Laboratory and free-living gait performance in adults with COPD and healthy controls

01 September 2025

Laboratory and free-living gait performance in adults with COPD and healthy controls

Joren Buekers[1,2,3], Dimitrios Megaritis[4], Sarah Koch[1,2,3], Lisa Alcock[5,6], Nadir Ammour[7], Clemens Becker[8], Stefano Bertuletti[9], Tecla Bonci[10], Philip Brown[11], Ellen Buckley[10], Sara C. Buttery[12], Brian Caulfied[13,14], Andrea Cereatti[15], Nikolaos Chynkiamis[4,16], Heleen Demeyer[17,18], Carlos Echevarria[5,11], Anja Frei[19], Clint Hansen[20], Jeffrey M. Hausdorff[21,22,23], Nicholas S. Hopkinson[12], Emily Hume[4], Arne Kuederle[24], Walter Maetzler[20], Claudia Mazzà[10], Encarna M. Micó-Amigo[5], Arne Mueller[25], Luca Palmerini[26], Francesca Salis[9], Kirsty Scott[10], Thierry Troosters[17], Beatrix Vereijken[27], Henrik Watz[28], Lynn Rochester[5,6,11], Silvia Del Din[5,6], Ioannis Vogiatzis[4,16] and Judith Garcia-Aymerich[1,2,3]

[1]ISGlobal, Barcelona, Spain. [2]Universitat Pompeu Fabra, Barcelona, Spain. [3]CIBER Epidemiología y Salud Pública, Barcelona, Spain. [4]Department of Sport, Exercise and Rehabilitation, Northumbria University Newcastle, Newcastle upon Tyne, UK. [5]Translational and Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK. [6]National Institute for Health and Care Research Newcastle Biomedical Research Centre, Newcastle University and The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK. [7]Clinical Science and Operations, GlobalDevelopment, Sanofi R&D, Chilly-Mazarin, France. [8]Robert Bosch Gesellschaft für Medizinische Forschung, Stuttgart, Germany. [9]Department of Biomedical Sciences, University of Sassari, Sassari, Italy. [10]Department of Mechanical Engineering and INSIGNEO Institute for In Silico Medicine, The University of Sheffield, Sheffield, UK. [11]The Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK. [12]National Lung and Heart Institute, Imperial College, London, UK. [13]Insight Centre for Data Analytics, University College Dublin, Dublin, Ireland. [14]School of Public Health, Physiotherapy and Sports Science, University College Dublin, Dublin, Ireland. [15]Polytechnic University of Torino, Department of Electronics and Telecommunications, Turin, Italy. [16]Thorax Research Foundation and First Department of Respiratory Medicine, National and Kapodistrian University of Athens, Sotiria General Chest Hospital, Athens, Greece. [17]KU Leuven, Department of Rehabilitation Sciences and Pulmonary Rehabilitation, Respiratory Division, University Hospital Gasthuisberg, Leuven, Belgium. [18]Department of Rehabilitation Sciences, Ghent University, Ghent, Belgium. [19]Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland. [20]Department of Neurology, University Hospital Schleswig-Holstein and Kiel University, Kiel, Germany. [21]Center for the Study of Movement, Cognition and Mobility, Neurological Institute, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel. [22]Sagol School of Neuroscience and Department of Physical Therapy, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. [23]Rush Alzheimer's Disease Center and Department of Orthopedic Surgery, Rush University Medical Center, Chicago, IL, USA. [24]Machine Learning and Data Analytics Lab, Department of Artificial Intelligence in Biomedical Engineering, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany. [25]Novartis Institutes for Biomedical Research, Basel, Switzerland. [26]Department of Electrical, Electronic and Information Engineering "Guglielmo Marconi", University of Bologna, Bologna, Italy. [27]Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology, Trondheim, Norway. [28]Pulmonary Research Institute at LungenClinic Grosshansdorf, Airway Research Center North, German Center for Lung Research (DZL), Grosshansdorf, Germany.

Corresponding author: Joren Buekers (joren.buekers@isglobal.org)

Shareable abstract (@ERSpublications)
Gait impairment of adults with COPD was only observed during relatively long walking bouts (>30 s) in free-living conditions but not during shorter (⩽30 s) walking bouts in either laboratory or free-living settings https://bit.ly/44vBpYp

Cite this article as: Buekers J, Megaritis D, Koch S, *et al*. Laboratory and free-living gait performance in adults with COPD and healthy controls. *ERJ Open Res* 2023; 0: 00159-2023 [DOI: 10.1183/23120541.00159-2023].

Abstract

Background Gait characteristics are important risk factors for falls, hospitalisations and mortality in older adults, but the impact of COPD on gait performance remains unclear. We aimed to identify differences in gait characteristics between adults with COPD and healthy age-matched controls during 1) laboratory tests that included complex movements and obstacles, 2) simulated daily-life activities (supervised) and 3) free-living daily-life activities (unsupervised).

Methods This case–control study used a multi-sensor wearable system (INDIP) to obtain seven gait characteristics for each walking bout performed by adults with mild-to-severe COPD (n=17; forced

Received: 14 Feb 2023
Accepted: 29 June 2023

expiratory volume in 1 s=57±19% predicted) and controls (n=20) during laboratory tests, and during simulated and free-living daily-life activities. Gait characteristics were compared between adults with COPD and healthy controls for all walking bouts combined, and for shorter (⩽30 s) and longer (>30 s) walking bouts separately.

Results Slower walking speed (−11 cm·s^{-1}, 95%CI: −20 to −3) and lower cadence (−6.6 steps·min^{-1}, 95% CI: −12.3 to −0.9) were recorded in adults with COPD compared to healthy controls during longer (>30 s) free-living walking bouts, but not during shorter (⩽30 s) walking bouts in either laboratory or free-living settings. Double support duration and gait variability measures were generally comparable between the two groups.

Conclusion Gait impairment of adults with mild-to-severe COPD mainly manifests during relatively long walking bouts (>30 s) in free-living conditions. Future research should determine the underlying mechanism(s) of this impairment to facilitate the development of interventions that can improve free-living gait performance in adults with COPD.

Introduction

COPD is characterised by persistent respiratory symptoms [1], airflow limitation [1] and extrapulmonary disease manifestations such as fatigue [2], weight loss [3] and comorbidities [4]. Adults with COPD are also prone to falls [5], which can lead to long-lasting pain, functional impairment, disability and death [6]. Even just fear of falling can lead to physical activity avoidance [7], which may in turn increase risk for exacerbations, hospital admissions and mortality in adults with COPD [8–10]. Since altered gait is one of the main risk factors for falls [11, 12], characterising gait is critical for preventing falls and their devastating consequences.

Walking speed is arguably the most intensively studied and validated gait characteristic [13]. It is an important predictor of multiple falls [11], incident disability and mortality in older adults [14]. Walking speed depends on two other gait characteristics: stride length (one stride is two consecutive steps) and cadence (the number of steps taken per minute). Another gait characteristic, double support duration, represents the duration of simultaneously having both feet in contact with the ground while walking and is generally increased in older adults [15]. Decreased stride length and cadence, and increased double support duration are all associated with an increased fall risk in older adults [11, 12]. Finally, gait variability measures (*e.g.*, coefficients of variation of stride duration, stride length or double support duration) represent movement consistency and stability (*i.e.*, gait not leading to falls, in spite of perturbations) [16, 17]. It has been argued that increased gait variability might even better predict increased fall risk in older adults than previously discussed average values [11, 18]. Q1

Despite the importance of the seven abovementioned gait characteristics as risk factors for falls, hospitalisations and mortality in older adults, relatively few studies have examined gait characteristics in COPD. Furthermore, the available literature shows inconsistencies on the impact of COPD on gait. Some studies identified a reduced walking speed, cadence, stride length and a higher double support duration for adults with COPD compared to healthy controls [19–21], while other studies did not [22, 23]. Based on a 2021 scoping review, we hypothesise that adults with COPD walk with a slower walking speed, lower cadence, shorter stride length, a longer double support duration and similar gait variability compared to healthy controls [13]. By analogy with other chronic conditions such as Parkinson's disease [24] and multiple sclerosis [25], we hypothesise that the degree of gait impairment in COPD is different during longer (>30 s) compared to shorter (⩽30 s) walking bouts, as symptoms that could affect gait, such as leg fatigue or dyspnoea [26], are more likely to be present during longer walking bouts. Another limitation of previous research is that differences in gait characteristics between adults with COPD and controls have almost exclusively been examined in a laboratory setting [27], without considering any of the complex movements (*e.g.*, starting to walk from a seated position) or obstacles (*e.g.*, a step) that are inherent to free-living walking outside of the laboratory. Consequently, available information on gait in COPD represents gait capacity, rather than free-living gait performance. We hypothesise that gait impairment in COPD is more pronounced during more complex activities and that therefore the impact of COPD on gait can mainly be observed in free-living conditions.

