An official European Respiratory Society statement on physical activity in COPD

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ABSTRACT   This European Respiratory Society (ERS) statement provides a comprehensive overview on physical activity in patients with chronic obstructive pulmonary disease (COPD). A multidisciplinary Task Force of experts representing the ERS Scientific Group 01.02 "Rehabilitation and Chronic Care" determined the overall scope of this statement through consensus. Focused literature reviews were conducted in key topic areas and the final content of this Statement was agreed upon by all members.

The current knowledge regarding physical activity in COPD is presented, including the definition of physical activity, the consequences of physical inactivity on lung function decline and COPD incidence, physical activity assessment, prevalence of physical inactivity in COPD, clinical correlates of physical activity, effects of physical inactivity on hospitalisations and mortality, and treatment strategies to improve physical activity in patients with COPD.

This Task Force identified multiple major areas of research that need to be addressed further in the coming years. These include, but are not limited to, the disease-modifying potential of increased physical activity, and to further understand how improvements in exercise capacity, dyspnoea and self-efficacy following interventions may translate into increased physical activity.

The Task Force recommends that this ERS statement should be reviewed periodically (*e.g.* every 5–8 years).

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An official ERS statement providing a comprehensive overview on physical activity in patients with COPD http://ow.ly/C6v78

Introduction

Chronic obstructive pulmonary disease (COPD) is a highly prevalent chronic respiratory disease affecting about 10% of the adult population above 40 years of age [1]. In addition to progressive chronic airflow limitation, patients with COPD commonly have multiple extrapulmonary effects and comorbidities, which are associated with physical inactivity [2, 3]. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has recommended regular physical activity for all COPD patients [2]. However, the clinical relevance of regular physical activity has not been addressed in depth. The purpose of this official European Respiratory Society (ERS) statement is to highlight the existing science regarding physical (in)activity in patients with COPD, including, but not limited to, its prevalence, determinants, consequences, measurement, and potential treatment.

Methods

An international group of pulmonologists, physiotherapists, movement scientists, exercise physiologists, health psychologists, social psychologists, and epidemiologists knowledgeable in the area of physical activity and/or COPD research was assembled into a Task Force by the leadership of the ERS Scientific Group 01.02 "Rehabilitation and Chronic Care". Contributors searched the scientific literature (PubMed and the Cochrane Library) for original studies and systematic reviews relevant to the topic. Selection of relevant studies and reviews was based on the expertise of the contributors. Draft contributions were shared among committee members, reviewed and revised iteratively. Members were vetted for potential conflicts of interest according to the policies and procedures of ERS. This document represents the consensus of these Task Force members.

Definitions

Physical activity can be defined as any bodily movement produced by skeletal muscles that results in energy expenditure [4]. Physical activity is a complex behaviour that can be characterised by type, intensity, duration, patterns and symptom experience. Exercise is a subset of physical activity. Exercise is physical activity that is planned, structured, repetitive and purposeful [4]. Physical activity also includes, but is not limited to, leisure-time, domestic and occupational activities [4, 5]. Activities of daily living are another subset of physical activity and this term refers to a set of basic, everyday tasks required for personal self-care and independent living [6, 7].

While physical inactivity can be defined simply as "an absence of physical activity" [8], it is commonly used to represent a level of physical activity that is below an optimal or specified threshold. This concept rests on the strong evidence that lower levels of physical activity are related to poor health and predict negative health outcomes [9]. In general, a healthy individual can be considered physically inactive if one of the following criteria is not met: 1) 30 min of at least moderate-intensity physical activity on ⩾5 days every week; 2) 20 min of vigorous-intensity physical activity on at least 3 days every week; or 3) an equivalent combination, which can also be accumulated in shorter bouts usually lasting 10 min of moderate (three times 10 min) or vigorous (two times 10 min) exercise [10, 11]. This represents a framework on which to base recommendations for physical activity promotion. However, the recommended intensity and duration of physical activity for the elderly may be different [12]. Furthermore, the extent to which these recommendations apply to persons with COPD is currently unknown.

In recent years, attention has been raised regarding the adverse health effects of a sedentary lifestyle [13]. A sedentary lifestyle is characterised by behaviours that do not increase skeletal muscle energy expenditure substantially above the resting level [14]. Sedentary individuals expend less than 10% of their total daily energy expenditure in performing moderate- or high-intensity activities [15].

