# Early View

Original article

# Accompanied *versus* unaccompanied walking for continuous oxygen saturation measurement during 6-min walk test in COPD: a randomised cross-over study

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Accompanied versus unaccompanied walking for continuous oxygen saturation measurement during 6-minute walk test in COPD: a randomised cross-over study

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### **Take Home Message:**

- Accompanied walking during a 6MWT *vs.* unaccompanied walking results in lower walked distance (mean difference -9.1 m, [95%CI -13.9 to -4.3]).
- No differences in nadir SpO<sub>2</sub> and oximetry artefacts were noted between accompanied and unaccompanied walking.

# **Abstract**

**Study question:** Is there is a difference in the 6-Minute Walk Test (6MWT) distance when the assessor accompanies the patient to continuously measure oxygen saturation (SpO<sub>2</sub>) compared to the patient walking unaccompanied?

**Methods:** We conducted a prospective randomised cross-over study to evaluate the impact of the assessor walking with the patient during 6MWT (6MWT<sub>with</sub>) versus patient walking alone (6MWT<sub>without</sub>). At the end of a pulmonary rehabilitation programme, each patient performed two 6MWTs in random order and separated by 30 minutes rest.

**Results:** 49 COPD patients (GOLD II-IV) were included. In a regression model adjusting for period and subject, accompanying the patient resulted in a lower walking distance (mean difference -9.1 m, [95%CI, -13.9 to -4.3], p=0.0004). Notably, six patients walked more than 30m further (minimal important difference, MID) in one of the two conditions (6MWT<sub>with</sub>: n=1, 6MWT<sub>without</sub>: n=5). There were no between-sequence-group differences in heart rate, dyspnoea and leg-fatigue, and SpO<sub>2</sub>. The median (interquartile range) number and duration of SpO<sub>2</sub> signal artefacts were high but not different between the experimental conditions (6MWT<sub>with</sub>: 17 [4, 24], 34s [7, 113], 6MWT<sub>without</sub>: 11 [3, 26], 24s [4, 62]).

Answer to the question: On a study population level, we observed a statistically significant difference in 6MWT distance between the two experimental conditions, however, the magnitude of difference is small and may not be considered clinically relevant. Nevertheless, in a clinical setting, unaccompanied walking resulted in a substantially higher walking distance pointing towards strictly standardised testing methodology, in particular in pre-post study designs.

# Introduction

The six-minute walk test (6MWT) is a field walking test to assess functional exercise capacity [1]. It is a widely used functional capacity test to evaluate a person's physical fitness, to assess effects of interventions such as rehabilitation programmes and for prognostic purposes [2]. Further, the test is commonly used to measure the lowest oxygen saturation (SpO<sub>2</sub>) during self-paced exercise [3]. Exercise-induced hypoxaemia is frequently observed in patients with pulmonary disorders [4,5] and the lowest SpO<sub>2</sub> does not necessarily occur at the end of the test [6,7]. Moreover, the extent of oxygen desaturation is important for determining the indication for supplemental oxygen during daily life activities, exercise therapy [4], and to gain indicators for the prognosis in chronic obstructive pulmonary disease (COPD) [8].

In 2002, the American Thoracic Society published a technical standard on the 6MWT suggesting that the assessor must not walk with the patient [9]. In an update published in 2014 by the European Respiratory Society and the American Thoracic Society, the document highlights the importance of the continuous measurement of SpO<sub>2</sub> during the 6MWT in pulmonary disorders [1]. Therefore, it has been recommended that the assessor accompanies the patient during the 6MWT to continuously monitor SpO<sub>2</sub> [i.e. to be able to capture the lowest (nadir) value during the test] [1].

Precise standardisation of testing methodology is of critical importance when conducting a 6MWT. It has been shown that small changes in the testing methodology (e.g., change in track length, track layout, supplemental oxygen, or verbal instructions) and learning experience due to repeated tests affect 6MWT distance [3,10–13]. No study has evaluated the impact of the assessor walking behind the patient versus standing aside on 6MWT distance, the primary outcome measure in a 6MWT test, in people with COPD.

This study was designed to assess the impact of the assessor accompanying the patient compared to the patient walking alone (i.e., the unaccompanied) on 6MWT distance and nadir SpO<sub>2</sub>.

### Material and methods

### Study design and study subjects

We conducted a randomised cross-over trial at the Berner Reha Zentrum AG, a specialised rehabilitation clinic located in Bern, Switzerland.

