

## Moderate-vigorous physical activity and all-cause mortality in COPD: could bouts matter?

To the Editor:

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Received: 13 Dec 2022 Accepted: 5 April 2023 In people with COPD, the amount and intensity of regular physical activity is related to risk of hospitalisation and mortality [1]. Previously, general physical activity guidelines for older adults required  $\geq$  30 min of at least moderate intensity exercise on  $\geq$ 5 days per week [2]; to achieve health benefits, activity needed to be performed in uninterrupted bouts  $\geq$ 10 min duration [2, 3]. For people with COPD, symptoms of breathlessness, functional limitations and poor exercise tolerance may make it difficult to meet these guidelines. Recently, physical activity guidelines have removed the recommendation for physical activity to be performed in bouts [4], as nonbouted activity has been associated with improved health, including cardiometabolic outcomes, frailty and mortality [5–7]. Bouts of physical activity of  $\geq$ 10 min duration are associated with improved maximal oxygen uptake, *i.e.* cardiorespiratory fitness [8, 9], a known prognostic indicator for people with COPD [10]. However, for people with COPD, especially severe disease, incidental physical activity accumulated alongside daily tasks may be more achievable than periods of dedicated exercise. If a mortality benefit from physical activity participation can be achieved without a minimum bout requirement in people with COPD, this could create opportunities for new activity promotion and exercise training strategies.

The aim of this analysis was to determine whether a mortality benefit is conferred by cumulative physical activity time alone, or whether bouts of activity may better achieve improved health outcomes in people with COPD.

This retrospective cohort study used device-measured physical activity data previously collected from individuals with COPD participating in pulmonary rehabilitation clinical trials conducted in Melbourne, Australia. The parent trials were investigating alternative models of rehabilitation delivery or impact of rehabilitation participation on immune function [11–13]. Common inclusion criteria were confirmed diagnosis of COPD; forced expiratory ratio <0.7; and age  $\geq$ 40 years. Ethics approval was provided by Alfred Health human research ethics committee (project ID 68534). All data included in this exploratory analysis represent baseline data on referral to pulmonary rehabilitation, and collected prior to any study intervention.

Participants wore the SenseWear armband (BodyMedia, Pittsburgh, PA, USA), a tri-axial accelerometer, for 7 days at baseline. The SenseWear armband contains sensors to measure galvanic skin response, heat flux and skin temperature when in contact with the skin. During wear time, a proprietary algorithm (version 8.0) estimated activity intensity (metabolic equivalents (METs)) and recorded data in 1-min epochs. A minimum 4 days of data ( $\geq$ 10 h wear time per day) was required for inclusion [14]. Physical activity was categorised using conventional MET cut-points for sedentary (<1.5 METs, not including time categorised as sleep), light intensity physical activity (LIPA;  $\geq$ 1.5<3 METs) and moderate–vigorous physical activity (MVPA;  $\geq$ 3 METs). Time in each activity intensity category (min·day<sup>-1</sup>), bouts of MVPA  $\geq$ 10 min and number of bouts of MVPA per day were determined. Sleep time was classified according to the SenseWear algorithm.

Baseline demographic features collected included age at recruitment, sex, smoking history and lung function. All-cause mortality at 31 July 2021 was ascertained from electronic medical records.

For this retrospective cohort, a sample size calculation was not performed and a sample of convenience was used. A total of 143 individuals consented to the three parent studies and undertook baseline



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For people with COPD, performance of physical activity in bouts confers a greater survival benefit than total physical activity alone, suggesting that the manner in which physical activity is undertaken may be important for people with COPD https://bit.ly/3Gy2Gjl

