



Pulmonary rehabilitation

Martijn A. Spruit^{1,2}

Affiliations: ¹Dept of Research and Education, CIRO+, Center of Expertise for Chronic Organ Failure, Horn, The Netherlands. ²REVAL - Rehabilitation Research Center, BIOMED - Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt University, Diepenbeek, Belgium.

Correspondence: M.A. Spruit, Dept of Research and Education, CIRO+, Center of Expertise for Chronic Organ Failure, Hornerheide 1, 6085 NM Horn, the Netherlands. E-mail: martijnspruit@ciro-horn.nl

ABSTRACT Pulmonary rehabilitation is a comprehensive intervention designed to improve the physical and psychological condition of people with chronic respiratory disease and promote the long-term adherence to health-enhancing behaviours. During the 2013 European Respiratory Society Annual Congress in Barcelona, Spain, a Clinical Year in Review session was held focusing on the latest developments in pulmonary rehabilitation. This review summarises some of the main findings of peer-reviewed articles focusing on pulmonary rehabilitation that were published in the 12 months prior to the 2013 Annual Congress.



@ERSpublications

Pulmonary rehabilitation is an important part of the integrated care of patients with chronic respiratory diseases <http://ow.ly/rAr82>

Introduction

Pulmonary rehabilitation is a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education and behaviour change, which are designed to improve the physical and psychological condition of people with chronic respiratory disease and promote the long-term adherence to health-enhancing behaviours [1]. It is acknowledged as a core component of the integrated care of people with chronic respiratory disease [2]. During the 12 months prior to the European Respiratory Society Annual Congress 2013 in Barcelona, Spain, numerous new and clinically relevant peer-reviewed English language articles related to the research field of pulmonary rehabilitation were published [3–30]. This review summarises some of the main findings.

Physical activity and pulmonary rehabilitation

Patients with chronic obstructive pulmonary disease (COPD) are physically less active compared to their peers [31, 32], resulting in a loss of lower limb muscle mass and muscle function [33–36]. Indeed, approximately 40% of patients with COPD do not achieve the recommended quantity and/or quality of physical activity [37–39]. This strengthens the rationale for exercise-based pulmonary rehabilitation programmes in patients with COPD [40]. DONAIRE-GONZALEZ *et al.* [37] were the first to point out that patients with severe and very severe COPD perform physical activities in fewer and shorter bouts than those with mild and moderate airflow limitation. These findings provide the first insight into physical activity patterns during the day in patients with COPD, which can be of great value for occupational therapists during pulmonary rehabilitation. Obviously, validated activity monitors need to be used to assess the impact of pulmonary rehabilitation on physical activity in patients with COPD [19, 41]. In the future, we need to optimise pulmonary rehabilitation components to influence meaningful and sustainable behaviour change [1]. This includes further developing strategies and ways to translate gains in exercise capacity into increased physical activity. EGAN *et al.* [42] showed that short-term and long-term improvements in exercise

Received: Nov 05 2013 | Accepted: Nov 21 2013

Conflict of interest: None declared.

Provenance: Submitted article, peer reviewed.

Copyright ©ERS 2014. ERR articles are open access and distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 3.0.

capacity did not transfer into increased daily physical activity in patients with COPD, confirming previous findings [43]. Perhaps we also need to focus on behavioural and environmental factors. Indeed, health benefits, enjoyment, continuation of an active lifestyle and functional reasons have been identified by patients with COPD as the main reasons to be physically active; while the weather, health problems, and lack of intrinsic motivation were reasons to be sedentary [44].

Comorbidities and pulmonary rehabilitation

Various authors have reported positive effects of pulmonary rehabilitation on functional exercise performance and/or disease-specific health status in COPD patients with and without self-reported comorbidities at baseline [45, 46]. These authors also confirmed previous observations that comorbidities are present in about 50–60% of the patients with COPD entering pulmonary rehabilitation [47, 48]. Again, self-reported comorbidities were used for analyses [45–48], most probably causing an underestimation of the true prevalence of comorbidities. Indeed, VANFLETEREN *et al.* [49] reported a prevalence of one or more comorbidities based on validated objective measurements in 97% of the patients with COPD entering pulmonary rehabilitation. These authors were also the first to report the presence of five clusters of comorbidities in patients with COPD entering pulmonary rehabilitation: less comorbidity, cardiovascular, cachectic, metabolic, and psychological [49]. Interestingly, the degree of airflow limitation, the functional exercise performance and most biomarkers of systemic inflammation were comparable between clusters. Thus, comorbidities need to be objectified during the initial assessment of pulmonary rehabilitation. To date, it remains unknown whether and to what extent clusters of comorbidities affect the response to pulmonary rehabilitation in patients with COPD or even the minimal important difference. Moreover, future studies may want to consider choosing innovative/explanatory outcomes in addition to the more conventional outcomes, such as exercise performance and health status. For example, OLIVEIRA *et al.* [50] showed that dyspnoeic, non-hypercapnic patients with COPD and well-established chronic heart failure with reduced left ventricular ejection fraction (<40%) have impaired cerebral oxygenation during progressive exercise compared to their COPD peers without chronic heart failure. As the coexistence of COPD and chronic heart failure is highly prevalent in patients admitted to the hospital or entering pulmonary rehabilitation [51–53], these findings warrant further research.

MCNAMARA *et al.* [7] hypothesised that land-based exercise training may exacerbate existing physical comorbidities. Therefore, a randomised controlled trial was designed to compare the effects of water-based exercise training with those of land-based exercise training or a usual care control group in COPD patients with physical comorbidities, including musculoskeletal conditions, peripheral vascular disease, neurological conditions, or obesity with a body mass index $\geq 32 \text{ kg}\cdot\text{m}^{-2}$ [7]. Water-based exercise training was significantly more effective than land-based exercise training and the non-exercising control group in improving incremental and endurance shuttle walk distances, and improving aspects of quality of life in patients with COPD with physical comorbidities [7]. These data suggest that water-based training may be more beneficial for patients with COPD and physical comorbidities compared to land-based exercise training. However, baseline values of the exercise tests were dissimilar, and the water-based group trained at significantly higher mean dyspnoea and exertion scores compared to the land-based group. This may partially explain the observed differences. Finally, diagnosis of the physical comorbidity was based on medical referral, patient history and physical examination, which may have underestimated the true prevalence of comorbidities. Therefore, additional studies are warranted on the effects of water-based training in patients with COPD and musculoskeletal comorbidities.