Consequences of physical inactivity in the general population and in chronic diseases other than COPD

Physical inactivity is a fundamental characteristic of many chronic diseases, both as a cause and as a consequence. Evidence suggests that reduced physical activity predisposes to greater incidence of cardiovascular disease [16, 17], obesity [18], diabetes [19, 20], cancer [21], dementia [22] and physical disability [23]. In addition to its effect on development of chronic disease, physical inactivity may develop or worsen as a result of many diseases, owing to the sequelae of the disease and/or the associated reduction in physiological reserve. These effects of physical inactivity to both potentiate and develop from chronic disease probably explain the fact that reduced physical activity, measured either subjectively or objectively, is associated with higher overall mortality rates in the elderly [24, 25]. The exact mechanisms whereby physical inactivity interacts with anatomical and physiological changes related to ageing and other pathological

cofactors to contribute to the evolution of disease or subsequent morbidity or mortality, however, is poorly understood within the human population.

Consequences of physical inactivity on lung function decline and COPD incidence

Several population-based epidemiological studies have assessed the longitudinal effect of regular physical activity on lung function decline or COPD incidence [26–30]; their main characteristics and results are summarised in table 1. Briefly, all studies show an inverse relationship between physical activity levels and the magnitude of lung function decline in at least one of the population subgroups or physical activity variables studied. However, the association between lower physical activity levels and faster lung function decline is not consistent across all population subgroups or physical activity variables. Potential explanations for such inconsistencies include selection bias, lack of adjustment for potential confounders and lack of consideration of changes in physical activity level during follow-up. Only one study overcomes such limitations and, interestingly, shows beneficial effects of regular physical activity on lung function decline and COPD risk in active smokers but not in former or never-smokers [29, 30].

Physical activity assessment

Questionnaires

The physical activity of patients with COPD can be assessed using questionnaires. These instruments are commonly used in epidemiological studies and large clinical trials because they are inexpensive and easy to use [31]. A variety of questionnaires exist that capture different aspects of physical activity such as amount, type, intensity, symptom experience and limitations in the performance of "activities of daily living" [31]. The selection of a questionnaire to measure physical activity requires that the specific questionnaire fits the study aim, is properly developed and has strong psychometric properties, for example, validation, test-retest reliability and responsiveness to change [32]. In the specific case of COPD studies, additional criteria could be considered to improve validity of the questionnaire, such as the inclusion of information on low-intensity activities [31, 33], or the availability of a version for interviewer-based administration [34]. Other practical issues include the availability of a culturally validated version, the time required for questionnaire administration and the ability to compare outcome levels across studies.

Recent systematic reviews have assessed all questionnaires available to measure physical activity in the elderly or chronically ill patients [35, 36]. From the 104 questionnaires identified in these systematic reviews, 15 were developed for use in patients with COPD. Validity was assessed in 85% of these instruments, test-retest-reliability in 69% and responsiveness in only 19%, and none of the instruments was based on a conceptual framework [37]. A current Innovative Medicines Initiative project is filling this gap by developing a valid patient reported outcome tool (PROactive) capturing physical activity experience in COPD (www.proactivecopd.com).

A common methodological issue is recall bias, which may become a limitation if not addressed in the development and validation process. GARFIELD et al. [38] assessed four questionnaires against physical activity measured directly by accelerometry and found that while the Stanford 7-Day Physical Activity Recall questionnaire could identify patients at both extremes of physical activity the other three had a poor relationship with directly measured activity. Also, in two other studies the relationship between questionnaire-derived physical activity measures and accelerometer-derived physical activity measures was either not given [39] or did not allow the authors to reliably identify extremely inactive patients [40].

Despite limitations of questionnaires when used on an individual level, some questionnaires might be used to measure physical activity in groups of patients with COPD. However, the choice depends on matching the question to be addressed with the psychometric properties of the instrument.

Step counters

Pedometers are small, lightweight, portable and nonintrusive devices which measure the number of steps performed in a given period of time. From that metric estimates of distance and energy expenditure can be made [31]. Many pedometers are available, and variability exists not only in cost but also in mechanism of step detection, data storage and sensitivity. Pedometers are most accurate at step counting, less accurate in distance estimates, and even less accurate at estimating energy expenditure [41]. Pedometers may underestimate the number of steps and energy expenditure during walking at slow speed, which is typical in patients with COPD [42–44]. This may limit their accuracy in patients with moderate-to-very severe disease. However, pedometers may have positive role as a motivational tool aiming to increase daily activity, especially in addition to other combined interventions [45–47].

