EUROPEAN RESPIRATORY REVIEW
REVIEW
J. BUEKERS ET AL.

Gait differences between COPD and healthy controls: systematic review and meta-analysis

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Low-quality evidence shows that people with COPD walk more slowly than healthy controls, which could contribute to an increased risk of falls. Evidence for alterations in spatial and temporal components of gait was inconclusive. https://bit.ly/3OD9q3u

Cite this article as: Buekers J, Delgado-Ortiz L, Megaritis D, *et al*. Gait differences between COPD and healthy controls: systematic review and meta-analysis. *Eur Respir Rev* 2024; 33: 230253 [DOI: 10.1183/16000617.0253-2023].

Received: 5 Dec 2023
Accepted: 6 Feb 2024

Abstract

Background Despite the importance of gait as a determinant of falls, disability and mortality in older people, understanding of gait impairment in COPD is limited. This study aimed to identify differences in gait characteristics during supervised walking tests between people with COPD and healthy controls.

Methods We searched 11 electronic databases, supplemented by Google Scholar searches and manual collation of references, in November 2019 and updated the search in July 2021. Record screening and information extraction were performed independently by one reviewer and checked for accuracy by a second. Meta-analyses were performed in studies not considered at a high risk of bias.

Results Searches yielded 21 085 unique records, of which 25 were included in the systematic review (including 1015 people with COPD and 2229 healthy controls). Gait speed was assessed in 17 studies (usual speed: 12; fast speed: three; both speeds: two), step length in nine, step duration in seven, cadence in six, and step width in five. Five studies were considered at a high risk of bias. Low-quality evidence indicated that people with COPD walk more slowly than healthy controls at their usual speed (mean difference (MD) $-19\ \mathrm{cm\cdot s^{-1}}$, 95% CI -28 to $-11\ \mathrm{cm\cdot s^{-1}}$) and at a fast speed (MD $-30\ \mathrm{cm\cdot s^{-1}}$, 95% CI -47 to $-13\ \mathrm{cm\cdot s^{-1}}$). Alterations in other gait characteristics were not statistically significant.

Conclusion Low-quality evidence shows that people with COPD walk more slowly than healthy controls, which could contribute to an increased falls risk. The evidence for alterations in spatial and temporal components of gait was inconclusive. Gait impairment appears to be an important but understudied area in COPD.

Introduction

COPD is a heterogenous lung condition characterised by chronic respiratory symptoms and, commonly, extrapulmonary complications [1]. Complications include fatigue [2], frailty [3], limb muscle dysfunction [4] and impaired balance [5], all of which are risk factors for falling [5–7]. Consequently, people with COPD have an even higher fall risk than healthy older people [5], even though fall prevalence estimates for healthy older people are already at 26.5% [8]. Falls can have devastating consequences: while fatal falls are the second leading cause of death due to unintentional injuries across all ages worldwide [9], non-fatal falls in older people may result in fractures, long-lasting pain, functional impairment and increased fear of falling [10, 11]. The high prevalence of osteoporosis in people with COPD further increases the risk of fall-related fractures in COPD [12]. In addition, the negative outcomes associated with falling may aggravate the disease status of people with COPD by decreasing the amount of physical activity they perform, which could in turn increase their risk for exacerbations, symptoms of depression [13], hospitalisations and mortality [14–16]. Hence, falls are crucial events for people with COPD.

Gait impairment, particularly reduced gait speed, is a main determinant of falls [17, 18], disability [19] and mortality [20] in older people. Gait impairment is most commonly assessed during supervised walking tests of gait performance, based on a set of gait characteristics such as gait speed, cadence, step/stride length and step width. In COPD, gait additionally has prognostic value for healthcare utilisation and mortality [21]. Nevertheless, our general understanding of gait impairment in COPD is limited [22]. In 2018, the first systematic review on the topic by ZAGO *et al*. [23] suggested that people with COPD might have a reduced step length and cadence, as well as altered gait variability, compared to healthy controls. However, the authors acknowledged that the low number of included studies (n=7) and small sample sizes represented important risks of bias in their narrative review. Because new studies on gait in COPD have emerged [22], a new systematic review with a more extensive literature search is warranted.

The objective of this systematic review was to identify differences in gait characteristics during supervised walking tests between people with COPD and healthy controls. The increased number of available studies is expected to allow for quantitative (meta-)analyses on the differences in gait characteristics between people with COPD and healthy controls. Unsupervised, real-world measurements of gait were not considered, because there are still too few COPD studies in this line of research to justify inclusion in this systematic review [22, 24].

Methods

This review consisted of a systematic review and subsequent meta-analyses. Methods adhered to the Cochrane Handbook for Systematic Reviews of Interventions [25] and are reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [26]. The protocol was registered in the PROSPERO repository (CRD42021293459) [27].

Search strategy and eligibility criteria

The search strategy was iteratively developed in collaboration with clinical experts, experts in biomechanics and an experienced research librarian. Briefly, we searched for relevant literature available from January 1999 in 11 electronic databases (MEDLINE, Embase, CINAHL, Cochrane Library, Scopus, Web of Science, IEEE Xplore, ACM Digital Library, ProQuest Dissertations, OpenGrey and National Information Centre's Projects in Progress Database), supplemented by Google Scholar searches and manual collation of references. The full search strategy for the different databases is provided in an online repository [28]. The original search was performed in November 2019 as part of a scoping review that mapped the clinical meaningfulness of gait and walking characteristics in four clinical cohorts (COPD, Parkinson's disease, multiple sclerosis and proximal femoral fracture) [22, 29]. The exact same search was then updated for COPD in July 2021. Further details on the search strategy have been published elsewhere [22, 27, 29].

Reference sheets were developed prior to the screening process, and all members of the review team were trained and completed consistency checks (Cohen's κ [30] and Fleiss' κ [31]) to ensure agreement among them. Records written in any of the languages spoken by members of the established review team (English, German, Spanish, French, Italian, Portuguese, Danish, Norwegian, Swedish, Hebrew, Dutch, Catalan or Russian) were eligible. During abstract screening, records passed to the next screening stage if at least one reviewer deemed them eligible. Records were only considered eligible if they reported original data on gait characteristics for at least 10 participants. Case studies, case series and reviews were excluded.

