



# Accumulating physical activity in at least 10-minute bouts predicts better lung function after 3-years in adults with cystic fibrosis

To the Editor:

In people with cystic fibrosis (CF) reduced fitness and lower levels of physical activity have been associated with poorer prognosis [1] and greater decline in lung function [2]. Despite the health benefits of being physically active [3], in people with CF adherence to exercise programmes is often poor [4], and prescribed exercise training programmes have seldom translated into increased daily physical activity [5].

We have previously shown that while adults with CF frequently achieve a total of 30 min of moderate-vigorous physical activity (MVPA) each day, in keeping with physical activity guidelines [6], time spent in MVPA was predominantly accumulated in short duration sequences [7]. For physical activity to result in improvements to cardiorespiratory fitness it needs to be performed in a single concerted effort of 30-min duration or in multiple bouts of activity to total 30 min in a day, where a bout must be at least 10 min in duration [6, 8]. Whether the pattern of physical activity participation, as opposed to the total volume of activity, is important to long-term clinical outcomes in people with CF has not been reported using objective measures. We sought to explore the relationship between objectively measured patterns of physical activity participation and markers of disease progression, namely lung function and need for hospitalisation, during a 3-year follow-up period in adults with CF.

Data were collected from adults with stable CF aged >18 years participating in a prospective, observational study conducted at two centres in Melbourne, Australia. All participants provided written, informed consent. A full description of the methods is published elsewhere [7]. In brief, physical activity was measured objectively (over 7 days) using the SenseWear Armband (SWA, Bodymedia, Pittsburgh, PA, USA) in adults with CF who were not experiencing a respiratory exacerbation. For this follow-up analysis, 3-year outcome data relating to survival, lung function and hospitalisation, for the same cohort of patients, was collected from the patient medical record. Lung function tests undertaken within an 8-week period either side of a participant's 3-year anniversary of study enrolment were eligible for inclusion in this analysis. The original study, and follow-up data collection, was approved by the relevant Human Research Ethics Committees (Alfred Health project 375/10 and Monash Health project 10347A).

Statistical analyses were conducted using IBM SPSS statistics (Version 24.0; IBM Corp., Armonk, NY, USA). We assessed if the pattern of physical activity could predict clinical outcomes over 3-years with stepwise multiple linear regression analysis using annual rate of change in lung function (forced expiratory volume in 1 s (FEV<sub>1</sub>)) and respiratory exacerbations requiring hospitalisation (none, 1–2 or >2) [9] as dependent variables. Predictor variables were pattern of physical activity categorised as attainment, or not, of: 1) 30 min of MVPA accumulated throughout the course of the day ( $\geq 30$ MVPA or  $< 30$ MVPA, respectively); or 2) 30 min of MVPA per day accumulated in bouts of at least 10 min in duration (MVPA-Bouts or MVPA-No Bouts, respectively), as well as total daily MVPA time (in minutes). Other predictor variables known to influence long-term outcomes in CF [9] were also included. Alpha was set at 0.05.



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**Achieving physical activity guidelines by undertaking multiple bouts of moderate-vigorous physical activity  $\geq 10$  min duration, but not shorter periods of activity, was independently associated with less decline in FEV<sub>1</sub> over 3 years among adults with CF** <http://ow.ly/yk6930ivCV8>

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At baseline, 65 adults (34 male) with stable CF, mean±SD age 28±7 years and mean±SD FEV<sub>1</sub> 68±20% predicted were recruited, with 61 individuals having valid physical activity data for inclusion in the original analysis. At 3-year follow-up spirometry data were available for n=56 (86%) (no lung function n=6; died n=2; lung transplant n=1), resulting in 53 complete cases (baseline valid physical activity and 3-year follow-up spirometry) for inclusion (table 1). At 3-year follow-up mean±SD FEV<sub>1</sub> was 65±24% predicted, while median respiratory-related hospital admissions and hospital days were 2 (interquartile range (IQR): 1–7) and 28 (IQR: 9–107), respectively. Mean±SD change in FEV<sub>1</sub> from baseline to 3-year follow-up was –0.11±0.33 L.

In a stepwise multiple linear regression model that included age, sex, body mass index, baseline FEV<sub>1</sub>, CF-related diabetes and pancreatic insufficiency, the only significant predictors of annual rate of change in FEV<sub>1</sub> were age ( $\beta$ =–0.006, SE of  $\beta$ =0.002, p=0.027) and MVPA-Bouts ( $\beta$ =0.081, SE of  $\beta$ =0.033, p=0.018). This model explained 32% of the variation in change in FEV<sub>1</sub> (F (1, 42)=6.12, p=0.018), of which 13% was attributable to MVPA-Bouts. When regression analysis was repeated using alternate patterns of physical activity ( $\geq$ 30MVPA or total MVPA time per day, rather than MVPA-Bouts) the model was no longer significant (p=0.16 and p=0.07, respectively). Pattern of physical activity accumulation was not an independent contributor to the model predicting exacerbations requiring hospitalisation at 3-year follow-up.