Patients with COPD and Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification II-IV [Forced expiratory volume in one second (FEV<sub>1</sub>) / Forced vital capacity (FVC) < 0.7, FEV<sub>1</sub> < 80% predicted] were included [14]. Precent predicted values and z-scores for FEV<sub>1</sub> and FVC were calculated based on equations by Quanjer et al. 2012 [15]. We excluded patients who were physically unable to perform a 6MWT (e.g., due to unstable cardiac disease) or who were unable to understand the instructions for the 6MWT (e.g. due to cognitive impairment, or insufficient knowledge of the language in which the instructions were given). The study protocol was approved by the Cantonal Ethics Committee Zurich (2019-00827) and the study was registered at clinicaltrials.gov (NCT04033783). Patients gave their written informed consent to participate in the study, after they were given at least 24 hours to decide [16]. The recruitment was performed consecutively between September and December 2019. All data were collected in REDCap, a secure, web-based application designed to support data capture for research studies and was hosted at Clinical Trials Center at University Hospital of Zurich.

### Randomisation and allocation concealment

We used simple randomisation (1:1 ratio) to randomly allocate patients into either one of two sequence groups: first assessment 6MWT with the assessor walking behind the patient (6MWT<sub>with</sub>) and second 6MWT with the patient walking alone (6MWT<sub>without</sub>), or vice versa. The randomisation list was created with R software [17] (coded as 0 = starting with 6MWT<sub>without</sub> or 1 = 6MWT<sub>with</sub>, n=60 to account for potential dropouts) using the R package blockrand [18]. The list was compiled by a biostatistician (SRH) who was not involved in the study recruitment, randomisation, or study-specific assessments. A person, not involved in the study, implemented the randomisation list into the database (REDCap, Research Electronic Data Capture, Vanderbilt, USA) [19] to ensure complete concealment of random allocation.

Randomisation within REDCap was always performed by the same person, after inclusion and exclusion criteria were evaluated.

### **Six-Minute Walk Test**

The 6MWT was performed on a 30m floor according to a recent technical standard [1]. All assessments were performed at the end of the inpatient pulmonary rehabilitation programme (1–7 days before leaving the clinic) and supervised by the same assessor (TFR) throughout the entire study. Patients and assessor were not blinded to the experimental condition. All included patients had already performed at least one and up to three 6MWTs prior to the study assessments, thus accounting for possible learning effects [3].

Prior to the study assessments, each patient had at least one hour of rest before starting the walking tests. After randomisation, each patient conducted two 6MWTs. Between the two tests, there was a resting phase of 30 minutes to allow heart rate and SpO<sub>2</sub> to reach pre-testing values [1]. Before each 6MWT patients received the standardised instruction for the test as described by Holland et al. [1] which has been translated by our research group into German. Additionally, all 6MWTs were monitored with pulse oximetry, using a handheld pulse oximeter (Covidien Nellcor PM10N, Dublin, Ireland). The sensor was attached to the patient's left middle finger and fixated with tape (Figure 1 a).

In one experimental condition, the assessor walked behind the patient during the 6MWT (6MWT<sub>with</sub>), and the pulse oximeter was held by the assessor who walked 1 metre behind and did not "pace" the patient, as recommended [1]. In the other experimental condition, the 6MWT was performed without the assessor walking with the patient (6MWT<sub>without</sub>) at the 15m mark of the 30m test course. In this condition, the pulse oximeter was placed around the trunk of the patient and fixed with a strap (Figures 1b and 1c). Walking aids and/or supplemental oxygen dose, if needed, were identical during both experimental conditions.

After completion of the two 6MWTs, patients filled out a self-administered questionnaire inquiring their subjective perception covering preferences, velocity, and safety during both 6MWTs.

### [INSERT FIGURE 1 HERE]

### **Analysis**

The sample size calculation was performed using a pre-defined difference of 30 metres between the 6MWTs under the two conditions, which is the established minimal important difference (MID) for patients with COPD [3]. We assumed a standard deviation of the change scores of the 6MWT of 73 metres [3], which equals an effect size of 0.41. To achieve a power of 80% to detect a difference of 30 metres with an assumed standard deviation of 73m, 49 patients were required, assuming a two-sided significance level of 0.05. The sample size calculation was performed with G\*Power 3.1.9.2 [20].

For the primary endpoint 6MWT distance (in metres), a linear regression model adjusting for the experimental condition (6MWT<sub>with</sub> *versus* 6MWT<sub>without</sub>, coded as 1, 0), period (1<sup>st</sup> test or 2<sup>nd</sup> test), and subject was performed [21].

Secondary outcomes were patient-reported perception of different aspects such as feeling of safety, self-perceived influence on gait velocity or interfering factors during the two versions of the 6MWT.