TABLE 1 Studies on physical inactivity and lung function decline or COPD incidence

First author [ref.]	Design and setting	Subjects and follow-up	Subjects' characteristics[#]	Physical activity assessment	Outcome(s)	Main Results
JAKES [26]	Population-based cohort UK	n=12 283 Mean 3.7 years follow-up	45% male Age: 59±9 years FEV1: 3.0±0.7 L in males, and 2.2±0.5 L in females	Standardised questionnaire	FEV1 decline mL·year^{-1}	Climbing more stairs is associated with slower FEV1 decline in females (-0.31, -0.11, -0.03 and 0.04% change in FEV1 in none, 1–5, 6–10 and >10 flights of stairs per day; p-value for trend <0.004) Participation in vigorous leisure time activities is associated with slower FEV1 decline in females (-0.22, -0.34, 0.27 and 0.03% change in FEV1 in none, <0.25, 0.25–1, and >1 h per week; p-value for trend<0.004) Based on a linear regression model adjusted for age, smoking status, and per cent change in weight No association found in males
PELKONEN [27]	Cohort of rural men with a high physical activity level Finland	n=186 25 years follow-up	100% male Age: 54±5 years FEV0.75: 2.9±0.6 L	Validated questionnaire	FEV0.75 decline mL·year^{-1}	Decline in FEV0.75 over 25 years was -44.4, -40.5 and -36.5 mL·year^{-1} for low, medium and high physical activity; p-value for trend=0.035 Based on a linear regression model adjusted for age, height and smoking habits
CHENG [28]	Convenience sample from a clinic USA	n=5707 Mean 1.6 years follow-up	87% male Age range: 25–55 years	Self-report	FEV1 and FVC decline mL·year^{-1}	Males who remained in the active category during the follow-up increased FEV1 by 50 mL and FVC by 70 mL while subjects who remained in the sedentary group reduced FEV1 and FVC by 30 and 20 mL, respectively Based on generalised least squared regressions adjusted for smoking and drinking habit change, age, baseline height, baseline lung function levels, and follow-up time No association found in females
GARCIA-AYMERICH [29]	Population-based cohort Denmark	n=6790 10 years follow-up	43% male Age: 52±12 years FEV1: 2.7±0.9 L FVC: 3.3±1.0 L	Validated questionnaire	COPD incidence (FEV1/FVC ⩽70%)	Active smokers with moderate-to-high physical activity show a reduced risk of developing COPD compared with the low physical activity group (OR=0.77; p=0.027) Based on logistic regression models adjusted for sex, age, education, BMI, weight change during follow-up, asthma, dyspnoea, sputum, smoking status and smoking duration No association found in former or never-smokers
					FEV1 and FVC decline mL·year^{-1}	Active smokers with moderate and high physical activity show a reduced FEV1 decline compared with those with low physical activity (relative change in FEV1 of +2.6 and +4.8 mL·year^{-1}, respectively; p-value for trend=0.006) Active smokers with moderate and high physical activity show a reduced FVC decline compared with those with low physical activity (relative change in FVC of +2.6 and +7.7 mL·year^{-1}, respectively; p-value for trend<0.0001) Based on linear regression models adjusted for sex, age, education, BMI, weight change during follow-up, ischaemic heart disease, dyspnoea, sputum, smoking status, smoking duration, alcohol consumption and baseline lung function levels No association found in former or never-smokers
GARCIA-AYMERICH [30]	Population-based cohort Denmark	n=6568 Mean 16 years follow-up	41% male Age: 49±11 years FEV1: 2.7±0.8 L FVC: 3.4±1.0 L	Validated questionnaire	COPD incidence (FEV1/FVC ⩽70%)	Subjects with moderate-to-high physical activity show a reduced risk of developing COPD compared with the low physical activity group (OR=0.79; p=0.025) Based on a logistic regression model adjusted for sex, age, education, BMI, sputum, asthma and smoking, and weighted using marginal structural models to allow repeated measures of physical activity, lung function and covariates
					FEV1 and FVC decline mL·year^{-1}	Subjects with moderate and high physical activity show a reduced FEV1 decline compared with those with low physical activity (relative change of +7.4 and +10.3 mL·year^{-1} for FEV1; p-value for trend<0.001) Subjects with moderate and high physical activity show a reduced FVC decline compared with those with low physical activity (relative change of +6.9 and +10.0 mL·year^{-1} for FVC; p-value for trend<0.001) Based on linear regression models adjusted for sex, age, education, BMI, sputum, smoking, alcohol and baseline lung function levels, and weighted using marginal structural models to allow repeated measures of physical activity, lung function and covariates

COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 s; FEV0.75: forced expiratory volume in 0.75 s; FVC: forced vital capacity; BMI: body mass index. [#]: subjects' characteristics are presented as mean±SD, unless otherwise stated.

