**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 Shrikrishna9,24, 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 Savi25, Sally Wootton11, Karina C. Furlanetto5, Li W. Cindy Ng20, Anouk W. Vaes1, Christine Jenkins26, Peter R. Eastwood27, Diana Jarreta28, Anne Kirsten23, Dina Brooks29, David R. Hillman27, Thaís Sant’Anna5, Kenneth Meijer30, Selina Dürr14, Erica P. A. Rutten1, Malcolm Kohler13, Vanessa S. Probst5,31, Ruth Tal-Singer32, Esther Garcia Gil28, Albertus C. den Brinker4, Jörg D. Leuppi14, Peter M. A. Calverley22, Frank W. J. M. Smeenk21, Richard W. Costello8, Marco Gramm23, Roger Goldstein29, Miriam T. J. Groenen1, Helgo Magnussen23, Emiel F. M. Wouters1,2, Richard L. ZuWallack33, Oliver Amft3,34&, Henrik Watz23&, Martijn A. Spruit1,35&.

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.

24Musgrove Park Hospital, Taunton and Somerset NHS Foundation Trust, Somerset, United Kingdom.

25Department of Pediatrics and Pediatric Neurology, Cystic Fibrosis Center, Sapienza University of Rome, Rome, Italy.

26Woolcock Institute of Medical Research, The University of Sydney, Camperdown, NSW, Australia.

27Department of Pulmonary Physiology, Sir Charles Gairdner Hospital, Perth, WA, Australia.

28AstraZeneca, Barcelona, Spain.

29Respiratory Medicine, West Park Healthcare Centre and Faculty of Medicine, University of Toronto, Toronto, Canada.

30Department of Human Movement Science, Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands.

31Center for Research in Health Sciences, University North of Paraná (UNOPAR), Londrina, Brazil.

32GlaxoSmithKline R&D, King of Prussia, PA, United States of America.

33Department of Pulmonary and Critical Care, Saint Francis Hospital and Medical Center, Hartford, CT, United States of America.

34ACTLab group, Chair of Sensor Technology, University Passau, Passau, Germany.

35REVAL - Rehabilitation Research Center, BIOMED - Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt University, Diepenbeek, Belgium.

\* Corresponding author

E-mail: rafaelmesquita14@ymail.com (RM)

¶These authors contributed equally to this work.

&Joint senior authors.

**Abstract**

**Background**

Physical activity in patients with chronic obstructive pulmonary disease (COPD) is insufficiently understood. We described physical activity measures and hourly patterns in patients with COPD after stratification for generic and COPD-specific characteristics; we compared these parameters between patients and healthy subjects; and we identified clusters of patients based on physical activity measures.

**Methods**

1001 patients with COPD (65% men; age, 67 years; FEV1, 49% predicted) and 66 healthy subjects (45% men; age, 65 years; FEV1, 107% predicted) were studied cross-sectionally. Daily physical activity measures and hourly patterns (i.e., graphic representation of the mean intensity per hour during a day) were analysed based on data from a multi-sensor armband. Principal component analysis (PCA) and cluster analysis were applied to physical activity data to identify clusters of patients with COPD.

**Results**

Age, body mass index (BMI), dyspnoea grade and the ADO index (including age, dyspnoea, 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 PCA components, which accounted for 60% of variance. Importantly, cluster 1 was characterized by higher BMI, lower FEV1, worse dyspnoea and higher ADO index compared to other clusters (*P*<0.05 for all).

**Conclusions**

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

**Introduction**

Physical activity levels in patients with COPD are mostly presented as a total amount or as an average of multiple measurement days [1-6]. Nevertheless, physical activity is a multi-dimensional construct, which should be described appropriate measures besides its total amount [7]. For example, patients with COPD have shown to perform bouts of moderate-to-vigorous physical activity, but the proportion of time in bouts and the frequency of bouts decreased with increasing severity [8].

A more detailed analysis of physical activity can be achieved by plotting physical activity hourly patterns [9, 10] and by applying cluster analysis to physical activity measures [9, 11, 12]. Physical activity hourly patterns provide graphic representations of the temporal trends of physical activity intensities over the course of a day [7, 10, 13]. These data will reveal whether and to what extent physical activities are concentrated during certain periods of the day [13]. Cluster analysis will be useful to identify subgroups of patients with distinct physical activity characteristics [14]. These detailed analyses will then lead to new insights regarding subgroups of patients with COPD with specific physical activity patterns, which may be used in further investigations and intervention strategies [6, 15, 16]. Indeed, the focus may be shifted from moderate-to-vigorous activities towards sedentary time and light activities [17].

Therefore, the contributions provided by this work are: 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 these 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.