Exploratory outcomes were pre- and post-test heart rate, dyspnoea and leg fatigue (0–10 Borg scale), and pulse oximetry data from the two 6MWTs per subject. Pulse oximetry data were used to quantify measurement artefacts and the lowest SpO<sub>2</sub> (nadir value) during the 6MWT. Pulse oximetry data was downloaded as csv data sheet from the pulse oximeter using Nellcor Analytics Tool (version 1.6.0). The lowest SpO<sub>2</sub> values were manually corrected, if needed, to obtain the true SpO<sub>2</sub> nadir without measurement artefacts. Exploratory outcomes were evaluated using the same adjusted linear regression model as for the primary endpoint.

Statistical analyses were performed using IBM SPSS Statistics version 26.0 [22] and R version 3.6.3 [17].

### Results

### **Patients**

51 patients were included in the study. Of those, 22 patients were randomised to the sequence group 6MWT<sub>with</sub> followed by 6MWT<sub>without</sub> and 29 were randomised to the sequence group 6MWT<sub>without</sub> followed by 6MWT<sub>with</sub>, respectively. Two patients of the 6MWT<sub>without</sub> then 6MWT<sub>with</sub> group were excluded from the analysis. One patient reported that he had to walk slower on the second 6MWT due to low back pain. The other patient was excluded due to a screening failure (i.e., lung function data did not adhere to inclusion criteria). Finally, data of 49 patients were analysed [23], see flow chart in Figure 2.

### [INSERT FIGURE 2 HERE]

Baseline characteristics are shown in Table 1. Pre– and post–walking test values for heart rate, SpO<sub>2</sub>, and perceived dyspnoea and leg fatigue are given in Table S1 in the online supplementary material. Overall, 6% (n=3) used a walking aid; 6% (n=3) used supplemental oxygen (ranging from 1 to 10 litres/minute); 37% (n=18) used both a walking aid and supplemental oxygen, and 51% (n=25) used neither a walking aid nor supplemental oxygen during the 6MWTs. The used walking aids and oxygen dose were the same during both experimental conditions.

### [INSERT TABLE 1 HERE]

### **6MWT** distance

Walking behind the patient during the 6MWT (6MWT<sub>with</sub>) resulted in a lower walking distance of -9.1 m [95%CI, -13.9 to -4.3], see Table 2. On the individual level, 5 patients (10%) walked equal to or greater/lesser than 30m further when walking alone (6MWT<sub>without</sub>). In contrast, one patient (2%) walked equal to or greater/lesser than 30m further when the test was accompanied (Figure S2).

### [INSERT TABLE 2 HERE]

# Pulse oximetry: SpO<sub>2</sub> and signal artefacts

There were no significant differences in SpO<sub>2</sub> nadir and pulse oximetry artefacts in absolute numbers and duration between the two experimental conditions, respectively (Table 2). The median (interquartile range) number and duration of SpO<sub>2</sub> signal artefacts were not different between experimental conditions (6MWT<sub>with</sub>: 17 [4, 24], 34s [7, 113], 6MWT<sub>without</sub>: 11 [3, 26], 24s [4, 62]). The nadir SpO<sub>2</sub> during all 6MWTs was in 61–69% of cases lower than the post-test SpO<sub>2</sub> (6MWT<sub>with</sub>: 30/49 cases, 6MWT<sub>without</sub> 34/49 cases). Among a total of 98 walking tests, a difference of ≥3% between SpO<sub>2</sub> post-test and SpO<sub>2</sub> nadir values was found for 7 tests (7%), while a difference of ≤2% was observed in 83 tests (85%).

# **Patient perceptions**

Patients perceptions during the 6MWT<sub>with</sub> are summarised in Table S3. 59% (n=29) of patients did not prefer any of the two 6MWTs, whereas 25% (n=12) preferred the 6MWT<sub>with</sub> and 16% (n=8) preferred the 6MWT<sub>without</sub>.

Patients favouring the 6MWT<sub>with</sub> noted "safety & supervision" (n=4), "less loneliness", "easier walking", "test goes by faster" (n=3), "self-induced reminder on breathing technique" (n=2), and "more motivating to walk together" (n=2) as reasons. On the other hand, patients preferring the 6MWT<sub>without</sub> reported feeling "more free and having no pressure while walking" (n=4), "choosing their own tempo" (n=3) and "being used to walk alone" (n=2) as their preferential reasons.

In addition, two patients who reported to feel "stressed" by the assessor accompanying them mentioned the "cable of the pulse oximeter" (n=1), "proximity of the assessor" (n=1) and "feeling a lower velocity of the assessor" (n=1) as reasons.

# **Discussion**

This randomised cross-over study investigated the impact of the assessor walking behind the patient compared to the patient walking alone on the distance covered during a 6MWT in people with COPD. We observed a lower walking distance in the test condition where the assessor accompanied the patient (6MWT<sub>with</sub>), compared to the condition where the patient was walking alone (6MWT<sub>without</sub>). No differences between study conditions were observed in nadir SpO<sub>2</sub> and the number and duration

of signal artefacts during pulse oximetry measurements. The majority of patients had no preference for either test condition.

