ASSOCIATIONS OF PHYSICAL ACTIVITY WITH DISEASE CHARACTERISTICS OF SEVERE ASTHMA, BRONCHIECTASIS, AND COPD

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Summary at glance

This is the first study in characterising and comparing the prevalence of physical activity between a severe asthma, bronchiectasis, COPD and a control population; and in testing the associations of key treatable and shared disease characteristics with the level of physical activity in obstructive airway diseases.

Abstract:

Background: Physical activity in obstructive airway diseases (OAD) is likely to be impaired. However, this has not been extensively studied outside of chronic obstructive pulmonary disease (COPD). We describe physical activity levels in severe asthma and bronchiectasis compared to moderate-severe COPD and to controls, and tested the cross-sectional associations of physical activity (steps/day) with shared disease characteristics in the OAD group.

Method: Adults with OAD (SA=62, COPD=67, bronchiectasis=60) and controls (n=63) underwent a multidimensional assessment, including device-measured physical activity levels.

Results: The OAD group included 189 participants (58.7% female), median [IQR] age 67 [58 - 72] years and mean forced expiratory volume in the first second percentage predicted (FEV_1%) of 69.4%. Demographic characteristics differed between groups. Compared to controls (52.4% female, aged 55 [34–64] years, median 7640 steps/day), those with severe asthma, bronchiectasis and COPD accumulated less steps/day: median difference -2255, -2289, and -4782, respectively ($p \leq 0.001$). Compared to COPD, severe asthma and bronchiectasis participants accumulated more steps/day: median difference 2375 and 2341, respectively ($p \leq 0.001$). No significant differences were found between the severe asthma and bronchiectasis group. Exercise capacity, FEV_1% predicted, dyspnoea and systemic inflammation differed between groups, but were each significantly associated with steps/day in OAD. In the multivariable model adjusted for all disease characteristics, exercise capacity and FEV_1% predicted remained significantly associated.

Conclusion: Physical activity impairment is common in OAD. The activity level was associated with shared characteristics of these diseases. Interventions to improve physical activity should be multifactorial and consider the level of impairment and the associated characteristics.

Key words: accelerometry, asthma, bronchiectasis, chronic obstructive pulmonary disease, motor activity.

List of abbreviations:

COPD: chronic obstructive pulmonary disease

OAD: obstructive airway diseases

PA: physical activity

BMI: body mass index

6MWT: 6-minute walk test

6MWD: 6-minute walk distance

AFL: airflow limitation

FEV1: forced expiratory volume in the first second

FVC: forced vital capacity

mMRC: modified Medical Research Council Dyspnoea Scale

Hs-CRP: high sensitivity C- reactive protein

MVPA: moderate and higher intensity physical activity

Short title:

Physical activity in airway diseases

Introduction

Asthma, chronic obstructive pulmonary disease (COPD) and bronchiectasis are obstructive airway diseases (OAD) that cause significant burden to individuals and health systems.[1]

Whilst these conditions have different pathophysiological processes,[2] there are commonalities. They are all chronic conditions affecting the lower respiratory airways,[1,3] and share similar clinical characteristics. Additionally, exacerbations are common, increasing the disease burden.[1] These shared characteristics may challenge the person's ability to perform daily activities, and often lead to deconditioning and poor health status.

It is well established that individuals with COPD are considerably less active than people without respiratory disease,[4-6] and that the degree of physical activity (PA) is associated with important disease outcomes.[7] The focus in COPD now is to develop and test interventions that improve PA and decrease sedentary time.[8,9] In severe asthma and bronchiectasis however, there has been little research that objectively characterises these behaviours, or that have focused on interventions to improve them.[10] In order to develop such interventions, data characterising PA are needed. Furthermore, the extent to which PA impairment is associated with shared clinical and biological characteristics in OAD populations is also unknown. Understanding these similarities and differences is important, in order to develop targeted interventions.

We have previously reported[11,12] that people with severe asthma have lower PA levels compared to controls, and that this behaviour is associated with important disease outcomes. In the present study, we aimed to characterise the degree and intensity of PA in people with severe asthma and bronchiectasis, compared to people with moderate-severe COPD and to people without respiratory disease. In addition, we sought to understand whether the PA

impairment likely to be found in OAD is associated with shared disease characteristics. We hypothesised that participants with severe asthma and bronchiectasis would engage in more PA than participants with COPD; but in lower activity levels than controls. Additionally, we hypothesised that in the OAD group, PA would be associated with characteristics shared by the three diseases.