During full-text screening, records were assessed independently by one reviewer and inclusions were checked for accuracy by a second. Disagreements were resolved through discussion or, when necessary, a third member of the review team. The entire process was conducted on DistillerSR, a specialised systematic review software [22, 29]. Records were only considered eligible if they included people with COPD as diagnosed by spirometry ("population") and healthy controls ("comparison"), and reported on gait characteristics during supervised walking tests ("outcome") in a case–control study ("study design"). The following gait characteristics, measured through any technology, were considered: gait speed ($cm \cdot s^{-1}$), step and stride length (cm; one stride is two consecutive steps), cadence (steps·min^{-1}), step and stride duration (s), swing duration (s), stance duration (s), single support duration (s), double support duration (s), step width (cm) and variability measures (standard deviation and coefficient of variation) of step and stride length, step and stride duration, swing duration, stance duration, single support duration, double support duration and step width.

Data extraction and critical appraisal

Data extraction forms were iteratively developed by two reviewers (J. Buekers and L. Delgado-Ortiz) according to reporting guidelines, established best practices and expert feedback. Each iteration of the form was piloted using between two and ten studies. One reviewer (J. Buekers) extracted all relevant information from included studies, and the second reviewer (L. Delgado-Ortiz) checked extractions for accuracy. The following data were extracted: year of publication, country, sample size for people with COPD and healthy controls, participants' characteristics (age, height and lung function), type of walking test, gait speed protocol (walking at a usual speed, fast speed or 6-min walk test (6MWT) speed, *i.e.* the submaximal speed maintained during a 6MWT), measurement method, examined gait characteristics, and measure of association and corresponding p-value for differences in gait characteristics between people with COPD and healthy controls. Individual authors were contacted and provided further information when values of gait characteristics could not be directly extracted from study reports.

Two reviewers (J. Buekers and L. Delgado-Ortiz) piloted different critical appraisal tools for case–control studies, and after discussion with a third reviewer (J. Garcia-Aymerich) agreed that a modified version of the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for case–control studies (supplementary material: appendix 1) [32, 33] best matched the objective of the current systematic review. The tool critically appraises three domains: participant selection, comparability and gait characteristics. Critical appraisal of all eligible studies was independently performed by two reviewers (J. Buekers and L. Delgado-Ortiz) and disagreements were resolved by discussion to reach consensus.

Data analysis

To allow for meta-analyses across included studies and following Cochrane's guidelines [25], stride length values were converted into step length values for one study (dividing by two) [34], cadence values expressed in strides·min^{-1} were converted into steps·min^{-1} in one study (multiplying by two) [35], female and male subgroups were combined in one study [36], subgroups of patients requiring and not requiring supplemental oxygen were combined in one study [37], and central tendency measures were converted into mean±SD based on the conversion equations of WAN *et al.* [25, 38] in one study [39].

Studies were considered eligible for meta-analysis if they 1) had a low risk of bias according to the modified JBI tool, 2) reported on sample sizes and 3) reported mean and SD of both groups (or mean difference (MD) and standard error (SE) between the groups) for the considered gait characteristic. Results of the random effects meta-analyses are presented as MD (95% CI). Meta-analyses were separately performed for different gait speed protocols (*i.e.* usual, fast and 6MWT speed), and were restricted to the most prominent gait characteristics by only meta-analysing gait characteristics for which a minimum of three studies could be included. Forest plots were generated to visualise the comparison of gait characteristics between people with COPD and healthy controls. Publication bias was assessed using funnel plots [25]. Statistical heterogeneity was tested using the I^2 statistic and the prediction interval (the latter only for meta-analyses that included at least ten studies [25, 40]). Meta-regression was performed for meta-analyses that included at least ten studies and had considerable heterogeneity (I^2>75%) [25], in order to understand how region (*i.e.* Europe, North America, Asia and South America; no studies were performed in other regions), measurement method (manually measuring time *versus* instrumented), distance walked during the walking test, or differences in mean age, height or forced expiratory volume in 1 s (FEV_1) contributed to the heterogeneity. A first sensitivity analysis excluded studies that did not control for a difference in age and/or height between people with COPD and healthy controls. A second sensitivity analysis excluded studies that examined gait characteristics during treadmill walking. Statistical analyses were performed using the R 4.1.2 programming language (metafor package) (www.r-project.org).

Certainty of evidence

The certainty of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, which contains four levels: very low, low, moderate or high certainty of evidence. The starting point for observational studies is at low certainty. The certainty level is decreased when there is serious risk of bias, inconsistency, indirectness, imprecision or publication bias, or increased when there is a large effect, a dose–response gradient or when residual confounding is more likely to reduce, rather than increase, a demonstrated effect [25, 41].

Results

Description of included studies

After removal of duplicates, 21 085 records (19 672 in the original search, 1413 in the updated search) were identified and screened on abstract (figure 1). Of those, 2977 (2903 in the original search, 82 in the updated search) were screened on full-text. Ultimately, 25 studies (n=1015 people with COPD and n=2229 healthy controls) were included in the current systematic review (figure 1), with nine originating from Europe, eight from North America, five from Asia and three from South America (table 1). Most studies were relatively small (median sample size (P25–P75): n=33 (20–42) participants with COPD, n=23 (20–40) healthy controls) and included people with COPD with FEV_1 values around 50% predicted (median (P25–P75) of the reported average FEV_1 values: 50 (47–54) % predicted) and with a median (P25–P75) reported average age of 69 (64–71) years.