### 6MWT distance

In this study, accompanying the patient resulted in a lower 6MWT distance of -9.1m [95% CI -13.9 to -4.3] compared to the patient walking alone. Our data suggests a systematic difference resulting in a lower 6MWT distance when the assessor walks behind the patient. On a population level, the magnitude of the observed difference of -9.1 m is small (about 2-3% of the total walking distance) and below the wellestablished MID for the 6MWT [3]. However, on an individual level, we noticed that about 10% (n=5) of the patients walked ≥30m further, when walking alone. In comparison only one participant walked further when accompanied. Unfortunately, the authors are not aware of any previous studies assessing the intra-day variability in 6MWT distance in people with (cardio)respiratory diseases that would facilitate the interpretation of the magnitude of observed effects. Numerous studies investigated the impact of changes in testing methodology on 6MWT distance such as additional verbal encouragement [24], use of different test instructions [13], walking with walking aids [25–30], supplemental oxygen [31–35] or compressed air [36], carrying oxygen devices [35,37], different track layouts [11,12] and track lengths [10] leading to differences in 6MWT distance ranging from -49.5 to 109 metres. Considering the huge variability arising from changes in testing methodology, our between-test difference seems rather small when interpreted on a population level. However, it is unclear to what extent additive or multiplicative interaction could occur when other additional methodological changes are applied. It is important to note that, in contrast to research settings, the risk for methodological changes might be even greater in clinical settings, for example when different assessors supervise walking tests.

# Pulse oximetry: SpO<sub>2</sub> and signal artefacts

In our study, no differences between the two walking test conditions were observed in nadir SpO<sub>2</sub> and the number and duration of signal artefacts during pulse oximetry measurements.

Oxygen desaturation is common in chronic lung diseases, especially during exercise [4,5], and the extent of desaturation during a 6MWT can provide important information regarding disease severity, prognosis [8] and supplemental oxygen

titration. It must be noted that the lowest SpO<sub>2</sub> does not always occur at the end of the 6MWT [6], one reason (among others) that continuous pulse oximetry monitoring during the 6MWT is recommended [1]. In general, pulse oximetry during 6MWT is a reliable measurement under the condition that a high-quality and stable signal is received [1,3]. Pulse oximeters need the pulse waveform to calculate the correct SpO<sub>2</sub> value [38]. In this study, the assessor held the pulse oximeter in order to clearly see the pulse waveforms. To ensure an adequate pulse wave signal we fixated the sensor with tape around the left middle finger and on the back of the hand. However, despite additional fixation we observed a high number (median 11–17) and long duration median (24–35 s) of signal artefacts in each single walking test.

Nonetheless, there were no differences in SpO<sub>2</sub> signal artefacts between the two experimental conditions suggesting that the assessor carrying the pulse oximeter when walking behind the patient did not introduce measurement bias.

Furthermore, we observed differences between the nadir and post-test SpO<sub>2</sub> values in 64/98 (65%) of the 6MWTs. Overall, the differences in SpO<sub>2</sub> recordings ranged from 0–12%. In 15/98 tests a difference  $\geq$ 3% between post-test and nadir SpO<sub>2</sub> was observed, whereas in 83/98 tests the difference was  $\leq$ 2%. Our results indicate little differences between the post-test SpO<sub>2</sub> and nadir SpO<sub>2</sub>. Our data confirm previous studies [6,7], demonstrating differences between nadir SpO<sub>2</sub> and post-exercise SpO<sub>2</sub> values underlying the need to continuously monitor SpO<sub>2</sub> during the 6MWT [1].

# Patient perceptions

Most patients did not prefer either of the two experimental conditions. If they preferred one condition over the other, it was mostly due to personal preference and experience (e.g. favourably walking alone at home).

Similarly, a majority of the patients did not feel their walking speed was negatively affected or bothered by the assessor walking behind them during the test. Slightly more dispersion was observed in the answers concerning if the patients felt driven. However, this contradicts the lower mean walking distance in the 6MWT<sub>with</sub>. Interestingly, one third of patients felt safer when the assessor walked behind them.

# Strengths & limitations

One strength of our study is the randomised crossover design [23] which minimises the inter-subject variability and confounding. Furthermore, all study assessments were conducted at the end of a pulmonary rehabilitation programme when patients were in stable clinical condition and potential learning effects for the 6MWT were diminished [39]. The latter is supported by the fact that all patients had performed at least one 6MWT and 72% of patients had performed two or three walking tests before inclusion into the study.