The analysis reported here indicates that accumulating 30 min of MVPA a day in bouts of at least 10-minutes duration is a significant independent predictor of less decline in lung function over 3-years in adults with CF. This would suggest that concerted efforts of moderately intense physical activity in bouts of purposeful exercise, such as brisk walking at speeds above 4.8 km per hour or cycling at more than

TABLE 1 Demographic details and clinical outcomes relative to physical activity performance

	$\geq$ 30MVPA	<30MVPA	MVPA-Bouts	MVPA-No Bouts
<b>Baseline</b>				
Subjects	33	28	21	40
Male:female	22:11	10:18	14:7	22:18
Age years	29.9±6	32.6±10	29.5±6	32.0±9
BMI kg·m <sup>-2</sup>	21.8±1.8	22.6±3.6	21.9±2.2	22.3±3.1
Pancreatic insufficiency	31	27	20	37
CF-related diabetes	7	7	5	9
FEV <sub>1</sub> L	2.8±0.9	2.3±1.0	2.9±1.0	2.3±0.9
FEV <sub>1</sub> % predicted	69±18	65±23	71±20	64±20
<b>1-year follow-up</b>				
FEV <sub>1</sub> L	2.8±0.9	2.2±1.1	2.9±0.9	2.3±1.0
FEV <sub>1</sub> % predicted	69±19	64±26	72±21	63±23
Annual change in FEV <sub>1</sub> L	–0.01±0.2	–0.03±0.2	0.02±0.2	–0.04±0.2
Hospitalisation frequency				
0	17	9	13	13
1–2	11	13	6	17
>2	5	6	2	10
Total hospitalisations, median (IQR)	0 (0–2)	1.5 (0–2)	0 (0–2)	1 (0–2)
Total hospital days, median (IQR)	0 (0–19)	27 (0–49)	0 (0–25)	12 (0–44)
<b>3-year follow-up</b>				
Complete cases	29	24	18	34
Male: Female	21:8	8:16	13:5	15:19
FEV <sub>1</sub> L	2.7±1.0	2.2±1.1	2.9±1.0	2.2±1.0
FEV <sub>1</sub> % predicted	66±20	63±28	71±21	61±25
Annual change FEV <sub>1</sub> L	–0.03±0.12	–0.05±0.09	0.01±0.1	–0.07±0.1
Hospitalisation frequency				
0	5	4	4	7
1–2	10	5	7	7
>2	14	15	7	20
Total hospitalisations, median (IQR)	2 (1–7)	4 (1–7)	2 (0.8–6)	4 (1–7)
Total hospital days, median (IQR)	19 (4–100)	51 (10–115)	17 (6–92)	44 (9–119)

Data are presented as n or mean±SD, unless otherwise stated. MVPA: moderate-vigorous physical activity;  $\geq$ 30MVPA: spent at least 30 min in MVPA daily; <30MVPA: did not achieve at least 30 min MVPA daily; MVPA-Bouts: achieved 30 min MVPA in bouts of  $\geq$ 10 min duration; MVPA-No Bouts: did not achieve 30 min MVPA in bouts of  $\geq$ 10 min duration; BMI: body mass index; CF: cystic fibrosis; FEV<sub>1</sub>: forced expiratory volume in 1 s; IQR: interquartile range.

8 km per hour [10], are necessary to achieve better outcomes in clinically relevant measures (specifically FEV<sub>1</sub>) in adults with CF, as opposed to only accumulating incidental physical activity through daily living. In our cohort, relatively few adults with CF were able to achieve 30 min of MVPA a day in bouts of at least 10-minutes duration. Whether failure to achieve 30 min of MVPA a day in bouts relates to physiological limitations, attitudes and behaviour relating to physical activity or time constraints imposed by other therapy requirements is not clear.

Very few studies have reported on the long-term relationship between physical activity and clinical outcomes, in particular lung function, in people with CF. COLLACO *et al.* [11], using US CF Foundation patient registry data, found adults who self-reported any exercise participation had a slower rate of decline in FEV<sub>1</sub> over 5 years. In a predominantly paediatric cohort, participants who were categorised as having higher levels of activity, based on self-report using the Habitual Activity Estimation Scale, had a slower rate of decline in FEV<sub>1</sub> over an average of 5-years of follow-up [2]. However, the nature, duration and intensity of exercise were not elucidated in these studies. By using the SenseWear Armband, a valid, objective measure of physical activity in adults with CF [12], we have described the pattern, not just volume, of physical activity associated with less decline in lung function over time. Such objective measures of physical activity provide composite information in terms of activity frequency, intensity and duration [13], and are able to overcome issues of bias due to memory recall that are associated with subjective measures of physical activity [14]. Despite this, objective measurement of physical activity remains subject to variations imposed by external factors such as weather or daylight hours. Although assessed over a multi-day period as recommended [15], the effect of changes in health, personal circumstances or season on physical activity in this cohort could not be controlled.

In the present analysis we found pattern of physical activity did not predict need for hospitalisation due to respiratory exacerbation over the 3-year follow-up. This is in keeping with the findings of SAVI *et al.* [9] who found no association between the number of pulmonary exacerbations in the preceding year and physical activity variables when corrected for clinical covariates. In our previous 1-year follow-up analysis we noted that, compared to those who did not, individuals who achieved physical activity recommendations in bouts of at least 10-min duration had significantly fewer hospital days and a trend towards fewer hospital admissions over 12-months [7]; however, physical activity was not an independent predictor of hospital time when controlling for other clinical variables. This serves to highlight the intricate interaction between changes in health status as a consequence of a progressive disease and the complex, multifaceted behaviour that is physical activity [13].

In conclusion, for adults with CF achieving physical activity guidelines by undertaking multiple bouts of MVPA  $\geq 10$  min duration in a day, but not shorter periods of physical activity, was independently associated with less decline in FEV<sub>1</sub> over 3 years. Understanding the pattern by which adults with CF undertake physical activity, and its effect on clinical outcomes, may enhance our ability to develop realistic and achievable interventions that promote meaningful physical activity participation in this population.

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