Referral, attendance and adherence to pulmonary rehabilitation

Pulmonary rehabilitation during and directly following hospitalisation because of a COPD exacerbation has shown to be very beneficial and cost-effective for patients with COPD [54–56]. Nevertheless, poor referral and uptake rates for early outpatient pulmonary rehabilitation programmes following hospitalisation for COPD exacerbations occur throughout the world [57–60]. This may, at least in part, be due to a combination of barriers for patients and/or referring physicians, such as: low knowledge of pulmonary rehabilitation for patients with COPD; low knowledge of how to refer patients with COPD to pulmonary rehabilitation programmes; actual or anticipated access difficulties for patients with COPD; and physicians questioning the need to do more to promote exercise behaviour change in patients with COPD [58, 60].

The use of long-term oxygen therapy and living alone have been identified as independent predictors of poor attendance in patients with stable COPD, whereas current smoking, poor shuttle walk distance and hospitalisation are independent predictors of poor adherence to pulmonary rehabilitation [61]. Thus, future international policy statements should be developed to increase patient access to pulmonary rehabilitation, increase the capacity of pulmonary rehabilitation programmes, increase availability and amount of payer funding, and enhance knowledge and awareness of pulmonary rehabilitation among patients with chronic

respiratory disease, healthcare providers and payers. Moreover, we need to define phenotypes to identify responders and nonresponders to pulmonary rehabilitation to optimise the impact of pulmonary rehabilitation [62].

New exercise training modalities and pulmonary rehabilitation

Supervised exercise training is the cornerstone of pulmonary rehabilitation programmes in order to increase exercise performance [1, 63]. Nevertheless, new types of exercise training have been studied in patients with COPD, including high-intensity knee extensor training, T'ai chi, non-linear exercise training and neuromuscular electrical stimulation (NMES).

High-intensity knee extensor training

Most patients with COPD experience a ventilatory limitation during the performance of whole-body endurance exercise training [64]. Training of specific, smaller, lower limb muscle groups will reduce the ventilatory load [64–66] and, in turn, may increase training load and muscle adaptations [11]. BRØNSTAD *et al.* [12] studied the effects of 6 weeks of high-intensity interval aerobic knee extensor exercise training (three times per week) on muscle oxygen uptake and mitochondrial respiration of the vastus lateralis muscle in subjects with COPD. Peak power and maximal mitochondrial respiration in vastus lateralis muscle were restored, and were similar to those of healthy elderly control subjects [12]. Thus, local muscle training seems a valuable exercise training strategy in reversing muscle dysfunction in patients with COPD. However, the sample size of BRØNSTAD *et al.* [12] was rather low (n=7) and, in turn, needs corroboration.

T'ai chi

T'ai chi is a traditional Chinese form of conditioning exercise derived from martial arts. When practised correctly, T'ai chi is thought to strengthen the body's vital energy and enhance the passage of this energy throughout the body to confer its health promoting effects [67]. T'ai chi is very popular in healthy and diseased subjects as it may improve physical and emotional functioning [68–75]. In a randomised controlled trial, LEUNG *et al.* [8] compared the effects of Sun-style T'ai chi, which is well known for its smooth flowing movements [76], with usual care in 42 patients with COPD. A twice weekly, supervised Sun-style T'ai chi training regimen in combination with an unsupervised, home-based T'ai chi training programme (including a T'ai chi training booklet and DVD) on the remaining 5 days a week (30 min per day) for a total duration of 12 weeks improved quadriceps muscle strength, balance, incremental and endurance shuttle walk test, health status and mood status compared to the usual care control group [8]. Indeed, the minimal important differences for health status and functional exercise performance were exceeded following T'ai chi [77–79]. This may, at least in part, be due to the relatively high metabolic load during T'ai chi. Indeed, patients with COPD used ~63% of their peak aerobic capacity during a session of Sun-style T'ai chi, which is similar to the mean oxygen uptake during a session of lower limb resistance training [64, 65]. Recently, other forms of T'ai chi have also appeared to be beneficial for patients with COPD [80–82]. Therefore, T'ai chi may even be considered as a long-term maintenance training strategy, due to the fact it can be performed by patients in their home setting.

Non-linear periodised exercise training

Most conventional exercise training programmes that form part of pulmonary rehabilitation use non-varied, linear progressive protocols [83–87]. In contrast, athletes frequently vary exercise training variables (*e.g.* volume, intensity and number of repetitions) to maximise physical performance by avoiding training plateaus [88]. Indeed, the energy systems used during treadmill walking, stationary cycling or resistance training are matched to optimise the physiological adaptation. Until recently, a comparison between conventional linear exercise training and non-linear periodised exercise training had not been performed in patients with COPD. Nevertheless, KLIJN *et al.* [89] compared a 10-week conventional exercise training programme (*i.e.* resistance training and endurance training three times per week) with non-linear periodised exercise training in patients with very severe COPD. Non-linear exercise training was safe and improved the cycle endurance time to a greater extent compared to conventional exercise training in COPD patients with and without a normal baseline fat-free mass index. A similar pattern was found for the changes in health status. However, these patients also received other non-exercising interventions, which may have influenced these results to some extent. Therefore, non-linear exercise training seems beneficial for patients with very severe COPD. Whether and to what extent gains in exercise capacity will also translate into improved activities of daily life remains unknown. Moreover, long-term effects were not studied. The current findings do, however, emphasise that conventional exercise training schedules may not be optimal for patients with COPD.