Limitations of the study include lack of masking of the outcome assessor which is not possible due to the design. However, all investigations were performed and supervised by the same person and following a standardised testing protocol, thus lessening measurement bias. With respect to pulse oximetry measurements, we acknowledge that finger probes, compared to forehead sensors, are more prone to inaccurate measurements due to motion artifacts or poor perfusion of fingertips. Additionally, pulse oximetry devices with Bluetooth connection already exist to assess SpO<sub>2</sub> remotely. However, Bluetooth devices may not be readily available in every clinical setting and additional time is required to analyse SpO<sub>2</sub> recordings to be able to determine the nadir value. Therefore, the chosen measurement methodology in our study may best reflect the typical clinical setting, in which handheld pulse oximeters are being used.

In conclusion, walking behind the patient during a 6MWT, compared to the patient walking alone, results in lower walking distance in the range of -13.9 to -4.3m. This difference is considered small but supports the need for strict standardisation of testing methodology, especially in repeated measures study designs, clinical settings and between-group comparisons.

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### References

- Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, McCormack MC, Carlin BW, Sciurba FC, Pitta F, Wanger J, MacIntyre N, Kaminsky DA, Culver BH, Revill SM, Hernandes NA, Andrianopoulos V, Camillo CA, Mitchell KE, Lee AL, Hill CJ, Singh SJ. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. Eur Respir J. 2014;44:1428–46.
- 2. Holland AE, Spruit MA, Singh SJ. How to carry out a field walking test in chronic respiratory disease. Breathe. 2015;11:128–39.
- 3. Singh SJ, Puhan MA, Andrianopoulos V, Hernandes NA, Mitchell KE, Hill CJ, Lee AL, Camillo CA, Troosters T, Spruit MA, Carlin BW, Wanger J, Pepin V, Saey D, Pitta F, Kaminsky DA, McCormack MC, MacIntyre N, Culver BH, Sciurba FC, Revill SM, Delafosse V, Holland AE. An official systematic review of the European Respiratory Society/American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. Eur Respir J. 2014;44:1447–78.
- Gestel AJR van, Clarenbach CF, Stöwhas AC, Teschler S, Russi EW, Teschler H, Kohler M. Prevalence and Prediction of Exercise-Induced Oxygen Desaturation in Patients with Chronic Obstructive Pulmonary Disease.
   Respiration. 2012;84:353–9.
- 5. Jenkins S, Čečins N. Six-minute walk test: observed adverse events and oxygen desaturation in a large cohort of patients with chronic lung disease. Intern Med J. 2011;41:416–22.
- 6. Fiore C, Lee A, McDonald C, Hill C, Holland A. Should oxyhaemoglobin saturation be monitored continuously during the 6-minute walk test? Chron Respir Dis. 2011;8:181–4.
- 7. Chuang M-L, Lin I-F, Chen S-P. Kinetics of Changes in Oxyhemoglobin Saturation During Walking and Cycling Tests in COPD. Respir Care. 2014;59:353–62.
- 8. Takigawa N, Tada A, Soda R, Date H, Yamashita M, Endo S, Takahashi S, Kawata N, Shibayama T, Hamada N, Sakaguchi M, Hirano A, Kimura G, Okada

- C, Takahashi K. Distance and oxygen desaturation in 6-min walk test predict prognosis in COPD patients. Respir Med. 2007;101:561–7.
- ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166:111–7.
- 10. Beekman E, Mesters I, Hendriks EJM, Klaassen MPM, Gosselink R, van Schayck OCP, de Bie RA. Course length of 30 metres versus 10 metres has a significant influence on six-minute walk distance in patients with COPD: an experimental crossover study. J Physiother. 2013;59:169–76.
- Bansal V, Hill K, Dolmage TE, Brooks D, Woon LJ, Goldstein RS. Modifying Track Layout From Straight to Circular Has a Modest Effect on the 6-min Walk Distance. Chest. 2008;133:1155–60.
- Sciurba F, Criner GJ, Lee SM, Mohsenifar Z, Shade D, Slivka W, Wise RA.
   Six-Minute Walk Distance in Chronic Obstructive Pulmonary Disease. Am J
   Respir Crit Care Med. 2003;167:1522–7.
- Weir NA, Brown AW, Shlobin OA, Smith MA, Reffett T, Battle E, Ahmad S, Nathan SD. The Influence of Alternative Instruction on 6-Min Walk Test Distance. Chest. 2013;144:1900–5.
- 14. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of chronic obstructive lung disease. [Internet]. [cited 2020 April 17]. Available from: https://www.goldcopd.org.
- 15. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, Enright PL, Hankinson JL, Ip MSM, Zheng J, Stocks J, Initiative the EGLF. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. Eur Respir J. 2012;40:1324–43.
- 16. Paterick TJ, Carson GV, Allen MC, Paterick TE. Medical Informed Consent: General Considerations for Physicians. Mayo Clin Proc. 2008;83:313–9.

