

Respiratory Medicine
Elsevier Editorial System(tm) for
Manuscript Draft

Manuscript Number: YRMED-D-20-00201

Title: Prognostication in COPD using physical function measures: Let's walk before we run away with conclusions.

Article Type: Correspondence

Keywords: COPD; physical function; 4MGS; SPPB

Corresponding Author: Dr. Adam Lewis, Ph.D.

Corresponding Author's Institution: Brunel University London

First Author: Adam Lewis, Ph.D.

Order of Authors: Adam Lewis, Ph.D.; Claire M Nolan, Ph.D; William D Man, Ph.D; Samantha S Kon, Ph.D; Joy Conway, Ph.D

Cover letter for Respiratory Medicine

Dear Editors,

We would like you to consider our correspondence paper titled 'Prognostication in COPD using physical function measures: Let's walk before we run away with conclusions.' for publication in Respiratory Medicine. We highlight the value and clinical relevance of measuring physical function in COPD prognostication, reported in a systematic review recently published in Respiratory Medicine(1). However, we believe other measures of physical function including the 4-metre gait speed and the Short Physical Performance Battery should also be considered for purposes of prognostication in COPD and associated data on these measures were not provided by Massierer et al(1). We present evidence for these simple and quick measures of physical function which indicate their prognostic utility in COPD.

We hope that you find our correspondence of interest.

Many thanks on behalf of all authors,

Adam Lewis

1. Massierer D, Alsowayan W, Lima VP, Bourbeau J, Janaudis-Ferreira T. Prognostic value of simple measures of physical function and muscle strength in COPD: A systematic review. Respiratory Medicine. 2020;161(105856):1-9.

Prognostication in COPD using physical function measures: Let's walk before we run away with conclusions.

Dr Adam Lewis PhD ^{1*} adam.lewis@brunel.ac.uk

Dr Claire M. Nolan PhD ^{2,3*} c.nolan@rbht.nhs.uk

Dr William D.C. Man PhD ^{2,3,4} w.man@rbht.nhs.uk

Dr Samantha S.C. Kon PhD ^{2,5} s.kon@rbht.nhs.uk

Professor Joy Conway PhD¹ joy.conway@brunel.ac.uk

*Contributed equally as joint first authors

Affiliations:

1. Brunel University London
2. Harefield Respiratory Research Unit, Royal Brompton and Harefield NHS Foundation Trust, UK
3. Harefield Pulmonary Rehabilitation Unit, Royal Brompton and Harefield NHS Foundation Trust, UK
4. National Heart and Lung Institute, Imperial College London, UK
5. The Hillingdon Hospital NHS Foundation Trust, London, UK

Corresponding author: Dr Adam Lewis, College of Health and Life Sciences, Brunel University London, Kingston Lane, Uxbridge, Middlesex, UB8 3PH

We read with great interest the recently published systematic review by Massierer and colleagues (1) that investigated the ability of simple measures of physical function and muscle strength to predict exacerbation, hospitalization and mortality in people with chronic obstructive pulmonary disease (COPD). The authors concluded that the measures with the greatest amount of evidence for prognostication were hand-grip strength and 1-minute sit to stand test. However, they reported that only a limited number of studies examining the prognostic ability of simple measures had been published, and that these studies lacked methodological rigor.

We congratulate the authors on reviewing this important topic. However, we believe that there are other simple measures with prognostic ability in COPD such as the 4-metre gait speed test (4MGS); and Short Physical Performance Battery (SPPB) that are not reported in this review. A possible reason for their exclusion is the search strategy employed by the authors. The search terms were mainly generic (e.g. *“performance”*, *“exercise”*) and specific names of simple measures (e.g. *“four-metre gait speed”*) were omitted. A possible advantage of using a broad search strategy should be the identification of a wide range of simple measures; indeed, the authors identified 10,561 articles. However, this strategy did not identify papers including the 4MGS and SPPB and despite searching for the terms *“gait”*, *“walk”* and *“SPPB”*. This suggests that the search strategy wasn't sufficiently comprehensive.

The 4MGS test, a measure of usual walking speed, is a surrogate marker of physical frailty (2). It is acceptable to patients, quick to perform can be adopted in almost any environment

including the home or hospital bedside. Gait speed has been shown to be a consistent predictor of adverse prognosis including all-cause mortality, hospitalisation and disability in older adults (3, 4). It has been identified as the best validated functional performance test for pharmacological trials in sarcopenia and frailty (5) and has been used as a stratification tool and clinical end-point in pharmacological trials in other diseases (6). In people with COPD, 4MGS is reliable (7), valid (7), responsive to intervention (pulmonary rehabilitation: minimal clinically important difference 0.11ms^{-1}) and time (12 months) (8). Particularly relevant to Massierer and colleagues' review, a prospective study by Kon et al involving 213 people hospitalised with an acute exacerbation of COPD demonstrated that 4MGS measured at hospital discharge independently predicted risk of 90-day hospital readmission (odds ratio (95% confidence interval (CI)) 7.12 (2.61 to 19.44)) (9).