Methods

Adults (≥18 years) with and without respiratory disease were recruited between March 2014 and June 2017 to a cross-sectional study that included measurement of PA.

Participants with physician-diagnosed severe asthma,[13] bronchiectasis,[14] or moderate-severe COPD[15] were recruited via the respiratory clinics at John Hunter Hospital (Newcastle, Australia), and the research databases of the Centre for Healthy Lungs and the Hunter Medical Research Institute (HMRI). Controls were recruited via the research database of the HMRI. Participants were required to be without exacerbation within the 4-weeks prior the study visits. Detailed inclusion and exclusion criteria are described in *appendix S-1*.

Ethics approval was granted from the Human Research Ethics Committees of the Hunter New England Local Health District (severe asthma, bronchiectasis, and controls ([08/08/20/3.10]; COPD [12/12/12/3.06]) and the University of Newcastle. The study was conducted according to Good Clinical Practice Guidelines and each participant provided written informed consent.

Measurements

Participants underwent a multidimensional assessment[3] involving measures of body mass index (BMI), comorbidities,[16] exacerbations, respiratory health status,[17] and smoking status. Further assessments included:

Exercise capacity.

The 6-minute walk test (6MWT) was performed according to current guidelines.[18] The predicted 6-minute walk distance (6MWD) was calculated.[19]

Airflow limitation (AFL)

Spirometry was used to measure post-bronchodilator forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC ratio (Medgraphics, CPFS/D™ USB Spirometer, BreezeSuite v7.1, MGC Diagnostics, Saint Paul, MN, USA). Predicted values were calculated using NHANES III reference equations.[20]

Dyspnoea

Scores ≥2 from the modified Medical Research Council Dyspnoea Scale (mMRC)[21] defined positive presence of dyspnoea. This cut-off is associated with higher risk of mortality in COPD.[22]

Airway inflammation

Eosinophil and neutrophil counts were obtained from induced sputum samples using nebulised 4.5% saline, or 0.9% according to FEV_1.[23] Total cell counts and cell viability (Trypan blue exclusion) from lower respiratory sputum portions were performed, followed by cytospins' preparation for differential cell counts using May-Grunwald–Giemsa.

Systemic inflammation

High-sensitivity C-reactive protein (hs-CRP) was measured in peripheral blood, and analysed using enzyme-linked immunosorbent assay.

Physical activity

Physical activity data were obtained from accelerations detected in the vertical axis using the ActiGraph wGT3X-BT (ActiGraph, Pensacola, Fl) accelerometer. The device was initialized[24] to collect accelerations at 30 Hz rate in epochs of 10-seconds. Participants wore the monitor for 14 consecutive days on a belt around their waist over the dominant hip; and removed the monitor during water-based activities. Data were summarised using the ActiLife 6.11.6 Data Analysis Software[24] and were considered valid if there were ≥4 days of recordings, with ≥10 hours of recording/day.[25] Non-wear time was removed[26] from the analysis. Moderate and vigorous PA (MVPA) was categorized according to the Freedson 1998 cut-point[27] (MVPA ≥1952 counts/minute).

For PA levels, we reported the average steps/day and the mean minutes/day in MVPA. For the diseases outcomes analysis , we reported steps/day, since it is an output easy to compare and that could be used as a motivational and informative tool for patients and clinicians.[28]

Statistical Analysis

Data were analysed using STATA 13 (Stata Corp., College Station, TX, USA). Differences between the severe asthma, bronchiectasis, COPD, and the control groups were assessed using one-way analysis of variance, Kruskal–Wallis, or Chi-square test as appropriate.

Analyses of the associations between PA and shared disease characteristics were performed by disease, and in the combined diseases group (OAD group). The associations between PA (dependant variable), disease characteristics (independent variables: 6MWD, FEV_1%predicted, dyspnoea score ≥2, hs-CRP, sputum eosinophils and sputum neutrophils), and potential confounders (current smoking and BMI) were separately estimated in the OAD group using simple linear regression analysis against steps/day. Confounders (BMI) and each

independent variable with a *P*-value <0.2 (6MWD, FEV_1%predicted, dyspnoea, sputum eosinophils, hs-CRP) were included into separate linear regression analyses to identify variables associated with PA. Age and sex were included in all models as biological confounders.