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assessment of physical activity. To determine the clinical relevance of physical activity duration and bout combinations, we examined four different ways to categorise physical activity accumulation: 1) accumulation of MVPA totalling  $\geq 30 \text{ min} \cdot \text{day}^{-1}$ ; 2) MVPA  $\geq 30 \text{ min} \text{ accumulated entirely in bouts} \geq 10 \text{ min on any one day in the monitoring period; 3) bout duration average <math>\geq 10 \text{ min across all included}$  days; and 4) MVPA  $\geq 30 \text{ min} \cdot \text{day}^{-1}$  and any bouts of MVPA  $\geq 10 \text{ min in the monitoring period. Physical activity categories were not mutually exclusive, as the effect of pattern of physical activity accumulation (total$ *versus*bouts) is not known. Kaplan–Meier curves for mortality were calculated and time to death (or censor) was reported in days from date of recruitment. Cox proportional hazards models were used to estimate hazard ratios for mortality according to achievement of physical activity (1–4 described earlier), as well as for cumulative physical activity time (all physical activity of at least light intensity (*i.e.*LIPA +MVPA) as classified by the SenseWear armband throughout the monitoring period irrespective of whether accumulated continuously or interrupted). Analyses accounted for potential confounders of the association between physical activity and mortality (*i.e.*sex, disease severity).

Out of 143 potentially eligible datasets, 122 were included in the analysis (table 1). Five individuals had participated in more than one of the parent trials, so only first eligible data were included. 16 participants did not have valid activity monitoring data for inclusion.

For the group as a whole, daily MVPA time was median 23 min (interquartile range (IQR) 6–55 min). 53 (43%) participants achieved MVPA  $\geq$ 30 min·day<sup>-1</sup>, with n=48 (39%) accumulating MVPA  $\geq$ 30 min of MVPA in bouts of  $\geq$ 10 min duration on any day. 46 (38%) participants achieved an average MVPA bout duration  $\geq$ 10 min (mean±sp bout duration 17±31 min); with 45 (37%) achieving MVPA  $\geq$ 30 min·day<sup>-1</sup> and any 10-min bout duration. At the census date, 35 (29%) were deceased and 1 (1%) had been transplanted. Time from physical activity monitoring to death or censor, was mean±sp 1283±633 days (3.5±1.7 years).

TABLE I Participant characteristics at baseline		
	Participants	Participants with insufficient physical activity data for inclusion
Participants	122	16
Male	59 (48)	4 (25)
Age, years	67±10	70±12
BMI, kg·m <sup>−2</sup>	27.2±6.6	27.4±5.2
Smoking status		
Current smokers	25 (21)	2 (13)
Ex-smokers	94 (77)	14 (87)
Never-smokers	3 (3)	0 (0)
Smoking history, pack-years	46±23	36±15
Spirometry		
FEV <sub>1</sub> , L	1.3±0.5	1.0±0.4
FEV1, % pred	49.6±19.9	51.0±22.4
FVC, L	2.7±0.7	2.2±0.8
FVC, % pred	78.9±21.4	78.9±26.5
FER	0.5±0.1	0.4±0.1
LTOT users	12 (10)	3 (19)
6MWD, m	417±103	360±102
Physical activity		
Sleep time, min∙day <sup>−1</sup>	408 (316–452)	
Sedentary time, min∙day <sup>−1</sup>	696 (588–1823)	
LIPA time, min·day <sup>−1</sup>	191 (111–250)	
MVPA time, min∙day <sup>−1</sup>	23 (6–55)	
Total physical activity time (LIPA+MVPA), min·day $^{-1}$	224 (116–336)	
MVPA bouts per day	0 (0—1)	
MVPA bout duration, min·day <sup>-1</sup>	4 (0-21)	
Activity monitor wear, days	6 (6–7)	
Activity monitor wear time, h∙day <sup>−1</sup>	22.9 (20.7–23.7)	

Data are presented as n, n (%), mean±sD or median (interquartile range). BMI: body mass index; FEV<sub>1</sub>: forced expiratory volume in 1 s; FVC: forced vital capacity; FER: forced expiratory ratio; LTOT: long-term oxygen therapy; 6MWD: 6-min walk distance; LIPA: light-intensity physical activity; MVPA: moderate–vigorous physical activity.

