

Northumbria Research Link

Citation: Demeyer, Heleen, Dueñas-Espín, Ivan, De Jongh, Corina, Louvaris, Zafeiris, Hornikx, Miek, Gimeno-Santos, Elena, Loeckx, Matthias, Vogiatzis, Ioannis, Janssens, Wim, Hopkinson, Nicholas, Rabinovich, Roberto, Karlsson, Niklas, Garcia-Aymerich, Judith and Troosters, Thierry (2016) Can health status questionnaires be used as a measure of physical activity in COPD patients? *European Respiratory Journal*, 47 (5). pp. 1565-1568. ISSN 0903-1936

Published by: European Respiratory Society

URL: <http://dx.doi.org/10.1183/13993003.01815-2015>
<<http://dx.doi.org/10.1183/13993003.01815-2015>>

This version was downloaded from Northumbria Research Link:
<http://nrl.northumbria.ac.uk/28981/>

Northumbria University has developed Northumbria Research Link (NRL) to enable users to access the University's research output. Copyright © and moral rights for items on NRL are retained by the individual author(s) and/or other copyright owners. Single copies of full items can be reproduced, displayed or performed, and given to third parties in any format or medium for personal research or study, educational, or not-for-profit purposes without prior permission or charge, provided the authors, title and full bibliographic details are given, as well as a hyperlink and/or URL to the original metadata page. The content must not be changed in any way. Full items must not be sold commercially in any format or medium without formal permission of the copyright holder. The full policy is available online: <http://nrl.northumbria.ac.uk/policies.html>

This document may differ from the final, published version of the research and has been made available online in accordance with publisher policies. To read and/or cite from the published version of the research, please visit the publisher's website (a subscription may be required.)

www.northumbria.ac.uk/nrl



CAN HEALTH STATUS QUESTIONNAIRES BE USED AS A MEASURE OF PHYSICAL ACTIVITY IN COPD PATIENTS?

Heleen Demeyer^{1,2}, Ivan Dueñas-Espín³, Corina De Jongh⁴, Zafeiris Louvaris⁵, Miek Hornikx^{1,2}, Elena Gimeno-Santos³, Matthias Loeckx^{1,2}, Ioannis Vogiatzis⁵, Wim Janssens², Nicholas S Hopkinson⁶, Roberto A Rabinovich⁷, Niklas Karlsson⁸, Judith Garcia-Aymerich³, Thierry Troosters^{1,2}, on behalf of the PROactive consortium

¹KU Leuven-University of Leuven, Department of Rehabilitation Sciences, B-3000 Leuven, Belgium

²University Hospitals Leuven, Department of Respiratory Diseases, B-3000 Leuven, Belgium

³Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain; CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain; Universitat Pompeu Fabra (UPF), Barcelona, Spain

⁴Department of General Practice, University Medical Center Groningen, Groningen, Netherlands

⁵Dept of Critical Care Medicine, Pulmonary Rehabilitation Centre, Evangelismos Hospital, M. Simou and G.P. Livanos Laboratories, National and Kapodistrian University of Athens, Thorax Foundation, Athens, Greece.

⁶NIHR Respiratory Biomedical Research Unit of the Royal Brompton and Harefield NHS foundation Trust and Imperial College London, London, UK

⁷ELEGI/Colt laboratory, UoE/MRC Centre for Inflammation Research, The University of Edinburgh, Edinburgh, Scotland

⁸Astra Zeneca, Mölndal, Sweden

Corresponding author:

Thierry Troosters
Respiratory Rehabilitation and Respiratory Division
UZ Gasthuisberg, Herestraat 49 bus 706, Onderwijs & Navorsing I, Labo Pneumologie,
B-3000 Leuven (Belgium)
Email : Thierry.Troosters@med.kuleuven.be
Phone +32.16.33.07.98

Take home message

Health status questionnaires provide only limited insight in the physical activity of patients with COPD

