



INVITED REVIEW SERIES: REHABILITATION IN CHRONIC RESPIRATORY DISEASES

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Organizational aspects of pulmonary rehabilitation in chronic respiratory diseases

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ABSTRACT

Adult patients with chronic respiratory diseases may suffer from multiple physical (pulmonary and extra-pulmonary), emotional and social features which necessitate a comprehensive, interdisciplinary rehabilitation programme. To date, pulmonary rehabilitation programmes show a lot of variation in setting, content, frequency and duration. Future projects should strive for a standard set of assessment measures to identify patients eligible for pulmonary rehabilitation, taking disease complexity into consideration, which should result in referral to an appropriate rehabilitation setting. Local circumstances may complicate this crucial endeavour.

Key words: chronic obstructive pulmonary disease, home-based, pulmonary rehabilitation, setting.

INTRODUCTION

Adult patients with chronic respiratory diseases, such as chronic obstructive pulmonary disease (COPD), asthma and interstitial lung disease (ILD), may suffer from multiple physical (pulmonary and extra-pulmonary), emotional and/or social limitations which necessitate a comprehensive, interdisciplinary pulmonary rehabilitation programme.¹ Indeed, the integrated care of these complex patients should reach beyond regular pulmonary drug treatment(s), as this will have no or only a partial effect on the physical, emotional and social conditions of these patients, and the burden of disease to patients and society is high.² In this review, we share our views on some of the

organizational aspects of a pulmonary rehabilitation programme, including its setting.

PULMONARY REHABILITATION

In 2013, an Official Task Force of the American Thoracic Society (ATS) and the European Respiratory Society (ERS) defined pulmonary rehabilitation as a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies, which include, but are not limited to, exercise training, education and behaviour change, designed to improve the physical and psychological condition of patients with chronic respiratory disease and to promote the long-term adherence of health-enhancing behaviours.¹ Despite the formal approval of this definition by the ATS Board of Directors and the ERS Executive Committee, large differences still exist (internationally, nationally and regionally) in the content and organizational aspects of rehabilitative interventions for adults with chronic respiratory disease.³

SETTINGS FOR PULMONARY REHABILITATION

To date, most pulmonary rehabilitation programmes have been offered in a hospital-based outpatient setting.³ However, rehabilitative interventions have also been provided in an inpatient setting, a community-based setting and at the patient's home.³ To date, clear evidence is lacking to allocate the most appropriate patient, to the most appropriate setting, for the most appropriate rehabilitative treatment, including medical and non-medical patient-tailored therapies. Internationally, there is also no expert consensus, mainly due to large differences in local situations.³ Historically, the degree of airflow limitation has been used to select patients with COPD for pulmonary rehabilitation.^{4,5} However, just using the degree of lung function impairment is not enough to truly understand the physical, emotional and social conditions of adults with a chronic respiratory disease.⁶⁻¹³ Indeed, dyspnoea, fatigue,

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dynamic hyperinflation, a reduced physical capacity, an impaired disease-specific health status and social deprivation already occur in patients with a mild degree of airflow limitation.¹⁴⁻¹⁷ Moreover, the degree of lung function impairment at entry to the pulmonary rehabilitation cannot forecast the efficacy of the programme.¹⁸⁻²¹

The degree of disease complexity, derived from a comprehensive initial assessment, should determine the type of intervention as well as the rehabilitation setting. Only then we can make the next step towards personalized medicine within the field of pulmonary rehabilitation. Figure 1 is an example of how patients with chronic respiratory disease, based on the degree of complexity, can be referred to the most appropriate type of care. So, patients without clear symptom burden and limitations during the performance of activities of daily life should receive healthy lifestyle recommendations and should be followed up over time to determine the degree of disease stability. Fast-developing e-health/m-health applications can support patients, family members and healthcare providers to monitor these well-functioning patients in their home environment.²²⁻²⁴ Patients who despite optimal medical therapy have a single physical, emotional or social limitation should be referred to an allied respiratory professional in primary care (i.e. physiotherapist, or psychologist, or dietician or social worker, etc.) for a targeted therapy. Patients with multiple physical, emotional and/or social limitations should be considered candidates for a comprehensive, hospital-based intervention, where interdisciplinary care can be provided by a dedicated and skilled team. The degree of care-dependency (including patients with chronic respiratory failure in need of non-invasive ventilation, or patients in the direct post-hospitalization phase^{25,26}) should then be used as criteria to refer patients to inpatient pulmonary rehabilitation programmes in specialized centres. Obviously, the proposed model needs to be substantiated by additional research projects, and its success also depends on the local availability of the different pulmonary rehabilitation settings. However, this approach is in line with new initiatives, such as COPDnet, where patients with COPD are referred to different care settings with a different treatment modality and intensity after an extensive screening in the secondary care setting.^{27,28}