We tested the interaction effects between diagnosis and each independent variables on steps/day (*table S-1*). A final model including all the independent variables was used to identify independent associations with PA in the OAD group. The association between exacerbation and PA was also tested in simple linear regression analyses *(appendix and table S-2).* Assumptions for linear regressions were met. Based on the observed effect size in the final regression model (f^2=0.916, adjusted R^2= 0.4782, $\alpha = 0.05$), the study has 100% power to detect the effect. Spearman's rank correlation tested relationships between steps/day and disease outcomes. A *P*-value <0.05 was considered statistically significant.

Results

A total of 296 participants (severe asthma=75, bronchiectasis=67, COPD=83, controls=71) completed the study and 252 (severe asthma=62, bronchiectasis=60, COPD=67, controls=63) were included in the analysis. Reasons for exclusion were: invalid accelerometer data (severe asthma=8, bronchiectasis=5, COPD=4, controls=5), not fulfilling the inclusion criteria after assessment (severe asthma=5, bronchiectasis=2, controls=3) or inability to complete all assessments (COPD=12).

The clinical characteristics of each group differed (Tables 1 and 2). As expected, the disease groups had worse clinical/biological characteristics than controls. The severe asthma and COPD groups had higher BMI, and both the bronchiectasis and COPD group were older than controls. Participants were treated according to current guidelines.[13,15]

Characterisation of physical activity

Compared to controls, the severe asthma and bronchiectasis groups had lower PA, with a median difference of around 2270 less steps/day (P<0.001 both), and a median of 19.7 (P=0.006) and 26.5 (P<0.0001) less minutes/day of MVPA, respectively. Compared to COPD, the severe asthma and bronchiectasis groups had higher PA levels, with a median of 2374 and 2341 more steps/day (P<0.0001 both), and a median of 13.6 (P<0.0001) and 6.8 (P=0.0024) more minutes/day of MVPA (Figure I). No significant differences were observed between the severe asthma and bronchiectasis population.

Characteristics associated with physical activity in OAD

After adjustment for significant confounders, 6MWD, FEV_1% predicted, dyspnoea, sputum eosinophils% and hs-CRP were all associated with steps/day in the combined OAD group (Table 3). Regression models by disease (Table 4) show a similar pattern, as indicated by

overlapping confidence intervals in forest plots (figure *S-1*). No statistically significant interactions for diagnosis were found between the independent variables and steps/day (table S-1). The correlations between some measured outcomes and steps/day are shown in Figure II. The 6MWD had the strongest correlation with PA, and the regression model explained 43% of the adjusted variance in steps/day. Every 100-metre increase in exercise capacity was associated with an increase of 1500 steps/day. Dyspnoea, AFL, systemic inflammation, and sputum eosinophils were weaker associations of PA, but statistically significant nonetheless. Associations between disease outcomes and MVPA are reported in *table S-3*.

The full regression model shows that better exercise capacity and lung function remained independently and positively associated with PA in OAD (Table 3). Dyspnoea, hs-CRP and sputum eosinophils were no longer significant. The full model explained 48% of the variance in steps/day in OAD.

Discussion

In this study we characterised the level of physical activity in a group of people with severe asthma and bronchiectasis, compared to moderate-severe COPD and controls. For the first time, we have shown that people with both severe asthma and bronchiectasis engage in lower levels of PA than people without respiratory disease, but higher levels compared to people with COPD. The intensity and volume of activity were similar in the severe asthma and bronchiectasis groups, and the degree of PA impairment in OAD could be explained in an important proportion by exercise capacity and AFL.

We aimed to characterise and compare the level of PA impairment in different OAD. A robust body of research exists in COPD, highlighting that PA is markedly decreased,[7] and that this

decrease is strongly associated with exacerbations and mortality.[7,29,30] As such, the promotion of PA in COPD is an important component of disease management,[9] and a desirable indirect outcome of pulmonary rehabilitation.[9,31]

Whilst the degree of physical inactivity and its impact is well established in COPD, in severe asthma and bronchiectasis there is a paucity of research that: characterises this important and modifiable risk-factor, that makes comparisons to disease groups with similar characteristics, or that has described the clinical associations of PA in these conditions. This is important in order to generate an evidence-base that can guide the direction of treatment interventions for severe asthma and bronchiectasis. Extrapolating what is known in COPD to these conditions may lead to the design of ineffective interventions. In an era of personalised medicine this new knowledge will help design individualised treatment programmes.