Therefore, the objectives of this study were to identify differences in gait characteristics between adults with COPD and healthy controls during 1) laboratory tests that include complex movements (*e.g.*, timed up and go) or obstacles (*e.g.*, walking over a step), 2) simulated daily-life activities (supervised) and (3) free-living daily-life activities (unsupervised). The generated insights will help to develop and evaluate early intervention and prevention strategies for improving free-living gait performance of adults with COPD, and consequently reduce their fall risk and fall-related complications.

Methods

Study design and participants

This multicentre, observational case–control study used data from the technical validation study of the IMI2-JU-funded Mobilise-D project (https://www.mobilise-d.eu/), which aimed to validate a new digital method for remote monitoring of mobility in different cohorts, including adults with COPD and healthy older adults [28, 29]. The study was approved by the London-Bloomsbury Research Ethics committee (19/LO/1507), medical faculty of Kiel University (D540/19), medical faculty of the University of Tübingen (647/2019BO2) and Helsinki Committee of the Tel Aviv Sourasky Medical Center (0551-19TLV). All participants provided written informed consent.

Clinically stable adults with COPD (post-bronchodilator forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC) ratio <0.70; smoking history equivalent to at least 10 pack-years; 4 weeks without antibiotics and/or oral corticosteroids to treat a moderate or severe exacerbation) were recruited from The Newcastle upon Tyne Hospitals NHS Foundation Trust (UK) and Sheffield Teaching Hospitals NHS Foundation Trust (UK). Candidates were excluded if they had undergone major lung surgery, had a lung tumour or a respiratory disease other than COPD, or had orthopaedic, neurological or other complaints that significantly impaired normal biomechanical movement patterns, as judged by the investigator. Healthy controls (>65 years) were recruited from The Newcastle upon Tyne Hospitals NHS Foundation Trust (UK), the University of Kiel (Germany), Robert Bosch Foundation for Medical Research (Germany) and the Tel Aviv Sourasky Medical Center (Israel). Data were collected between July 2020 and July 2021.

Participants were excluded if they were unable to walk 4 m independently with or without walking aid, had shoe size <36 European Union (3 UK), Montreal Cognitive Assessment score ⩽15 or an occurrence of any of the following within 3 months prior to inclusion: myocardial infarction, hospitalisation for unstable angina, stroke, coronary artery bypass graft, percutaneous coronary intervention or implantation of a cardiac resynchronisation therapy device.

Procedures

Gait characteristics were obtained during laboratory tests, simulated daily-life activities and free-living daily-life activities using the INertial module with DIstance Sensors and Pressure insoles (INDIP) system, a validated multi-sensor system including pressure insoles, distance sensors at the ankles, and magneto-inertial sensors on the shoes and lower back [28, 30–33] (supplementary figure E1).

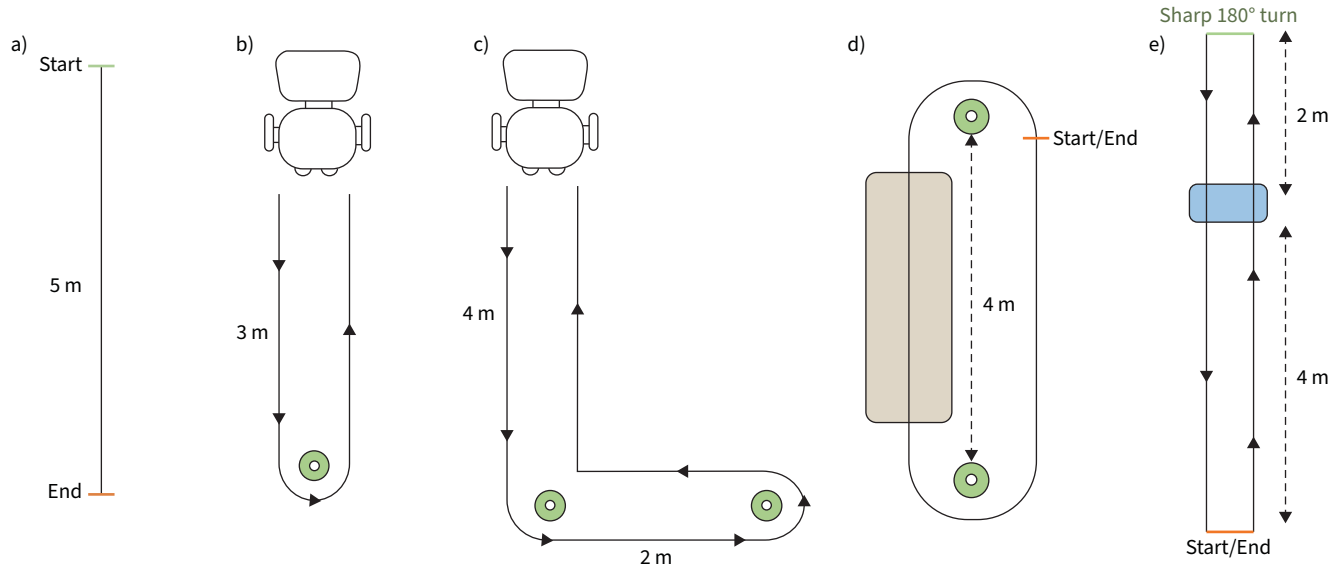
Laboratory tests included five structured mobility tasks with increasing complexity, performed at the participants' preferred walking speed (figure 1) [28]. When needed, the use of arm rests or handrails was permitted during the tests. Simulated daily-life activities were based on a series of supervised daily-life tasks performed in the laboratory while sitting and moving around a room, such as picking up objects and setting the table [28] (figure 2).

Free-living daily-life activities consisted of 2.5 h of unsupervised activities in a habitual environment (home/work/community) chosen by the participant. The duration of the measurements was chosen as a trade-off between experimental, clinical and technical requirements [28]. The free-living activities were unstructured, but participants were encouraged to complete several specific tasks, such as rise from a chair and walk to another room, walk up and down a set of stairs, and walk outdoors. Hence, these activities should not be interpreted as entirely regular daily-life routines.

Variables

Participant characteristics were collected for all participants including age, sex, height, body mass index, falls in the previous year, walking aid usage, living arrangement, education and pain while walking. Additionally, the COPD group completed the COPD assessment test and performed a 6-min walk test according to American Thoracic Society (ATS) guidelines. Pulmonary function (FEV_1 and FVC) for participants with COPD was obtained from medical records completed within 6 months prior to participant inclusion.