To run a hospital-based pulmonary rehabilitation programme for the most complex patients with COPD,

the involvement of multiple, skilled healthcare professionals with COPD-specific knowledge seems imperative.¹ For example, physiotherapists should be aware of the various treatment possibilities, including neuromuscular electrical stimulation^{29,30} and exercise training combined with non-invasive ventilation³¹; or dieticians should be trained to modulate patient's nutritional pattern, taking body composition abnormalities (i.e. cachexia and obesity^{7,32}) and cardiovascular risk factors (i.e. hypertension, hyperglycaemia and hyperlipidaemia³³) into consideration. However, multiple surveys show a huge variation in the number of healthcare disciplines available within and between countries.^{3,34-36} Moreover, the content of pulmonary rehabilitation programmes as well as its frequency and duration vary to a great extent.^{3,34-36} These disparities may, at least partially, be caused by differences in the local reimbursement of pulmonary rehabilitation services,³⁷ ranging from paying out of pocket by the patient up to full reimbursement by insurance, employer and/or government.³ This will complicate bench marking of key indicators of structure, process and performance, and, in turn, confuse quality control of existing and new pulmonary rehabilitation services.³⁸

HOME-BASED PULMONARY REHABILITATION

Home-based 'pulmonary rehabilitation' is emerging as a new format of pulmonary rehabilitation,³⁹ which mostly consist of a home-based exercise training programme (i.e. walking, stationary cycling and/or resistance exercises using body weight, resistance bands and/or water-filled bottles), education by providing a self-management manual and sometimes coaching using motivational interviewing. This approach, applying some of the core components of pulmonary rehabilitation, confers short-term improvements in the level of breathlessness, exercise tolerance and disease-specific quality of life, with no significant difference compared to outpatient pulmonary rehabilitation.³⁹ To date, however, it is not possible to exclude non-inferiority.⁴⁰

The development of home-based intervention is, at least in part, the result of (i) a lack of financial resources to start up new rehabilitation locations in

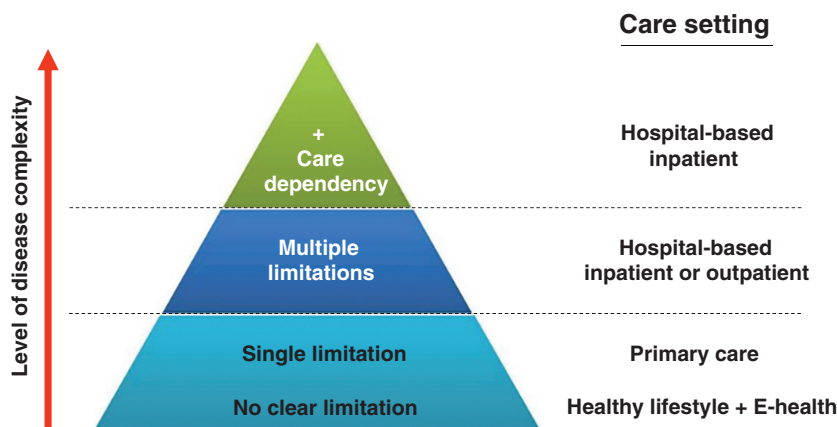


Figure 1 The most appropriate setting for pulmonary rehabilitation based on patient's level of disease complexity.

rural areas⁴¹; (ii) local healthcare policies⁴²; (iii) initiatives by local researchers/clinicians; (iv) the unwillingness of payers to expand the capacity of existing programmes; (v) a reduction of costs of healthcare in general, and pulmonary rehabilitation in particular; (vi) patient choice⁴³; and/or (vii) ignoring the complexity and heterogeneity in a subgroup of patients with high degree of unpredictability of the clinical course.⁴⁴