Our severe asthma and bronchiectasis populations moved a median of 5360 steps/day each, resulting in a median difference of 2350 more steps compared to our COPD population. Previous studies conducted in severe asthma[32] and bronchiectasis[33] have reported a median of approximately 6000 steps/day, which is consistent with our results. When compared with severe asthma, our bronchiectasis population also accumulated fewer minutes of MVPA, although not statistically significant. These differences were explained by the fact that our bronchiectasis participants were mostly females, a trend previously reported.[34] Overall our data confirm that PA impairment exists in severe asthma and bronchiectasis, but to a lesser degree than in COPD.

Whilst we highlight the importance of characterising these behaviours in specific disease groups, we also combined the disease populations to identify if shared clinical characteristics of OAD are associated with PA. In the recently proposed 'treatable traits' management

approach,[35] deconditioning was proposed as an extrapulmonary trait to be addressed. We suggest that PA itself is a trait to be targeted, and we report that this occurs albeit to different degrees across diagnosis groups. These groups also shared clinical and biological features that were all associated with PA impairment. Therefore, we have identified potential treatment targets that might address the physical inactivity trait, not only in COPD but also in severe asthma and bronchiectasis.

The 6MWD explained the highest proportion of variance in steps/day in the OAD group. This test has been endorsed as a valid outcome measure in people with chronic respiratory disease to measure functional exercise capacity,[18] and is an important predictor of COPD mortality.[36,37] Despite being widely used in COPD and increasingly validated in bronchiectasis,[38] it is not routinely recommended in severe asthma,[13] and thus, assessment of functional exercise capacity in severe asthma is scarce.[39] The reasons for its underuse may relate to fear of provoking exercise-induced bronchoconstriction, or that "uncontrolled asthma" is listed as one of the guideline contraindications.[18] We did not encounter any adverse-events performing the test in our severe asthma population.

FEV_1% predicted was also independently associated with the level of PA in the OAD group. Considering that the degree of AFL categorises disease severity, and that increased severity has been associated with lower activity levels,[12,33,40] these results are somewhat expected. Interesting though, in the full model AFL was a stronger predictor of steps/day than dyspnoea, despite the latter being one of the most disabling symptoms in diseases such as COPD and severe asthma.

Activity-related dyspnoea was common in our OAD population. We found that higher dyspnoea scores (≥2) modestly explained the adjusted variance in PA in the individual model,

but it did not remain significant in the full model. It could be that breathlessness alone is not enough to explain the PA impairment found in these diseases, and that the evaluation of symptoms in different domains could give a more accurate picture. This is in line with recommendations made in COPD guidelines.[15]

In our full multivariate model, the inflammatory markers of hs-CRP and sputum eosinophils were not independently associated with PA, despite displaying a moderate to weak associations individually. This is probably related to the strong association found with the 6MWD, which by itself accounted for most of the variance in PA. Despite this, systemic inflammation was still significantly associated with steps/day in the OAD group, which is in line with evidence in COPD[7] and in severe asthma.[11]

Exercise capacity was a better predictor of PA than AFL. This may be due to the fact that functional exercise capacity gives an estimate of the person's ability to endure exercise,[9] which is a subset of PA.[41] In COPD, the mechanisms behind exercise limitation are multifactorial, and include the impairment of the ventilatory, cardiovascular, metabolic and locomotor muscle systems.[42] It is likely that these mechanisms also play a role in severe asthma and bronchiectasis, especially in patients showing a degree of overlap between these conditions.

Lastly, in the general population, PA has been positively associated with the prevention of different chronic diseases.[43,44] Considering the comorbidity burden found in OAD populations, the promotion of PA may generate benefits beyond respiratory symptoms alone.

Our study has some limitations. Its cross-sectional design does not infer causality of our findings. Additionally, we have not considered important comorbidities, disease

characteristics, sociodemographic and environmental characteristics nor behaviours (i.e. sedentary time) that may impact in the engagement of PA or interact with diseases' outcomes. Lastly, our populations are not demographically nor clinically matched, which limit comparison of our findings. Nevertheless, diagnosis was not a significant interaction in the relationship between the independent variables and steps/day.

Conclusion

Physical activity impairment is a shared behavioural characteristic of people with COPD, severe asthma and bronchiectasis. Shared clinical characteristics, such as exercise capacity and AFL explain an important proportion of this impairment in OAD. Both of these traits can be targeted by specific treatments, making PA impairment a "treatable trait" that requires consideration in the management of these diseases. Treatment studies aimed at improving PA in these populations are needed and our data may inform such interventions.