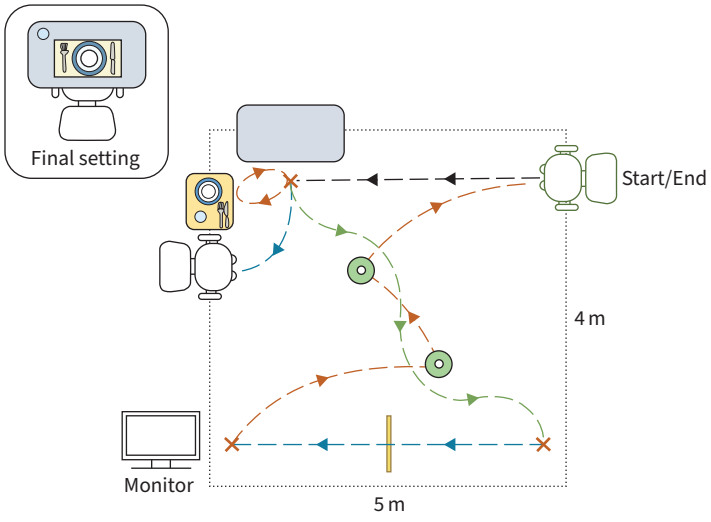
For the laboratory tests, simulated daily-life activities and free-living daily-life activities, we collected: the number of walking bouts, walking bout duration (s), walking bout length (cm) and the number of turns per walking bout. A walking bout was defined as a walking sequence containing at least two consecutive strides of both feet. The start and end of a walking bout were determined by a resting period or any non-walking activity for at least 3 s [30, 34].



Laboratory test	Procedure
a) Straight walking test	Participants walked 5 m from a standing start. This trial was performed twice for each of three self-selected speeds: comfortable, slow and fast. As the different trials were considered to be conceptually very similar (*i.e.*, no complex movements or obstacles), only the first trial at a comfortable walking speed was analysed in the current study
b) Timed up and go	Participants stood up from a chair, walked 3 m in a straight line, made a 180° turn, walked back to the chair and sat down
c) L-test	Participants stood up from a chair, walked straight, turned 90° to the left around a cone, walked straight to the second cone, made a 180° turn to the left, walked straight before making a final 90° turn to the right and returning to the chair to sit down
d) Surface test	Participants completed an oval circuit (made up of two cones that were 4 m apart) twice, during which they walked over a 2 m carpeted mat
e) Hallway obstacle test	Participants walked back and forth along a 6 m walkway stepping up and down a step positioned in the walkway

FIGURE 1 Visualisation of laboratory tests. Reproduced and modified from Scott *et al.* [29] with permission from the publisher. Q3

For every walking bout, seven gait characteristics were calculated using the INDIP system: walking speed ($cm \cdot s^{-1}$), cadence ($steps \cdot min^{-1}$; number of steps taken per minute), stride length (cm; length of two consecutive steps), double support duration (s; duration of simultaneously having both feet in contact with the ground), stride duration (duration of two consecutive steps) variability (%; coefficient of variation of



Step	Description
One	Rise from the green chair and walk to the cross
Two	Set the grey table for dinner using the objects on the yellow table
Three	Move the grey chair to the grey table and sit down for 1-min break
Four	Stand up and move objects back to the yellow table
Five	Walk across the lab to the next cross while snaking around the cones
Six	Walk to the next cross while stepping over the small object on the floor
Seven	Stand and watch a 1-min video on the monitor
Eight	Pick up the cones and return to sit in the green chair

FIGURE 2 Visualisation of simulated daily-life activities. Reproduced and modified from Scott *et al.* [29] with permission from the publisher.

stride duration), stride length variability (%; coefficient of variation of stride length) and double support duration variability (%; coefficient of variation of double support duration). Of note, the acceleration and deceleration phase at the start and end of each laboratory test was included for the calculation of the gait characteristics (see the definition of a walking bout above), as this more closely reflects free-living conditions [34].

Statistical analyses

Statistical power to identify differences in gait characteristics between adults with COPD and healthy controls was estimated as 86%, based on walking speed data from previous studies (standard deviation of 20 $cm \cdot s^{-1}$ and expected differences of 20 $cm \cdot s^{-1}$ [19, 21, 22, 26, 35–37]), α=0.05, and our sample size of 17 adults with COPD and 20 healthy controls, using the GRANMO power calculator (https://www.imim.es/ofertadeserveis/software-public/granmo/).

Participant and gait characteristics are presented as mean$\pm_{SD}$ for normally distributed continuous variables and as n (%) for categorical variables. Normality was tested for all variables using histograms. Participant characteristics, the number of walking bouts per participant and the total time spent walking during daily-life activities were compared between adults with COPD and healthy controls using unpaired t-tests, Wilcoxon rank-sum or Fisher's exact tests, as appropriate.

Gait characteristics and walking bout duration were compared between adults with COPD and healthy controls using linear regression models adjusted for age, height and walking bout length. For the five laboratory tests (all including one walking bout by design), regression analyses were performed with one observation per participant. For the simulated and free-living daily-life activities (consisting of multiple walking bouts per participant), mixed effect regression models with a random intercept for individuals were used. To test whether the impact of COPD on gait performance was affected by walking bout duration, the previous models were additionally stratified by walking bout duration, using a cut-off based on scientific literature (*i.e.*, shorter ($\leqslant$30 s) and longer (>30 s) walking bouts) [24, 25]. Two sensitivity analyses were performed: 1) the mixed effect regression models for simulated and free-living daily-life activities were additionally adjusted for the number of turns per walking bout; and 2) models were stratified using additional cut-offs at 20 and 40 s.

Data preparation and statistical analyses were performed in JupyterLab using the Python 3.5 and the R 4.1.2 programming languages.

Results

Participant characteristics

17 adults with mild-to-severe COPD and 20 healthy age-matched controls were included in the study. There were no statistically significant differences between the groups regarding sex distribution, age, height, body mass index, falls in the previous year, walking aid usage, living arrangement, education and pain while walking (table 1). Three adults with COPD and seven healthy controls had an insufficient number of strides during the straight walking test to identify a walking bout, and one healthy control did not perform the simulated daily-life activities.

Gait characteristics during laboratory tests

Walking speed ranged between 89 and 106 $cm \cdot s^{-1}$ for adults with COPD and between 91 and 106 $cm \cdot s^{-1}$ for healthy controls during the different tests (table 2). No statistically significant differences in gait characteristics during the laboratory tests were found between adults with COPD and healthy controls, except for less stride duration variability (−1.1%, 95% CI: −2.1 to −0.1) for adults with COPD during the surface test (table 2; figures 3 and 4). All walking bouts during the laboratory tests were shorter walking bouts (*i.e.*, $\leqslant$30 s), except for the surface test of one participant with COPD (walking bout of 34 s). Therefore, no stratification was conducted.

Gait characteristics during simulated daily-life activities

Participants with COPD and healthy controls performed 88 and 96 walking bouts with an average walking speed of 59±21 $cm \cdot s^{-1}$ and 60±24 $cm \cdot s^{-1}$, respectively, during the simulated daily-life activities (table 3). Adults with COPD had less stride length variability (−5.8%, 95% CI: −11.2 to −0.4; figures 5 and 6). All walking bouts were shorter (*i.e.*, $\leqslant$30 s) and therefore no stratification was conducted. Sensitivity analyses in which the models were additionally adjusted for the number of turns provided similar results (supplementary figures E2 and E3).

