our study were not validated using a new sample of patients with COPD. Third, other outcomes which may influence physical activity levels in patients with COPD, such as comorbidities,(30) were not available. Fourth, the sample of healthy subjects is rather small, especially if compared with the total COPD sample. Notwithstanding, this sample is larger and more diverse than that of previous studies(REFPittaAJRCCM2005;WaschkiRespirMed2012;TrootersRespirMed2010) and did not seem to be a limiting factor for finding significant results (Table 3). Finally, some of our findings need to be interpreted in light of the number of multiple comparison tests performed. Nonetheless, multiple findings in the same direction rather than a single statistically significant result are suggestive that these are not due to chance alone.

**Clinical relevance**

Patients with COPD spent more time in sedentary activities than healthy subjects. Indeed, around 80% of the daily time of patients with COPD was spent in activities of very light intensity (Table 2). Previous studies in COPD have focused on the time in moderate-to-vigorous intensity,(6, 10, 31) but there is emerging literature in other populations suggesting that health benefits can be achieved by decreasing sedentary behavior and increasing the participation in light intensity physical activities.(32-34)

Physical activity hourly patterns and physical activity clustering provide details on the duration and intensity of physical activities over the course of a day, as well as identify groups with specific physical activity patterns, which can broaden the understanding of physical activity in patients with COPD. Indeed, this seems necessary information to tailor physical activity enhancing interventions.

To date, interventions targeting physical activity enhancement had limited impact in patients with COPD,(15, 31, 35) but none of these interventions targeted specific physical activity patterns. Identifying groups with specific physical activity patterns may lead to more important improvements in physical activity.

To conclude, in a large and multicenter sample of patients with COPD, daily physical activity measures and hourly patterns were found to vary considerably depending on the clinical characteristic. Compared with healthy subjects, patients spent not only less time in higher intensities of physical activity, but also more time in lower intensities. Five clusters of patients were identified, each with distinct physical activity measures and hourly patterns. The present data show that outcome measures need to be clearly delineated when evaluating interventions aiming to promote physical activity in patients with COPD.

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**REFERENCES**

1. Pitta F, Troosters T, Spruit MA, *et al*. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005;171:972-7.

2. Waschki B, Spruit MA, Watz H, *et al*. Physical activity monitoring in copd: Compliance and associations with clinical characteristics in a multicenter study. *Respir Med* 2012;106:522-30.

3. Garcia-Aymerich J, Lange P, Benet M, *et al*. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: A population based cohort study. *Thorax* 2006;61:772-8.

4. Waschki B, Kirsten A, Holz O, *et al*. Physical activity is the strongest predictor of all-cause mortality in patients with copd: A prospective cohort study. *Chest* 2011;140:331-42.

5. Vaes AW, Garcia-Aymerich J, Marott JL, *et al*. Changes in physical activity and all-cause mortality in copd. *Eur Respir J* 2014;44:1199-1209.

6. Watz H, Waschki B, Meyer T, *et al*. Physical activity in patients with copd. *Eur Respir J* 2009;33:262-72.

7. Depew ZS, Karpman C, Novotny PJ, *et al*. Correlations between gait speed, 6-minute walk distance, physical activity, and self-efficacy in patients with severe chronic lung disease. *Respir Care* 2013;58:2113-9.

8. Egan C, Deering BM, Blake C, *et al*. Short term and long term effects of pulmonary rehabilitation on physical activity in copd. *Respir Med* 2012;106:1671-9.

9. Bussmann JB, van den Berg-Emons RJ. To total amount of activity..... And beyond: Perspectives on measuring physical behavior. *Front Psychol* 2013;4:463.

10. Donaire-Gonzalez D, Gimeno-Santos E, Balcells E, *et al*. Physical activity in copd patients: Patterns and bouts. *Eur Respir J* 2013;42:993-1002.

11. Lee PH, Yu YY, McDowell I, *et al*. A cluster analysis of patterns of objectively measured physical activity in hong kong. *Public Health Nutr* 2013;16:1436-44.

12. Hecht A, Ma S, Porszasz J, *et al*. Methodology for using long-term accelerometry monitoring to describe daily activity patterns in copd. *COPD* 2009;6:121-29.

13. Trilk JL, Pate RR, Pfeiffer KA, *et al*. A cluster analysis of physical activity and sedentary behavior patterns in middle school girls. *J Adolesc Health* 2012;51:292-8.

14. Wardlaw AJ, Silverman M, Siva R, *et al*. Multi-dimensional phenotyping: Towards a new taxonomy for airway disease. *Clin Exp Allergy* 2005;35:1254-62.

15. Cindy Ng LW, Mackney J, Jenkins S, *et al*. Does exercise training change physical activity in people with copd? A systematic review and meta-analysis. *Chron Respir Dis* 2012;9:17-26.

16. Vaes AW, Cheung A, Atakhorrami M, *et al*. Effect of 'activity monitor-based' counseling on physical activity and health-related outcomes in patients with chronic diseases: A systematic review and meta-analysis. *Ann Med* 2013;45:397-412.

17. Vestbo J, Hurd SS, Agusti AG, *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: Gold executive summary. *Am J Respir Crit Care Med* 2013;187:347-65.

18. Rabe KF, Hurd S, Anzueto A, *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: Gold executive summary. *Am J Respir Crit Care Med* 2007;176:532-55.