- R Core Team. R: A language and environment for statistical computing.
   [Internet]. Vienna, Austria: R Foundation for Statistical Computing; 2018.
   Available from: https://www.R-project.org/
- Snow G. blockrand: Randomization for Block Random Clinical Trials [Internet].
   2020 [cited 2020 November 23]. Available from: https://CRAN.R-project.org/package=blockrand
- Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42:377–81.
- 20. Faul F, Erdfelder E, Lang A-G, Buchner A. G\*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39:175–91.
- 21. Stephen S. Senn. Cross-over Trials in Clinical Research. 2nd Edition. WILEY; 2002. 364 p.
- 22. IBM SPSS Statistics for Windows. Armonk, NY: IBM Corp.; 2019.
- 23. Dwan K, Li T, Altman DG, Elbourne D. CONSORT 2010 statement: extension to randomised crossover trials. BMJ. 2019;366:I4378.
- 24. Guyatt GH, Pugsley SO, Sullivan MJ, Thompson PJ, Berman L, Jones NL, Fallen EL, Taylor DW. Effect of encouragement on walking test performance. Thorax. 1984;39:818–22.
- 25. Gupta R, Goldstein R, Brooks D. The acute effects of a rollator in individuals with COPD. J Cardpulm Rehabil. 2006;26:107–11.
- Honeyman P, Barr P, Stubbing DG. Effect of a walking aid on disability, oxygenation, and breathlessness in patients with chronic airflow limitation. J Cardpulm Rehabil. 1996;16:63–7.
- 27. Probst VS, Troosters T, Coosemans I, Spruit MA, Pitta F de O, Decramer M, Gosselink R. Mechanisms of improvement in exercise capacity using a rollator in patients with COPD. Chest. 2004;126:1102–7.

- 28. Roomi J, Yohannes AM, Connolly MJ. The effect of walking aids on exercise capacity and oxygenation in elderly patients with chronic obstructive pulmonary disease. Age Ageing. 1998;27:703–6.
- 29. Solway S, Brooks D, Lau L, Goldstein R. The short-term effect of a rollator on functional exercise capacity among individuals with severe COPD. Chest. 2002;122:56–65.
- 30. Vaes AW, Annegarn J, Meijer K, Cuijpers MWJ, Franssen FME, Wiechert J, Wouters EFM, Spruit MA. The effects of a 'new' walking aid on exercise performance in patients with COPD: a randomized crossover trial. Chest. 2012;141:1224–32.
- 31. Davidson AC, Leach R, George RJ, Geddes DM. Supplemental oxygen and exercise ability in chronic obstructive airways disease. Thorax. 1988;43:965–71.
- 32. Fujimoto K, Matsuzawa Y, Yamaguchi S, Koizumi T, Kubo K. Benefits of Oxygen on Exercise Performance and Pulmonary Hemodynamics in Patients With COPD With Mild Hypoxemia. Chest. 2002;122:457–63.
- 33. Rooyackers JM, Dekhuijzen PN, Van Herwaarden CL, Folgering HT. Training with supplemental oxygen in patients with COPD and hypoxaemia at peak exercise. Eur Respir J. 1997;10:1278–84.
- 34. Jolly EC, Di Boscio V, Aguirre L, Luna CM, Berensztein S, Gené RJ. Effects of supplemental oxygen during activity in patients with advanced COPD without severe resting hypoxemia. Chest. 2001;120:437–43.
- 35. Woodcock AA, Gross ER, Geddes DM. Oxygen relieves breathlessness in 'pink puffers'. Lancet Lond Engl. 1981;1:907–9.
- 36. McDonald CF, Blyth CM, Lazarus MD, Marschner I, Barter CE. Exertional oxygen of limited benefit in patients with chronic obstructive pulmonary disease and mild hypoxemia. Am J Respir Crit Care Med. 1995;152:1616–9.
- 37. Crisafulli E, Beneventi C, Bortolotti V, Kidonias N, Fabbri LM, Chetta A, Clini EM. Energy Expenditure at Rest and during Walking in Patients with Chronic

- Respiratory Failure: A Prospective Two-Phase Case-Control Study. PLOS ONE. 2011;6:e23770.
- 38. Chan ED, Chan MM, Chan MM. Pulse oximetry: understanding its basic principles facilitates appreciation of its limitations. Respir Med. 2013;107:789–99.
- 39. Hernandes NA, Wouters EFM, Meijer K, Annegarn J, Pitta F, Spruit MA. Reproducibility of 6-minute walking test in patients with COPD. Eur Respir J. 2011;38:261–7.