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Table 1: Demographics and clinical characteristics of participants

	Severe asthma[#] (n=62)	Bronchiectasis[#] (n=60)	COPD[X] (n=67)	Control[&] (n=63)	P- value*	OAD (n=189)
Age, years	58.0 [43.0 – 68.0][X#]	68.0 [62.0 – 73.0][&#]	70.0 [64.0 - 75.0][&]	55.0 [34.0 – 64.0]	**<0.0001**	67.0 [58.0 - 72.0]
Females, %	51.6[#]	86.7[&#x]	38.8	52.4	**<0.001**	58.7
BMI, kg/m²	28.6 [24.6 - 33.7][&#]	25.6 [21.7 - 27.6][X#]	30.1 [26.9 - 33.5][&]	25.3 [22.3 - 27.6]	**<0.0001**	27.7 [23.8 - 31.6]
Years since diagnosis	27.6 [15.1 – 51.0]	16.0 [5.0 - 57.0]	6.0 [3.0 – 14.0]	N/A		14.6 [5.0-41.0]
Current smoker, %	8.1	1.7	0.0	0.0	**0.031**	3.2
Smoking Pack/years	0.0 [0.0 - 5.4][X]	0.0 [0.0 - 2.1][X]	42.6 [31.3 - 70.5][&]	0.0 [0.0 – 3.0]	**<0.0001**	5.0 [0 – 36.0]
CCI score ≥1, %	27.9	35.0	100.0	3.17	**<0.001**	55.9
Medication, % participant prescribed						
OCS, %	40.3	3.0	3.0	0.0		15.0
Combination ICS/LABA, %	97.0	63.3	70.2	0.0		77.0
ICS, %	13.0	5.0	16.4	0.0		12.0
LAMA, %	52.0	38.3	91.0	0.0		61.4
LABA, %	0.0	2.0	16.4	0.0		6.4
Omalizumab, %	11.3	N/A	N/A	N/A		3.7
Mepolizumab, %	6.5	N/A	N/A	N/A		2.1

*Results reported as median [interquartile range] or percentage. OAD group not included in the hypothesis tests. *P-value correspond to the differences within group (COPD, SA, BE, Controls). Between groups differences: X = result statistically significant different with COPD group; & = result statistically significant different with Control group; #= result statistically significant different between severe asthma and bronchiectasis group. COPD: chronic obstructive pulmonary disease; OAD: obstructive airway disease group; BMI: body mass index; CCI: Charlson Comorbidity Index; OCS: oral corticosteroid; ICS/LABA: inhaled corticosteroid/ long acting beta agonist; LAMA: long-acting muscarinic antagonist.*

Table 2: Clinical and biological characteristics

	Severe asthma[#] (n=62)	Bronchiectasis[#] (n=60)	COPD[X] (n=67)	Control[&] (n=63)	P- value*	OAD (n=189)
Post FEV_1% predicted, %	75.8 (70.4, 81.3)[&X]	76.9 (70.9, 82.8)[&X]	56.4 (52.5, 60.3)[&]	100.6 (96.7, 104.5)	**<0.0000**	69.4 (66.2, 72.5)
Post FVC % predicted, %	87.5 (83.1, 91.8)[&X]	81.1 (76.3, 86.0)[&]	78.7 (74.6, 82.7)[&]	96.6 (93.2, 100.1)	**<0.0000**	82.3 (79.7, 84.9)
Post FEV_1/FVC ratio	0.66 [0.56 - 0.77][&X]	0.73 [0.65 - 0.79][&X]	0.56 [0.44 - 0.67][&]	0.82 [0.77 - 0.86]	**<0.0001**	0.66 [0.55 - 0.76]
6MWD, m	477.8(452.0, 503.5)[&X]	453.4 (424.2, 482.6)[&X]	383.5 (353.5, 413.6)[&]	609.5 (589.0, 629.9)	**<0.0000**	435.9(418.6, 453.1)
6MWD % predicted, %	72.1 [64.7 - 82.6][&]	76.6 [62.9 - 82.0][&X]	66.0 [46.9 - 77.2][&]	86.8 [77.9 - 92.7]	**<0.0001**	70.9 [59.1 - 80.1]
Dyspnea score ≥ 2, %	50.0[&]	32.0[&X#]	53.0[&]	0.0	**<0.001**	45.2
GOLD quadrant, %	N/A	N/A	B= 17.9; C=4.5; D=76.1	N/A		N/A
GOLD stage, %	N/A	N/A	2= 64.2; 3=30.0; 4=6.0	N/A		N/A
Oxygen dependent, %	0	3.3	3.8	0	**<0.001**	2.6
Severe exacerbation, n	190[X]	18[#X]	44	0	**<0.001**	
SGRQ, score	41.2 [27.5 - 55.1][X]	36.0 [23.8 - 52.5][X]	50.3 [39.5 - 66.6]	N/A	**<0.0001**	45.2 [32 - 58]
Hs-CRP, mg/L	1.8 [1.0 – 6.0][&]	2.8 [1.4 – 7.0][&]	3.8 [1.9 – 10.0][&]	1.1 [0.6 - 2.5]	**<0.0001**	2.9 [1.4 - 7.8]
Eosinophils, %	3.6 [0.8 - 13.5][&#]	1.3 [0.6 -2.1][&#]	1.8 [0.75 - 3.8][&]	0.45 [0.0 – 1.0]	**<0.0001**	1.5 [0.75 - 4]
Neutrophils, %	35.0 [17.8 - 59.3][#]	78.1 [61.3 - 85.3][&X#]	48.8 [29.5 - 71.8][&]	27.3 [15.5 - 42.8]	**<0.0001**	53.3 [28.5 - 79.3]