Neuromuscular electrical stimulation

NMES involves the application of an electrical current through electrodes placed on the skin over the targeted muscles, thereby depolarising motor neurons and, in turn, inducing skeletal muscle contractions [90]. NMES does not evoke dyspnoea in patients with very severe COPD [66]. Therefore, NMES may be of clinical interest to patients with COPD who are admitted to the hospital with an exacerbation. Indeed, patients with COPD are physically less active during a hospital admission [91, 92] and, in turn, experience a further decline in quadriceps muscle function [93]. GIAVEDONI *et al.* [94] presented some pilot data on the feasibility, safety and efficacy of 14 sessions of high-frequency NMES during a COPD exacerbation. NMES was safe, well-tolerated and improved quadriceps muscle strength compared to the nonstimulated control leg [94]. In another pilot study, CHAPLIN *et al.* [95] compared effects of high-frequency NMES (50 Hz) with low-frequency NMES (35 Hz) in patients with COPD admitted to hospital with an exacerbation. Isometric quadriceps muscle strength increased in both groups, while the endurance shuttle walk distance tended to improve significantly compared to baseline. Both studies support previous findings that NMES is effective in counteracting quadriceps muscle dysfunction [96]. To date, the use of NMES in daily clinical practice seems rather limited [97]. This may partly be due to the fact that the optimal NMES frequency remains currently unknown in patients with COPD. Nevertheless, based on the currently available evidence [1, 90], NMES should be considered for use in early rehabilitation of patients with COPD admitted to the hospital [1].

Pulmonary rehabilitation in chronic respiratory disease other than COPD

Most pulmonary rehabilitation programmes enrol patients with COPD [97]. In addition, patients with other types of chronic respiratory disease are considered for comprehensive pulmonary rehabilitation programmes, as these patients also seem to benefit [1, 98, 99]. Indeed, patients with chronic respiratory disease other than COPD also suffer from daily symptoms, muscle weakness, exercise intolerance, impaired mood status, poor quality of life and physical inactivity, despite optimal medical treatment [100–106]. Most of the new studies confirm the positive effects of exercise-based pulmonary rehabilitation in patients with nonsmall cell lung cancer (pre-/post-lung resection) [107–117], chronic respiratory failure due to kyphoscoliosis [118], pre-/post-lung transplantation [119–122], cystic fibrosis [123], bronchiectasis [124], severe respiratory failure receiving extracorporeal membrane oxygenation [125, 126], interstitial lung disease [6, 127–129], and pulmonary arterial hypertension [130–132]. Existing COPD pulmonary rehabilitation programmes can be adapted to the particular needs of patients with chronic respiratory disease other than COPD, in particular the non-exercising parts [30]. Unfortunately, the referral rates for pulmonary rehabilitation for these patients are still poor due to various barriers [133]. For example, NWOSU *et al.* [134] identified a lack of knowledge of services or referral mechanisms, waiting lists, inadequate rehabilitation services, and the perception that patients do not want rehabilitation as the main barriers for referral of lung cancer patients to pulmonary rehabilitation. Further research in this field is necessary [135].

Novel targets/outcomes in pulmonary rehabilitation

Quality of life, 6-min walk test and dyspnoea have been identified as the three most important outcomes of pulmonary rehabilitation [97]. Nevertheless, several other outcomes have been used to evaluate the efficacy of pulmonary rehabilitation [1], including health transitions, advance care planning and balance.

Health transitions

HALDING *et al.* [136] used qualitative outcomes to evaluate the effects of pulmonary rehabilitation in patients with COPD. Using interviews, 18 patients with COPD reported that participation in pulmonary rehabilitation was perceived as a time of increasing awareness of opportunities for health and well-being with strengthened hope [136]. Thus, pulmonary rehabilitation promotes significant behavioural changes towards health promotion [137].

Indeed, patients undergoing pulmonary rehabilitation experience a complex health behaviour change process [138]. Healthcare professionals need to guide patients through this process by applying an autonomy supportive counselling style, teaching and training self-management skills, and by providing patient-tailored advice [138].

Advance care planning

Advance care planning is the process whereby patients, in consultation with healthcare professionals, family members and significant others, make individual decisions about their future healthcare, should they become incapable of participating in medical treatment decisions [139]. Advance care planning, taking into account the burden of treatment, outcome of treatment and likelihood of outcome, has an important role in patients with severe to very severe chronic respiratory disease [140, 141]. However, physicians rarely discuss prognosis, dying and palliative care [141]; thus, the quality of patient–physician end-of-life care

communication needs to improve. Inclusion of an advance care planning information session in pulmonary rehabilitation and/or maintenance programmes could support a practical solution. BURGE *et al.* [142] studied the introduction of a structured group advance care planning information session from the perspective of participants in pulmonary rehabilitation and maintenance programmes. Only 24% of the patients had previously heard of advance care planning. Most patients appreciated the advance care planning information session and thought pulmonary rehabilitation was an appropriate setting. Therefore, inclusion of advance care planning education into existing pulmonary rehabilitation and maintenance programmes for people with chronic respiratory disease should be contemplated [29].

Balance

Patients with COPD may suffer from a disturbed balance [143] and, in turn, a higher susceptibility to falling [144, 145]. LEUNG *et al.* [8] reported increased balance in patients with COPD following 12 weeks of T'ai chi compared to a non-exercising control group. BEAUCHAMP *et al.* [146] randomly assigned patients with COPD to pulmonary rehabilitation with or without specific balance training, consisting of exercises focusing on stance, transitions, gait, and functional strength. Scores on the Berg Balance Scale and the Balance Evaluation Systems Test improved significantly compared to the control group, while the Activities-Specific Balance Confidence scale did not show group differences [146]. Therefore, balance training as part of pulmonary rehabilitation seems feasible and effective in patients with COPD. Nevertheless, future studies need to assess the long-term effects of balance training on the risk of falling and fractures. Moreover, the optimal outcome to assess balance remains to be determined, as postural control and fear of falling can be assessed using various outcomes and tools [147]. The Berg Balance Scale, the Short Physical Performance Battery, and the Activities-Specific Balance Confidence scale are the most frequently used instruments to assess postural control and fear of falling [147]. Nevertheless, subtle gait changes that have previously been related to fall risk are not always captured by these subjective assessments. Therefore, accelerometry based gait analysis should be considered as an additional objective approach to screen patients with COPD at risk for falling [148].

Conclusion

Between September 2012 and September 2013, numerous peer-reviewed studies have been published focusing on the multiple aspects related to pulmonary rehabilitation. Most of these studies confirm the clinical importance of pulmonary rehabilitation as part of the integrated care of patients with chronic respiratory diseases.