Activity monitors

Accelerometers are portable electronic devices that are worn on the body to detect acceleration and thereby reflect bodily movement. They quantify activity counts, and may provide an estimate of time spent above or below a pre-specified activity level, number of steps and energy expenditure [31]. The use of accelerometers has received increasing interest since they add objective data which cannot be obtained from questionnaires or pedometers.

Accelerometers can detect movement along one axis (uni-axial accelerometers), two axes (bi-axial accelerometers) or three axes (tri-axial accelerometers). Uni-axial devices provide information similar to pedometers, but with the advantage of assessing acceleration in addition to simply detecting steps. Bi-axial and tri-axial devices allow for detection of movement in a wider range of physical activities and are, therefore, more sensitive than uni-axial devices [48]. Activity monitors sometimes combine accelerometers with other physiological sensors (*e.g.* heart rate or skin temperature) or are used in conjunction with positioning systems with the objective of increasing their accuracy to estimate daily physical activity and energy expenditure [49–51].

The validity of activity monitors for assessment of physical activity in patients with COPD has been the subject of many investigations in recent years [31, 39, 42, 43, 49, 52–61]. Two studies in COPD patients recently investigated the validity of six widely used accelerometers in comparison to the "gold standards" of indirect calorimetry and doubly-labelled-water [62, 63]. Among the six devices, the DynaPort MiniMod (McRoberts BV, the Hague, the Netherlands), the Actigraph GT3X (Actigraph, Pensacola, FL, USA) and the SenseWear Armband (BodyMedia, Inc., Pittsburgh, PA, USA) (all employing triaxial accelerometers) were valid and responsive for use in COPD [62, 63]. These devices were demonstrated to be valid in other studies in COPD as well [42, 43, 49, 52, 54–56, 58].

Several factors may influence the outcome of physical activity monitoring. Vibration from vehicle travel can falsely elevate activity counts measured by some devices, although this may be reduced by filtering the accelerometer signal [64]. The number of assessment days and hours of use per day are also important factors that may influence the reliability of the physical activity assessment [65, 66]. Interestingly, compared with the other days of the week Sundays seem to be days of less physical activity in GOLD stage I to III patients [65]. A recent study demonstrates that for cross-sectional analyses 2 to 3 days are sufficient for reliable measurement of physical activity in GOLD stage IV patients, whereas up to 5 days of measurement are required in patients with GOLD stage I [65]. For measurements that aim to assess longitudinal changes 4 days were shown to be sufficient to demonstrate treatment effects following pulmonary rehabilitation in moderate-to-severe COPD, when weekends were excluded from the analysis [67].

The use of accelerometers certainly presents limitations. It should be noted that there is little uniformity in output from the various types of accelerometers, which makes it difficult to compare studies using different devices [68]. Another limitation is that estimates of energy expenditure for individual patients may be inaccurate, especially among those with functional limitations due to chronic diseases that affect walking speed and efficiency of movement [69]. Furthermore, purchase costs vary considerably between devices.

Doubly labelled water

The doubly labelled water (DLW) method provides an indirect assessment of total energy expenditure by the body over a substantial period of time (*e.g.* 2 weeks). The technique has been described elsewhere [70]. Briefly, known doses of deuterium and ^{18}O are ingested ($^{2}H_2O$ and $H_2^{18}O$). The deuterium washes out of the body through the urine, whereas the ^{18}O is eliminated as urine water and CO_2. The difference between the wash out of the two (typically measured in urine samples) provides an estimate of CO_2 production by the body, which can be converted to energy expenditure [71].