TABLE 1 Participant characteristics

	COPD	Healthy controls	p-value
Participants, n	17	20	
Sex, n (%)			
Male	9 (53)	11 (55)	1.00
Female	8 (47)	9 (45)	
Age years, mean±SD	69±9	72±6	0.37
Height cm, mean±SD	169±7	166±10	0.37
Body mass index kg·m^{-2}, mean±SD	25.9±5.2	27.1±3.6	0.43
Participants who fell in previous year, n (%)	1 (6)	3 (15)	0.61
Participants who use a walking aid, n (%)	1 (6)	1 (5)	1.00
Living arrangement, n (%)			
Alone	3 (18)	7 (35)	0.29
With somebody	14 (83)	13 (65)	
Education, n (%)			
⩽12 years	11 (65)	8 (40)	0.19
>12 years	6 (35)	12 (60)	
Pain while walking (visual analogue scale, 0–100), median (IQR)	7 (18)	1 (9)	0.12
6-min walk distance m, mean±SD	358±89	/	/
FEV_1 L, mean±SD	1.54±0.59	/	/
FEV_1 % predicted, mean±SD	57±19	/	/
GOLD stage, n (%)			
I	3 (18)	/	/
II	6 (35)	/	/
III	8 (47)	/	/
IV	0 (0)	/	/
FVC L, mean±SD	2.98±0.75	/	/
FVC % predicted, mean±SD	86±25	/	/
FEV_1/FVC, mean±SD	0.52±0.14	/	/
COPD assessment test score, mean±SD	20±9	/	/

p-values represent the comparison between adults with COPD and healthy controls based on t-test or Fisher's exact test, as appropriate. FEV_1: forced expiratory volume in 1 s; GOLD: Global Initiative for Chronic Obstructive Lung Disease; FVC: forced vital capacity.

Gait characteristics during free-living daily-life activities

Participants with COPD and healthy controls performed 1035 (90% shorter and 10% longer) and 1330 (88% shorter and 12% longer) walking bouts, respectively, during the 2.5 h of unsupervised, free-living activities

TABLE 2 Gait characteristics during laboratory tests

	Straight walking test		Timed up and go		L-test		Surface test		Hallway obstacle test	
	COPD	CON	COPD	CON	COPD	CON	COPD	CON	COPD	CON
Participants, n	14	13	17	20	17	20	17	20	17	20
Walking bout duration s	3.3±0.5	3.7±0.6	5.7±1.5	5.5±1.6	13.6±2.9	11.9±2.1	22.9±4.1	17.4±5.5	13.3±2.3	11.9±2.3
Walking speed cm·s^{-1}	102±17	106±11	106±19	105±25	92±16	91±16	98±14	100±16	89±13	92±17
Cadence steps·min^{-1}	101±10	106±9	112±13	114±16	101±9	104±8	101±8	105±8	99±10	101±9
Stride length cm	121±12	120±11	114±15	110±18	109±14	104±16	116±13	115±16	107±10	110±18
Double support duration s	0.37±0.07	0.38±0.07	0.33±0.06	0.36±0.10	0.39±0.07	0.38±0.09	0.38±0.05	0.38±0.09	0.38±0.06	0.39±0.07
Stride duration variability %	4±2	4±1	5±3	6±3	5±2	6±2	**3±1**[#]	**5±1**	13±4	12±4
Stride length variability %	7±5	5±2	20±7	19±6	21±6	22±4	12±2	15±4	21±3	22±4
Double support duration variability %	6±7	7±4	11±5	12±8	10±5	12±5	9±5	10±5	16±8	16±6

Data are presented as mean±SD unless otherwise indicated. Every test consisted of only one walking bout. All tests/walking bouts were shorter (*i.e.*, ⩽30 s), except for the surface test of one participant with COPD (walking bout of 34 s). CON: healthy age-matched controls. [#]: statistically significant differences between patients with COPD and healthy controls based on β coefficients (95% CI) from linear regression models adjusted for age, height and walking bout length.

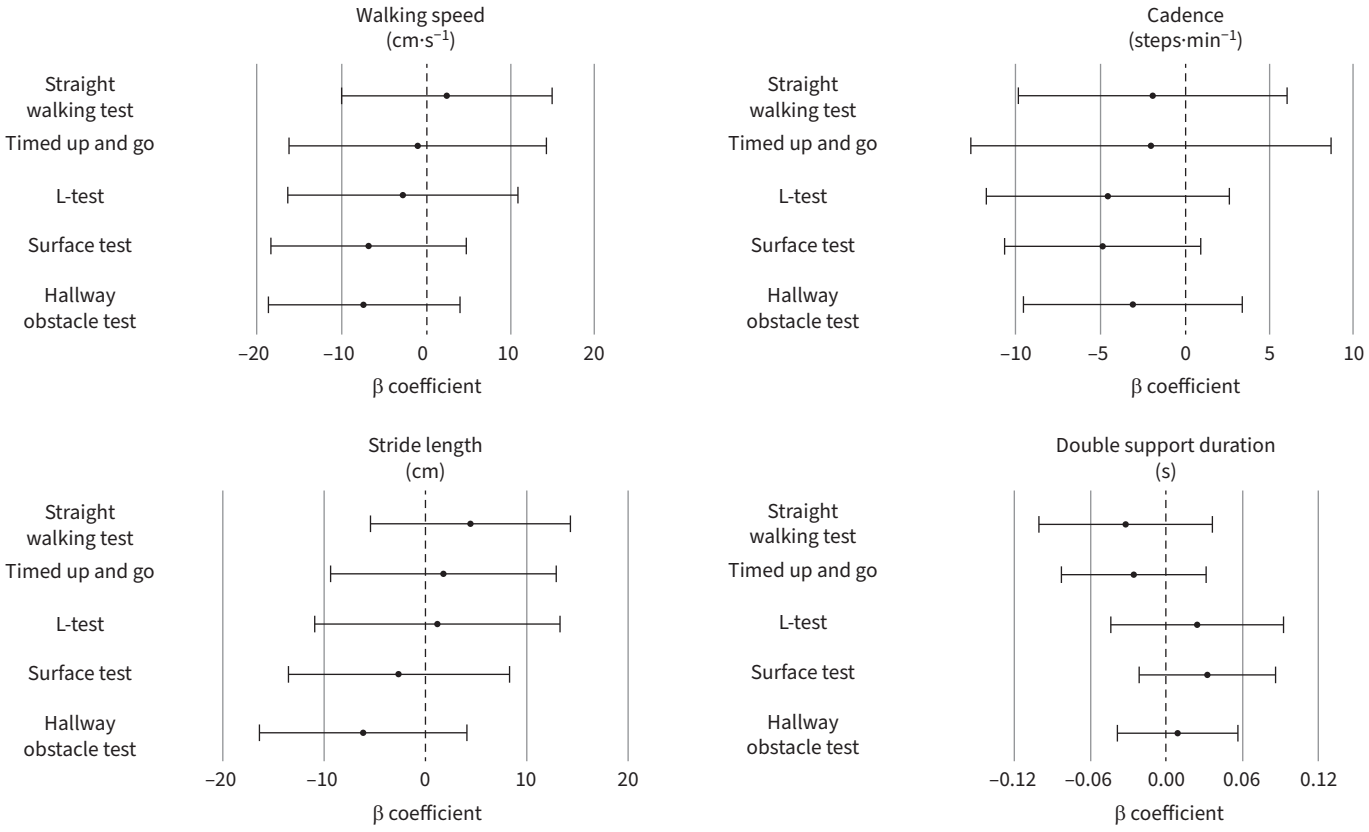


FIGURE 3 Differences in walking speed, cadence, stride length and double support duration between adults with COPD and healthy controls during laboratory tests, expressed as β coefficient (95% CI) of a linear regression model adjusted for age, height and walking bout length. The healthy controls were used as the reference group.

(table 3). All participants performed both shorter and longer walking bouts. Healthy controls spent more time walking during the 2.5 h of free-living activities than adults with COPD, originating from more time spent walking during, and longer durations of, longer walking bouts (table 3; supplementary figure E4).

Walking speed during shorter bouts was 57±20 cm·s^{-1} for patients with COPD and 54±21 cm·s^{-1} for healthy controls, increasing to 71±23 cm·s^{-1} for COPD and 85±29 cm·s^{-1} for controls during longer bouts (table 3). No statistically significant differences in gait characteristics were observed between adults with COPD and healthy controls when all free-living walking bouts were considered together, or during shorter free-living walking bouts (figures 5 and 6). During longer free-living walking bouts, adults with COPD had a slower walking speed (−11 cm·s^{-1}, 95% CI: −20 to −3) and lower cadence (−6.6 steps·min^{-1}, 95% CI: −12.3 to −0.9) compared to healthy controls, and a trend towards a shorter stride length (p=0.08) (figure 5). Sensitivity analyses 1) additionally adjusting the models for the number of turns (supplementary figures E2 and E3) and 2) using cut-offs at 20 s or 40 s for separating shorter and longer walking bouts provided similar results (supplementary figures E5 and E6).