References

- 1 Spruit MA, Singh SJ, Garvey C, *et al.* 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–e64.
- 2 Nici L, ZuWallack R. An official American Thoracic Society workshop report: the integrated care of the COPD patient. *Proc Am Thorac Soc* 2012; 9: 9–18.
- 3 Puhan MA, Siebeling L, Zoller M, *et al.* Simple functional performance tests and mortality in COPD. *Eur Respir J* 2013; 42: 956–963.
- 4 Blanco I, Santos S, Gea J, *et al.* Sildenafil to improve respiratory rehabilitation outcomes in COPD: a controlled trial. *Eur Respir J* 2013; 42: 982–992.
- 5 Marvisi M, Herth FJ, Ley S, *et al.* Selected clinical highlights from the 2012 ERS congress in Vienna. *Eur Respir J* 2013; 41: 1219–1227.
- 6 Huppmann P, Sczepanski B, Boensch M, *et al.* Effects of inpatient pulmonary rehabilitation in patients with interstitial lung disease. *Eur Respir J* 2013; 42: 444–453.
- 7 McNamara RJ, McKeough ZJ, McKenzie DK, *et al.* Water-based exercise in COPD with physical comorbidities: a randomised controlled trial. *Eur Respir J* 2013; 41: 1284–1291.
- 8 Leung RW, McKeough ZJ, Peters MJ, *et al.* Short-form Sun-style t'ai chi as an exercise training modality in people with COPD. *Eur Respir J* 2013; 41: 1051–1057.
- 9 Gouzi F, Préfaut C, Abdellaoui A, *et al.* Blunted muscle angiogenic training-response in COPD patients *versus* sedentary controls. *Eur Respir J* 2013; 41: 806–814.
- 10 Paddison JS, Effing TW, Quinn S, *et al.* Fatigue in COPD: association with functional status and hospitalisations. *Eur Respir J* 2013; 41: 565–570.
- 11 Lazaar AL, Greenhaff PL. Impaired muscle mitochondrial density and/or function: a COPD-specific mitochondrialopathy or simply deconditioning? *Eur Respir J* 2012; 40: 1070–1071.
- 12 Brønstad E, Rognmo O, Tjonna AE, *et al.* High-intensity knee extensor training restores skeletal muscle function in COPD patients. *Eur Respir J* 2012; 40: 1130–1136.
- 13 Warnier MJ, van Riet EE, Rutten FH, *et al.* Smoking cessation strategies in patients with COPD. *Eur Respir J* 2013; 41: 727–734.
- 14 Kon SS, Patel MS, Canavan JL, *et al.* Reliability and validity of 4-metre gait speed in COPD. *Eur Respir J* 2013; 42: 333–340.
- 15 Queiroga F Jr, Nunes M, Meda E, *et al.* Exercise tolerance with helium-hyperoxia *versus* hyperoxia in hypoxaemic patients with COPD. *Eur Respir J* 2013; 42: 362–370.
- 16 Laveneziana P, Garcia G, Joureau B, *et al.* Dynamic respiratory mechanics and exertional dyspnoea in pulmonary arterial hypertension. *Eur Respir J* 2013; 41: 578–587.