**Materials and Methods**

*Please, see File S1 for all details.*

**Study Design and Participants**

In this multicentre, post-hoc, cross-sectional study, objectively assessed physical activity data from 10 countries (i.e., United Kingdom (UK), Ireland, the Netherlands, Germany, Switzerland, Italy, Spain, the United States of America (USA), Brazil, and Australia) were analysed. Published and/or unpublished physical activity data from previous studies as assessed by the SenseWear Armband or SenseWear Mini Armband activity monitors (both from BodyMedia Inc., Pittsburgh, PA, USA) were considered for analysis. From all studies, only the baseline data was used (in studies that included longitudinal analyses), which means that the subjects included in the current analysis were not undergoing any specific intervention at the time of assessment. Subjects were included if they had: COPD with a post-bronchodilator forced expiratory volume in the first 1 second (FEV1) / forced vital capacity (FVC) ratio <0.70 [18], clinical stability at the time of physical activity assessment, and complete data for age, gender, BMI and daily physical activity measures. The Netherlands and the UK also provided data on healthy elderly subjects, who were 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/institutional review boards (details of the ethics committees/institutional review boards can be found in File S1), 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.

**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. Moreover, the SenseWear Armband or SenseWear Mini Armband activity monitors were used to assess physical activity [19-22]. Physical activity intensities were classified as follows [23]: 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 as acceptable [1], with the device being used for ≥22 hours·day-1 [24]. Only recordings during waking hours of weekdays were considered for the cluster analysis, since physical activity measures during the weekend are known to be different [1] and therefore could bias the analyses. The physical activity measures represent the average of all valid weekdays. Weekend days were used only for the presentation of daily physical activity hourly patterns. 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; S1 Table in File S1). Steps-per-day data were not included in the current analysis as this outcome is subject to inaccuracy unless the subject walks at higher speeds [25].

**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. The influence of seasons on daily physical activity measures was minimal (S2 Table in File S1) and therefore this was not taken into consideration throughout the analyses. Spearman coefficient was used to investigate correlations, when appropriate. Area Under the Curve (AUC)-values of each hourly pattern were calculated and presented with their 95% confidence intervals in order to quantitatively represent time-varying averages of the hourly patterns. *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).

Cluster analysis was adopted to identify subgroups with distinct physical activity profiles. Firstly, Principal Component Analysis (PCA) was used to compress the information contained in the high-dimensional feature set (180 dimensions) to a lower subspace that is both able to account for the desired variance of the data (set to 60%) and convenient for data visualization (3 dimensions). 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 [26]. The normalized mean over pairwise clustering distances was used as an instability measure [26]. Feature extraction, PCA and cluster analysis were performed using Matlab R2012b (Mathworks Inc., USA).

**Results**

**General Characteristics**

In total, 1001 patients with COPD were analysed (Table 1). Majority of patients were men, had a normal-to-overweight BMI, moderate-to-severe degree of airflow limitation, were categorized to GOLD group D, and only a small proportion used LTOT. Characteristics per country can be found in S3 Table in File S2.

**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 | 7 |
|  | Normal weight | 37 |
|  | Overweight | 34 |
|  | Obese | 22 |
| mMRC dyspnoea 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 | 9 |
|  | 2 | 40 |
|  | 3 | 34 |
|  | 4 | 17 |
| GOLD 2011 classification, %\* |  |  |
|  | A | 29 |
|  | B | 16 |
|  | C | 17 |
|  | D | 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, dyspnoea, and airflow 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. This value is lower than 10 minutes due to the averaging process, in which days without bouts of ≥10 minutes were also taken into account. Daily hourly patterns showed similar patterns between weekdays and weekend days, with the peak of intensity occurring before midday (Fig. 1). This similarity was confirmed by the AUC-values (0.30 for weekdays and 0.29 for weekend days; S4 Table in File S2).

**Fig. 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).

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

|  |  |  |  |
| --- | --- | --- | --- |
| **Physical activity measure** | **Very light intensity** | **Light intensity** | **Moderate-to-vigorous intensity** |
| **General physical activity** |  |  |  |
| Time, min∙day-1 | 803 (710 – 901) | 142 (92 – 194)† | 52 (26 – 99)†,‡ |
| EE, METs-min∙day-1 | 1032 (822 – 1327) | 435 (291 – 655)† | 267 (132 – 550)†,‡ |
| **≥10-minute bouts of physical activity** |  |  |  |
| Time, min∙day-1\* | 657 (539 – 780) | 7 (0 – 22)† | 6 (0 – 22)† |
| Frequency, bouts∙day-1\* | 18 (16 – 21) | 1 (0 – 2)† | 1 (0 – 2)† |
| Average duration, min∙bout-1\* | 32 (27 – 39) | 13 (12 – 14)† | 14 (12 – 17)†,‡ |
| EE, METs-min∙day-1\* | 847 (626 – 1168) | 26 (0 – 77)† | 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 dyspnoea 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 (S5-S13 Tables in File S2). Daily physical activity hourly patterns after stratification for the abovementioned characteristics are presented in fig. 2 and S1 Fig., showing a noticeable influence of age, BMI, mMRC dyspnoea grades, and ADO index scores. The AUC-values for these parameters varied between 0.25 and 0.36 (S4 Table in File S2). 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; Fig. 3).

**Fig. 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).** Figs. A, C, E, and G represent weekdays, while figs. B, D, F, and H represent weekend days. Data pooled per hour as mean (95% confidence intervals).