# **Captions**

Figure 1: Sensor fixation with tape and experimental conditions

- a) Sensor fixation with tape
- b) 6MWT<sub>without</sub>: Patient walking alone with pulse oximeter around the trunk (6MWT<sub>without</sub>)
- c) 6MWT<sub>with</sub>: Assessor walking behind the patient (6MWT<sub>with</sub>)

Figure 2: Flow chart

# **Tables**

Table 1: Patient characteristics

Variable	6MWT <sub>with</sub> then 6MWT <sub>without</sub> n=22	6MWT <sub>without</sub> then 6MWT <sub>with</sub> n=27	Complete Sample n=49	
Age, years	67 ± 8	71 ± 9	69 ± 9	
Sex, n (%)				
female	9 (41)	11 (41)	29 (59)	
male	13 (59)	16 (59)	20 (41)	
GOLD stages, n (%)				
II	4 (18)	9 (33)	13 (26)	
III	11 (50)	13 (48)	24 (49)	
IV	7 (32)	5 (19)	12 (25)	
FEV <sub>1</sub> , % predicted	38 ± 11	45 ± 14	42 ± 13	
FEV <sub>1</sub> , z-score	$-3.7 \pm 0.7$	$-3.2 \pm 0.9$	-3.4± 0.8	
FEV <sub>1</sub> /FVC ratio	$0.47 \pm 0.07$	$0.49 \pm 0.09$	$0.48 \pm 0.08$	
FEV <sub>1</sub> /FVC ratio, z-score	$-3.5 \pm 0.7$	$-3.1 \pm 0.9$	-3.28 ± 0.86	
6MWT on admission, m	268 ± 96	267 ± 92	267 ± 96	
6MWTs prior to study inclusion, n (%)				
1 test	6 (27)	8 (30)	14 (28)	
2 tests	9 (41)	10 (37)	19 (39)	
3 tests	7 (32)	9 (33)	16 (33)	

Data are given as mean ± standard deviation or number (percent).

6MWT six-minute walk test, 6MWT<sub>without</sub> patient walking alone during 6MWT, 6MWT<sub>with</sub> assessor walking behind the patient during 6MWT, BMI body mass index, FEV<sub>1</sub> Forced expiratory volume in one second, FVC forced vital capacity, GOLD Global Initiative for Chronic Obstructive Lung Disease.

Table 2: Differences in walking distance and oxygen saturation between the two experimental conditions.

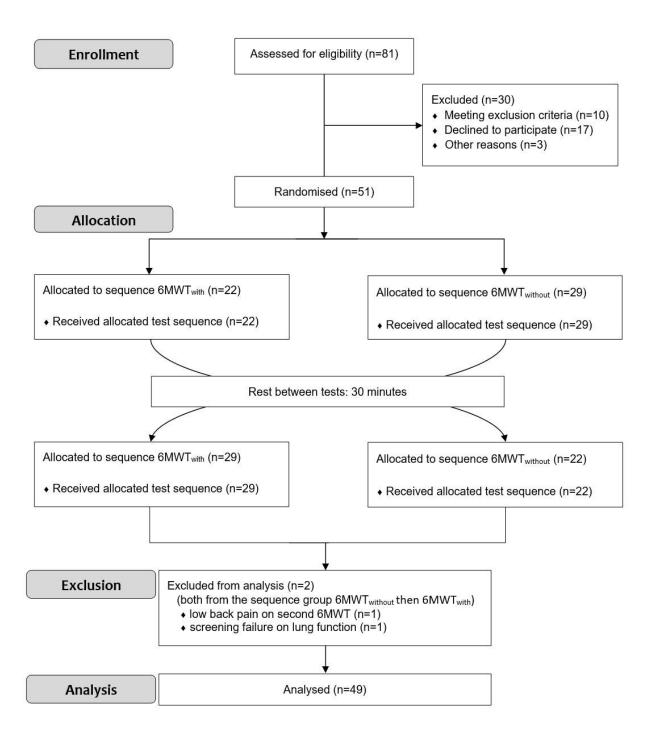
Outcome	$6MWT_{with}$	6MWT <sub>without</sub>	Mean difference	p-value
6MWT, m	337.8 ± 85.7	346.5 ± 86.4	-9.1 [-13.9 to -4.3]	0.0004
SpO <sub>2</sub> nadir, %	85.1 ± 5.4	85.0 ± 5.6	0.06 [-0.49 to 0.62]	0.82
SpO <sub>2</sub> artefact, n	17 [4, 24]	11 [3, 26]	0.60 [-3.76 to 4.96]	0.78
SpO <sub>2</sub> artefact,	34 [7, 113]	24 [4, 62]	17.9 [-5.45 to 41.2]	0.13
seconds				

Data are given as mean ± standard deviation or median [interquartile range].