A longer time to death was seen in all analyses which included completion of activity in bouts (bouts of MVPA  $\geq 10 \text{ min}$  for a total of 30 min·day<sup>-1</sup>: Chi-squared 3.73, p=0.05; any bouts of MVPA  $\geq 10 \text{ min}$ : Chi-squared 6.56, p=0.01; MVPA  $\geq 30 \text{ min·day}^{-1}$  and any bouts of MVPA  $\geq 10 \text{ min}$ : Chi-squared 8.31, p=0.004), but not for undertaking MVPA  $\geq 30 \text{ min·day}^{-1}$  (Chi-squared 3.04, p=0.081).

Accounting for sex and percentage predicted forced expiratory volume, any bouts of MVPA  $\geq 10$  min (hazard ratio (HR) 2.91, 95% CI 1.26–6.70), or MVPA  $\geq 30$  min·day<sup>-1</sup> and any bouts of MVPA  $\geq 10$  min (HR 3.49, 95% CI 1.44–8.45) were both associated with an increased likelihood of survival, whereas MVPA  $\geq 30$  min·day<sup>-1</sup> (HR 1.84, 95% CI 0.89–3.77) and total physical activity time (HR 0.99, 95% CI 0.97–1.01) were not. When models included 6-min walk distance (6MWD), the effect of MVPA bouts was no longer evident.

The results of this study suggest that in people with COPD, achieving physical activity in bouts is associated with a survival benefit that exceeds that attributable to physical activity duration alone. Approximately one-third of participants were able to achieve any  $\geq 10$  min bouts of MVPA, similar to older adults with other chronic health conditions [15]. The lack of impact of physical activity duration alone on survival contrasts with findings in two studies of up to 5000 community-dwelling adults, where greater physical activity conferred a mortality benefit at >5 years' follow-up [6, 16]. Our findings have implications for physical activity recommendations in COPD, which may not be consistent with those in healthy adults. It was interesting to note that the survival benefit associated with physical activity bouts was no longer evident once 6MWD was included in the model, suggesting that the ability to perform physical activity in bouts may reflect greater physical capacity. This reinforces the need for interventions that can improve physical capacity in COPD (*e.g.* exercise training), if patients are to achieve physical activity patterns that are associated with longer-term benefits. The role of interventions that specifically target increased physical activity in people with COPD, including bouts, remains unclear [17].

A limitation of the present work is the use of previously collected data, which limits the available sample size for the physical activity intensity categories considered. However, this approach is in keeping with other recent exploratory analyses of the impact of physical activity level on mortality [18]. Furthermore, we only considered the influence of time spent in MVPA and total physical activity and as such the relative effect, if any, of LIPA in isolation on mortality in this cohort is not described. We chose to look at the impact of bouts of physical activity of ≥10 min duration as the 10-min exercise threshold is associated with improvements in cardiorespiratory fitness, i.e. maximal oxygen uptake [8, 9], a known predictor of prognosis in people with COPD [10]. While it may be challenging for many people with COPD to accumulate physical activity in bouts of  $\geq 10$  min [19], evidence for the effect of shorter activity bout durations, e.g. 1 min, 2 min or 5 min, on cardiorespiratory fitness is scarce. In a systematic review on the association between physical activity bout duration and health, included studies describing the effect of physical activity in bouts of <10 min were largely single, nonrandomised cohort or cross-sectional studies which did not report on the impact on cardiorespiratory fitness [5]. No randomised controlled trials reported outcomes for physical activity bouts <10 min [5]. In a small cohort study of sedentary older individuals, bouts of MVPA <10 min achieved similar cardiovascular outcomes including lower blood pressure, as did 30-60 min periods of exercise; however, exercise capacity was not evaluated, and adherence to the longer duration training was poor [20]. Whether short bouts or unbouted physical activity achieves cardiovascular improvements in people with COPD of a magnitude to confer survival benefit remains to be determined. Additionally, the possibility of other unmeasured confounders to the relationship between physical activity and mortality cannot be excluded.

In contrast to recommendations for healthy individuals, in people with COPD performance of physical activity in bouts confers a greater survival benefit than total physical activity alone. Achieving physical activity in bouts may reflect greater physical capacity. This suggests that, in addition to interventions that enhance physical capacity, the manner in which physical activity is undertaken may also be important for long-term health benefits in people with COPD.

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