*Results reported as mean (95% confidence interval) (post FEV1% predicted, FVC % predicted and 6MWD), median [interquartile range] or percentage. OAD group not included in the hypothesis tests. *P-value correspond to the differences within group (COPD, SA, BE, Controls). Between groups differences: X = result statistically significant different with COPD group; & = result statistically significant different with Control group; #= result statistically significant different between severe asthma and bronchiectasis group. COPD: chronic obstructive pulmonary disease; OAD: obstructive airway disease group; FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity; 6MWD: 6-minute walk distance; GOLD: Global Initiative for Chronic Obstructive Lung Disease, Severe exacerbation: total number in last year as per severe asthma and GOLD guidelines definitions (bronchiectasis as per GOLD guidelines). SGRQ: Saint George Respiratory Questionnaire; hs-CRP: high sensitivity C-reactive protein.*

473 *Table 3: Associations of physical activity in obstructive airways diseases*

Separate models for clinical and biological outcomes	**Associations of steps/day with disease characteristics in OAD**		
	Coefficient (95%CI)	**Significance**	**Adj. R^2**
a. 6MWD (m)	15.10 (12.10, 18.10)	**<0.001**	0.433
b. FEV_1% predicted (%)	52.62 (34.99, 70.25)	**<0.001**	0.153
Reference: ≤1 scores **c. Dyspnoea (≥2 score)**	-1689.4 (-2476, -902.1)	**<0.001**	0.204
d. hs-CRP (mg/L)	-36.96 (-61.35, -12.56)	**0.003**	0.190
e. Eosinophils (%)	50.25 (0.40, 100.11)	**0.048**	0.161
Full model	**Independent associations of steps/day in OAD**		**Adj. R^2 = 0.478**
6MWD (m)	12.40 (8.51, 16.28)	**<0.001**	
FEV_1% predicted (%)	18.96 (0.53, 37.40)	**0.044**	
Dyspnoea (≥2 score)	-42.40 (-813.95, 729.16)	0.914	
hs-CRP (mg/L)	0.69 (-20.33, 21.71)	0.948	
Eosinophils (%)	25.88 (-14.49, 66.24)	0.207	
BMI (kg/m^2)	-54.15 (-104.05, -4.26)	**0.034**	
Age	-27.74 (-55.3 -0.19)	**0.048**	

Each model adjusted for confounders: age, gender, and BMI (except FEV_1%predicted). Dyspnoea was transformed into a binary variable and considered positive when scores were ≥2. Confounders (BMI, age and sex) explained a 13% of the variance in steps/day in the full model. Sex not significant in the full model. OAD: obstructive airway diseases; 6MWD: 6-minute walk distance; FEV1% predicted: forced expiratory volume in the first second; hs-CRP: high sensitivity C-reactive protein; BMI: body mass index. Statistically significant results in bold

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Table 4: Regression models of associations of disease characteristics with steps/day by diagnosis