Discussion

Our study was the first to examine differences in free-living gait performance between adults with mild-to-severe COPD and age-matched healthy controls. Walking speed and cadence were significantly reduced in the COPD group during longer (>30 s) free-living walking bouts, and there was a non-significant trend towards a shorter stride length for adults with COPD during these bouts. Opposed to our hypothesis, no differences were observed in walking speed, cadence or stride length during shorter walking bouts in either laboratory or free-living settings. Double support duration and gait variability measures were generally comparable between adults with COPD and healthy controls.

The most important finding of the current study is that mild-to-severe COPD was associated with walking at a slower speed and lower cadence during longer free-living walking bouts, while no differences were

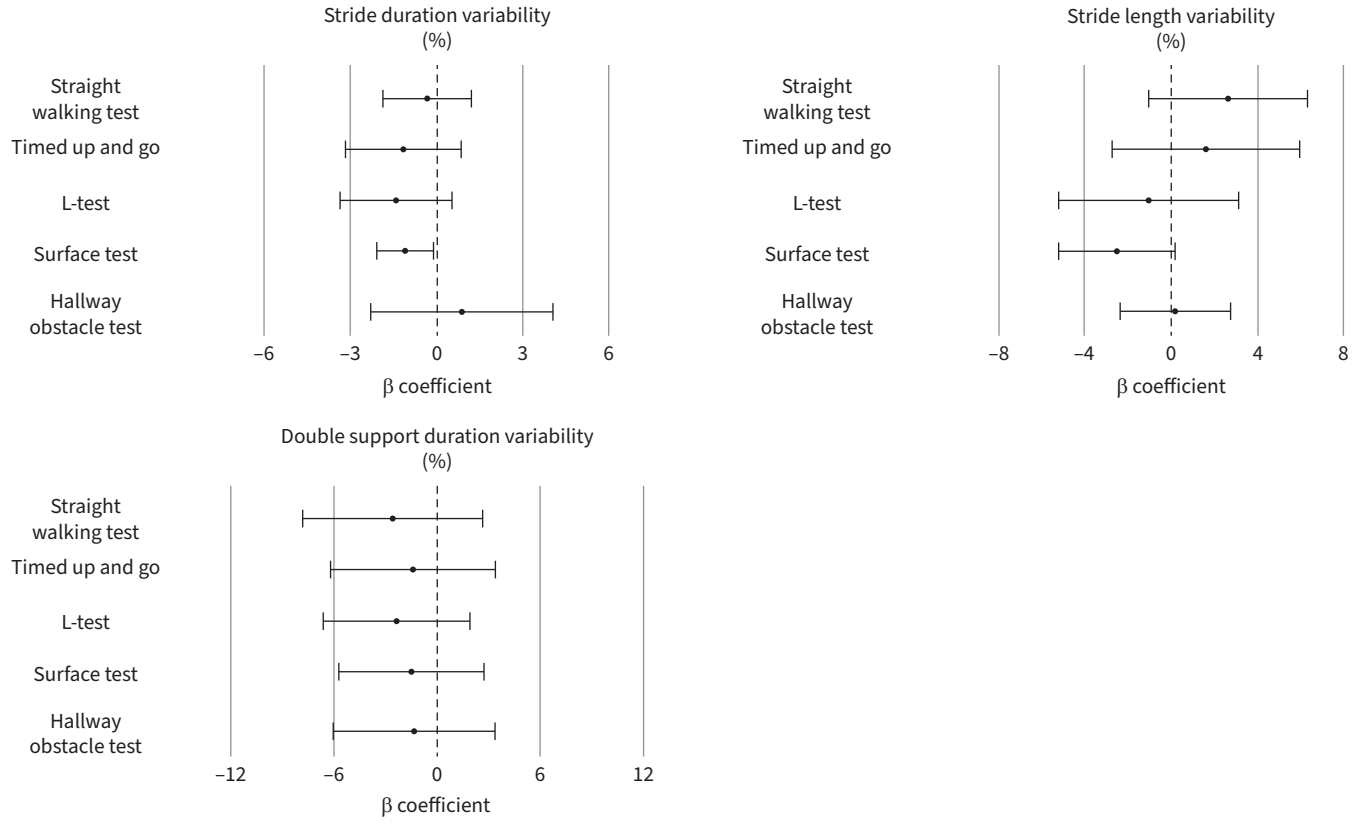


FIGURE 4 Differences in gait variability measures between adults with COPD and healthy controls during laboratory tests, expressed as β coefficient (95% CI) of a linear regression model adjusted for age, height and walking bout length. The healthy controls were used as the reference group.

TABLE 3 Gait characteristics (on the walking bout level) during the simulated and free-living daily-life activities (analyses for all free-living bouts combined, and for shorter (⩽30 s) and longer (>30 s) walking bouts separately)

	Simulated daily-life activities		Free-living activities (all bouts)		Free-living activities (bouts ⩽30 s)		Free-living activities (bouts >30 s)	
	COPD	CON	COPD	CON	COPD	CON	COPD	CON
Walking bouts,	88	96	1035	1330	932	1168	103	162
Participants	17	19	17	20	17	20	17	20
Walking bouts per participant	5±2	5±1	61±25	66±27	55±24	58±26	6±3	8±4
Total time spent walking min	0.6 (0.2)	0.6 (0.2)	**17 (8)**[#]	**26 (10)**	11 (8)	11 (4)	**7 (4)**[#]	**12 (9)**
Walking bout duration s[¶]	6 (4)	6 (4)	10 (12)	10 (12)	9 (9)	9 (8)	**44 (27)**[+]	**56 (64)**
Walking speed cm·s^{-1}	59±25	60±24	59±21	58±25	57±20	54±21	**71±23**[+]	**85±29**
Cadence steps·min^{-1}	89±13	91±12	84±12	85±14	84±12	84±14	**87±11**[+]	**96±14**
Stride length cm	79±28	77±26	82±23	80±26	80±22	77±24	96±25	104±25
Double support duration s	0.56±0.23	0.62±0.32	0.57±0.19	0.58±0.21	0.57±0.19	0.60±0.22	0.52±0.15	0.46±0.12
Stride duration variability %	22±16	25±15	19±10	19±10	19±10	19±10	19±7	17±8
Stride length variability %	**31**[+]**±20**	**36±19**	31±14	30±14	32±14	31±14	30±11	24±11
Double support duration variability %	33±32	36±31	27±21	26±20	26±21	25±20	34±18	30±18

Data are presented as n, mean±SD and median (IQR). CON: healthy age-matched controls. [#]: statistically significant differences between patients with COPD and healthy controls based on p-values from Wilcoxon rank-sum test; [¶]: walking bout duration during free-living daily-life activities was transformed using Box-Cox for the comparison between patients with COPD and healthy controls; [+]: statistically significant differences between patients with COPD and healthy controls based on β coefficients (95% CI) from mixed effect models with a random intercept for individuals and adjusted for age, height and walking bout length.