**Fig. 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).**

**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. The comparison of daily physical activity measures in very light and light intensities can be found in S14 Table in File S2. Patients with COPD spent more time in very light intensity than healthy subjects, but there was no difference for the time in light intensity. Fig. 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. This was also supported by the AUC-values (S4 Table in File S2).

**Fig. 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).

**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 dyspnoea 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 ≥10-min bouts, min∙day-1 | 29 (10 – 73) | 6 (0 – 20) | <0.0001 |
| Frequency of ≥10-min bouts, bouts∙day-1 | 2 (1 – 4) | 0 (0 – 1) | <0.0001 |
| Average duration of ≥10-min bouts, min∙bout-1 | 16 (14 – 22) | 13 (12 – 16) | <0.001 |
| 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 Physical Activity 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 File S2. Cluster analysis, performed on the 3 principal components, identified five distinct clusters (Fig. 5; see S1 Video for a 3-dimensional video of Fig. 5). Table 4 presents the characteristics and physical activity measures of these groups. Cluster 1 (n=216, 22%) was characterized by higher BMI, more dyspnoea, 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. Cluster 2 (n=415, 41%) had had more dyspnoea 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%) was characterized by less time in very light intensity and more time in moderate-to-vigorous intensity compared to other clusters. Fig. 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. Moreover, increasing AUC-values were found from clusters 1 to 5 (S4 Table in File S2).

**Fig. 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 File S2.

**Fig. 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).

**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 dyspnoea 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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥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 ≥10-min bouts, min∙bout-1 | 12 (11 – 13) | 12 (11 – 14) | 14 (13 – 15)†,‡ | 12 (11 – 14)§ | 13 (11 – 14) | <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 ≥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 ≥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 ≥10-min bouts, min∙bout-1 | 14 (11 – 16) | 14 (12 – 15) | 14 (12 – 17) | 17 (15 – 21)†,‡,§ | 20 (17 – 25)†,‡,§ | <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 are that 1) daily physical activity measures and hourly patterns vary considerably after stratification for generic and COPD-specific characteristics; 2) patients with COPD exhibit physical activity hourly patterns at lower intensities in comparison with healthy subjects; and 3) 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 characteristic in patients with COPD, corroborating previous findings [27, 28]. Interestingly, comparable time in very light and moderate-to-vigorous intensities was found between GOLD groups A and C, and B and D (S13 Table in File S2). This suggests that symptoms of dyspnoea, 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.

Patients with COPD are physically less active compared to healthy subjects [24, 29]. The present study is the first to confirm this finding after a pairwise matching for gender, age and BMI. 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) [30]. Reducing the time in very light intensity by increasing the time in light intensity may be an important strategy for achieving health benefits [17].

**Clusters of Patients with COPD Based on Daily Physical Activity Measures**

The present study is the first to cluster patients with COPD based only on objectively assessed 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 [31] 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 [31]. On the other hand, more inactive clusters were also observed (clusters 1, 2 and 3). In middle-aged Chinese adults, Lee et al [9] 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 dyspnoea 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 Considerations**

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.

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. Moreover, some types of patients with COPD might be underrepresented, such as patients from primary care. 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. Third, other characteristics which may influence physical activity levels in patients with COPD, such as comorbidities [32], were not available. 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 increasing the time in moderate-to-vigorous intensity [1, 8, 33], but there is emerging literature in other populations suggesting that health benefits can be achieved by decreasing time in very light intensity and increasing the participation in light intensity physical activities [17, 34-36].

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, we were able to show that cluster 1 is probably at increased risk of having a worse prognosis due to the combination of health-threatening characteristics (e.g., more time very light intensity, less time in moderate-to-vigorous intensity). Moreover, identifying groups with specific physical activity patterns seems to be useful information for tailoring physical activity enhancing interventions. To date, interventions targeting physical activity enhancement had limited impact in patients with COPD [15, 33, 37], but none of these interventions targeted specific physical activity patterns.

**Conclusion**

To conclude, in a large and multicentre 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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**Supporting Information**

**S1 Fig. Daily physical activity hourly patterns of the patients with chronic obstructive pulmonary disease after stratification for: A and B – age groups (< or ≥ median, 67 years); C and D – gender; E and F – long-term oxygen therapy (LTOT) use (yes or no), data available for 707 subjects only; G and H – diffusion capacity of the lung for carbon monoxide (DLCO) groups (< or ≥ median, 51% predicted), data available for 505 subjects; and I and J – age, dyspnoea, and airflow obstruction (ADO) index groups(< or ≥ median, 4 points).** Figs. A, C, E, G, and I represent weekdays, whilst figs. B, D, F, H, and J represent weekend days. Data pooled per hour as mean (95% confidence intervals).

(TIFF)

**S1 Video. 3-dimensional video of the five clusters identified according to the three principal component analysis (PCA) components.**

(AVI)

**File S1 Supporting Materials and Methods.**

(DOC)

**File S2 Supporting Results.**

(DOC)