The biggest drawback of the technique in the context of physical activity assessment in COPD is that it does not allow separation of energy expenditure linked to physical activity and energy expenditure linked to basal metabolic rate or diet-induced metabolism. Thus, although the DLW technique is used to estimate total energy expenditure in patients with COPD [63, 72, 73] its ability to estimate physical activity is compromised by a number of assumptions that may be correct for healthy subjects but not for patients with COPD. For example, one study used DLW in severe COPD and concluded that active energy expenditure was even higher in COPD compared with controls, which might be related to the increased oxygen cost of breathing and decreased mechanical efficiency in patients with COPD [72]. By contrast, actual physical activity levels are lower in patients with COPD [65]. The DLW technique should probably be restricted to questions about caloric balance in patients with COPD rather than questions concerning the amount and intensity of physical activity. It can be questioned whether the technique should remain the "gold standard" to validate monitors that measure the amount and intensity of movement in COPD, even though DLW will very likely remain a "gold standard" for measuring the caloric cost of physical activity.

Levels of physical activity in patients with COPD

Patients with COPD have significantly lower levels of physical activity as compared with healthy controls [65, 74–81]. Existing data show that time spent walking is significantly lower in COPD patients compared with healthy, age-matched persons [74, 76, 77, 80, 82]. These findings appear to be consistent across settings, cultural background, geographic area and methods used to measure physical activity. In addition, movement intensity of patients with COPD is lower compared with age-matched healthy subjects, which indicates that patients with COPD walk at a slower pace [74]. Current data suggest that patients with COPD reduce their physical activity early in the course of the disease [83–85]. Accordingly, most patients do not meet currently recommended physical activity levels. For example, in one study only 26% of 177 patients with a mean forced expiratory volume in 1 s (FEV_1) 52% predicted achieved at least 30 consecutive minutes of moderate intensity activity on at least 5 days; this increased to 50% if the 30 min was accomplished in bouts of at least 10 min each [86]. Corroborating these results, another study reported that only 29% of 73 patients with COPD achieved a mean of at least 30 min of moderate physical activity summed up throughout the day [87]. Compared with controls, COPD patients had a reduction by 50% of their minutes of moderate physical activity per day, which was even more reduced when bouts of at least 10 min were compared between controls and COPD patients [88].

Factors associated with physical activity in COPD

This section addresses associations between physical activity and clinical characteristics of patients with COPD, such as disease severity, comorbidities, exacerbations and behavioural factors. Since most of the studies are cross-sectional it is not possible to draw conclusions regarding the directionality of the established associations [89]. It should be acknowledged that, in general, physical activity is dependent of many factors, which include biological, behavioural, genetic, social, environmental, cultural and policy factors [90]. In this section we will discuss those aspects that are specifically studied in COPD.

Lung function

FEV_1 shows a weak-to-moderate positive association with objectively measured physical activity in patients with COPD (table 2) [39, 65, 74, 77, 79, 80, 91, 92]. In general, FEV_1 explains only a small proportion of the variation in physical activity in subjects with COPD. Directly measured maximal voluntary ventilation may provide an increased correlation with physical activity in this population [92]. Fewer studies have investigated the relationship between physical activity and other lung function measures. While three studies found weak-to-moderate positive associations between physical activity and diffusion capacity [74, 80, 93], one study showed a strong and independent linear association [94]. A robust inverse association was found between dynamic hyperinflation (measured in the laboratory during cardiopulmonary exercise test on a stationary cycle ergometer) and physical activity [95]. Overall, while increasing severity of lung function impairment is associated with reduced physical activity in subjects with COPD, the relationship is relatively weak. Therefore, levels of physical activity cannot be accurately predicted from resting lung function parameters.

Exercise performance

Physical fitness, which can be measured by various exercise tests, comprises a set of attributes that relates to the ability to perform physical activity [4]. Accordingly, most studies in COPD have found moderately positive associations between either 6-min walking distance or peak work rate in an incremental exercise test and objectively measured physical activity (table 3) [40, 65, 74, 79, 96].

Two studies evaluated the predictive power of the 6-min walking distance to identify physically inactive COPD patients with an objectively measured physical activity level lower than 1.4 (*i.e.* <40% of total daily energy expenditure is related to physical activity). In both studies 6-min walking distance, even though moderately associated with physical activity, was found to be of limited value to reliably identify physically inactive COPD patients [40, 65].

Self-efficacy

Self-efficacy, an individual's belief in his or her capability of performing a specific task in a specific situation, is influenced by expectations of ability to perform the task and its outcome [97]. Theoretically, higher levels of self-efficacy may be associated with increased physical activity; and higher levels of physical activity may result in enhanced self-efficacy belief. However, self-efficacy for walking, assessed in COPD using the Self-Efficacy Questionnaire – Walking (SEQ-W) instrument, was only weakly associated with objectively measured physical activity [91]. Furthermore, in another study of 165 patients with COPD, general self-efficacy as measured with the General Self-Efficacy Scale (SES6) was not associated with physical activity [98].