16 studies (64%) measured gait characteristics during a 4–15 m-long walkway, four (16%) during a 6MWT, three (12%) during treadmill walking (for 3, 5 or 6 min), one (4%) during a 3-step gait protocol and one (4%) during a Timed Up and Go test (table 1). 15 studies (60%) used an instrumented approach (force plates and/or optical instrumentation, accelerometer, Locomètre device or treadmill walking speed) to calculate gait characteristics, and ten studies (40%) manually measured the time to complete the walking test to determine gait speed. In 17 studies (68%), participants walked at their usual speed, in six (24%) at a fast speed, and in four (16%) at their 6MWT speed. Of the four studies based on a 6MWT, only Liu *et al.* [34]

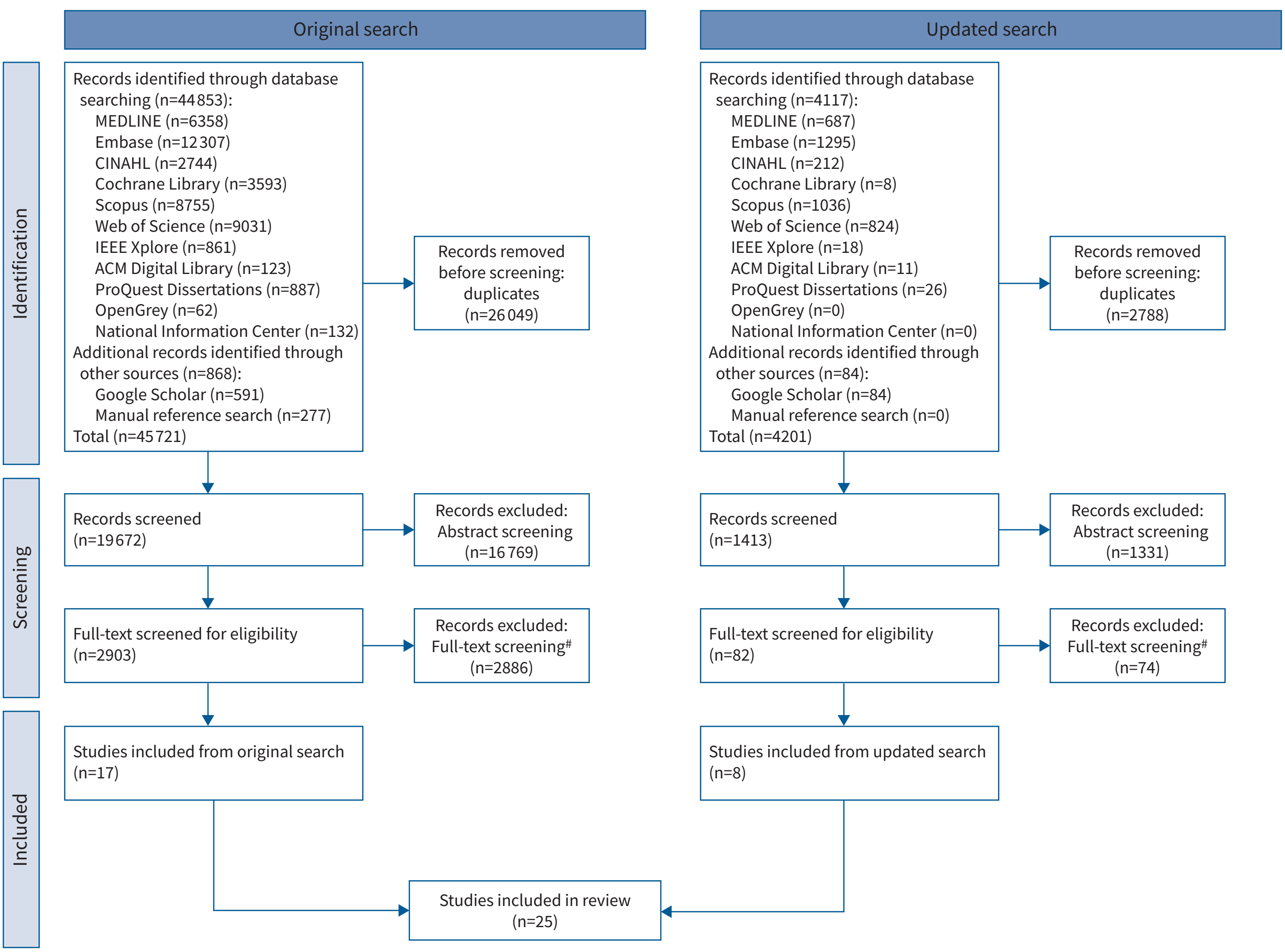

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram showing how records were screened for eligibility in the scoping review by Polhemus *et al.* [22], and how records were further screened for inclusion in the current systematic review. #: details on the reasons for excluding records are provided in supplementary tables S2 and S3.