To the editor

Acting to address the amount of physical activity (PA) of patients with Chronic Obstructive Pulmonary Disease (COPD) is recommended as part of the GOLD recommendations [1]. A level lower than approximately 5000 steps ('sedentary lifestyle index') is associated with significantly increased health risks [2,3]. Actively screening to identify patients below this threshold could be an important step towards targeting interventions to increase PA. Potential screening tools include activity monitors (objective assessment) or self-reported questionnaires (subjective assessment) to measure the amount of PA [4]. The latter method, feasible in clinical practice, may not result in an accurate representation in an individual patient, as questionnaire responses tend to misclassify PA [5]. Although more accurate and widely used in research, activity monitoring is not yet commonly included in patients' routine assessment. Several health status questionnaires in routine clinical use, contain a domain or dimension related to PA [6]. In the analytical framework of Leidy, et al. functional performance has been defined as the physical, psychological, social, occupational and spiritual activities that people actually do in the normal course of their lives to meet basic needs, fulfill usual roles, and maintain their health and well-being [7]. A review by Kocks, et al., proposed that these could be used in the measurement of functional performance (defined as 'what a patient is actually doing') and that this would be a more practical alternative to PA monitoring [8]. Whether this approach is sufficiently valid as a representation for PA levels in clinical practice remains to be established.

The aims of the present analyses were (i) to describe the relationship between objectively measured PA and responses to health status questionnaires and (ii) to assess the utility of these questionnaires to screen for severe physical inactivity (SPI) in this population.

Data from two hundred thirty-five COPD patients (diagnosis confirmed with a post-bronchodilator spirometry) recruited from five centers across Europe [Leuven(Belgium), Athens (Greece), Groningen (The Netherlands), London and Edinburgh (UK)], as part of the PROactive project

(www.proactivecopd.com) were included in this analysis. Patients were current or ex-smokers (+10 pack years) without comorbidities significantly interfering with their ability to exercise and without respiratory conditions other than COPD. Further study details are available in the paper reporting the primary analyses of the present study [9]. PA was measured for 14 days during waking hours using the Dynaport Movemonitor (©McRoberts; The Hague, the Netherlands), which has been validated in this population [10,11]. Patients with a minimum of four valid days, defined as days with at least eight hours of wearing time, were included in this analysis [12]. SPI was defined as a step count lower than 5000 per day [2]. At the end of this measurement period, several questionnaires were administered including: Chronic Respiratory Disease Questionnaire Self-administered Standardised Format (CRDQ-SAS), COPD assessment test (CAT), Clinical COPD questionnaire (CCQ) and modified Medical Research Council dyspnea questionnaire (mMRC). Relations between PA (number of daily steps, STEPS) and different health status questionnaires were investigated using Spearman correlations. The ability of questionnaires to predict SPI was analyzed using logistic regression analysis with SPI as outcome and different questionnaires as explanatory variables, each included in a separate analysis. Area under the curve (AUC) was retrieved if the regression analysis was significant. AUC values are a measure of accuracy and are considered as excellent (≥ 0.90), good (0.80-0.89), fair (0.70-0.79) or poor (< 0.70). ROC curves were drawn for the different questionnaires, including total scores and the subdomain with the best discriminative property. A cutoff was suggested for each of the questionnaires (using the total score or subdomain, giving the highest AUC) putting an equal weight to sensitivity and specificity. Likelihood ratios were calculated as the ratio between sensitivity and (1-specificity). Likelihood ratios above 10 are considered to provide strong evidence for diagnostic purposes [13].

Nine patients did not have a valid PA measurement and were excluded from the analysis, one patient did not complete the questionnaires, resulting in 225 patients (67% male, mean \pm SD of 67 \pm 8 years, FEV₁ 56 \pm 20%_{pred}, 6MWD 426 \pm 129m (68 \pm 19%_{pred}), with a median [Q1-Q3] step count of 4287 [2971-6331] steps.day⁻¹ representing all GOLD stages I/II/III/IV (12%/47%/32%/9% respectively) included in