	Associations of steps/day with disease outcomes by disease		
	6MWD (m)		
	Coefficient (95%CI)	Significance	Adj. R2
Severe asthma	12.76 (6.27, 19.26)	**<0.001**	0.259
COPD	12.01 (7.63, 16.39)	**<0.001**	0.485
Bronchiectasis	17.37 (12.26, 22.47)	**<0.001**	0.503
	FEV_1% predicted (%)		
Severe asthma	33.71 (2.04, 65.38)	**0.037**	0.060
COPD	46.20 (4.52, 87.88)	**0.030**	0.055
Bronchiectasis	45.52 (15.77, 75.27)	**<0.01**	0.124
	Dyspnoea (≥2 score) ***(versus scores ≤1)***		
Severe asthma	-1534.53 (-2966.27, -102.80)	**0.036**	0.129
COPD	-1310.93 (-2536.58, -85.28)	**0.036**	0.286
Bronchiectasis	-2270.94 (-3710.32, -831.56)	**0.003**	0.213
	hs-CRP (mg/L)		
Severe asthma	-45.82 (-84.92, -6.72)	**0.022**	0.153
COPD	-15.52 (-52.71, 21.67)	0.407	0.243
Bronchiectasis	-84.34 (-132.33, -36.35)	**<0.001**	0.279
	Eosinophils (%)		
Severe asthma	87.87 (16.34, 159.40)	**0.017**	0.124
COPD	22.99 (-50.20, 96.18)	0.532	0.239
Bronchiectasis	-113.40 (-351.35, 124.55)	0.343	0.103

Models adjusted for confounders: age, sex, and BMI (except FEV_1% predicted). Dyspnoea was transformed into a binary variable and considered positive when scores were ≥2. OAD: obstructive airway diseases; 6MWD: 6-minute walk distance; FEV1% predicted: forced expiratory volume in the first second; hs-CRP: high sensitivity C-reactive protein; BMI: body mass index. Statistically significant results in bold

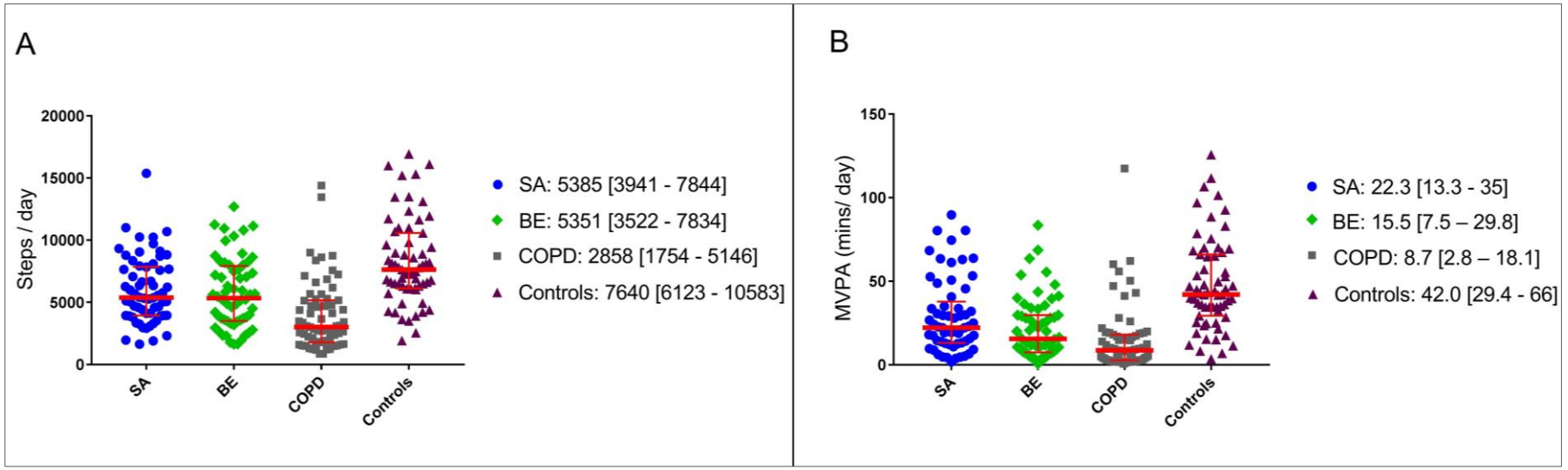

Figure I: Physical activity comparison for steps/day (A) and MVPA (B).
MVPA: moderate and vigorous physical activity; SA: severe asthma; BE: bronchiectasis; COPD: chronic obstructive pulmonary disease; Controls: adults with no respiratory disease; SA n=62; BE n=60; COPD n=67; Controls n=63