- 17 Hilde JM, Skjørten I, Hansteen V, *et al.* Haemodynamic responses to exercise in patients with COPD. *Eur Respir J* 2013; 41: 1031–1041.
- 18 Jackson AS, Shrikrishna D, Kelly JL, *et al.* Vitamin D and skeletal muscle strength and endurance in COPD. *Eur Respir J* 2013; 41: 309–316.
- 19 Rabinovich RA, Louvaris Z, Raste Y, *et al.* Validity of physical activity monitors during daily life in patients with COPD. *Eur Respir J* 2013; 42: 1205–1215.
- 20 Vogiatzis I, Louvaris Z, Habazettl H, *et al.* Cerebral cortex oxygen delivery and exercise limitation in patients with COPD. *Eur Respir J* 2013; 41: 295–301.
- 21 Spruit MA, Polkey MI, Celli B, *et al.* Predicting outcomes from 6-minute walk distance in chronic obstructive pulmonary disease. *J Am Med Dir Assoc* 2012; 13: 291–297.
- 22 Vaes AW, Cheung A, Atakhorrami M, *et al.* Effect of ‘activity monitor-based’ counseling on physical activity and health-related outcomes in patients with chronic diseases: a systematic review and meta-analysis. *Ann Med* 2013; 45: 397–412.
- 23 Fermoselle C, Rabinovich R, Ausín P, *et al.* Does oxidative stress modulate limb muscle atrophy in severe COPD patients? *Eur Respir J* 2012; 40: 851–862.
- 24 Garvey C, Spruit MA, Hill K, *et al.* International COPD Coalition Column: pulmonary rehabilitation-reaching out to our international community. *J Thorac Dis* 2013; 5: 343–348.
- 25 Stoilkova A, Janssen DJ, Franssen FM, *et al.* Coping styles in patients with COPD before and after pulmonary rehabilitation. *Respir Med* 2013; 107: 825–833.
- 26 Stoilkova A, Wouters EF, Spruit MA, *et al.* The relationship between coping styles and clinical outcomes in patients with COPD entering pulmonary rehabilitation. *COPD* 2013; 10: 316–323.
- 27 Gloeckl R, Marinov B, Pitta F. Practical recommendations for exercise training in patients with COPD. *Eur Respir Rev* 2013; 22: 178–186.
- 28 Hill K, Vogiatzis I, Burtin C. The importance of components of pulmonary rehabilitation, other than exercise training, in COPD. *Eur Respir Rev* 2013; 22: 405–413.
- 29 Stoilkova A, Janssen DJ, Wouters EF. Educational programmes in COPD management interventions: a systematic review. *Respir Med* 2013; 107: 1637–1650.
- 30 Holland AE, Wadell K, Spruit MA. How to adapt the pulmonary rehabilitation programme to patients with chronic respiratory disease other than COPD. *Eur Respir Rev* 2013; 23: 577–586.
- 31 Waschki B, Spruit MA, Watz H, *et al.* Physical activity monitoring in COPD: compliance and associations with clinical characteristics in a multicenter study. *Respir Med* 2012; 106: 522–530.
- 32 Van Remoortel H, Hornikx M, Demeyer H, *et al.* Daily physical activity in subjects with newly diagnosed COPD. *Thorax* 2013; 68: 962–963.
- 33 Natanek SA, Gosker HR, Slot IG, *et al.* Pathways associated with reduced quadriceps oxidative fibres and endurance in COPD. *Eur Respir J* 2013; 41: 1275–1283.
- 34 Shrikrishna D, Patel M, Tanner RJ, *et al.* Quadriceps wasting and physical inactivity in patients with COPD. *Eur Respir J* 2012; 40: 1115–1122.
- 35 Seymour JM, Spruit MA, Hopkinson NS, *et al.* The prevalence of quadriceps weakness in COPD and the relationship with disease severity. *Eur Respir J* 2010; 36: 81–88.
- 36 Carrai R, Scano G, Gigliotti F, *et al.* Prevalence of limb muscle dysfunction in patients with chronic obstructive pulmonary disease admitted to a pulmonary rehabilitation centre. *Clin Neurophysiol* 2012; 123: 2306–2311.
- 37 Donaire-Gonzalez D, Gimeno-Santos E, Balcells E, *et al.* Physical activity in COPD patients: patterns and bouts. *Eur Respir J* 2013; 42: 993–1002.
- 38 Hernandez NA, Sant’Anna T, Furlanetto K, *et al.* Which is the variable of physical activity monitoring that better correlates with functional exercise capacity in COPD? *Eur Respir J* 2013; 42: Suppl. 57, 1983s.
- 39 Hernandez NA, de Castro Teixeira D, Probst VS, *et al.* Profile of the level of physical activity in the daily lives of patients with COPD in Brazil. *J Bras Pneumol* 2009; 35: 949–956.
- 40 Spruit MA, Wouters EF. New modalities of pulmonary rehabilitation in patients with chronic obstructive pulmonary disease. *Sports Med* 2007; 37: 501–518.
- 41 Annegarn J, Spruit MA, Uszko-Lencer NH, *et al.* Objective physical activity assessment in patients with chronic organ failure: a validation study of a new single-unit activity monitor. *Arch Phys Med Rehabil* 2011; 92: 1852–1857.
- 42 Egan C, Deering BM, Blake C, *et al.* Short term and long term effects of pulmonary rehabilitation on physical activity in COPD. *Respir Med* 2012; 106: 1671–1679.
- 43 Ng LWC, Mackney J, Jenkins S, *et al.* Does exercise training change physical activity in people with COPD? A systematic review and meta-analysis. *Chron Respir Dis* 2012; 9: 17–26.
- 44 Hartman JE, ten Hacken NH, Boezen HM, *et al.* Self-efficacy for physical activity and insight into its benefits are modifiable factors associated with physical activity in people with COPD: a mixed-methods study. *J Physiother* 2013; 59: 117–124.
- 45 Walsh JR, McKeough ZJ, Morris NR, *et al.* Metabolic disease and participant age are independent predictors of response to pulmonary rehabilitation. *J Cardiopulm Rehabil Prev* 2013; 33: 249–256.
- 46 Carreiro A, Santos J, Rodrigues F. Impact of comorbidities in pulmonary rehabilitation outcomes in patients with chronic obstructive pulmonary disease. *Rev Port Pneumol* 2013; 19: 106–113.
- 47 Crisafulli E, Costi S, Luppi F, *et al.* Role of comorbidities in a cohort of patients with COPD undergoing pulmonary rehabilitation. *Thorax* 2008; 63: 487–492.
- 48 Crisafulli E, Gorgone P, Vagaggini B, *et al.* Efficacy of standard rehabilitation in COPD outpatients with comorbidities. *Eur Respir J* 2010; 36: 1042–1048.
- 49 Vanfleteren LE, Spruit MA, Groenen M, *et al.* 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: 728–735.
- 50 Oliveira MF, Arbex F, Alencar MC, *et al.* Heart failure impairs cerebral oxygenation during exercise in patients with COPD. *Eur Respir J* 2013; 42: 1423–1426.
- 51 Freixa X, Portillo K, Paré C, *et al.* Echocardiographic abnormalities in patients with COPD at their first hospital admission. *Eur Respir J* 2013; 41: 784–791.
- 52 Kawut SM. COPD: CardioPulmonary Disease? *Eur Respir J* 2013; 41: 1241–1243.