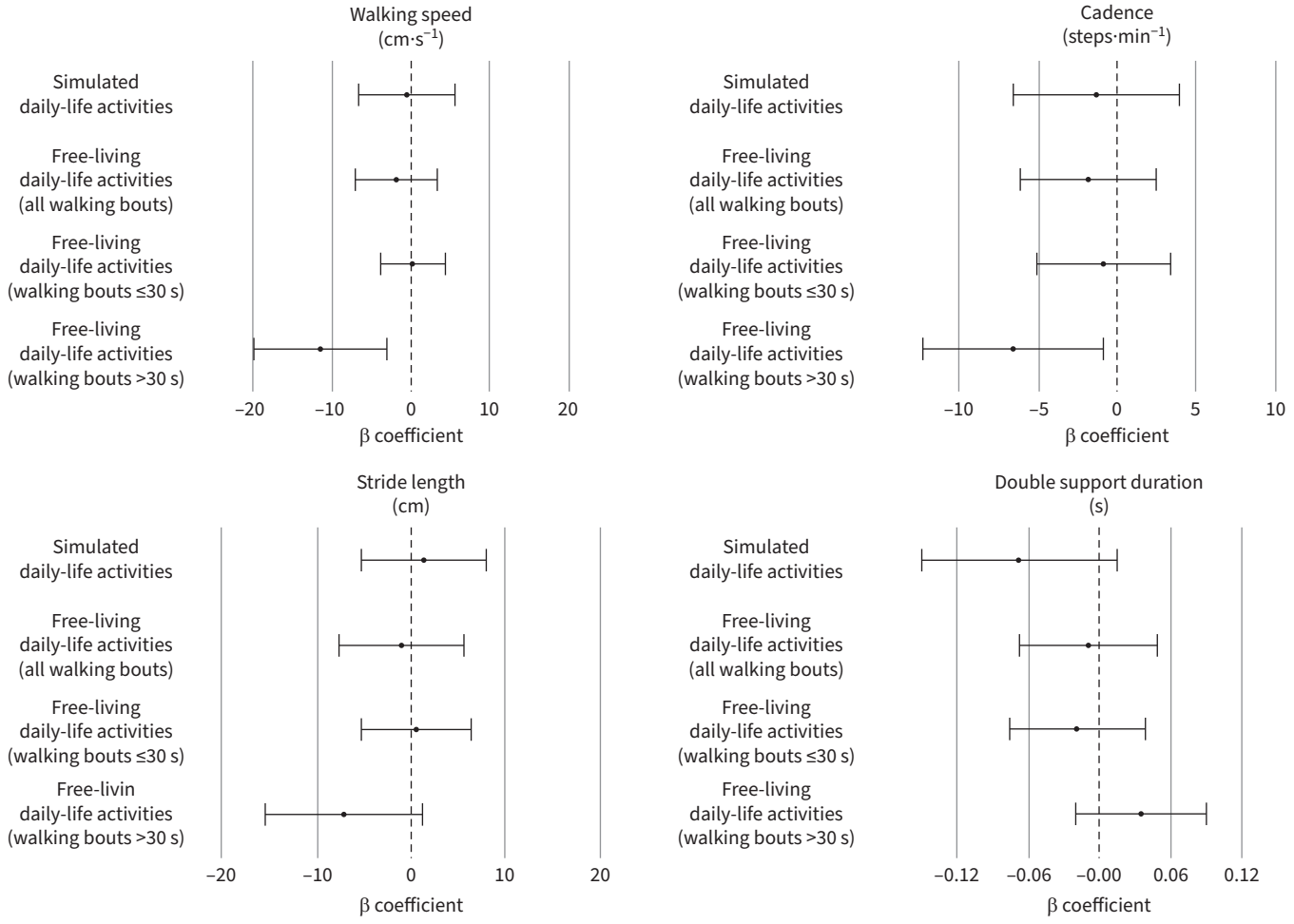


FIGURE 5 Differences in walking speed, cadence, stride length and double support duration between adults with COPD and healthy controls during simulated and free-living daily-life activities, expressed as β coefficient (95% CI) of a linear mixed effects model with random intercepts for participants. The healthy controls were used as the reference group. Models were adjusted for age, height and walking bout length.

observed during shorter bouts. Specifically, walking speed changed from 54±21 cm·s^{-1} in shorter bouts to 85±29 cm·s^{-1} in longer bouts among healthy participants, while in COPD it only increased from 57 ±20 cm·s^{-1} to 71±23 cm·s^{-1}. The underlying mechanisms of this attenuated increase in walking speed and cadence during longer walking bouts of adults with COPD could be pathological (*e.g.*, due to poor exercise capacity [19, 38]) and/or behavioural (*e.g.*, a coping mechanism to maintain a tolerable dyspnoea sensation [26] or a compensatory strategy to maintain balance and reduce fall risk [39]).

Previous research has provided contradictory results on the presence/absence of differences in gait characteristics between adults with COPD and healthy controls during laboratory tests [19–23, 26, 35, 36]. Careful screening of scientific literature did not identify consistent differences in sample size, disease severity or walking bout durations between these studies that could explain the observed inconsistencies. These inconsistencies might still originate from other methodological or clinical differences between studies that were not systematically reported, such as differences in the starting procedure (static *versus* dynamic start) [40] or dyspnoea levels of participants [41]. Hence, comparisons of current results with previous literature should only be done cautiously. Nevertheless, the observed slower walking speed and lower cadence during free-living conditions in our study corresponds with the results of the largest laboratory-based study to date on gait in COPD (n=196 adults with COPD walking on an electronic walkway), suggesting that the reduced walking speed in COPD is related to a decrease in cadence [36]. The walking speed during the straight walking test of the healthy controls in the current study was slower than for healthy older adults in previous reports [42]. This can most likely be attributed to the inclusion of