19. Puhan MA, Garcia-Aymerich J, Frey M, *et al*. Expansion of the prognostic assessment of patients with chronic obstructive pulmonary disease: The updated bode index and the ado index. *Lancet* 2009;374:704-11.

20. Colbert LH, Matthews CE, Havighurst TC, *et al*. Comparative validity of physical activity measures in older adults. *Med Sci Sports Exerc* 2011;43:867-76.

21. Mackey DC, Manini TM, Schoeller DA, *et al*. Validation of an armband to measure daily energy expenditure in older adults. *J Gerontol A Biol Sci Med Sci* 2011;66:1108-13.

22. Hill K, Dolmage TE, Woon L, *et al*. Measurement properties of the sensewear armband in adults with chronic obstructive pulmonary disease. *Thorax* 2010;65:486-91.

23. Cavalheri V, Donaria L, Ferreira T, *et al*. Energy expenditure during daily activities as measured by two motion sensors in patients with copd. *Respir Med* 2011;105:922-9.

24. Garber CE, Blissmer B, Deschenes MR, *et al*. American college of sports medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Med Sci Sports Exerc* 2011;43:1334-59.

25. von Luxburg U. Clustering stability: An overview. *Foundations and trends in machine learning* 2010;2:235-74.

26. Garcia-Aymerich J, Serra I, Gomez FP, *et al*. Physical activity and clinical and functional status in copd. *Chest* 2009;136:62-70.

27. Gimeno-Santos E, Frei A, Steurer-Stey C, *et al*. Determinants and outcomes of physical activity in patients with copd: A systematic review. *Thorax* 2014;69:731-9.

28. Pate RR, O'Neill JR, Lobelo F. The evolving definition of "Sedentary". *Exerc Sport Sci Rev* 2008;36:173-8.

29. De Bourdeaudhuij I, Verloigne M, Maes L, *et al*. Associations of physical activity and sedentary time with weight and weight status among 10- to 12-year-old boys and girls in europe: A cluster analysis within the energy project. *Pediatr Obes* 2013;8:367-75.

30. Watz H, Waschki B, Kirsten A, *et al*. The metabolic syndrome in patients with chronic bronchitis and copd: Frequency and associated consequences for systemic inflammation and physical inactivity. *Chest* 2009;136:1039-46.

31. Troosters T, Sciurba FC, Decramer M, *et al*. Tiotropium in patients with moderate copd naive to maintenance therapy: A randomised placebo-controlled trial. *NPJ Prim Care Respir Med* 2014;24:14003.

32. Pau M, Leban B, Collu G, *et al*. Effect of light and vigorous physical activity on balance and gait of older adults. *Arch Gerontol Geriatr* 2014;59:568-73.

33. Loprinzi PD, Lee H, Cardinal BJ. Daily movement patterns and biological markers among adults in the united states. *Prev Med* 2014;60:128-30.

34. Duvivier BM, Schaper NC, Bremers MA, *et al*. Minimal intensity physical activity (standing and walking) of longer duration improves insulin action and plasma lipids more than shorter periods of moderate to vigorous exercise (cycling) in sedentary subjects when energy expenditure is comparable. *PloS one* 2013;8:e55542.

35. Nguyen HQ, Gill DP, Wolpin S, *et al*. Pilot study of a cell phone-based exercise persistence intervention post-rehabilitation for copd. *Int J Chron Obstruct Pulmon Dis* 2009;4:301-13.

**FIGURE LEGENDS**

**Figure 1** Daily physical activity hourly patterns of the 1001 patients with chronic obstructive pulmonary disease during weekdays (A) and weekend days (B). Data pooled per hour as mean (95% confidence intervals).

**Figure 2** Daily physical activity hourly patterns of the patients with chronic obstructive pulmonary disease after stratification for: A and B – modified Medical Research Council (mMRC) grades, data available for 868 subjects only; C and D – body mass index (BMI) classification; E and F – Global Initiative for Chronic Obstructive Lung Disease (GOLD) grades (1 to 4); and G and H – GOLD groups (A to D). Figures A, C, E, and G represent weekdays, while figures B, D, F, and H represent weekend days. Data pooled per hour as mean (95% confidence intervals).

**Figure 3** Spearman’s correlation between forced expiratory volume in the first second (% predicted) and the daily time in activities of moderate-to-vigorous intensity for 1001 patients with chronic obstructive pulmonary disease (*r*s=0.20, *P*<0.0001).

**Figure 4** Daily physical activity hourly patterns of healthy subjects and matched patients with chronic obstructive pulmonary disease during weekdays (A) and weekend days (B). Data pooled per hour as mean (95% confidence intervals).

**Figure 5** The five clusters identified. A: Graph in 3 dimensions presenting the three principal component analysis (PCA) components; B: Graph in 2 dimensions presenting the 1st and 2nd components; C: Graph in 2 dimensions presenting the 1st and 3rd components; and D: Graph in 2 dimensions presenting the 2nd and 3rd components. Details about the relationship between components and clusters can be found in the online supplement.

**Figure 6** Daily physical activity hourly pattern of the clusters of patients with chronic obstructive pulmonary disease during weekdays (A and C) and weekend days (B and D), and before (A and B) and after (C and D) synchronization of the waking up moment. Data pooled per hour as mean (95% confidence intervals).