While the home-based approach seems worth pursuing in patients with a chronic respiratory disease who are not too complex, multiple questions remain unanswered. Is the training intensity during the home-based programme intense enough to improve exercise capacity in COPD patients with a mildly impaired exercise tolerance at the start of the intervention⁴⁵? Does an exercise-based intervention in the patient's home deal with the complexity that patients with chronic respiratory disease may experience? Is a home-based intervention also feasible, safe and effective in patients with chronic respiratory disease other than COPD? Does a home-based exercise training programme qualify as a pulmonary rehabilitation programme? Indeed, the term 'home-based pulmonary rehabilitation' seems erroneously chosen. A true comprehensive pulmonary rehabilitation programme is like a Swiss army knife. At first, a Swiss army knife looks just a simple pocket knife. However, if you look carefully, it is much more than just a knife and you have to be an expert to carefully apply all its features (Fig. 2). The same is true for pulmonary rehabilitation. At first, pulmonary rehabilitation seems just to be exercise training, providing some educational sessions and a self-management manual. However, based on comprehensive assessment at the start of the programme, physical, emotional and social treatable traits can be identified, which can be addressed by a dedicated, interdisciplinary pulmonary rehabilitation team using targeted therapies.⁴⁶ Here, we should never forget the wise words of Aristotle: 'The whole is greater than the sum of its parts'.

As stated before, the choice of treatment (monodisciplinary vs interdisciplinary) and the location of treatment (home- vs hospital-based) should be made on

well-defined criteria, and should not be determined by local limitations. To date, daily clinical practice is not organized in such way. Obviously, if the choice for a home-based exercise training is necessary due to lack of other settings and/or the preference of the patient, this seems much better than doing nothing.³⁹ However, it is appreciated that a home-based exercise training programme will not be able to cover all needs and preferences of patients with complex chronic respiratory disease and, in turn, causes a fragmentation of necessary interdisciplinary care. Indeed, the effects of a conventional, home-based exercise training programme on the performance of activities of daily life and daily symptoms beyond dyspnoea (i.e. anxiety, depression and fatigue) remain unknown,³⁹ while this is clearly shown following a comprehensive, hospital-based pulmonary rehabilitation programme.^{47,48} The home-based approach does also not allow to truly target the training interventions to the possibilities/limitations of each individual patient. The one-size-fits-all approach (i.e. a home-based walking programme) seems acceptable for patients with a mild degree of complexity. However, for patients with hypercapnia, hypoxaemia, very severe dyspnoea and/or recently hospitalized/frail patients,^{49,50} this approach seems to ignore many available possibilities, including but not limited to exercise training (on a stationary bicycle or treadmill, to really target and monitor the optimal training intensity⁵¹) combined with non-invasive ventilation with or without oxygen supplements^{52,53}; neuromuscular electrical stimulation for severely dyspnoeic and weakened patients²⁹; whole-body vibration⁵⁴; resistance training using adequate apparatus⁵⁵; etc.

MANAGEMENT FOR CHRONIC LUNG DISEASE IN PRIMARY CARE

The current trend is to move the disease management of patients with chronic respiratory disease more and more towards primary care and the home setting. However, timely referral by the general practitioner

Condition	Proposed management
→ Cachexia	→ Nutritional supplements / anabolic agents
→ Obesity	→ Diet and meal replacements
→ Exercise intolerance	→ Exercise training (+ pursed lips breathing)
→ Muscle weakness	→ Exercise training
→ Depression/anxiety	→ Cognitive behavioural therapy
→ Poor coping skills	→ Education + goal setting
→ Co-morbidities	→ Specific co-morbidity treatment
→ Physical inactivity	→ Physical activity coaching
	→ Supervised daily outdoor walks
→ Current smoking	→ Smoking cessation
→ Excessive mucus	→ Mucus evacuating techniques
→ Inspiratory muscle weakness	→ Inspiratory muscle training
→ Poor exacerbation management skills	→ Education + skills training
→ Poor inhalation technique	→ Education + skills training
→ Problematic ADL	→ Home adaptations and aids
	→ ADL training / energy conservation technology



Figure 2 The multitarget approach during pulmonary rehabilitation. ADL, activity of daily living.

(GP) to the next level of care (horizontally or vertically) is imperative. Accumulating evidence shows that there is still room for major improvement. To date, only a minority of outpatients with severe to very severe COPD attending an outpatient clinic are referred for respiratory primary care (i.e. nurse specialist (35%); physiotherapist (53%); and occupational therapist, dietician, social worker or psychologist (all <15%)) while they clearly are in need of such support and care. Indeed, fatigue was reported by 89% of the patients, while muscle weakness was reported by 75%; 47% of the patients had an abnormal low or obese BMI; 45% were dependent on personal care; 52% had a low mood and 85% of the patients had self-perceived mobility problems.⁵⁶

Upon referral by the GP to a hospital-based, outpatient consultation by a chest physician, 50% of the patients with COPD (mean forced expiratory volume in 1 s (FEV₁): 56% predicted) had clear exercise intolerance, physical inactivity and multiple exacerbations in the last 12 months.⁵⁷ These data suggest that GP-guided medical care to patients with COPD is insufficient to stabilize (or even improve) patients' physical, emotional and/or social condition. So, patients with mild to severe COPD can already enter the vicious dyspnoea-inactivity circle in the primary care setting, without being recognized.⁵⁸

WHAT DO PATIENTS WANT?