the present analyses. Sixty percent of patients were defined as severely inactive. The health status questionnaires (and their subdomains) CCQ_{symptoms} , $CRDQ-SAS_{\text{mental}}$, $CRDQ-SAS_{\text{mastery}}$ were poorly correlated ($abs(r) < 0.3$); CAT, CCQ_{total} , CCQ_{mental} , $CCQ_{\text{functional state}}$, $CRDQ-SAS_{\text{total}}$, $CRDQ-SAS_{\text{dyspnea}}$, $CRDQ-SAS_{\text{fatigue}}$ were weakly related ($0.5 < abs(r) \leq 0.3$); the mMRC score was moderately related ($r = -0.52$) to STEPS ($p < 0.01$ for all). All scores, except from the $CRDQ-SAS_{\text{mental}}$ score, were significant predictors of SPI ($p \leq 0.01$ for all). Only mMRC and $CCQ_{\text{functional state}}$ scores showed a fair discriminative property (AUC respectively 0.719 and 0.724). Other questionnaires resulted in a poor discrimination ($AUC < 0.7$). ROC curves were built for the different questionnaires including the total score and the best discriminative subdomain (see Figure 1). To predict SPI, a mMRC score ≥ 2 resulted in a positive predictive value (PPV) of 79%, accuracy (ACC) of 67% and positive likelihood ratio (LR+) of 2.27. A CAT score ≥ 13 resulted in a PPV of 73%, ACC of 64% and LR+ of 1.78. A $CCQ_{\text{functional state}}$ score ≥ 1.5 results in a PPV of 76%, ACC of 67% and LR+ of 2.06. A $CRDQ-SAS_{\text{dyspnea}}$ score ≤ 5.3 results in PPV of 76%, ACC of 68% and LR+ of 2.10.

The present data show that responses to health status questionnaires are only loosely related to the amount of PA and their use cannot therefore be recommended as a *standalone* screening tool for SPI because of low sensitivity and specificity. Two explanations can be proposed for the very low to moderate associations observed between these questionnaires which mainly capture symptoms and PA. First, none of these questionnaires use PA as a main concept and thus they are not designed to give a reliable assessment of the PA level [6]. The questionnaires mainly reflect symptoms that are indirectly associated with PA. Second, it is plausible that there is an interplay between the volume (amount*intensity) of PA and the symptom experience. Patients may decrease their level of PA to avoid symptoms. This leads to the hypothesis that symptoms can depend on the PA level and therefore fail to give a reliable estimate of the actual underlying PA level. Indeed, patients' perception of PA includes not only the amount of PA but also symptoms experienced during and adaptations related to PA [14,9].

A good screening tool for inactive patients would be able to identify truly inactive patients (sensitivity) without including too many active patients (specificity). Depew, et al. concluded that the mMRC is the best predictor of SPI, compared to two PA questionnaires, self-efficacy and the ADO-index [15]. These authors proposed a mMRC score of 3 as a triage for SPI (defined as $PAL < 1.4$, i.e. the ratio of active to total energy expenditure) [15]. Above this cutoff, 84% of patients identified as severely inactive were indeed inactive (PPV 84%). However, it resulted in a sensitivity of 36% meaning that only the minority of inactive patients were identified by this screening tool. Based on the ROC analysis, for mMRC we chose a cutoff of 2 points, which also resulted in a majority of patients above this threshold to be inactive (PPV 79%) with a sensitivity of 65%. These results suggest that this cutoff could be used in clinical practice as a first screening tool to identify severely inactive patients. However, a significant proportion of patients with an mMRC of 0 or 1 are inactive (NPV 56%). Therefore, PA should still be measured to identify inactive patients with a mMRC below 2. A comparable conclusion can be drawn based on the $CCQ_{functional\ state}$ domain, using a cut off ≥ 1.5 (PPV 76%, NPV 57%). In the review of Kocks, et al., [8] the questionnaires were judged mainly based on the use in a primary care setting (e.g. practical use, responsiveness). These authors also concluded the mMRC and $CCQ_{functional\ state}$ to be the most suited questionnaires to measure functional performance [8]. The present study shows that this conclusion only holds true in terms of PPV whereas NPV is poor.