- 53 Wilke S, Spruit MA, Otkinska M, *et al.* Echocardiographic abnormalities in patients with COPD entering pulmonary rehabilitation. *Eur Respir J* 2013; 42: Suppl. 57, 4656s.
- 54 Puhan MA, Gimeno-Santos E, Scharplatz M, *et al.* Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2011; 5: CD005305.
- 55 Man WD, Polkey MI, Donaldson N, *et al.* Community pulmonary rehabilitation after hospitalisation for acute exacerbations of chronic obstructive pulmonary disease: randomised controlled study. *BMJ* 2004; 329: 1209.
- 56 Revitt O, Sewell L, Morgan MD, *et al.* A short out-patient pulmonary rehabilitation programme reduces readmission following a hospitalisation for an exacerbation of COPD. *Respirology* 2013; 18: 1063–1068.
- 57 Jones SE, Green SA, Clark AL, *et al.* Pulmonary rehabilitation following hospitalisation for acute exacerbation of COPD: referrals, uptake and adherence. *Thorax* 2013 [In press DOI: 10.1136/thoraxjnl-2013-204227].
- 58 Johnston K, Grimmer-Somers K, Young M, *et al.* Which chronic obstructive pulmonary disease care recommendations have low implementation and why? A pilot study. *BMC Res Notes* 2012; 5: 652.
- 59 Johnston K, Young M, Grimmer K, *et al.* Frequency of referral to and attendance at a pulmonary rehabilitation program amongst patients admitted to a tertiary hospital with chronic obstructive pulmonary disease. *Respirology* 2013; 18: 1089–1094.
- 60 Johnston KN, Young M, Grimmer KA, *et al.* Barriers to, and facilitators for, referral to pulmonary rehabilitation in COPD patients from the perspective of Australian general practitioners: a qualitative study. *Prim Care Respir J* 2013; 22: 319–324.
- 61 Hayton C, Clark A, Olive S, *et al.* Barriers to pulmonary rehabilitation: characteristics that predict patient attendance and adherence. *Respir Med* 2013; 107: 401–407.
- 62 Walsh JR, McKeough ZJ, Morris NR, *et al.* Performance-based criteria are used in participant selection for pulmonary rehabilitation programs. *Aust Health Rev* 2013; 37: 331–336.
- 63 Wadell K, Janaudis Ferreira T, Arne M, *et al.* Hospital-based pulmonary rehabilitation in patients with COPD in Sweden – a national survey. *Respir Med* 2013; 107: 1195–1200.
- 64 Probst VS, Troosters T, Pitta F, *et al.* Cardiopulmonary stress during exercise training in patients with COPD. *Eur Respir J* 2006; 27: 1110–1118.
- 65 Sillen MJ, Janssen PP, Akkermans MA, *et al.* The metabolic response during resistance training and neuromuscular electrical stimulation (NMES) in patients with COPD, a pilot study. *Respir Med* 2008; 102: 786–789.
- 66 Sillen MJ, Wouters EF, Franssen FM, *et al.* Oxygen uptake, ventilation, and symptoms during low-frequency versus high-frequency NMES in COPD: a pilot study. *Lung* 2011; 189: 21–26.
- 67 Spruit MA, Polkey MI. Tai chi for individuals with COPD: an ancient wisdom for a 21st century disease? *Eur Respir J* 2013; 41: 1005–1007.
- 68 Blake H, Hawley H. Effects of Tai Chi exercise on physical and psychological health of older people. *Curr Aging Sci* 2012; 5: 19–27.
- 69 Wang C, Schmid CH, Rones R, *et al.* A randomized trial of tai chi for fibromyalgia. *N Engl J Med* 2010; 363: 743–754.
- 70 Li F, Harmer P, Fitzgerald K, *et al.* Tai chi and postural stability in patients with Parkinson's disease. *N Engl J Med* 2012; 366: 511–519.
- 71 Hochberg MC, Altman RD, April KT, *et al.* American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken)* 2012; 64: 465–474.
- 72 Chen M, He M, Min X, *et al.* Different physical activity subtypes and risk of metabolic syndrome in middle-aged and older Chinese people. *PloS One* 2013; 8: e53258.
- 73 Pan L, Yan J, Guo Y. Effects of Tai Chi training on exercise capacity and quality of life in patients with chronic heart failure: a meta-analysis. *Eur J Heart Fail* 2013; 15: 316–323.
- 74 Chi I, Jordan-Marsh M, Guo M, *et al.* Tai chi and reduction of depressive symptoms for older adults: a meta-analysis of randomized trials. *Geriatr Gerontol Int* 2013; 13: 3–12.
- 75 Lu X, Hui-Chan CW, Tsang WW. Effects of Tai Chi training on arterial compliance and muscle strength in female seniors: a randomized clinical trial. *Eur J Prev Cardiol* 2013; 20: 238–245.
- 76 Wikipedia. Sun-style tai chi ch'uan. http://en.wikipedia.org/wiki/Sun-style_tai_chi_ch'uan Date last updated: December 8, 2013. Date last accessed: September 18, 2013.
- 77 Pepin V, Laviolette L, Brouillard C, *et al.* Significance of changes in endurance shuttle walking performance. *Thorax* 2011; 66: 115–120.
- 78 Singh SJ, Jones PW, Evans R, *et al.* Minimum clinically important improvement for the incremental shuttle walking test. *Thorax* 2008; 63: 775–777.
- 79 Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertain the minimal clinically important difference. *Control Clin Trials* 1989; 10: 407–415.
- 80 Chan AW, Lee A, Suen LK, *et al.* Tai chi Qigong improves lung functions and activity tolerance in COPD clients: a single blind, randomized controlled trial. *Complement Ther Med* 2011; 19: 3–11.
- 81 Chan AW, Lee A, Suen LK, *et al.* Effectiveness of a Tai chi Qigong program in promoting health-related quality of life and perceived social support in chronic obstructive pulmonary disease clients. *Qual Life Res* 2010; 19: 653–664.
- 82 Yan JH, Guo YZ, Yao HM, *et al.* Effects of Tai Chi in patients with chronic obstructive pulmonary disease: preliminary evidence. *PloS One* 2013; 8: e61806.
- 83 Spruit MA, Gosselink R, Troosters T, *et al.* Resistance versus endurance training in patients with COPD and peripheral muscle weakness. *Eur Respir J* 2002; 19: 1072–1078.
- 84 Spruit MA, Gosselink R, Troosters T, *et al.* Low-grade systemic inflammation and the response to exercise training in patients with advanced COPD. *Chest* 2005; 128: 3183–3190.
- 85 Spruit MA, Troosters T, Trappenburg JC, *et al.* Exercise training during rehabilitation of patients with COPD: a current perspective. *Patient Educ Couns* 2004; 52: 243–248.
- 86 Vogiatzis I, Nanas S, Roussos C. Interval training as an alternative modality to continuous exercise in patients with COPD. *Eur Respir J* 2002; 20: 12–19.
- 87 Vogiatzis I, Simoes DC, Stratakos G, *et al.* Effect of pulmonary rehabilitation on muscle remodelling in cachectic patients with COPD. *Eur Respir J* 2010; 36: 301–310.
- 88 American College of Sports Medicine. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 2009; 41: 687–708.