Home-based exercise training programmes are well perceived by patients with COPD. Besides the increased exercise capacity, patients report that the intervention is flexible and convenient, as it reduces travel burden, and training can be done at a suitable time.⁴³ Then again, starting the home-based intervention can be challenging due to the persistent inactive lifestyle; some patients report physical limitations that clearly limited their capability to perform walking exercises at home; and doing the same exercise each day is somewhat uninteresting.⁴³

So, walking programmes in the home-based setting seem feasible, safe and effective to increase exercise performance to some extent. Nevertheless, patients with chronic respiratory disease state that hospital-based pulmonary rehabilitation programmes are indispensable as (i) the social aspect of exercising together with other patients is anticipated as enjoyable; (ii) patients can learn from each other's experiences; (iii) the dedicated staff members quickly understand the patient; (iv) patients receive and provide emotional support from peers; and (v) the supervised setting was thought of as a safe environment.⁵⁹ So, besides the proposed stratification of patients based on the degree of complexity (Fig. 1), patients' preferences should also be added to the equation.

Self-referral to pulmonary rehabilitation is only possible in about one-third of the pulmonary rehabilitation programmes, and is more common in North America compared to Europe.³ Therefore, patients are still relying on the referral by healthcare professionals, who really have to start thinking about referral for an initial screening in patients with clear daily limitations.⁶⁰

Approximately two-fifths of patients with chronic respiratory disease stated that their healthcare provider had never told them about pulmonary rehabilitation or its benefits⁶¹. This explains, at least in part, that currently <2% of the patients with chronic respiratory disease are referred to some kind of rehabilitative intervention.³⁶

To conclude, patients and healthcare professionals have to combine the most appropriate pulmonary and extra-pulmonary targeted therapies, for patients with a chronic respiratory disease who are still symptomatic despite otherwise optimal medical therapy, aiming at relevant outcomes. Local circumstances may complicate this crucial endeavour.

The Authors

Professor Dr M.A.S. (1975) published >250 peer-reviewed articles mainly on pulmonary rehabilitation and physical inactivity in patients with chronic lung disease. He was the lead author on the 2013 ATS/ERS Statement on Pulmonary Rehabilitation; the ERS awarded him the ERS COPD Research Award in 2013; and he was elected Fellow of the ERS in 2016. Professor Dr E.F.M.W. (1953) published >700 peer-reviewed articles on extra-pulmonary treatable traits and the integrated care of complex patients with COPD. He is Head of the Department of Respiratory Medicine, Director of the Centre for Chronic Diseases at Maastricht University Medical Centre and Chairman of the Board of Directors of CIRO. He was elected Fellow of the ERS in 2014.

Abbreviations: ADL, Activity of daily living; ATS, American Thoracic Society; BMI, body mass index; ERS, European Respiratory Society; GP, general practitioner.

REFERENCES

- 1 Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, Hill K, Holland AE, Lareau SC, Man WD *et al.*; ATS/ERS Task Force on Pulmonary Rehabilitation. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am. J. Respir. Crit. Care Med.* 2013; **188**: e13–64.
- 2 Foo J, Landis SH, Maskell J, Oh YM, van der Molen T, Han MK, Mannino DM, Ichinose M, Punekar Y. Continuing to confront COPD international patient survey: economic impact of COPD in 12 countries. *PLoS One* 2016; **11**: e0152618.
- 3 Spruit MA, Pitta F, Garvey C, ZuWallack RL, Roberts CM, Collins EG, Goldstein R, McNamara R, Surpas P, Atsuyoshi K *et al.*; ERS Rehabilitation and Chronic Care, and Physiotherapists Scientific Groups; American Association of Cardiovascular and Pulmonary Rehabilitation; ATS Pulmonary Rehabilitation Assembly and the ERS COPD Audit team. Differences in content and organisational aspects of pulmonary rehabilitation programmes. *Eur. Respir. J.* 2014; **43**: 1326–37.
- 4 McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst. Rev.* 2015: CD003793.
- 5 Qaseem A, Wilt TJ, Weinberger SE, Hanania NA, Criner G, van der Molen T, Marciniuk DD, Denberg T, Schunemann H, Wedzicha W *et al.*; American College of Physicians; American College of Chest Physicians; American Thoracic Society; European Respiratory Society. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. *Ann. Intern. Med.* 2011; **155**: 179–91.