TABLE 2 Relationship between FEV1 and physical activity in some representative cross-sectional studies

First author [ref.]	Design and setting	Subjects n (males/females)	Physical activity assessment	Main objective	Correlation coefficient	p-value	Main results
STEELE [39]	Single-centre convenience sample USA	47 (44/3)	Accelerometer	Feasibility of accelerometer measurement	0.62	<0.001	Preliminary data suggesting that a triaxial movement sensor is a reliable, valid and stable measure of walking and daily physical activity in COPD patients
BELZA [91]	Single-centre convenience sample USA	63 (60/3)	Accelerometer	Evaluation of correlates of physical activity	0.37	<0.01	Physical activity is most significantly related to walking abilities
PITTA [74]	Single-centre convenience sample Belgium	50 (36/14)	Accelerometer	Comparison of physical activity in COPD with healthy subjects	0.28	<0.05	Patients with COPD are markedly inactive in daily life. Functional exercise capacity is the strongest correlate of physical activity
WALKER [80]	Single-centre convenience sample UK	23 (12/11)	Accelerometer	Evaluation of lower limb activity and the association of laboratory assessments with physical activity before and after rehabilitation in COPD	0.57	<0.001	Physical activity in patients with COPD is closely related to leg activity, which is reduced compared with controls of similar age
HERNANDES [77]	Single-centre convenience sample Brazil	40 (18/22)	Accelerometer	Evaluation of physical activity and its clinical correlates in COPD in Brazil	0.17	NS	Physical activity correlates only moderately with maximal and functional exercise capacity
WATZ [65]	Single-centre convenience sample Germany	163 (122/41)	Accelerometer	Various analyses of physical activity and its clinical correlates in COPD	0.42	<0.01	Clinical characteristics of patients with COPD only incompletely reflect their physical activity
WASCHKI [79]	Multi-centre convenience sample UK, the Netherlands	127 (79/48)	Accelerometer	Evaluation of compliance with wearing an accelerometer and the relationship of disease characteristics with physical activity in a multicentre study	0.65[#]	<0.001	Excellent compliance with wearing a physical activity monitor in a multicentre study. Consistent associations of physical activity with relevant disease characteristics in a multicentre study

FEV1: forced expiratory volume in 1 s; COPD: chronic obstructive pulmonary disease; NS: nonsignificant. [#]: Standardised regression β-coefficient adjusted for age, sex, study site and body mass index >30 kg·m^{-2}.

TABLE 3 Relationship between exercise tolerance and physical activity in some representative cross sectional studies

First author [ref.]	Design and setting	Subjects n (males/females)	Main objective	Physical activity assessment	Exercise tolerance assessment	Correlation coefficient	p-value	Main results
STEELE [39]	Single-centre convenience sample USA	47 (44/3)	Feasibility of accelerometer measurement	Accelerometer	6MWD	0.74	<0.001	Preliminary data suggesting that a triaxial movement sensor is a reliable, valid and stable measure of walking and daily physical activity in COPD patients
BELZA [91]	Single-centre convenience sample USA	63 (60/3)	Evaluation of correlates of physical activity	Accelerometer	6MWD	0.60	<0.001	Physical activity is most significantly related to walking abilities
PITTA [74]	Single-centre convenience sample Belgium	50 (36/14)	Comparison of physical activity in COPD with healthy subjects	Acclerometer	6MWD % pred W_{max} % pred Peak V'_{O_2} % pred	0.76 0.64 0.33	<0.0001 <0.0001	Patients with COPD are markedly inactive in daily life Functional exercise capacity is the strongest correlate of physical activity
ELIASON [96]	Multicentre convenience sample Sweden	44 (28/16)	Associations between physical activity and clinical characteristics of COPD	Accelerometer	6MWD	0.34[#]	0.03	Mean physical activity level and physical activity of at least moderate intensity are positively associated with exercise capacity
WASCHKI [79]	Multicentre convenience sample UK, the Netherlands	127 (79/48)	Evaluation of compliance with wearing an accelerometer and the relationship of disease characteristics with physical activity in a multicentre study	Accelerometer	6MWD	0.47[¶]	<0.001	Excellent compliance with wearing a physical activity monitor in a multicentre study Consistent associations of physical activity with relevant disease characteristics in a multicentre study
WATZ [65]	Single-centre convenience sample Germany	163 (122/41)	Various analyses of physical activity and its clinical correlates in COPD	Accelerometer	6MWD	0.46	<0.001	Relation to clinical outcomes
VAN GESTEL [40]	Single-centre convenience sample Switzerland	70 (49/21)	Predicting physical activity levels from 6MWD	Accelerometer	6MWD	0.69	<0.001	6MWD cannot reliably predict physical inactivity

