



Early View

Research letter

A comparison of daily physical activity profiles between adults with severe asthma and healthy controls

Jill Neale, Mark W. Orme, Sally Majd, Stacey Chantrell, Sally J. Singh, Peter Bradding, Ruth H. Green, Rachael A. Evans

Please cite this article as: Neale J, Orme MW, Majd S, *et al.* A comparison of daily physical activity profiles between adults with severe asthma and healthy controls. *Eur Respir J* 2020; in press (<https://doi.org/10.1183/13993003.02219-2019>).

This manuscript has recently been accepted for publication in the *European Respiratory Journal*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJ online.

Manuscript word count 1316, 14 references, 1 figure

A comparison of daily physical activity profiles between adults with severe asthma and healthy controls

Jill Neale ^{1,3}, Mark W. Orme ^{1,2}, Sally Majd ^{1,2,3}, Stacey Chantrell ^{1,2}, Sally J. Singh ^{1,2,3}, Peter Bradding ^{1,2,3}, Ruth H. Green ^{1,2,3}, Rachael A. Evans ^{1,2,3}

1. Leicester Biomedical Research Centre (Respiratory), Glenfield Hospital, Leicester, UK.
2. Department of Respiratory Sciences, University of Leicester, Leicester, UK.
3. Department of Respiratory Medicine, Thoracic Surgery and Allergy, Glenfield Hospital, University Hospitals of Leicester NHS trust, Leicester, UK

Correspondence

Dr Rachael Evans
Glenfield Hospital, Groby Road, Leicester, UK.
Email: re66@leicester.ac.uk

Summary of the take home message (256 characters including spaces – for social media)

Compared to controls, adults with severe #asthma attain fewer daily steps and reduced sustained moderate-vigorous #physicalactivity which are associated with worse quality of life. Physical activity and #exercise interventions are needed for severe asthma.

INTRODUCTION

Severe asthma is associated with a substantial burden of disease including premature death and reduced quality adjusted life years[1]. Care in specialist centres is associated with reduced exacerbation rates and healthcare utilisation, but at the cost of increased use of systemic steroids and increased body mass index (BMI)[2]. Common co-comorbidities such as metabolic syndrome and type 2 diabetes are associated with low levels of moderate-vigorous physical activity (MVPA)[3]. Guidelines recommend that adults accumulate either ≥ 150 minutes of moderate intensity activity or ≥ 75 minutes of vigorous intensity activity per week, accumulated in bouts of any length [4]. Adults with severe asthma may avoid MVPA due to negative expectations and fear-avoidance beliefs[5]. A few small studies have reported that daily step count and time spent in MVPA may be reduced in adults with severe asthma compared to controls[6-8]. However, results are conflicting when physical activity levels are adjusted for confounders such as age, gender, obesity and smoking[7]. Furthermore, adults with severe asthma have reduced health-related quality of life (HRQoL) but whether physical activity levels impact on HRQoL is unknown[9].

Therefore, the aims of our study were to compare physical activity levels and how physical activity is accumulated between adults with severe asthma and healthy controls, and to identify whether physical activity is associated with HRQoL in severe asthma. We hypothesised that adults with severe asthma would be less physically active than age and sex-matched healthy participants and that being less physically active would be associated with worse HRQoL.

METHODS

Patients were recruited as part of a study (approved by the National Research Ethics Service Committee of the East Midlands Ref. 127552) involving Asthma-Tailored Pulmonary Rehabilitation[10] from a UK difficult-to-treat asthma service. Inclusion criteria were age 18-80 years, severe asthma (step 4–5 treatment according to SIGN/BTS guidelines[11]), were not

undertaking regular exercise and had not previously completed pulmonary rehabilitation. Age (within one year) and sex individually-matched healthy controls with no history of major medical illness and who were not undertaking regular exercise were recruited from a database of people who had previously expressed an interest in participating in research, and from advertisements within the hospital.

Participant Characteristics

All participants had their ethnicity and smoking status documented, and BMI calculated. Medications were documented and spirometry was performed in those with severe asthma.

Outcomes

Physical activity was measured for seven days, with the season recorded, using a SenseWear Pro3 Armband worn on the non-dominant upper arm during waking hours. A threshold of ≥ 8 hours per day of wear-time was used to determine adequate adherence, and those with ≥ 4 valid days of data were included in the analysis[12]. For each 60-second epoch, step count, stationary time (absence of steps), light activity (≥ 1.5 to < 3.0 metabolic equivalent of task (METs) with steps taken), MVPA (≥ 3.0 METs with steps taken) and MVPA in ≥ 10 -minute bouts were extracted and summed for each day. In participants with severe asthma, HRQoL was measured using the EuroQoL (EQ-5D-3L), Chronic Respiratory Questionnaire (CRQ) and Asthma QoL Questionnaire (AQLQ)[10].