https://doi.org/10.1183/16000617.0253-2023

TABLE 1 Characteristics of the included studies

Study	Country	Participants, n		Age (years), mean±SD		Height (cm), mean±SD		FEV$_1$ (% pred), mean±SD		Type of walking test	Gait speed protocol	Measurement method	Gait characteristics	p-value	Measure of association
		COPD	CON	COPD	CON	COPD	CON	COPD	CON						
Jirange 2021 [39]	India	42	45	61.9±4.6	60.5±6.2	–	–	37.3±8.0	–	3-step gait protocol	Usual speed	Force plate	Step/stride length Step/stride duration Swing duration	0.23 0.6 0.04	Mann–Whitney U test
Sepúlveda-Loyola 2021 [42]	Brazil	39	35	69±6	69±7	160±10	160±9	49±13[#]	98±16	4 m walkway	Usual speed	Measure time	Gait speed	>0.05	t-test
Fallahtafti 2020 [43]	USA	17	23	64.3±7.6	59.9±6.6	167±11[#]	163±7	–	–	6 min treadmill	Usual speed	Optical	Step length Step duration Step width	0.49 <0.001 0.007	t-test
Hassan 2020 [44]	Canada	15	20	70.7±8.0	69.1±6.9	169±10	164±9	52.3±20.3[#]	92.6±11.7	5 m walkway	Usual speed Fast speed	Force plate	Gait speed	0.005 0.001	t-test
Park 2020 [45]	USA	34	22	69.0±1.4	70.4±1.7	165±1	167±1	44.2±3.1[#]	96.9±3.0	4 m walkway	Usual speed Fast speed	Measure time	Gait speed	<0.001 <0.001	t-test
Iwakura 2019 [46]	Japan	34	16	71±8	72±6	166±5	164±7	57±28[#]	102±19	10 m walkway	Usual speed	Measure time and tri-axial accelerometer	Gait speed Step length Cadence Step duration SD	<0.001 <0.001 <0.001 0.001	t-test
Navarro-Cruz 2019 [47]	Spain	26	10	78.8±7.1	76.6±4.1	–	–	53.4±35.6	–	4 m walkway	Usual speed	Measure time	Gait speed	0.02	t-test
Pineda-Zuluaga 2019 [36]	Colombia	35	36	67.9±12.6	68.6±10.0	158±10	157±10	–	–	4 m walkway	Usual speed	Measure time	Gait speed	>0.05	t-test
Franssen 2018 [48]	The Netherlands	68	742	60.9±2.8	60.4±2.9	–	–	67.6 (60.4–80.4)[#,¶]	99.5 (90.4–109.6)[¶]	6 m walkway including 180° turn	Fast speed	Measure time	Gait speed	0.03	Mann–Whitney U test
Heraud 2018 [49]	France	25	20	64.6±7.4	69.3±6.9	165±9	165±10	47.9±15.5[#]	111.6±24.1	15 m walkway	Usual speed	Locomètre device	Gait speed Stride duration COV	0.22 0.33	Two-way ANOVA
Sanseverino 2018 [50]	Brazil	11	11	65±3	65±3	–	–	45±5[#]	108±7	5 min on treadmill	Usual speed	Treadmill speed	Gait speed	<0.001	t-test

Continued

TABLE 1 Continued

Study	Country	Participants, n		Age (years), mean±SD		Height (cm), mean±SD		FEV_1 (% pred), mean±SD		Type of walking test	Gait speed protocol	Measurement method	Gait characteristics	p-value	Measure of association
		COPD	CON	COPD	CON	COPD	CON	COPD	CON						
Liu 2017 [34]	The Netherlands	80	38	62.3±7.2	62.1±6.3	170±9	172±8	55.8±19.4#	118.6±16.5	Treadmill 6MWT	6MWT speed	Optical and force plate	Step/stride length	<0.001	t-test
													Cadence	<0.001	
													Step/stride duration	<0.001	
													Stance duration	<0.001	
													Swing duration	<0.001	
													Double support duration	<0.001	
													Step width	0.056	
													Step/stride length COV	<0.001	
													Step/stride duration COV	0.10	
													Stance duration COV	0.003	
													Swing duration COV	0.58	
													Double support duration COV	0.001	
													Step width COV	0.01	
Morlino 2017 [51]	Italy	40	28	70.7±7.1	69.5±6.7	–	–	50.2±21.1#	116.0±14.1	4 m walkway	Usual speed	Force plate	Gait speed	<0.001	t-test
													Step length	<0.05	
													Cadence	<0.05	
													Single support duration	0.07	
													Double support duration	<0.05	
													Step width	0.39	
													Step length COV	<0.001	
													Step duration COV	>0.05	
													Step width COV	>0.05	
Yentes 2017 [52]	USA	20	20	63.6±9.7	62.5±8.2	176±11#	168±10	54.3±19.2#	100.3±16.2	3 min treadmill	Usual speed	Optical	Step length	>0.05	Regression model
													Step duration	0.02	
													Step width	>0.05	
													Step length SD	>0.05	
													Step duration SD	0.03	
													Step width SD	0.007	
													Step length COV	>0.05	
													Step duration COV	>0.05	
													Step width COV	>0.05	

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https://doi.org/10.1183/16000617.0253-2023

TABLE 1 Continued

Study	Country	Participants, n		Age (years), mean±SD		Height (cm), mean±SD		FEV_1 (% pred), mean±SD		Type of walking test	Gait speed protocol	Measurement method	Gait characteristics	p-value	Measure of association
		COPD	CON	COPD	CON	COPD	CON	COPD	CON						
Iwakura 2016 [53]	Japan	22	13	71.6±6.9	71.5±5.6	165±5	165±6	52.8±20.6#	94.7±26.7	4 m walkway	Usual speed	Measure time	Gait speed	<0.001	t-test
Bairapareddy 2016 [54]	India	42	45	61.9±4.6	60.5±6.2	–	–	–	–	TUG	Fast speed	Force plate	Swing duration	<0.01	–
Lahousse 2015 [55]#	The Netherlands	196	898	75.5±5.5#	74.2±5.2	171±9#	167±9	80.8±18.7#	110.9±16.3	5.79 m walkway	Usual speed	Force plate	Gait speed Cadence	>0.05 <0.05	Regression model
Nantsupawat 2015 [56]	USA	14	–	69.7±6	–	–	–	36.9±15.6	–	6–10 m walkway	Usual speed	Optical	Gait speed Step length Cadence Double support duration	<0.05 >0.05 >0.05 <0.05	95% confidence interval
Yentes 2015 [57]	USA	17	21	63.8±8.6	65.3±7.7	172±12	166±16	50.2±21.0#	101.7±11.0	10 m walkway	Usual speed	Optical and force plate	Gait speed Step/stride length Step/stride duration Stance duration Double support duration Step width	>0.05 >0.05 >0.05 >0.05 >0.05 >0.05	Regression model
Rutkowski 2014 [58]	Poland	33	48	65.7±10.4#	58.7±11.8	–	–	–	–	4 m mat during 6MWT	6MWT speed	Force plate	Stride length Stride duration	<0.05 <0.05	Repeated measures ANOVA
Annegarn 2012 [35]	The Netherlands	79	24	64.3±8.9	63.7±5.9	167±9#	173±7	53.5±18.7#	124.9±21.0	6MWT	6MWT speed	Tri-axial accelerometer	Cadence	<0.05	ANOVA
Horie 2011 [59]	Japan	60	60	76.8±6.8	76.3±1.8	151±8	152±8	–	–	11 m walkway	Fast speed	Measure time	Gait speed	0.005	t-test
Roig 2011 [60]	Canada	21	21	71.2±8.1	67.4±8.6	160±10	170±10	47.2±12.9#	98.1±11.9	5 m walkway	Usual speed	Measure time	Gait speed	<0.001	Regression model
Annegarn 2010 [61]	The Netherlands	15	12	63.7±3.9#	33.3±2.3	–	–	48.9±15.6	–	6MWT	6MWT speed	Tri-axial accelerometer	Stride duration	<0.01	–
Butcher 2004 [37]	Canada	30	21	70.6±2.7	68.1±1.9	164±3	163±2	37.8±8.9#	105.2±3.15	10 m walkway	Fast speed	Measure time	Gait speed	0.002	ANCOVA