- 6 Augustin IML, Spruit MA, Houben-Wilke S, Franssen FME, Vanfleteren L, Gaffron S, Janssen DJA, Wouters EFM. The respiratory physiome: clustering based on a comprehensive lung function assessment in patients with COPD. *PLoS One* 2018; **13**: e0201593.
- 7 Machado FVC, Schneider LP, Fonseca J, Belo LF, Bonomo C, Morita AA, Furlanetto KC, Felcar JM, Rodrigues A, Franssen FME *et al.* Clinical impact of body composition phenotypes in patients with COPD: a retrospective analysis. *Eur. J. Clin. Nutr.* 2019; doi: 10.1038/s41430-019-0390-4. [Epub ahead of print].
- 8 Van Herck M, Spruit MA, Burtin C, Djamin R, Antons J, Goertz YMJ, Ebadi Z, Janssen DJA, Vercoelen JH, Peters JB *et al.* Fatigue is highly prevalent in patients with asthma and contributes to the burden of disease. *J. Clin. Med.* 2018; **7**: 471.
- 9 Houben-Wilke S, Janssen DJA, Franssen FME, Vanfleteren L, Wouters EFM, Spruit MA. Contribution of individual COPD assessment test (CAT) items to CAT total score and effects of pulmonary rehabilitation on CAT scores. *Health Qual. Life Outcomes* 2018; **16**: 205.
- 10 Nakken N, Spruit MA, van den Bogaart EHA, Crutzen R, Muris JWM, Wouters EFM, Janssen DJA. Identifying causes of perceptual differences in problematic activities of daily life between patients with COPD and proxies: a qualitative study. *Aust. Occup. Ther. J.* 2019; **66**: 44–51.
- 11 Goertz YMJ, Looijmans M, Prins JB, Janssen DJA, Thong MSY, Peters JB, Burtin C, Meertens-Kerris Y, Coors A, Muris JWM *et al.* Fatigue in patients with chronic obstructive pulmonary disease: protocol of the Dutch multicentre, longitudinal, observational FANTASIGUE study. *BMJ Open* 2018; **8**: e021745.
- 12 Liu WY, Spruit MA, Delbressine JM, Willems PJ, Franssen FME, Wouters EFM, Meijer K. Spatiotemporal gait characteristics in patients with COPD during the gait real-time analysis interactive lab-based 6-minute walk test. *PLoS One* 2017; **12**: e0190099.
- 13 Smid DE, Franssen FME, Gonik M, Miravittles M, Casanova C, Cosio BG, de Lucas-Ramos P, Marin JM, Martinez C, Mir I *et al.* Redefining cut-points for high symptom burden of the Global Initiative for Chronic Obstructive Lung Disease classification in 18,577 patients with chronic obstructive pulmonary disease. *J. Am. Med. Dir. Assoc.* 2017; **18**: 1097.e11–24.
- 14 McNamara RJ, Houben-Wilke S, Franssen FME, Smid DE, Vanfleteren L, Groenen MTJ, Uszko-Lencer N, Wouters EFM, Alison JA, Spruit MA. Determinants of functional, peak and endurance exercise capacity in people with chronic obstructive pulmonary disease. *Respir. Med.* 2018; **138**: 81–7.
- 15 Ofir D, Laveneziana P, Webb KA, Lam YM, O'Donnell DE. Mechanisms of dyspnea during cycle exercise in symptomatic patients with GOLD stage I chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* 2008; **177**: 622–9.
- 16 Elbehairy AF, Ciavaglia CE, Webb KA, Guenette JA, Jensen D, Mourad SM, Nader JA, O'Donnell DE; Canadian Respiratory Research Network. Pulmonary gas exchange abnormalities in mild chronic obstructive pulmonary disease. Implications for dyspnea and exercise intolerance. *Am. J. Respir. Crit. Care Med.* 2015; **191**: 1384–94.
- 17 Smid DE, Spruit MA, Houben-Wilke S, Muris JWM, Rohde GGU, Wouters EFM, Franssen FME. Burden of COPD in patients treated in different care settings in the Netherlands. *Respir. Med.* 2016; **118**: 76–83.
- 18 Augustin IML, Wouters EFM, Houben-Wilke S, Gaffron S, Janssen DJA, Franssen FME, Spruit MA. Comprehensive lung function assessment does not allow to infer response to pulmonary rehabilitation in patients with COPD. *J. Clin. Med.* 2018; **8**: pii: E27.
- 19 Spruit MA, Augustin IM, Vanfleteren LE, Janssen DJ, Gaffron S, Pennings HJ, Smeenk F, Pieters W, van den Bergh JJ, Michels AJ *et al.*; CIO+ Rehabilitation Network. Differential response to pulmonary rehabilitation in COPD: multidimensional profiling. *Eur. Respir. J.* 2015; **46**: 1625–35.