6MWD: 6-min walking distance; COPD: chronic obstructive pulmonary disease; W_{max}: maximal workload; V'_{O_2}: oxygen uptake. [#]: standardised regression β-coefficient; [¶]: standardised regression β-coefficient adjusted for age, sex, study site and body mass index >30 kg·m^{-2}.

Sociodemographic factors and environment

Several sociodemographic and environmental factors, including ethnicity, socioeconomic status, job availability, education level, patient choices about where to live, and seasonal variations in temperature and humidity, have the potential to influence performance of daily physical activity among persons with COPD.

Among healthy adults, lower physical activity levels have been associated with lower socioeconomic status, lower education level and non-Caucasian race [99–101]. However, this may not be the case for patients with COPD, since two studies have demonstrated a relationship between lower physical activity levels and higher socioeconomic status [102, 103]. In these studies, it is difficult to distinguish the impact of socioeconomic status from that of other influences, such as geographical location and ethnic and cultural differences, but it is possible that increased dependence on walking and public transportation among persons of lower socioeconomic status accounts for the findings. Also, both studies focused on persons with severe airflow limitation; hence the findings may not be applicable to patients with less severe lung function impairment.

Weather, climate and altitude conditions can also influence physical activity levels among persons with COPD. Extremes of heat or cold and/or high environmental levels of particulates or other air pollutants can trigger increased symptoms, bronchoconstriction and acute exacerbations [104–106] and may pose a barrier to exercise and activity adherence [107, 108]. Accordingly, seasonal variations in daily physical activity have been reported [93, 109–111], with a tendency for lower activity during periods with lower temperature. High altitude environments may also influence physical activity levels, since elevation in altitude leads to worsening resting and/or exercise hypoxaemia and reduced exercise tolerance among patients with COPD [112]. Geographical location *per se* may not strongly influence activity levels (*e.g.* independently of other factors such as climate, altitude or socioeconomic status) as no significant differences in physical activity were observed among patients with varying severity of COPD across diverse geographical locations in Europe and the USA [78, 79]. Finally, physical activity levels may be influenced by the day of the week; total activity and activity intensity were lower on Sundays or during the weekend as compared with other days [63, 65].

Exacerbations of COPD

Physical activity is dramatically reduced during and after hospitalisation due to an exacerbation of COPD [113, 114]. Furthermore, recovery time is prolonged over several weeks and physical activity may not return to pre-exacerbation activity levels [113, 114].

Even patients with milder exacerbations, which do not require hospitalisation, tend to stay indoors during the exacerbation period [115]. Moreover, patients with a history of frequent exacerbations reduce their time spent outdoors at a faster rate compared with those with infrequent exacerbations, and thus are more likely to become housebound [115]. This was confirmed by another study demonstrating that a history of more than one exacerbation was correlated with lower physical activity levels [79].

Comorbidities

Comorbidities are common in COPD [116–118] and may independently impact physical activity levels. A cross-sectional study of 170 patients with COPD demonstrated that left ventricular cardiac dysfunction (assessed by elevated N-terminal pro-brain natriuretic peptide and echocardiographic assessment of diastolic function) was associated with reduced physical activity levels, independent of COPD severity assessed by GOLD stage or the multidimensional BODE (body mass index, airflow obstruction, dyspnoea, exercise capacity) score [119]. In this study, depression, anaemia, systemic arterial blood pressure and nutritional depletion were not associated with reduced physical activity levels [119]. In the same cohort, physical activity levels were significantly lower among patients with metabolic syndrome and COPD across all GOLD stages as compared with the patients without metabolic syndrome [120]. It is not yet clear which of the components of metabolic syndrome contributed to this finding. For instance, obese COPD patients have lower activity levels compared with underweight and normal weight patients [121, 122]. Furthermore, diabetes is strongly associated with inactivity in COPD, independent of other confounders [102]. In a cohort of newly diagnosed COPD patients, physical inactivity was more strongly associated with the presence of comorbidities compared with airflow obstruction [123].