FEV_1: forced expiratory volume in 1 s; COPD: patients with chronic obstructive pulmonary disease; CON: healthy controls; COV: coefficient of variation; 6MWT: 6-min walk test; TUG: Timed Up and Go. #: significantly different from healthy controls (p<0.05); ¶: data represented as median (P25–P75).

mentioned that instructions were standardised according to the European Respiratory Society/American Thoracic Society guidelines [62]; the other three studies did not report on any guidelines.

Gait speed was assessed in 17 studies (68%), step length in nine (36%), step duration in seven (28%), cadence in six (24%), step width in five (20%), and the remaining gait characteristics in less than five studies (table 1 and supplementary figure S1).

We considered five studies at a high risk of bias and excluded them from the meta-analyses (supplementary table S1) because of an unfavourable appraisal for selection and comparability criteria (two studies), because insufficient information was provided in conference abstracts (two studies) or because values for healthy controls were extracted from another study (one study).

Gait differences between people with COPD and healthy controls: meta-analyses

A minimum of three studies eligible for meta-analyses were identified for gait speed (usual speed and fast speed), step length (usual speed), step duration (usual speed), cadence (usual speed) and step width (usual speed) (supplementary figure S1).

Meta-analyses on gait speed were performed separately depending on the gait speed protocol. At a usual speed, a meta-analysis of 13 studies (n=419 people with COPD and n=1151 healthy controls) indicated that people with COPD walked more slowly than healthy controls (MD −19 $cm \cdot s^{-1}$, 95% CI −28 to −11 $cm \cdot s^{-1}$; p<0.001) and there was evidence of considerable heterogeneity (I^2=88%; 95% prediction interval −48 to 10 $cm \cdot s^{-1}$) (figure 2). The weighted mean usual gait speed was 100 $cm \cdot s^{-1}$ for people with COPD and 119 $cm \cdot s^{-1}$ for healthy controls. At a fast speed, people with COPD also walked more slowly than healthy controls (five studies; n=207 people with COPD and n=865 healthy controls; MD −30 $cm \cdot s^{-1}$, 95% CI −47 to −13 $cm \cdot s^{-1}$; p<0.001), with evidence of considerable heterogeneity (I^2=91%). The weighted mean fast gait speed was 113 $cm \cdot s^{-1}$ for people with COPD and 138 $cm \cdot s^{-1}$ for healthy controls.

Step length, step duration, cadence and step width at their usual speed did not differ significantly between people with COPD and healthy controls (figure 3), although point estimates indicated a smaller step length (six studies; n=170 people with COPD and n=153 healthy controls; MD −4 cm, 95% CI −9 to 1 cm; p=0.11), longer step duration (four studies; n=96 people with COPD and n=109 healthy controls; MD=0.05 s, 95% CI −0.01 to 0.12 s; p=0.10) and lower cadence (three studies; n=174 people with COPD and n=942 healthy controls; MD −10 $steps \cdot min^{-1}$, 95% CI −21 to 1 $steps \cdot min^{-1}$; p=0.06) in people with COPD, all with evidence of considerable heterogeneity (I^2=81% for step length, I^2=82% for step duration and I^2=95% for cadence). Step width was similar in both groups (four studies; n=94 people with COPD and n=92 healthy controls; MD 0 cm, 95% CI −1 to 1 cm; p=0.48), without evidence of heterogeneity (I^2=23%).

Funnel plots did not reveal publication bias for any of the gait characteristics (supplementary figures S2–S7). Only gait speed at a usual speed fulfilled the *a priori* determined criteria for performing meta-regression (*i.e.* for meta-analyses that included at least ten studies and had considerable statistical heterogeneity). No clear associations were found between mean differences in usual gait speed and length of the walking test (β=0.0 $cm \cdot s^{-1}$ per metre, 95% CI −0.2 to 0.1 $cm \cdot s^{-1}$ per metre; p=0.60) or measurement method (β=12.5 $cm \cdot s^{-1}$, 95% CI −3.8 to 28.7 $cm \cdot s^{-1}$; p=0.13; manually measuring time as reference group), or mean differences in age (β=0.3 $cm \cdot s^{-1}$ per year, 95% CI −3.8 to 4.3 $cm \cdot s^{-1}$ per year; p=0.90), height (β= −1.4 $cm \cdot s^{-1}$ per cm, 95% CI −3.6 to 0.7 $cm \cdot s^{-1}$ per cm; p=0.20), or FEV_1 (β=0.1 $cm \cdot s^{-1}$ per % predicted, 95% CI −0.4 to 0.2 $cm \cdot s^{-1}$ per % predicted; p=0.61) between COPD and healthy controls. Studies originating from Asia (reference group; n=2; both studies performed by Iwakura *et al.* [46, 53]) reported a larger decrease in usual gait speed in people with COPD compared to studies originating from Europe (β=34.2 $cm \cdot s^{-1}$, 95% CI 11.9 to 56.4 $cm \cdot s^{-1}$; p=0.003), North America (β=27.0 $cm \cdot s^{-1}$, 95% CI 5.1 to 49.0 $cm \cdot s^{-1}$; p=0.02) and South America (β=33.6 $cm \cdot s^{-1}$, 95% CI 10.7 to 56.5 $cm \cdot s^{-1}$; p=0.004).