- 89 Klijn P, van Keimpema A, Legemaat M, *et al.* Nonlinear exercise training in advanced COPD is superior to traditional exercise training. A randomized trial. *Am J Respir Crit Care Med* 2013; 188: 193–200.
- 90 Sillen MJ, Speksnijder CM, Eterman RM, *et al.* Effects of neuromuscular electrical stimulation of muscles of ambulation in patients with chronic heart failure or COPD: a systematic review of the English-language literature. *Chest* 2009; 136: 44–61.
- 91 Pitta F, Troosters T, Probst VS, *et al.* Physical activity and hospitalization for exacerbation of COPD. *Chest* 2006; 129: 536–544.
- 92 Borges RC, Carvalho CR. Physical activity in daily life in Brazilian COPD patients during and after exacerbation. *COPD* 2012; 9: 596–602.
- 93 Spruit MA, Gosselink R, Troosters T, *et al.* Muscle force during an acute exacerbation in hospitalised patients with COPD and its relationship with CXCL8 and IGF-I. *Thorax* 2003; 58: 752–756.
- 94 Gavedoni S, Deans A, McCaughey P, *et al.* Neuromuscular electrical stimulation prevents muscle function deterioration in exacerbated COPD: a pilot study. *Respir Med* 2012; 106: 1429–1434.
- 95 Chaplin EJ, Houchen L, Greening NJ, *et al.* Neuromuscular stimulation of quadriceps in patients hospitalised during an exacerbation of COPD: a comparison of low (35 Hz) and high (50 Hz) frequencies. *Physiother Res Int* 2013; 18: 148–156.
- 96 Abdellaoui A, Préfaut C, Gouzi F, *et al.* Skeletal muscle effects of electrostimulation after COPD exacerbation: a pilot study. *Eur Respir J* 2011; 38: 781–788.
- 97 Spruit MA, Pitta F, Garvey C, *et al.* Differences in content and organizational aspects of pulmonary rehabilitation programs. *Eur Respir J* 2013 [In press DOI: 10.1183/09031936.00145613].
- 98 Güell MR, Cejudo P, Rodríguez-Trigo G, *et al.* Standards for quality care in respiratory rehabilitation in patients with chronic pulmonary disease. *Arch Bronconeumol* 2012; 48: 396–404.
- 99 Kon SS, Clark AL, Dilaver D, *et al.* Response of the COPD assessment test to pulmonary rehabilitation in unselected chronic respiratory disease. *Respirology* 2013; 18: 974–977.
- 100 Pugh ME, Buchowski MS, Robbins IM, *et al.* Physical activity limitation as measured by accelerometry in pulmonary arterial hypertension. *Chest* 2012; 142: 1391–1398.
- 101 Fox BD, Langleben D, Hirsch A, *et al.* Step climbing capacity in patients with pulmonary hypertension. *Clin Res Cardiol* 2013; 102: 51–61.
- 102 Watanabe F, Taniguchi H, Sakamoto K, *et al.* Quadriceps weakness contributes to exercise capacity in nonspecific interstitial pneumonia. *Respir Med* 2013; 107: 622–628.
- 103 Marcellis RG, Lenssen AF, Kleynen S, *et al.* Exercise capacity, muscle strength, and fatigue in sarcoidosis: a follow-up study. *Lung* 2013; 191: 247–256.
- 104 Walsh JR, Chambers DC, Davis RJ, *et al.* Impaired exercise capacity after lung transplantation is related to delayed recovery of muscle strength. *Clin Transplant* 2013; 27: E504–E511.
- 105 Akhtar AA, Ali MA, Smith RP. Depression in patients with idiopathic pulmonary fibrosis. *Chron Respir Dis* 2013; 10: 127–133.
- 106 Yilmaz E, Özalevli S, Ersöz H, *et al.* Comparison of health-related quality of life and exercise capacity according to stages in patients with non-small cell lung cancer. *Tuberk Toraks* 2013; 61: 131–139.
- 107 Hwang CL, Yu CJ, Shih JY, *et al.* Effects of exercise training on exercise capacity in patients with non-small cell lung cancer receiving targeted therapy. *Support Care Cancer* 2012; 20: 3169–3177.
- 108 Divisi D, Di Francesco C, Di Leonardo G, *et al.* Preoperative pulmonary rehabilitation in patients with lung cancer and chronic obstructive pulmonary disease. *Eur J Cardiothorac Surg* 2013; 43: 293–296.
- 109 Morano MT, Araújo AS, Nascimento FB, *et al.* Preoperative pulmonary rehabilitation versus chest physical therapy in patients undergoing lung cancer resection: a pilot randomized controlled trial. *Arch Phys Med Rehabil* 2013; 94: 53–58.
- 110 Schmidt-Hansen M, Page R, Hasler E. The effect of preoperative smoking cessation or preoperative pulmonary rehabilitation on outcomes after lung cancer surgery: a systematic review. *Clin Lung Cancer* 2013; 14: 96–102.
- 111 Stigt JA, Uil SM, van Riesen SJ, *et al.* A randomized controlled trial of postthoracotomy pulmonary rehabilitation in patients with resectable lung cancer. *J Thorac Oncol* 2013; 8: 214–221.
- 112 Vandenbos F, Fontas É, Dunais B, *et al.* Intérêt de la réhabilitation respiratoire après résection pulmonaire pour tumeur [Pulmonary rehabilitation after lung resection for tumor – a feasibility study]. *Rev Mal Respir* 2013; 30: 56–61.
- 113 Hoffman AJ, Brintnall RA, Brown JK, *et al.* Virtual reality bringing a new reality to post-thoracotomy lung cancer patients via a home-based exercise intervention targeting fatigue while undergoing adjuvant treatment. *Cancer Nurs* 2014; 37: 23–33.
- 114 Harada H, Yamashita Y, Misumi K, *et al.* Multidisciplinary team-based approach for comprehensive preoperative pulmonary rehabilitation including intensive nutritional support for lung cancer patients. *PloS One* 2013; 8: e59566.
- 115 Coats V, Maltais F, Simard S, *et al.* Feasibility and effectiveness of a home-based exercise training program before lung resection surgery. *Can Respir J* 2013; 20: e10–e16.
- 116 Bagan P, Oltean V, Ben Abdesselam A, *et al.* Réhabilitation et VNI avant exérèse pulmonaire chez les patients a haut risque opératoire [Pulmonary rehabilitation and non-invasive ventilation before lung surgery in very high-risk patients]. *Rev Mal Respir* 2013; 30: 414–419.
- 117 Stefanelli F, Meoli I, Cobuccio R, *et al.* High-intensity training and cardiopulmonary exercise testing in patients with chronic obstructive pulmonary disease and non-small-cell lung cancer undergoing lobectomy. *Eur J Cardiothorac Surg* 2013; 44: e260–e265.
- 118 Cejudo P, López-Marquez I, López-Campos JL, *et al.* Randomized controlled trial of exercise training in chronic respiratory failure due to kyphoscoliosis. *Respir Care* 2013 [In press DOI: 10.4187/respcare.02484].
- 119 Jastrzebski D, Ochman M, Ziora D, *et al.* Pulmonary rehabilitation in patients referred for lung transplantation. *Adv Exp Med Biol* 2013; 755: 19–25.
- 120 Dierich M, Tecklenburg A, Fuehner T, *et al.* The influence of clinical course after lung transplantation on rehabilitation success. *Transpl Int* 2013; 26: 322–330.
- 121 Li M, Mathur S, Chowdhury NA, *et al.* Pulmonary rehabilitation in lung transplant candidates. *J Heart Lung Transplant* 2013; 32: 626–632.
- 122 Florian J, Rubin A, Mattiello R, *et al.* Impact of pulmonary rehabilitation on quality of life and functional capacity in patients on waiting lists for lung transplantation. *J Bras Pneumol* 2013; 39: 349–356.