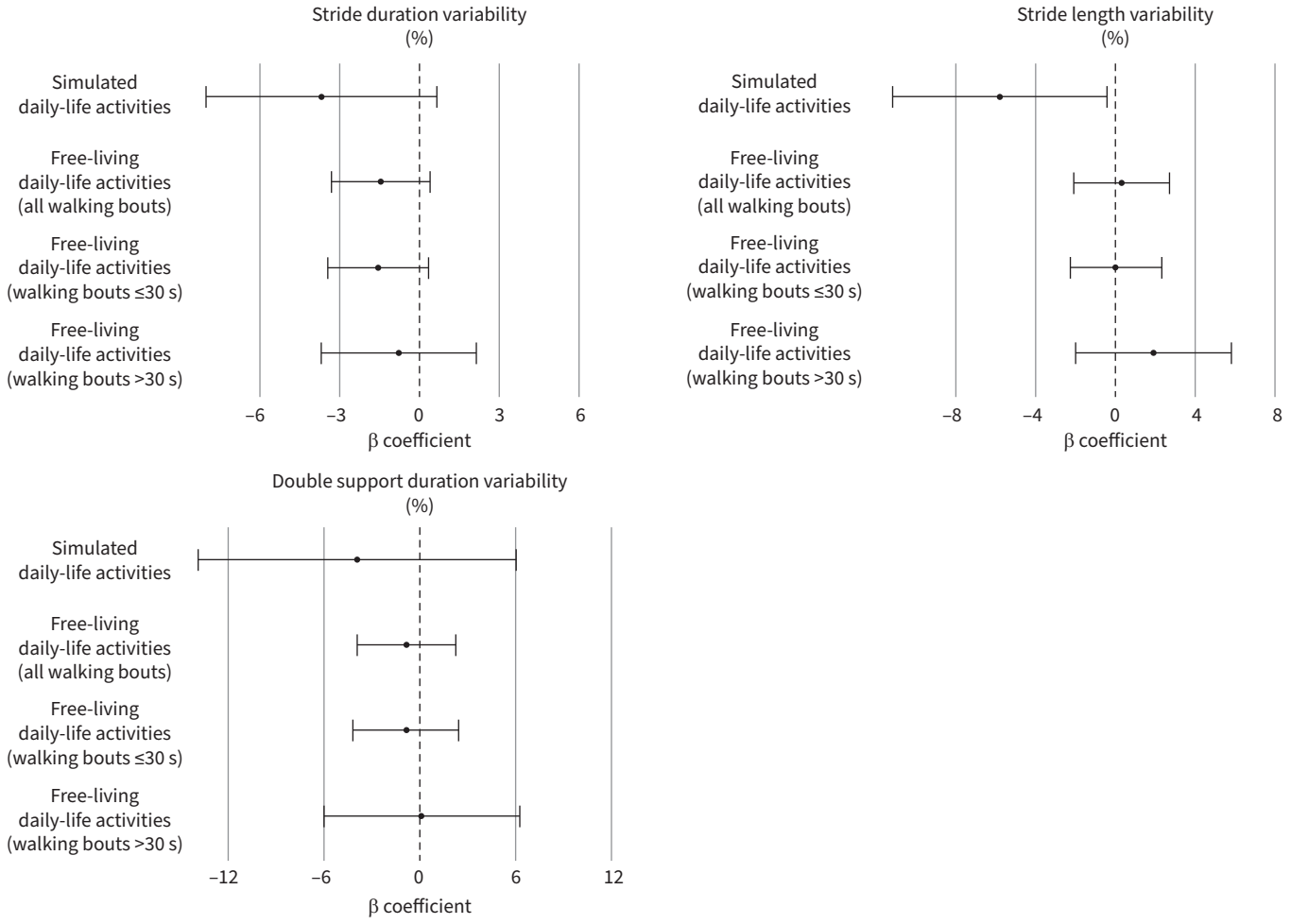


FIGURE 6 Differences in gait variability measures between adults with COPD and healthy controls during simulated and free-living daily-life activities, expressed as β coefficient (95% CI) of a linear mixed effects model with random intercepts for participants. The healthy controls were used as the reference group. Models were adjusted for age, height and walking bout length.

the acceleration and deceleration phase at the start and end of each laboratory test in the current study (*i.e.*, a static start), while other laboratory-based studies often excluded this acceleration/deceleration phase (*i.e.*, dynamic start).

We generally did not observe differences in double support duration or gait variability measures between adults with COPD and healthy controls. In combination with the absence of an association between double support duration/gait variability measures and fall history in COPD [36], this could suggest that stability during walking is not markedly affected in COPD and that these gait characteristics might be of secondary importance in this population. Of note, we observed less stride duration variability in adults with COPD during the surface test, and less stride length variability during the simulated daily-life activities, which could be the result of an inability to adjust gait when faced with a change in walking surface or obstacle [17], or a chance finding.

A clear implication of the present study is the need to consider walking bout duration and include a sufficient number of longer bouts in future studies on gait in COPD. Furthermore, examining the distribution of bout duration over multiple days might reveal differences in walking behaviour between adults with COPD and healthy controls, as already suggested by the 2.5 h of free-living measurements in the current study (supplementary figure E4). From a clinical perspective, the observed gait impairment suggests that free-living gait performance of adults with COPD can be improved, potentially by improving exercise capacity (*e.g.*, through pulmonary rehabilitation [43]) and/or reducing exertional dyspnoea (*e.g.*,

through bronchodilator therapy [44]). Ultimately, this could reduce fall risk and increase quality of life and survival of adults with COPD.

The main strength of this study was the collection of gait characteristics in free-living conditions in adults with COPD. By using a multi-sensor wearable system and combining laboratory tests, simulated daily-life activities and free-living daily-life activities, we were able to show that adults with mild-to-severe COPD experience gait impairment during free-living activities that may not be observable during short laboratory tests or simulated daily-life activities. Other strengths of the study include the use of a control group and the adjustment for both participant characteristics (age and height) and walking bout length in the regression analyses.

The study also had some potential limitations. Firstly, the sample size was relatively small. Nevertheless, the performed power calculation indicated that our sample size had high power (*i.e.*, 86%) to respond to the study objectives. Secondly, data were collected during the COVID-19 pandemic, which might have prevented adults with very severe COPD from participating, and which might have affected the activities performed during the free-living measurements. The COVID-19 pandemic also disrupted the recruitment strategy (which intended to distribute the recruitment of participants over five different centres to ensure generalisability [28]), and participants were unevenly recruited by the different centres. Thirdly, gait characteristic values obtained during the straight walking test cannot directly be compared with values obtained in other laboratory-based studies, as most studies exclude the acceleration/deceleration phase at the start/end of a straight walking test. Fourthly, the relatively short duration of free-living measurements (*i.e.*, 2.5 h) might not be representative of all daily-life activities and routines of the participants. Finally, free-living gait characteristics could have been affected by environmental factors (*e.g.*, slope, house/apartment size, meteorological factors), which were not assessed or controlled for in the current study

In conclusion, gait impairment in adults with mild-to-severe COPD occurred during longer walking bouts (>30 s) with an attenuated increase in walking speed and cadence, compared to healthy controls. These differences were not observed during shorter walking bouts (⩽30 s). Double support duration and gait variability measures were generally comparable between the two groups. Future research should replicate our analyses in larger studies and determine the underlying mechanism(s) of this gait impairment during longer bouts to facilitate the development of interventions that can improve free-living gait performance in adults with COPD.

Provenance: Submitted article, peer reviewed.

Acknowledgements: The authors acknowledge all the members of the Mobilise-D work package 2 for continuous discussion and critical input. They are particularly grateful to the participants in the study for their time and enthusiastic contribution, especially during the pandemic. Full membership of the Mobilise-D consortium is available on the website https://www.mobilise-d.eu/partners. Q2

Support statement: This work was supported by the Mobilise-D project that has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement number 820820. This JU receives support from the European Union's Horizon 2020 research and innovation programme, and the European Federation of Pharmaceutical Industries and Associations (EFPIA). S. Del Din and L. Rochester were also supported by the Innovative Medicines Initiative 2 (IMI2) JU project IDEA-FAST – grant agreement 853981. S. Del Din, L. Alcock and L. Rochester were also supported by the National Institute for Health Research (NIHR) Newcastle Biomedical Research Centre (BRC) based at The Newcastle upon Tyne Hospital NHS Foundation Trust, Newcastle University and the Cumbria, Northumberland and Tyne and Wear NHS Foundation Trust, and by the NIHR/Welcome Trust Clinical Research Facility infrastructure at Newcastle upon Tyne Hospitals NHS Foundation Trust. C. Mazzà and E. Buckley were also supported by the Sheffield BRC based at the Sheffield Teaching Hospital and the University of Sheffield. The Barcelona Institute for Global Health (ISGlobal) receives support from the Spanish Ministry of Science, Innovation and Universities through the "Centro de Excelencia Severo Ochoa 2019–2023" Programme (CEX 2018-000806-S), and support from the Generalitat de Catalunya through the CERCA Programme. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, the Department of Health, the IMI, the European Union, the EFPIA or any Associated Partners. Funding information for this article has been deposited with the Crossref Funder Registry.

Conflict of interest: A. Mueller is an employee of Novartis and holds shares in this company. L. Palmerini is cofounder of and owns shares in mHealth Technologies (https://mhealthtechnologies.it/). S. Del Din reports consultancy activity with Hoffmann-La Roche Ltd. outside the scope of this study. I. Vogiatzis is an associate editor of this journal . The other authors have nothing to disclose.