Both sensitivity analyses (excluding three studies that did not control for age and/or height, despite a significant difference between people with COPD and healthy controls; or excluding three studies that examined gait characteristics during treadmill walking), provided similar results for gait speed and step length (supplementary figures S8–S11), while meta-analyses of step duration and step width could not be conducted owing to an insufficient number of studies.

Certainty of evidence

All gait characteristics started at a low certainty of evidence rating (table 2). Usual gait speed, fast gait speed, step length, step duration and cadence were downgraded one level due to the high statistical

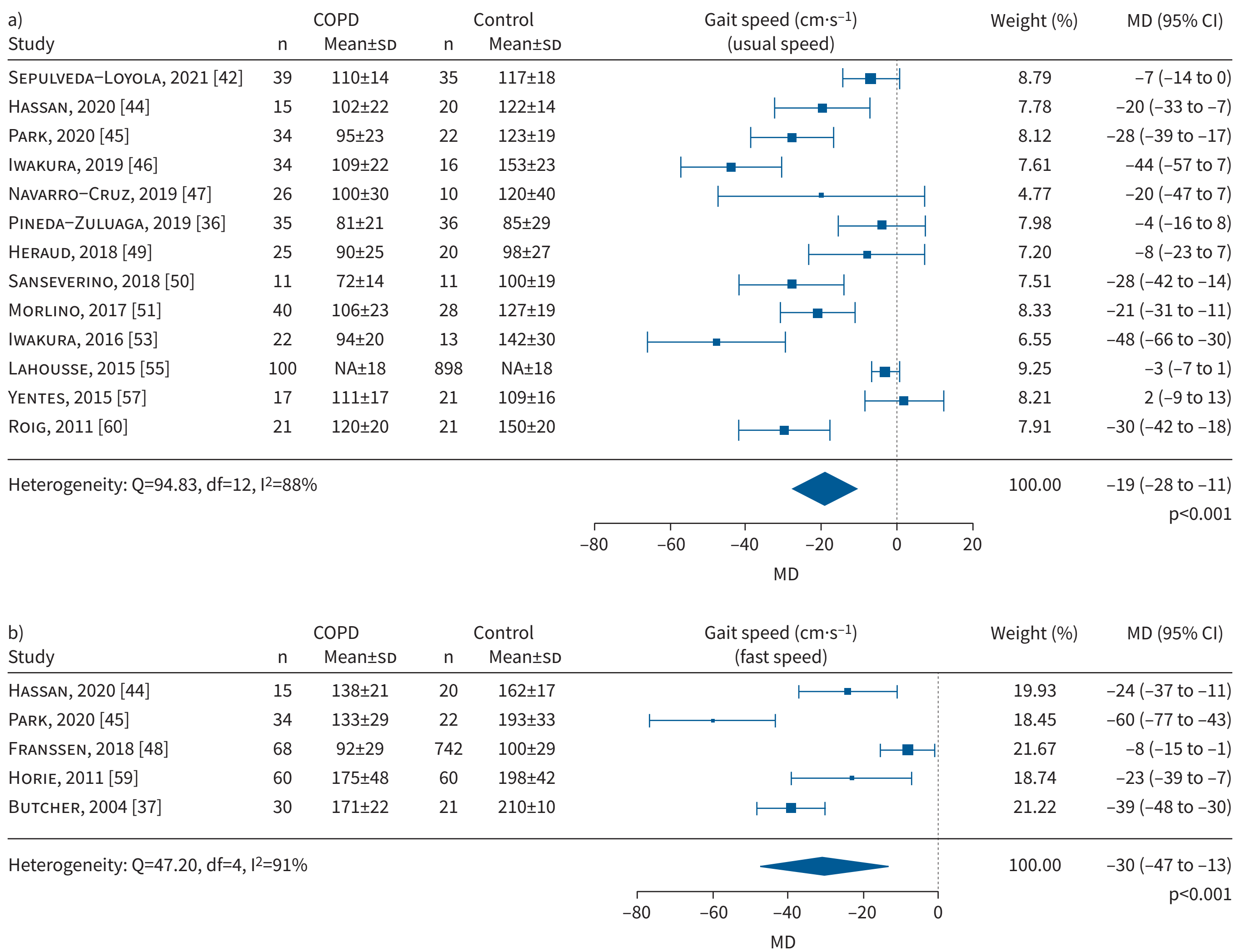

FIGURE 2 Differences in gait speed ($cm \cdot s^{-1}$) at a) usual speed and b) fast speed between people with COPD and healthy controls. MD: mean difference.

heterogeneity between studies (serious inconsistency; figures 2 and 3). Step length, step duration and cadence were downgraded another level due to imprecision of results. Usual gait speed and fast gait speed were upgraded one level because of the large effect size (figure 2). Consequently, usual gait speed, fast gait speed and step width had a low certainty of evidence, while step length, step duration and cadence had a very low certainty of evidence (table 2).

Discussion

This systematic review showed that people with COPD walk more slowly than healthy controls at their usual speed and at a fast speed. The evidence around other gait characteristics, such as alterations in step length, step duration and cadence at a usual speed, is inconclusive. A relatively small number of studies (except for gait speed) were identified, with relatively small sample sizes and considerable heterogeneity between them.