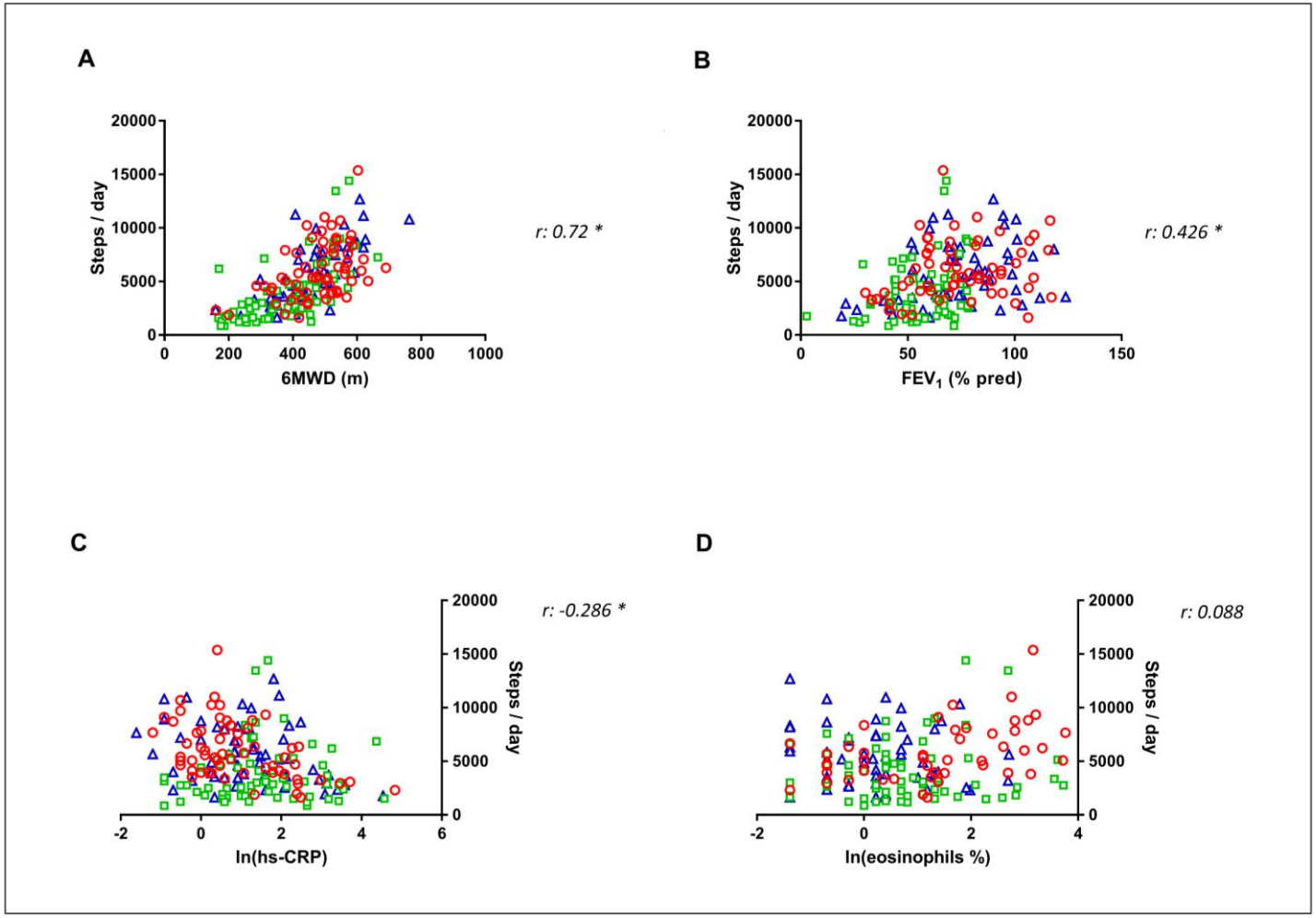

Figure II: Pearson's correlation of physical activity (steps/day) with 6MWT (A); FEV_1% predicted (B); hs-CRP (C); and Sputum eosinophils% (D). SA: severe asthma; COPD: chronic obstructive pulmonary disease, BE: bronchiectasis; 6MWD: 6-minute walk distance; FEV_1: forced expiratory volume in the first second; CRP: high sensitivity C-reactive protein. Hs-CRP and eosinophils % transformed to natural logarithm.