- 20 Vaes AW, Delbressine JML, Mesquita R, Goertz YMJ, Janssen DJA, Nakken N, Franssen FME, Vanfleteren L, Wouters EFM, Spruit MA. The impact of pulmonary rehabilitation on activities of daily living in patients with COPD. *J. Appl. Physiol.* (1985) 2018; doi: 10.1152/jappphysiol.00790.2018. [Epub ahead of print].
- 21 Vanfleteren MJ, Koopman M, Spruit MA, Pennings HJ, Smeenk F, Pieters W, van den Bergh JJ, Michels AJ, Wouters EF, Groenen MT *et al.* Effectiveness of pulmonary rehabilitation in patients with chronic obstructive pulmonary disease with different degrees of static lung hyperinflation. *Arch. Phys. Med. Rehabil.* 2018; **99**: 2279–86.e3.
- 22 Kamei T, Yamamoto Y, Kanamori T, Nakayama Y, Porter SE. Detection of early-stage changes in people with chronic diseases: a telephone monitoring-based telenursing feasibility study. *Nurs. Health Sci.* 2018; **20**: 313–22.
- 23 Donner CF, Raskin J, ZuWallack R, Nici L, Ambrosino N, Balbi B, Blackstock F, Casaburi R, Dreher M, Effing T *et al.* Incorporating telemedicine into the integrated care of the COPD patient a summary of an interdisciplinary workshop held in Stresa, Italy, 7–8 September 2017. *Respir. Med.* 2018; **143**: 91–102.
- 24 Buekers J, De Boever P, Vaes AW, Aerts JM, Wouters EFM, Spruit MA, Theunis J. Oxygen saturation measurements in telemonitoring of patients with COPD: a systematic review. *Expert Rev. Respir. Med.* 2018; **12**: 113–23.
- 25 Spruit MA, Singh SJ, Rochester CL, Greening NJ, Franssen FME, Pitta F, Troosters T, Nolan C, Vogiatzis I, Cline EM *et al.* Pulmonary rehabilitation for patients with COPD during and after an exacerbation-related hospitalisation: back to the future? *Eur. Respir. J.* 2018; **51**: 1701312.
- 26 Puhana MA, Gimeno-Santos E, Cates CJ, Troosters T. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst. Rev.* 2016; **12**: CD005305.
- 27 Koolen EH, van der Wees PJ, Westert GP, Dekhuijzen R, Heijdra YF, van 't Hul AJ. Evaluation of the COPDnet integrated care model in patients with COPD: the study protocol. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2018; **13**: 2237–44.
- 28 Koolen EH, van der Wees PJ, Westert GP, Dekhuijzen R, Heijdra YF, van 't Hul AJ. The COPDnet integrated care model. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2018; **13**: 2225–35.
- 29 Sillen MJ, Franssen FM, Delbressine JM, Vaes AW, Wouters EF, Spruit MA. Efficacy of lower-limb muscle training modalities in severely dyspnoeic individuals with COPD and quadriceps muscle weakness: results from the DICES trial. *Thorax* 2014; **69**: 525–31.
- 30 Hill K, Cavalheri V, Mathur S, Roig M, Janaudis-Ferreira T, Robles P, Dolmage TE, Goldstein R. Neuromuscular electrostimulation for adults with chronic obstructive pulmonary disease. *Cochrane Database Syst. Rev.* 2018; **5**: CD010821.
- 31 Gloeckl R, Andrianopoulos V, Stegmann A, Oversohl J, Schneeberger T, Schoenheit-Kenn U, Hitzl W, Dreher M, Koczulla AR, Kenn K. High-pressure non-invasive ventilation during exercise in COPD patients with chronic hypercapnic respiratory failure: a randomized, controlled, cross-over trial. *Respirology* 2018; **xxx**: xxx. <https://doi.org/10.1111/resp.13399>.
- 32 Vanfleteren LE, Spruit MA, Groenen M, Gaffron S, van Empel VP, Bruijnzeel PL, Rutten EP, Op 't Roodt J, Wouters EF, Franssen FM. Clusters of comorbidities based on validated objective measurements and systemic inflammation in patients with chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* 2013; **187**: 728–35.
- 33 Breyer MK, Spruit MA, Hanson CK, Franssen FM, Vanfleteren LE, Groenen MT, Bruijnzeel PL, Wouters EF, Rutten EP. Prevalence of metabolic syndrome in COPD patients and its consequences. *PLoS One* 2014; **9**: e98013.
- 34 Yohannes AM, Connolly MJ. Pulmonary rehabilitation programmes in the UK: a national representative survey. *Clin. Rehabil.* 2004; **18**: 444–9.
- 35 Brooks D, Sottana R, Bell B, Hanna M, Laframboise L, Selvanayagarajah S, Goldstein R. Characterization of pulmonary rehabilitation programs in Canada in 2005. *Can. Respir. J.* 2007; **14**: 87–92.
- 36 Wadell K, Janaudis Ferreira T, Arne M, Lisspers K, Stallberg B, Emtner M. Hospital-based pulmonary rehabilitation in patients