There was low-quality evidence that people with COPD walk more slowly than healthy controls, at both their usual speed ($-19\ cm \cdot s^{-1}$) and at a fast speed ($-30\ cm \cdot s^{-1}$). The considerable statistical heterogeneity that was observed for both speeds (I^2=88% for usual speed; I^2=91% for fast speed) and the wide prediction interval for usual gait speed (95% prediction interval of −48 to $10\ cm \cdot s^{-1}$) indicate that the exact magnitude of the gait speed reduction in COPD is uncertain, and that it will not be observed in all studies. In some studies, see for example the study of Yentes *et al.* [57], patients with COPD might even walk faster than healthy controls. This corroborates the general notion that COPD is a very heterogeneous

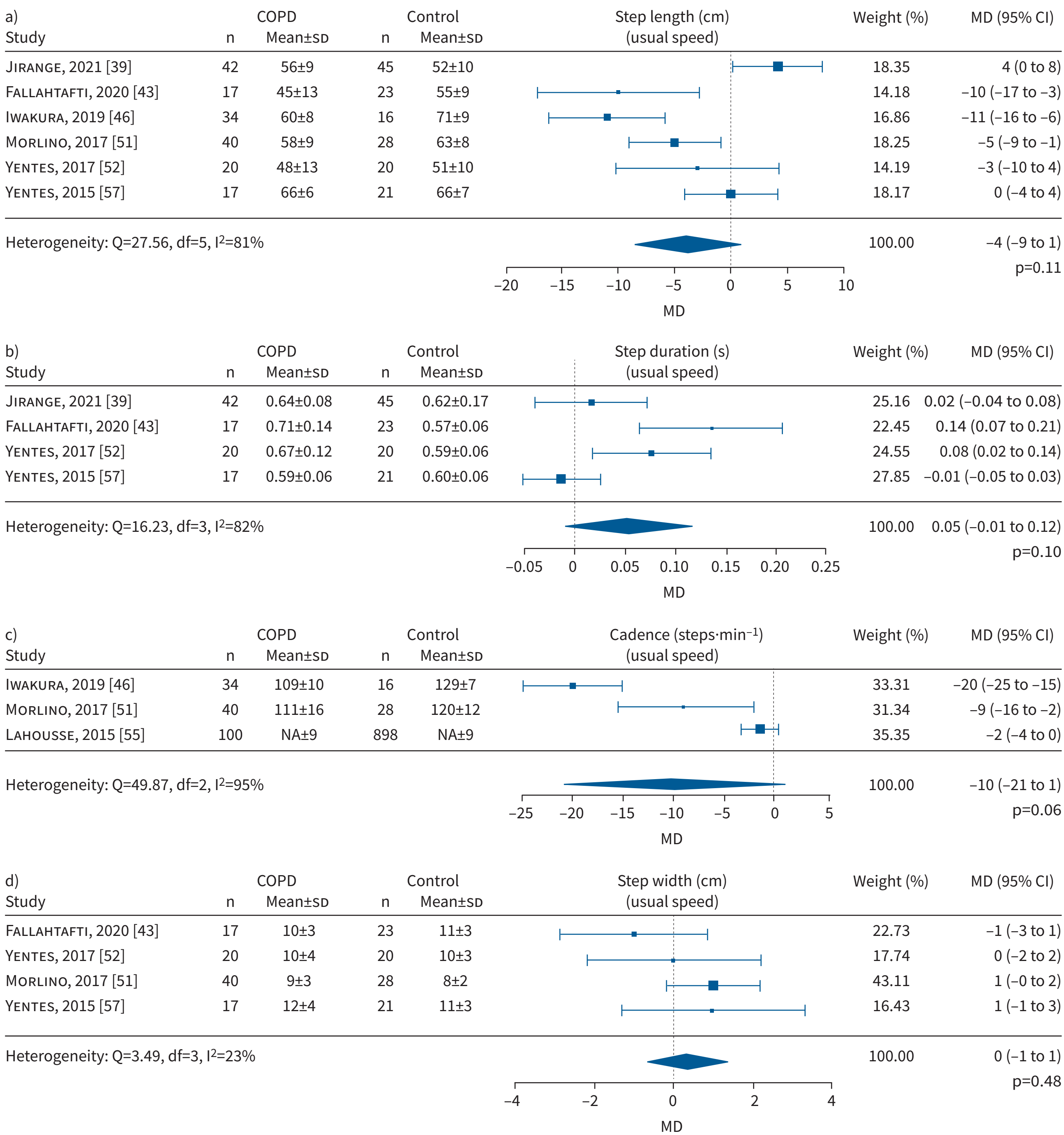

FIGURE 3 Differences in a) step length (cm), b) step duration (s), c) cadence (steps·min^{-1}) and d) step width (cm) at usual speed between people with COPD and healthy controls. For the study of Lahousse *et al.* [55], data could only be obtained for a subgroup of people with COPD (*i.e.* moderate and severe COPD, 100 out of 196 examined people with COPD). MD: mean difference.

disease [1, 63, 64]. Still, the point estimates of −19 cm·s^{-1} and −30 cm·s^{-1} for usual and fast gait speed, respectively, indicate that, generally, people with COPD have a clinically relevant reduction in their gait speed, given that a difference of merely 10 cm·s^{-1} in gait speed (in either cross-sectional analyses or as a change over time) has a relevant impact on people's health. In older people, a gait speed reduction of 10 cm·s^{-1} has been associated with poorer health status, poorer physical functioning, increased and longer

TABLE 2 Grading of Recommendations Assessment, Development and Evaluation (GRADE) certainty of evidence assessment

Outcome	Studies, n	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Certainty
Gait speed (usual speed)	13	Observational	Not serious	Serious (−1)	Not serious	Not serious	Large effect (+1)	Low
Gait speed (fast speed)	5	Observational	Not serious	Serious (−1)	Not serious	Not serious	Large effect (+1)	Low
Step length (usual speed)	6	Observational	Not serious	Serious (−1)	Not serious	Serious (−1)	None	Very low
Step duration (usual speed)	4	Observational	Not serious	Serious (−1)	Not serious	Serious (−1)	None	Very low
Cadence (usual speed)	3	Observational	Not serious	Serious (−1)	Not serious	Serious (−1)	None	Very low
Step width (usual speed)	4	Observational	Not serious	Not serious	Not serious	Not serious	None	Low

hospital stays, higher costs of care, increased mortality and increased fall risk [17, 18, 65–68]. In COPD, a 10 $cm \cdot s^{-1}$ reduction in gait speed increased the risk for hospital readmission (OR 1.43, 95% CI 1.13 to 1.80, per 10 $cm \cdot s^{-1}$ reduction) [69]. Yet, further research is needed to assess the effect of the identified gait speed reduction on other relevant COPD outcomes, including falls [5, 70–73]. Interestingly, the identified mean usual gait speed for people with COPD corresponds exactly with the gait speed threshold that is considered a marker of increased fall risk (*i.e.* 100 $cm \cdot s^{-1}$) [74, 75].