- 123 Dassios T, Katelari A, Doudounakis S, *et al.* Aerobic exercise and respiratory muscle strength in patients with cystic fibrosis. *Respir Med* 2013; 107: 684–690.
- 124 Mandal P, Sidhu MK, Kope L, *et al.* A pilot study of pulmonary rehabilitation and chest physiotherapy *versus* chest physiotherapy alone in bronchiectasis. *Respir Med* 2012; 106: 1647–1654.
- 125 Rahimi RA, Skrzat J, Reddy DR, *et al.* Physical rehabilitation of patients in the intensive care unit requiring extracorporeal membrane oxygenation: a small case series. *Phys Ther* 2013; 93: 248–255.
- 126 Rehder KJ, Turner DA, Hartwig MG, *et al.* Active rehabilitation during extracorporeal membrane oxygenation as a bridge to lung transplantation. *Respir Care* 2013; 58: 1291–1298.
- 127 Ho SC, Lin HC, Kuo HP, *et al.* Exercise training with negative pressure ventilation improves exercise capacity in patients with severe restrictive lung disease: a prospective controlled study. *Respir Res* 2013; 14: 22.
- 128 Johnson-Warrington V, Williams J, Bankart J, *et al.* Pulmonary rehabilitation and interstitial lung disease: aiding the referral decision. *J Cardiopulm Rehabil Prev* 2013; 33: 189–195.
- 129 Kenn K, Gloeckl R, Behr J. Pulmonary rehabilitation in patients with idiopathic pulmonary fibrosis – a review. *Respiration* 2013; 86: 89–99.
- 130 Becker-Grunig T, Klose H, Ehlken N, *et al.* Efficacy of exercise training in pulmonary arterial hypertension associated with congenital heart disease. *Int J Cardiol* 2013; 168: 375–381.
- 131 Weinstein AA, Chin LM, Keyser RE, *et al.* Effect of aerobic exercise training on fatigue and physical activity in patients with pulmonary arterial hypertension. *Respir Med* 2013; 107: 778–784.
- 132 Babu AS, Padmakumar R, Maiya AG. A review of ongoing trials in exercise based rehabilitation for pulmonary arterial hypertension. *Indian J Med Res* 2013; 137: 900–906.
- 133 Cavalheri V, Jenkins S, Hill K. Physiotherapy practice patterns for patients undergoing surgery for lung cancer: a survey of hospitals in Australia and New Zealand. *Intern Med J* 2013; 43: 394–401.
- 134 Nwosu AC, Bayly JL, Gaunt KE, *et al.* Lung cancer and rehabilitation – what are the barriers? Results of a questionnaire survey and the development of regional lung cancer rehabilitation standards and guidelines. *Support Care Cancer* 2012; 20: 3247–3254.
- 135 Agostini P, Reeve J, Dromard S, *et al.* A survey of physiotherapeutic provision for patients undergoing thoracic surgery in the U.K. *Physiotherapy* 2013; 99: 56–62.
- 136 Halding AG, Heggdal K. Patients' experiences of health transitions in pulmonary rehabilitation. *Nurs Inq* 2012; 19: 345–356.
- 137 de Sousa Pinto JM, Martín-Nogueras AM, Morano MT, *et al.* Chronic obstructive pulmonary disease patients' experience with pulmonary rehabilitation: a systematic review of qualitative research. *Chron Respir Dis* 2013; 10: 141–157.
- 138 Meis JJ, Bosma CB, Spruit MA, *et al.* A qualitative assessment of COPD patients' experiences of pulmonary rehabilitation and guidance by healthcare professionals. *Respir Med* 2013 [In press DOI: 10.1016/j.rmed.2013.11.001].
- 139 Singer PA, Robertson G, Roy DJ. Bioethics for clinicians: 6. Advance care planning. *CMAJ* 1996; 155: 1689–1692.
- 140 Spruit MA, Janssen DJ, Franssen FM, *et al.* Rehabilitation and palliative care in lung fibrosis. *Respirology* 2009; 14: 781–787.
- 141 Janssen DJ, Spruit MA, Schols JM, *et al.* A call for high-quality advance care planning in outpatients with severe COPD or chronic heart failure. *Chest* 2011; 139: 1081–1088.
- 142 Burge AT, Lee A, Nicholes M, *et al.* Advance care planning education in pulmonary rehabilitation: a qualitative study exploring participant perspectives. *Palliat Med* 2013; 27: 508–515.
- 143 Roig M, Eng JJ, MacIntyre DL, *et al.* Postural control is impaired in people with COPD: an observational study. *Physiother Can* 2011; 63: 423–431.
- 144 Roig M, Eng JJ, MacIntyre DL, *et al.* Falls in people with chronic obstructive pulmonary disease: an observational cohort study. *Respir Med* 2011; 105: 461–469.
- 145 Beauchamp MK, Hill K, Goldstein RS, *et al.* Impairments in balance discriminate fallers from non-fallers in COPD. *Respir Med* 2009; 103: 1885–1891.
- 146 Beauchamp MK, Janaudis-Ferreira T, Parreira V, *et al.* A randomized controlled trial of balance training during pulmonary rehabilitation for individuals with COPD. *Chest* 2013; 144: 1803–1810.
- 147 Oliveira CC, Lee A, Granger CL, *et al.* Postural control and fear of falling assessment in people with chronic obstructive pulmonary disease: a systematic review of instruments, international classification of functioning, disability and health linkage, and measurement properties. *Arch Phys Med Rehabil* 2013; 94: 1784–1799.
- 148 Senden R, Savelberg HH, Grimm B, *et al.* Accelerometry-based gait analysis, an additional objective approach to screen subjects at risk for falling. *Gait Posture* 2012; 36: 296–300.