Statistical Analysis

Analyses were performed using SPSS v.25.0. Data are presented as mean [SD] or median [interquartile range] for continuous outcomes, dependent on normality, and as counts and percentages for categorical variables. Independent t-tests or Mann-Whitney U tests were used to compare between group differences. Analysis of covariance was used to determine the differences in physical activity levels between groups when controlling for wear-time and BMI. Multivariable linear regression was used to investigate the relationship between physical activity and HRQoL after

controlling for wear-time, age (yr), FEV1 (L) and BMI (kg/m²). To detect a difference of 2000 steps between adults with severe asthma and healthy controls with a SD of 3000 steps, for 90% power at the 2-sided 5% significance level, 48 participants in each group would be needed [7].

RESULTS

96 participants (n=48 severe asthma, n=48 healthy controls) were recruited, mean[SD] age 55 [13]yr, 35% male with similar ethnicity (severe asthma 90% Caucasian, 10% South Asian; healthy controls 85% Caucasian, 15% South Asian, p=0.76) and smoking status (severe asthma 71% never-smokers, 25% ex-smokers, 4% current; healthy controls 71% never-smokers, 29% ex-smokers, 0% current, p=0.34). BMI was significantly higher in adults with severe asthma 33.0 [6.7](kg/m²) compared to healthy controls 26.4 [4.4](kg/m²), p<0.001. For severe asthma, the mean [SD] FEV1 was 1.9 [0.7]L, FEV1 %predicted 71.2 [20.1]% and FEV1/FVC 0.7 [0.1], and 50% were prescribed oral steroids. The EQ-5D-3L index-score was median [IQR] 0.8 [0.38]units, total CRQ score 85.6 [19.6] and AQLQ total score 4.98 [1.11].

Figure 1 shows that daily step count, time spent doing ≥10 minute bouts of MVPA and total MVPA were significantly less in adults with severe asthma compared to healthy controls (all p<0.001). The mean (SD) valid days for the severe asthma group was 6.71 [0.63] days versus 6.90 [0.37] days, p=0.126. However, adults with severe asthma wore the activity monitor significantly less per day (severe asthma mean [SD] 772 [108]min vs healthy control 826 [96]min, p=0.011) and this was predominantly due to adults with severe asthma putting on the monitor 53min later on average than the healthy participants, p=0.002. In our data, there was no association between season and daily physical activity levels therefore we did not adjust for seasonality. After adjusting for BMI and wear-time, adults with severe asthma completed fewer steps (p=0.009) and less time spent doing sustained (≥10 minute bouts) MVPA (p=0.012) but the difference in total MVPA became non-significant and there were no differences in stationary time.

Steps per day were positively associated with EQ-5D-3L score ($\beta=0.31$, $p=0.045$), AQLQ overall score ($\beta=0.36$, $p=0.039$) and CRQ total score ($\beta=0.40$, $p=0.030$), after adjusting for wear-time, age, FEV1 and BMI. Stationary time was not associated with any of the HRQoL questionnaire total scores: EQ-5D-3L ($\beta=-0.014$, $p=0.94$), AQLQ ($\beta=-0.29$, $p=0.19$) and CRQ ($\beta=-0.37$, $p=0.097$). Time Spent doing ≥ 10 Minute Bouts of MVPA was positively associated with total scores for AQLQ ($\beta=0.44$, $p=0.021$) and CRQ ($\beta=0.60$, $p=0.003$), but not EQ-5D-3L score ($\beta=0.18$, $p=0.29$). Total MVPA was also positively associated with total scores for AQLQ ($\beta=0.39$, $p=0.028$) and CRQ ($\beta=0.46$, $p=0.014$), but not EQ-5D-3L ($\beta=0.19$, $p=0.24$).

DISCUSSION

Our results demonstrate that adults with severe asthma are less physically active compared with their healthy peers. We provide further novel data showing adults with severe asthma accumulate MVPA in shorter bouts (fewer ≥ 10 minute bouts of MVPA), and that disease-specific HRQoL is positively related to physical activity levels.

With adequate power our data confirms previous suggestions that adults with severe asthma perform fewer steps than healthy controls[6, 7]. Similar to another study, after appropriate adjustment total MVPA was not significantly lower in adults with severe asthma compared to controls but we cannot exclude a type II error[7]. However, we identified that for adults with severe asthma the deficit in physical activity is within MVPA of >10 minute bouts, which are necessary to gain maximum benefit for cardiometabolic health[4]. As adults with severe asthma have an increased cardiometabolic risk[3, 13], modification of contributing lifestyle factors such as low-levels of MVPA should be prioritised.

Lower physical activity levels (step count, total MVPA and >10 min bouts of MVPA) were associated with worse HRQoL, and most strongly associated with time spent performing ≥ 10 minute bouts of MVPA, in contrast to stationary time where there was no association. A previous study in adults with

severe asthma showed a positive association between HRQoL (AQLQ scores) and MVPA[6], estimating that the clinically important difference in AQLQ was associated with approximately 30 minutes greater daily MVPA[6].