The use of simple clinical tests, e.g. six minute walk test, were also shown to fail in predicting SPI [16]. Taking all this into account we can conclude that neither health status questionnaires, nor simple clinical tests can replace objective measurement of PA in COPD patients. The mMRC dyspnea and $CCQ_{functional\ state}$ score could be recommended as easy first screening tests to identify severely inactive patients but will misclassify patients as 'not severely inactive' below the proposed thresholds. Therefore, objective PA measurement should be recommended in the clinical routine assessment of COPD patients.

Acknowledgements

The PROactive Consortium members are as follows. Nathalie Ivanoff: Almirall, Barcelona, Spain; Niklas Karlsson and Solange Corriol-Rohou: AstraZeneca AB, Mölndal, Sweden; Ian Jarrod: British Lung Foundation, London, UK; Damijen Erzen: Boehringer Ingelheim, Nieder-Ingelheim, Germany; Caterina Brindicci, Tim Higenbottam and Mario Scuri: Chiesi Farmaceutici S.A. Parma, Italy; Paul McBride: Choice Healthcare Solutions, Hitchin, UK; Nadia Kamel: European Respiratory Society, Lausanne, Switzerland; Margaret Tabberer: GlaxoSmithKline, Uxbridge, UK; Thierry Troosters and Fabienne Dobbels,: Katholieke Universiteit Leuven, Leuven, Belgium; Judith Garcia-Aymerich, Municipal Institute of Medical Research, Barcelona, Spain; Pim de Boer: Netherlands Asthma Foundation, Amersfoort, The Netherlands; Karoly Kulich and Alastair Glendenning: Novartis, Basel, Switzerland; Katja Rudell and Frederick J. Wilson: Pfizer Walton Oaks, UK; Michael I. Polkey and Nick S. Hopkinson: Royal Brompton and Harefield NHS Foundation Trust, London, UK; Ioannis Vogiatzis: Thorax Research Foundation, Athens, Greece; Enkeleida Nikai: UCB, Brussels, Belgium; Thys van der Molen and Corina De Jong: University Medical Center, Groningen, The Netherlands; Roberto A. Rabinovich and Bill MacNee: University of Edinburgh, Edinburgh, UK; Milo A. Puhan and Anja Frei: University of Zurich, Zurich, Switzerland.

Support statement

The PROactive project is funded by the Innovative Medicines Initiative Joint Undertaking (IMU JU) #115011. This work was supported by the Flemish Research Foundation (grant # G.0871.13). WJ is a post-doctoral research fellow of the FWO-Flanders.