- with COPD in Sweden – a national survey. *Respir. Med.* 2013; **107**: 1195–200.
- 37 Janssens W, Corhay JL, Bogaerts P, Derom E, Frusch N, Dang DN, Kibanda J, Rutten D, Thyryon L, Troosters T *et al.* How resources determine pulmonary rehabilitation programs: a survey among Belgian chest physicians. *Chron. Respir. Dis.* 2019; **16**: 1479972318767732.
- 38 Camp PG, Cheung W. Are we delivering optimal pulmonary rehabilitation? The importance of quality indicators in evaluating clinical practice. *Phys. Ther.* 2018; **98**: 541–8.
- 39 Wuytack F, Devane D, Stovold E, McDonnell M, Casey M, McDonnell TJ, Gillespie P, Raymakers A, Lacasse Y, McCarthy B. Comparison of outpatient and home-based exercise training programmes for COPD: a systematic review and meta-analysis. *Respirology* 2018; **23**: 272–83.
- 40 Horton EJ, Mitchell KE, Johnson-Warrington V, Apps LD, Sewell L, Morgan M, Taylor RS, Singh SJ. Comparison of a structured home-based rehabilitation programme with conventional supervised pulmonary rehabilitation: a randomised non-inferiority trial. *Thorax* 2018; **73**: 29–36.
- 41 Holland AE, Mahal A, Hill CJ, Lee AL, Burge AT, Cox NS, Moore R, Nicolson C, O'Halloran P, Lahham A *et al.* Home-based rehabilitation for COPD using minimal resources: a randomised, controlled equivalence trial. *Thorax* 2017; **72**: 57–65.
- 42 Franssen FM, Rutten EP, Groenen MT, Vanfleteren LE, Wouters EF, Spruit MA. New reference values for body composition by bioelectrical impedance analysis in the general population: results from the UK Biobank. *J. Am. Med. Dir. Assoc.* 2014; **15**: 448.e1–6.
- 43 Lahham A, McDonald CF, Mahal A, Lee AL, Hill CJ, Burge AT, Cox NS, Moore R, Nicolson C, O'Halloran P *et al.* Home-based pulmonary rehabilitation for people with COPD: a qualitative study reporting the patient perspective. *Chron. Respir. Dis.* 2018; **15**: 123–30.
- 44 Houben-Wilke S, Augustin IM, Vercoulen JH, van Ranst D, Bij de Vaate E, Wempe JB, Spruit MA, Wouters EFM, Franssen FME. COPD stands for complex obstructive pulmonary disease. *Eur. Respir. Rev.* 2018; **27**: 180027.
- 45 Lahham A, McDonald CF, Cox NS, Rawlings S, Nichols A, Moore R, Liacos A, Holland AE (eds). The impact of pulmonary rehabilitation on people with mild chronic obstructive pulmonary disease: a randomised controlled trial. International Conference of the American Thoracic Society, San Diego, CA. 2018; https://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2018.197.1_MeetingAbstracts.A2154.
- 46 Wouters EF, Augustin IM. Process of pulmonary rehabilitation and program organization. *Eur. J. Phys. Rehabil. Med.* 2011; **47**: 475–82.
- 47 Rutten EP, Spruit MA, McDonald ML, Rennard S, Agusti A, Celli B, Miller BE, Crim C, Calverley PM, Hanson C *et al.* Continuous fat-free mass decline in COPD: fact or fiction? *Eur. Respir. J.* 2015; **46**: 1496–8.
- 48 Peters JB, Boer LM, Molema J, Heijdra YF, Prins JB, Vercoulen JH. Integral health status-based cluster analysis in moderate-severe COPD patients identifies three clinical phenotypes: relevant for treatment as usual and pulmonary rehabilitation. *Int. J. Behav. Med.* 2017; **24**: 571–83.