Our data is from a single-centre but our patient characteristics are representative of a typical UK severe asthma service[14]. We are not inferring causality with the association between physical activity levels and HRQoL due to our cross-sectional study design because, while we adjusted for significant differences in BMI and monitor wear-time, residual confounding cannot be excluded.

In conclusion, steps per day and sustained MVPA are significantly lower in adults with severe asthma and a lower frequency of ≥ 10 minute bouts of MVPA is associated with worse HRQoL. These novel findings highlight the need for physical activity and exercise interventions for adults with severe asthma.

REFERENCES

1. Global Asthma Report. www.globalasthmareport.org. Date last updated: 2018. Date last accessed: November 7 2019.
2. Sweeney J, Brightling CE, Menzies-Gow A, Niven R, Patterson CC, Heaney LG, Network BTSDA. Clinical management and outcome of refractory asthma in the UK from the British Thoracic Society Difficult Asthma Registry. *Thorax* 2012; 67(8): 754-756.
3. Peters MC, McGrath KW, Hawkins GA, Hastie AT, Levy BD, Israel E, Phillips BR, Mauger DT, Comhair SA, Erzurum SC, Johansson MW, Jarjour NN, Coverstone AM, Castro M, Holguin F, Wenzel SE, Woodruff PG, Bleecker ER, Fahy JV, National Heart Ln, and Blood Institute Severe Asthma Research Program. Plasma interleukin-6 concentrations, metabolic dysfunction, and asthma severity: a cross-sectional analysis of two cohorts. *Lancet Respir Med* 2016; 4(7): 574-584.
4. UK Chief Medical Officers' Physical Activity Guidelines. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/832868/uk-chief-medical-officers-physical-activity-guidelines.pdf. Date last updated: 7th September 2019. Accessed Jan 2020.
5. Janssens T, Dupont L, Von Leupoldt A. Exercise fear-avoidance beliefs and self-reported physical activity in young adults with asthma and healthy controls. *Eur Respir J* 2018: 52.
6. Cordova-Rivera L, Gibson PG, Gardiner PA, Powell H, McDonald VM. Physical Activity and Exercise Capacity in Severe Asthma: Key Clinical Associations. *J Allergy Clin Immunol Pract* 2018; 6(3): 814-822.
7. Bahmer T, Waschki B, Schatz F, Herzmann C, Zabel P, Kirsten AM, Rabe KF, Watz H, Group E-S. Physical activity, airway resistance and small airway dysfunction in severe asthma. *Eur Respir J* 2017: 49(1).
8. Hennegrave F, Le Rouzic O, Fry S, Behal H, Chenivresse C, Wallaert B. Factors associated with daily life physical activity in patients with asthma. *Health Sci Rep* 2018: 1(10): e84.
9. Stucky BD, Sherbourne CD, Edelen MO, Eberhart NK. Understanding asthma-specific quality of life: moving beyond asthma symptoms and severity. *Eur Respir J* 2015; 46(3): 680- 687.
10. Majd S, Apps LD, Hudson N, Hewitt S, Eglinton E, Murphy A, Bradding P, Singh S, Green R, Evans R. Protocol for a feasibility study to inform the development of a multicentre randomised controlled trial of asthma-tailored pulmonary rehabilitation versus usual care for individuals with severe asthma. *BMJ Open* 2016; 6(3): e010574.
11. British Thoracic Society. British guideline on the management of asthma; A national clinical guideline. Date: 2014. Date last accessed November 7 2019.
12. Demeyer H, Burtin C, Van Remoortel H, Hornikx M, Langer D, Decramer M, Gosselink R, Janssens W, Troosters T. Standardizing the analysis of physical activity in patients with COPD following a pulmonary rehabilitation program. *Chest* 2014; 146(2): 318-327.

13. Moore LE, Bhutani M, Petersen SR, McMurtry MS, Byers BW, Tedjasaputra V, Stickland MK. Physical activity, fitness, and vascular health in patients with asthma. *J Allergy Clin Immunol* 2015; 136(3): 809-811.e803.

14. Apps LD, Chantrell S, Majd S, Eglinton E, Singh SJ, Murphy AC, Bradding P, Green RH, Hudson N, Evans RA. Patient Perceptions of Living with Severe Asthma: Challenges to Effective Management. *J Allergy Clin Immunol Pract* 2019. Nov - Dec;7(8):2613-2621.

Figure title and legend

Figure 1. A comparison of physical activity levels between adults with severe asthma and healthy participants

A comparison of physical activity levels between adults with severe asthma (SA) and healthy participants (non-adjusted data).

* $p < 0.001$ between SA and healthy participants, MVPA: Moderate to Vigorous Physical Activity