The evidence on alterations in spatial (step length) and temporal (step duration and cadence) components of gait was considered to be of very low quality, and our findings remain inconclusive. Although there was a trend towards a smaller step length, longer step duration and lower cadence, the results did not reach statistical significance. This was most likely due to the small number of included studies and the considerable statistical heterogeneity between them. Hence, it is still unclear whether the reduced gait speed in people with COPD originates from alterations in spatial gait characteristics (*e.g.* a reduction in step length stemming from limited quadriceps strength [46, 76]) and/or temporal gait characteristics (*e.g.* alterations in step duration and cadence due to limited exercise capacity [55, 77]). Of note, step width seemed to be unaltered in people with COPD.

The collected evidence was limited for most gait characteristics (except for gait speed). Moreover, the low number of relevant studies and the differences in gait speed protocols prevented meta-analysis of the results for many gait characteristics. When meta-analyses were possible, results showed considerable heterogeneity (I^2>75% for gait speed, step length, step duration and cadence). Consequently, current meta-analyses could not confirm the conclusions from Zago *et al.* [23], which suggested, based on a narrative summary of seven studies, that people with COPD have a reduced step length and cadence, and altered gait variability. Of note, evidence on the difference in gait characteristics between people with COPD and healthy controls is accumulating quickly (11 of the 25 included studies were published between 2018 and 2021), which warrants an update of this systematic review in the next few years.

Post hoc meta-regressions for usual gait speed suggested that variable differences in mean age, height or FEV_1 between included people with COPD and healthy controls did not contribute to the observed statistical heterogeneity. Furthermore, meta-regression showed that differences in the length of the walking tests or measurement method did not seem to contribute to the observed heterogeneity either. The statistically significant effect of region on the observed heterogeneity (*i.e.* larger differences between COPD and healthy controls in Asia) is largely the result of the two Asian studies carried out by the same group of authors. Hence, other (under-reported) clinical differences (*e.g.* different comorbidities), methodological differences (*e.g.* differences in the starting procedure, such as static *versus* dynamic start, or walking surface [78]) and small sample sizes are most likely behind the observed heterogeneity.

Our findings have implications for COPD research and clinical practice. Future research should identify and better understand the mechanisms underlying the reduced gait speed in COPD. In order to reduce methodological diversity, we recommend systematically using the 4 m gait speed test at usual speed and with a static start to assess gait characteristics in people with COPD, because this was the most commonly used walking test in this systematic review (table 1), and because it can be implemented as part of the Short Physical Performance Battery (SPPB) in diverse clinical settings [79]. A generally accepted protocol is available from the National Institute on Aging study [80]. Alternatively, unsupervised, real-world measurements of gait might have a higher ecological validity than supervised walking tests. However, real-world measurements of gait are still in their infancy [22, 24]. In clinical practice, supervised walking tests of gait can easily be added as part of routine patient care (*e.g.* as part of the SPPB) for an improved risk assessment of falls, hospitalisations and mortality, or to assess how gait is affected by interventions such as pulmonary rehabilitation.

The main strengths of the current study were the extensive literature search that was developed as a collaboration between clinical experts, experts in biomechanics and an experienced research librarian and the methodological rigour in accordance with Cochrane guidelines [25]. Applying this methodological rigour in a multidisciplinary team extended the time required to finalise this systematic review, and therefore the most recently published studies in this fast-moving area could not yet be included. The main limitations of the study were that meta-analyses could not be performed in some cases, and substantial heterogeneity resulted in (very) low-quality evidence for others. In addition, meta-analyses could not be stratified for clinically relevant subgroups (*e.g.* stratification based on disease severity) owing to the scarcity of reporting on subgroup results. Nevertheless, these limitations identified areas for future research, as discussed above.

In conclusion, low-quality evidence shows that people with COPD walk more slowly than healthy controls at their usual speed and at a fast speed, which could contribute to their increased fall risk. The evidence for alterations in spatial (step length) and temporal (step duration and cadence) components of gait was inconclusive. Gait impairment appears to be an important but understudied area in COPD.

Points for clinical practice

- We recommend systematically using the 4 m gait speed test at usual speed and with a static start to assess gait characteristics in people with COPD, in order to reduce methodological diversity. This can be implemented as part of the Short Physical Performance Battery (SPPB) in diverse clinical settings.
- Supervised walking tests of gait can easily be added as part of routine patient care (*e.g.* as part of the SPPB) for an improved risk assessment of falls, hospitalisations and mortality, or to assess how gait is affected by interventions such as pulmonary rehabilitation.

Questions for future research

- Future research should aim to identify and better understand the mechanisms underlying the reduced gait speed in COPD.
- Future studies on gait in COPD should increase the number and range of included people with COPD, and add stratified analyses based on clinically relevant subgroups (*e.g.* stratification based on disease severity).

Provenance: Submitted article, peer reviewed.

Conflict of interest: A. Polhemus is a paid employee of Merck & Co, Inc. and IQVIA AG. S.C. Buttery reports educational speaker fees for Pulmonx. J. Garcia-Aymerich reports speaker honoraria from Chiesi and a grant from AstraZeneca paid to her institution for a COVID-19-related project and is also a paid advisory board member for AstraZeneca. All other authors report no conflicts of interest.

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). 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 IMI, the European Union, the EFPIA or any associated partners. L. Delgado-Ortiz receives funding from the grant "Contratos Predoctorales de Formación en Investigación en Salud (PFIS) 2021 of the AES with Exp. FI21/00113" from ISCIII, and the European Social Fund Plus (ESF+). Funding information for this article has been deposited with the Crossref Funder Registry.

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