- 49 Marengoni A, Vetrano DL, Manes-Gravina E, Bernabei R, Onder G, Palmer K. The relationship between COPD and frailty: a systematic review and meta-analysis of observational studies. *Chest* 2018; **154**: 21–40.
- 50 Spruit MA, Gosselink R, Troosters T, Kasran A, Gayan-Ramirez G, Bogaerts P, Bouillon R, Decramer M. Muscle force during an acute exacerbation in hospitalised patients with COPD and its relationship with CXCL8 and IGF-I. *Thorax* 2003; **58**: 752–6.
- 51 Probst VS, Troosters T, Coosemans I, Spruit MA, Pitta Fde O, Decramer M, Gosselink R. Mechanisms of improvement in exercise capacity using a rollator in patients with COPD. *Chest* 2004; **126**: 1102–7.
- 52 Vitacca M, Ambrosino N. Non-invasive ventilation as an adjunct to exercise training in chronic ventilatory failure: a narrative review. *Respiration* 2019; **97**: 3–11.
- 53 Edvardsen A, Jarosch I, Grongstad A, Wiegand L, Gloeckl R, Kenn K, Spruit MA. A randomized cross-over trial on the direct effects of oxygen supplementation therapy using different devices on cycle endurance in hypoxemic patients with interstitial lung disease. *PLoS One* 2018; **13**: e0209069.
- 54 Gloeckl R, Heinzelmann I, Kenn K. Whole body vibration training in patients with COPD: a systematic review. *Chron. Respir. Dis.* 2015; **12**: 212–21.
- 55 Spruit MA, Gosselink R, Troosters T, De Paepe K, Decramer M. Resistance versus endurance training in patients with COPD and peripheral muscle weakness. *Eur. Respir. J.* 2002; **19**: 1072–8.
- 56 Janssens DJ, Spruit MA, Uszko-Lencer NH, Schols JM, Wouters EF. Symptoms, comorbidities, and health care in advanced chronic obstructive pulmonary disease or chronic heart failure. *J. Palliat. Med.* 2011; **14**: 735–43.
- 57 Koolen EH, Van Hees HW, Van Lummel RC, Dekhuijzen R, Djamin RS, Spruit MA, Van 't Hul AJ. Can do' versus 'do do': a novel concept in patients with chronic obstructive pulmonary disease. 2019; https://erj.ersjournals.com/content/52/suppl_62/PA5424.
- 58 Ramon MA, Ter Riet G, Carsin AE, Gimeno-Santos E, Agusti A, Anto JM, Donaire-Gonzalez D, Ferrer J, Rodriguez E, Rodriguez-Roisin R *et al.*; PAC-COPD Study Group. The dyspnoea-inactivity vicious circle in COPD: development and external validation of a conceptual model. *Eur. Respir. J.* 2018; **52**: pii: 1800079.
- 59 Fischer MJ, Scharloo M, Abbink JJ, Thijs-Van A, Rudolphus A, Snoei L, Weinman JA, Kaptein AA. Participation and drop-out in pulmonary rehabilitation: a qualitative analysis of the patient's perspective. *Clin. Rehabil.* 2007; **21**: 212–21.
- 60 Rochester CL, Vogiatzis I, Holland AE, Lareau SC, Marciniuk DD, Puhon MA, Spruit MA, Masefield S, Casaburi R, Clini EM *et al.*; ATS/ERS Task Force on Policy in Pulmonary Rehabilitation. An official American Thoracic Society/European Respiratory Society policy statement: enhancing implementation, use, and delivery of pulmonary rehabilitation. *Am. J. Respir. Crit. Care Med.* 2015; **192**: 1373–86.
- 61 Rochester CL, Vogiatzis I, Powell P, Masefield S, Spruit MA. Patients' perspective on pulmonary rehabilitation: experiences of European and American individuals with chronic respiratory diseases. *ERJ Open Res.* 2018; **4**: 00085-2018.