The SPPB is a standardised objective assessment tool of lower limb function that consists of three components that test standing balance, usual gait speed (4MGS), and ability to stand from a sitting position (10). It requires no complex equipment, is quick to perform and easily applicable in community and home settings, even by untrained operators. The SPPB is frequently used in epidemiological studies of community-dwelling older adults, and consistently identifies those at greater risk of mortality, nursing home admission, hospitalisation, and disability (11). Expert consensus groups have recommended the SPPB both as a primary functional outcome measure in frail older persons (5) and as a screening tool for sarcopenia (12). In people with COPD, the SPPB has been shown to be a valid assessment tool that may detect functional impairment, loss of muscle mass, and structural muscle abnormality (13). Singer and colleagues, demonstrated that in 262 people listed for

lung transplant (32% COPD) the SPPB was associated with increased risk of delisting or death before lung transplant (hazard ratio (95% CI) 1.53 (1.19 to 1.59) (14). Furthermore, Fermont et al (15) recently showed in a prospective observational 5 year longitudinal study data from 714 COPD patients, that a poorer SPPB score was associated with higher incidence rate for exacerbation related hospitalisations (incidence rate ratio (IRR) 1.08 per 1 point decrease, 95% CI 1.01 to 1.14) and length of stays (IRR 1.18 per 1 point decrease, 95% CI 1.10 to 1.27). For these reasons, we believe that 4MGS and SPBB are valuable prognostic measures that can be used in the clinical management and future studies of people with COPD.

In summary, we believe that an alternative search strategy may have identified simple measures not described in the review by Massierer and colleagues, thus enabling a greater understanding of tools with prognostic value in COPD.

Conflicts of Interest: The authors declare no conflicts of interest

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

References

1. Massierer D, Alsayyan W, Lima VP, Bourbeau J, Janaudis-Ferreira T. Prognostic value of simple measures of physical function and muscle strength in COPD: A systematic review. *Respiratory Medicine*. 2020;161(105856):1-9.
2. European Medicines Agency. Overview of comments on 'Points to consider on frailty: Evaluation instruments for baseline characterisation of clinical trial populations' 2018 [Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2018/02/WC500244286.pdf].
3. Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, et al. Gait speed and survival in older adults. *Jama*. 2011;305(1):50-8.
4. Steffen TM, Hacker TA, Mollinger L. Age-and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and gait speeds. *Phys Ther*. 2002;82(2):128-37.
5. Functional outcomes for clinical trials in frail older persons: time to be moving. *J Gerontol A Biol Sci Med Sci*. 2008;63(2):160-4.
6. Goodman AD, Brown TR, Edwards KR, Krupp LB, Schapiro RT, Cohen R, et al. A phase 3 trial of extended release oral dalfampridine in multiple sclerosis. *Ann Neurol*. 2010;68(4):494-502.
7. Kon SS, Patel MS, Canavan JL, Clark AL, Jones SE, Nolan CM, et al. Reliability and validity of 4-metre gait speed in COPD. *Eur Respir J*. 2013;42(2):333-40.
8. Kon SS, Canavan JL, Jones SE, Nolan CM, Clark AL, Dickson MJ, et al. Minimum clinically important difference for the COPD Assessment Test: a prospective analysis. *Lancet Respiratory Medicine*. 2014;2(3):195-203.
9. Kon SS, Jones SE, Schofield SJ, Banya W, Dickson MJ, Canavan JL, et al. Gait speed and readmission following hospitalisation for acute exacerbations of COPD: a prospective study. *Thorax*. 2015.
10. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol*. 1994;49(2):M85-94.
11. Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci*. 2000;55(4):M221-31.
12. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*. 2010;39(4):412-23.
13. Patel MS, Mohan D, Andersson YM, Baz M, Kon SS, Canavan JL, et al. Phenotypic characteristics associated with reduced short physical performance battery score in COPD. *Chest*. 2014;145(5):1016-24.
14. Singer JP, Diamond JM, Gries CJ, McDonough J, Blanc PD, Shah R, et al. Frailty phenotypes, disability, and outcomes in adult candidates for lung transplantation. *Am J Respir Crit Care Med*. 2015;192(11):1325-34.
15. Fermont JM, Bolton CE, Fisk M, Mohan D, Macnee W, Cockcroft JR, et al. Risk assessment for hospital admission in patients with COPD; a multi-centre UK prospective observational study. *PLoS One*. 2020;15(2):e0228940.