References

1. From the *Global Strategy for the Diagnosis, Management and Prevention of COPD*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2015; accessed 18-8-2015.
2. Tudor-Locke C, Craig CL, Thyfault JP, Spence JC. A step-defined sedentary lifestyle index: <5000 steps/day. *Appl Physiol Nutr Metab* 2013; 38: 100-114.
3. Waschki B, Kirsten A, Holz O, Muller KC, Meyer T, Watz H, Magnussen H. Physical Activity Is the Strongest Predictor of All-Cause Mortality in Patients With COPD A Prospective Cohort Study. *Chest* 2011; 140: 331-342.
4. Watz H, Pitta F, Rochester CL, Garcia-Aymerich J, ZuWallack R, Troosters T, Vaes AW, Puhan MA, Jehn M, Polkey MI, Vogiatzis I, Clini EM, Toth M, Gimeno-Santos E, Waschki B, Esteban C, Hayot M, Casaburi R, Porszasz J, McAuley E, Singh SJ, Langer D, Wouters EF, Magnussen H, Spruit MA. An official European Respiratory Society statement on physical activity in COPD. *Eur Respir J* 2014; 44: 1521-1537.
5. Garfield BE, Canavan JL, Smith CJ, Ingram KA, Fowler RP, Clark AL, Polkey MI, Man WD. Stanford Seven-Day Physical Activity Recall questionnaire in COPD. *Eur Respir J* 2012; 40: 356-362.
6. Williams K, Frei A, Vetsch A, Dobbels F, Puhan MA, Rudell K. Patient-reported physical activity questionnaires: a systematic review of content and format. *Health Qual Life Outcomes* 2012; 10: 28.
7. Leidy NK. Functional status and the forward progress of merry-go-rounds: toward a coherent analytical framework. *Nurs Res* 1994; 43: 196-202.
8. Kocks JW, Asijee GM, Tsiligianni IG, Kerstjens HA, van der MT. Functional status measurement in COPD: a review of available methods and their feasibility in primary care. *Prim Care Respir J* 2011; 20: 269-275.
9. Gimeno-Santos E, Raste Y, Demeyer H, Louvaris Z, de JC, Rabinovich RA, Hopkinson NS, Polkey MI, Vogiatzis I, Tabberer M, Dobbels F, Ivanoff N, de Boer WI, van der Molen T, Kulich K, Serra I, Basagana X, Troosters T, Puhan MA, Karlsson N, Garcia-Aymerich J. The PROactive instruments to measure physical activity in patients with chronic obstructive pulmonary disease. *Eur Respir J* 2015.
10. Rabinovich RA, Louvaris Z, Raste Y, Langer D, van RH, Giavedoni S, Burtin C, Regueiro EM, Vogiatzis I, Hopkinson NS, Polkey MI, Wilson FJ, Macnee W, Westerterp KR, Troosters T. Validity of physical activity monitors during daily life in patients with COPD. *Eur Respir J* 2013; 42: 1205-1215.
11. Van Remoortel H, Raste Y, Louvaris Z, Giavedone S, Burtin C, Langer D, Wilson F, Rabinovich R, Vogiatzis I, Hopkinson NS, Troosters T. Validity of six activity monitors in chronic obstructive pulmonary disease: a comparison with indirect calorimetry. *PLoS ONE* 2012; 7: e39198.

12. Demeyer H, Burtin C, van Remoortel H., Hornikx M, Langer D, Decramer M, Gosselink R, Janssens W, Troosters T. Standardizing the analysis of physical activity in patients with COPD following a pulmonary rehabilitation program. *Chest* 2014; 146: 318-327.
13. Deeks JJ, Altman DG. Diagnostic tests 4: likelihood ratios. *BMJ* 2004; 329: 168-169.
14. Dobbels F, de JC, Drost E, Elberse J, Feridou C, Jacobs L, Rabinovich R, Frei A, Puhan MA, de Boer WI, van der Molen T, Williams K, Pinnock H, Troosters T, Karlsson N, Kulich K, Rudell K. The PROactive innovative conceptual framework on physical activity. *Eur Respir J* 2014; 44: 1223-1233.
15. DePew ZS, Garofoli AC, Novotny PJ, Benzo RP. Screening for severe physical inactivity in chronic obstructive pulmonary disease: the value of simple measures and the validation of two physical activity questionnaires. *Chron Respir Dis* 2013; 10: 19-27.
16. van Gestel AJ, Clarenbach CF, Stowhas AC, Rossi VA, Sievi NA, Camen G, Russi EW, Kohler M. Predicting daily physical activity in patients with chronic obstructive pulmonary disease. *PLoS One* 2012; 7: e48081.

Figure caption

Figure 1 ROC analyses of modified Medical Research council dyspnea questionnaire (mMRC), with a range 0 to 4 [panel A], COPD assessment test (CAT), with a range 0-40 [panel B], total score (dotted line) and functional state domain score (solid line) of the Clinical COPD questionnaire (CCQ), with a range 0 to 6 for both [panel C]; total score (dotted line) and dyspnea domain score (solid line) of the Chronic Respiratory Disease Questionnaire self-administered standardized format (CRDQ-SAS), with a range 1 to 7 for both [panel D]. mMRC \geq 2 resulted in a sensitivity (SENS) of 65%, specificity (SPEC) of 71%; CAT \geq 13 resulted in 64% SENS and 64% SPEC, CCQ_{functional state} \geq 1.5 in 66% SENS and 68% SPEC, CRDQ-SAS_{dyspnea} \leq 5.3 in 67% SENS and 68% SPEC.