6MWT six-minute walk test, 6MWT<sub>without</sub> patient walking alone during 6MWT, 6MWT<sub>with</sub> assessor walking behind the patient during 6MWT, SpO<sub>2</sub> oxygen saturation.

Mean differences [95% CI lower to upper limit] between 6MWT<sub>with</sub> versus 6MWT<sub>without</sub> and SpO<sub>2</sub> outcomes were analysed with a linear regression model adjusting for the experimental condition, period, and subject.





# **ONLINE SUPPLEMENTARY MATERIAL**

# Accompanied versus unaccompanied walking for continuous oxygen saturation measurement during 6-minute walk test in COPD: a randomised cross-over study

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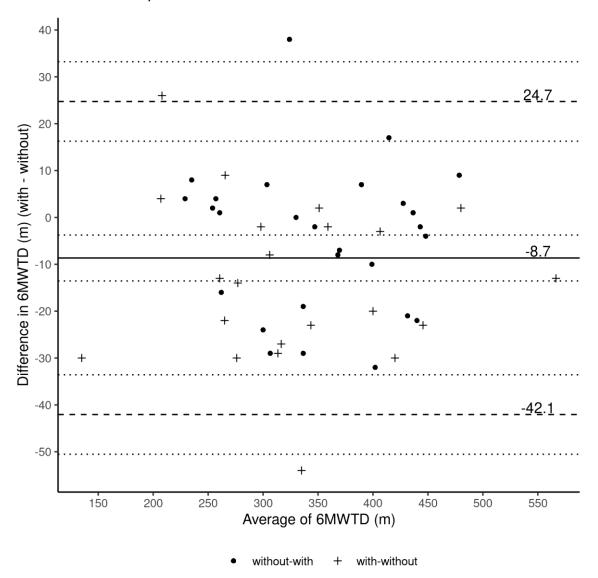
# Results

Table S1. Pre- and post-test conditions in the two experimental conditions

	6MW	6MWT <sub>with</sub> n=22		6MWT <sub>without</sub> n=27	
	n=2				
Outcome	pre-test	post-test	pre-test	post-test	
Heart rate, bpm	89 ± 13	109 ± 14	89 ± 13	108 ± 12	
SpO <sub>2</sub> , %	94 ± 2	86 ± 6	94 ± 3	86 ± 6	
SpO <sub>2</sub> nadir, %		85 ± 5		85 ± 6	
Dyspnoea, 0-10	$0.2 \pm 0.7$	3.5 ± 2.1	$0.2 \pm 0.6$	3.5 ± 2.1	
Leg fatigue, 0-10	$0.4 \pm 0.9$	2.7 ± 1.6	$0.4 \pm 0.9$	2.7 ± 1.4	

Data are given as mean  $\pm$  standard deviation. Perceived dysphoea and leg fatigue were measured using a 0-10 Borg Scale. 6MWT six-minute walk test, 6MWT without patient walking alone during 6MWT, 6MWT with assessor walking behind the patient during 6MWT, bpm, beats per minute, SpO<sub>2</sub> oxygen saturation.

**Figure S2.** Bland-Altman plot showing differences in six-minute walking distance between the two experimental conditions.



6MWTD: 6-Minute Walk Test distance. The solid line represents the mean difference, and the dashed lines represents the upper and lower limits of agreement (mean difference  $\pm$  1.96 x standard deviation of the differences). The dotted lines indicate the 95% confidence intervals of the mean difference and the lower and upper limits of agreement. Mean difference: -8.7m [95% CI, -13.5 to -3.8]. Lower limit of agreement: -42.1m [95% CI, -50.5 to -33.6]. Upper limit of agreement: 24.8m [95% CI, 16.3 to 33.2].

**Table S3.** Patient perceptions during the two 6MWTs (n=49)

	6MWT <sub>v</sub>	vith	6MWT <sub>without</sub>	either	
Which test did you like more?	12 (25%)		8		29
			(16%)	(59%)	
Questions concerning the					
assessor accompanying	absolutely	a little bit	moderate	strong	very
the patient	not				strong
To which extent did you feel	46	2	1	0	0
slowed down by the assessor	(94%)	(4%)	(2%)	(0%)	(0%)
accompanying you?					
To which extent did you feel	37	9	1	1	1
pushed forward by the	(76%)	(18%)	(2%)	(2%)	(2%)
assessor accompanying					
you?					
To which extent did you feel	47	1	1	0	0
bothered by the assessor	(96%)	(2%)	(2%)	(0%)	(0%)
accompanying you?					
Did you feel safer because	29	8	2	8	2
the assessor accompanied	(60%)	(16%)	(4%)	(16%)	(4%)
you?					

6MWT six-minute walk test,  $6MWT_{without}$  patient walking alone during 6MWT,  $6MWT_{with}$  assessor accompanying the patient during 6MWT.