References

1 Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD. 2021. Available from: http://goldcopd.org/
2 Goërtz YMJ, Spruit MA, Van t'Hul AJ, *et al.* Fatigue is highly prevalent in patients with COPD and correlates poorly with the degree of airflow limitation. *Ther Adv Vaccines* 2019; 13: 1753466619878128.
3 Agustí AGN, Noguera A, Sauleda J, *et al.* Systemic effects of chronic obstructive pulmonary disease. *Eur Respir J* 2003; 21: 347–360.
4 Vanfleteren LEGW, Spruit MA, Groenen M, *et al.* Clusters of comorbidities based on validated objective measurements and systemic inflammation in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2013; 187: 728–735.
5 Núñez-Cortés R, Padilla-Acevedo P, Vergara-Peña F, *et al.* Clinical assessment of balance and functional impairments in people with stable chronic obstructive pulmonary disease: a systematic review and meta-analysis. *ERJ Open Res* 2022; i: 00164-2022.
6 Kannus P, Sievänen H, Palvanen M, *et al.* Prevention of falls and consequent injuries in elderly people. *Lancet* 2005; 366: 1885–1893.
7 Cumming RG, Salkeld G, Thomas M, *et al.* Prospective study of the impact of fear of falling on activities of daily living, SF-36 scores, and nursing home admission. *J Gerontol A Biol Sci Med Sci* 2000; 55: 299–305.
8 Garcia-Aymerich J, Lange P, Benet M, *et al.* Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population based cohort study. *Thorax* 2006; 61: 772–778.
9 Garcia-Aymerich J, Farrero E, Félez MA, *et al.* Risk factors of readmission to hospital for a COPD exacerbation: a prospective study. *Thorax* 2003; 58: 100–105.
10 Garcia-Rio F, Rojo B, Casitas R, *et al.* Prognostic value of the objective measurement of daily physical activity in patients with COPD. *Chest* 2012; 142: 338–346.
11 Callisaya ML, Blizzard L, Schmidt MD, *et al.* Gait, gait variability and the risk of multiple incident falls in older people: a population-based study. *Age Ageing* 2011; 40: 481–487.
12 Verghese J, Holtzer R, Lipton RB, *et al.* Quantitative gait markers and incident fall risk in older adults. *J Gerontol A Biol Sci Med Sci* 2009; 64: 896–901.
13 Polhemus A, Ortiz LD, Brittain G, *et al.* Walking on common ground: a cross-disciplinary scoping review on the clinical utility of digital mobility outcomes. *NPJ Digit Med* 2021; 4: 149.
14 Studenski S, Perera S, Patel K, *et al.* Gait speed and survival in older adults. *J Am Med Assoc* 2011; 305: 50–58.
15 Winter DA, Patla AE, Frank JS, *et al.* Biomechanical walking pattern changes in the fit and healthy elderly. *Phys Ther* 1990; 70: 340–347. www.clubcampestrepopayan.com
16 Sekiya N, Nagasaki H, Ito H, *et al.* Optimal walking in terms of variability in step length. *J Orthop Sport Phys Ther* 1997; 26: 266–272.
17 Bruijn SM, Meijer OG, Beek PJ, *et al.* Assessing the stability of human locomotion: a review of current measures. *J R Soc Interface* 2013; 10: 20120999.
18 Maki BE. Gait changes in older adults: predictors of falls or indicators of fear? *J Am Geriatr Soc* 1997; 45: 313–320.
19 Iwakura M, Okura K, Shibata K, *et al.* Gait characteristics and their associations with clinical outcomes in patients with chronic obstructive pulmonary disease. *Gait Posture* 2019; 74: 60–65.
20 Liu WY, Spruit MA, Delbressine JM, *et al.* Spatiotemporal gait characteristics in patients with COPD during the Gait real-time analysis interactive lab-based 6-minute walk test. *PLoS One* 2017; 12: e0190099.
21 Morlino P, Balbi B, Guglielmetti S, *et al.* Gait abnormalities of COPD are not directly related to respiratory function. *Gait Posture* 2017; 58: 352–357.
22 Yentes JM, Schmid KK, Blanke D, *et al.* Gait mechanics in patients with chronic obstructive pulmonary disease. *Respir Res* 2015; 16: 31.
23 Jirange P, Vaishali K, Sinha MK, *et al.* A cross-sectional study on balance deficits and gait deviations in COPD patients. *Can Respir J* 2021; 2021: 6675088.
24 Rehman RZU, Guan Y, Shi JQ, *et al.* Investigating the impact of environment and data aggregation by walking bout duration on parkinson's disease classification using machine learning. *Front Aging Neurosci* 2022; 14: 808518.
25 Storm FA, Nair KPS, Clarke AJ, *et al.* Free-living and laboratory gait characteristics in patients with multiple sclerosis. *PLoS One* 2018; 13: e0196463.
26 Sanseverino MA, Pecchiari M, Bona RL, *et al.* Limiting factors in walking performance of subjects with COPD. *Respir Care* 2018; 63: 301–310.
27 Polhemus AM, Bergquist R, De Basea M B, *et al.* Walking-related digital mobility outcomes as clinical trial endpoint measures: protocol for a scoping review. *BMJ Open* 2020; 10: e038704.
28 Mazzà C, Alcock L, Aminian K, *et al.* Technical validation of real-world monitoring of gait: a multicentric observational study. *BMJ Open* 2021; 11: e050785.

29 Scott K, Bonci T, Alcock L, *et al.* Design and validation of a multi-task, multi-phase protocol for real-world gait simulation. *J Neuroeng Rehabil* 2022; 19: 141.

30 Salis F, Bertuletti S, Bonci T, *et al.* A multi-sensor wearable system for the assessment of diseased gait in real-world conditions. *Front Bioeng Biotechnol* 2023; 11: 1143248.

31 Salis F, Bertuletti S, Bonci T, *et al.* A method for gait events detection based on low spatial resolution pressure insoles data. *J Biomech* 2021; 127: 1–7.

32 Bertuletti S, Della Croce U, Cereatti A. A wearable solution for accurate step detection based on the direct measurement of the inter-foot distance. *J Biomech* 2019; 84: 274–277.

33 Caruso M, Sabatini AM, Knaflitz M, *et al.* Orientation estimation through magneto-inertial sensor fusion: a heuristic approach for suboptimal parameters tuning. *IEEE Sens J* 2021; 21: 3408–3419.

34 Kluge F, Del Din S, Cereatti A, *et al.* Consensus based framework for digital mobility monitoring. *PLoS One* 2021; 16: e0256541.

35 Heraud N, Alexandre F, Gueugnon M, *et al.* Impact of chronic obstructive pulmonary disease on cognitive and motor performances in dual-task walking. *COPD* 2018; 15: 277–282.

36 Lahousse L, Verlinden VJA, Van Der Geest JN, *et al.* Gait patterns in COPD: the Rotterdam study. *Eur Respir J* 2015; 46: 88–95.

37 Roig M, Eng JJ, MacIntyre DL, *et al.* Deficits in muscle strength, mass, quality, and mobility in people with chronic obstructive pulmonary disease. *J Cardiopulm Rehabil Prev* 2011; 31: 120–124.

38 McCamley JD, Pisciotta EJ, Yentes JM, *et al.* Gait deficiencies associated with peripheral artery disease are different than chronic obstructive pulmonary disease. *Gait Posture* 2017; 57: 258–264.

39 Menz HB, Lord SR, Fitzpatrick RC. Age-related differences in walking stability. *Age Ageing* 2003; 32: 137–142.

40 Stuck AK, Bachmann M, Füllemann P, *et al.* Effect of testing procedures on gait speed measurement: a systematic review. *PLoS One* 2020; 15: e0234200.

41 Karpman C, Benzo R. Gait speed as a measure of functional status in COPD patients. *Int J COPD* 2014; 9: 1315–1320.

42 Boyer KA, Johnson RT, Banks JJ, *et al.* Systematic review and meta-analysis of gait mechanics in young and older adults. *Exp Gerontol* 2017; 95: 63–70.

43 Spruit MA, Singh SJ, Garvey C, *et al.* An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med* 2013; 188: e13–e64.

44 O'Donnell DE, Elbehairy AF, Faisal A, *et al.* Exertional dyspnoea in COPD: the clinical utility of cardiopulmonary exercise testing. *Eur Respir Rev* 2016; 25: 333–347.

Author Queries

Journal: ERJOR

Manuscript: ERJOR-00159-2023

Q1 Are you referring to "mean values" in the sentence ending "…fall risk in older adults than previously discussed average values [11, 18]"?

Q2 This link did not work when tested on 6 July 2023.

Q3 ERS: For figures 1 and 2, please check wording for permission and check that permission has been obtained from the publisher.

Q4 Please explain data in bold type in tables 2 and 3.