Quadriceps muscle strength and mass, which are commonly reduced in patients with COPD, were positively correlated with physical activity in several studies [74, 79, 85]. In one study quadriceps muscle strength was predictive of physical activity, independent of FEV_1 [79]. By contrast, handgrip strength did not correlate with physical activity in patients with COPD [94, 119].

Mood disturbances such as symptoms of anxiety and depression are highly prevalent in patients with COPD [124]. Of the six studies examining the relationship between physical activity and depression in patients with COPD [79, 80, 119, 125–127], only two found significant associations [80, 127]. In one study higher

levels of anxiety were associated with higher levels of physical activity, whereas more depressive symptoms were associated with lower physical activity only when anxiety was part of the statistical model [127].

Systemic inflammation

In the general population a growing body of evidence demonstrates that physical activity, inflammation and immunity are tightly linked, with regular moderate physical activity reducing systemic inflammation [128–131]. Potential mechanisms underlying these observations include the release of anti-inflammatory myokines by contracting skeletal muscles [132]. In COPD, four studies have demonstrated that higher levels of low-grade systemic inflammation are associated with lower levels of physical activity even after adjusting for relevant confounders [79, 94, 119, 133]. Whether anti-inflammatory mechanisms of regular physical activity or COPD-specific mechanisms of systemic inflammation underlie the associations between systemic inflammation and physical activity in COPD needs to be elucidated in further longitudinal studies [134].

Health status

Various assessments of health status have been related to physical activity measurements in patients with COPD. Most studies showed that an impaired health status assessed either by generic or disease-specific instruments is weakly to moderately related to a lower amount and intensity of physical activity [79, 91, 102, 135, 136]. Changes in physical activity over time parallel trends in health status [137]. Since most health status questionnaires have items addressing physical activity this could obviously affect these relationships.

Symptoms

Breathlessness on exertion is the primary symptom limiting exercise, which in turn leads to reduced physical activity in patients with COPD [138]. Accordingly, patients' perception of breathlessness on exertion is reported to be a barrier for participation in exercise and activities of daily living [110, 139]. Indeed, greater levels of dyspnoea as measured by the modified Medical Research Council dyspnoea scale are related to lower levels of physical activity in patients with COPD [65, 79].

Fatigue is also reported to be a frequent symptom in patients with COPD [140]. There is one study that evaluated the association of fatigue assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue questionnaire and physical activity. After adjusting for several confounders physical activity was demonstrated to be associated with fatigue in patients with COPD [79]. Whether, and to what extent, pain symptoms may affect physical activity in patients with COPD remains currently unknown.

Effect of physical inactivity on hospitalisations in patients with COPD

To date, seven prospective longitudinal studies have assessed the association between levels of regular physical activity and hospital admission or readmission due to COPD exacerbations [30, 113, 141–145]. All studies consistently showed a statistically significant association of low physical activity levels with increased risk of hospitalisations. Although all studies reported associations adjusted for confounders, just one study adjusted for previous COPD hospitalisations, which is one of the most important risk factors for readmission [146]. Importantly, the studies have shown that the amount of regular physical activity needed to obtain a significant effect on admissions due to COPD is relatively small, equivalent to walking or cycling for 2 h per week [30, 113, 141–145].

Effects of physical inactivity on survival in COPD

Three longitudinal studies with a follow-up of 3–12 years have demonstrated that low levels of physical activity predict all-cause mortality in patients with COPD after controlling for relevant confounding factors [144, 145, 147]. The relationship was consistent across differing settings, patient characteristics and methods used to measure physical activity. In one study that separated respiratory-related from cardiovascular and all-cause mortality, the greatest effect was on the former [144]. Recently, an assessment of physical activity has also been included as a prognostic factor in a multidimensional prognostic score for stable COPD patients [148].

Whether, and to what extent, improvements in physical activity levels may lower the risk of dying remains unknown in patients with COPD. It seems reasonable to hypothesise that patients who have a decline in physical activity over time have a worse prognosis compared with those patients who remain physically active.

Treatment strategies to improve physical activity
Pharmacological therapy

While it is well-known that bronchodilators improve dyspnoea and exercise tolerance, only a few studies have investigated the impact of bronchodilator therapy on physical activity [149–151]. Two studies had positive results with regard to improvements in physical activity following bronchodilator treatment. Of

these, one study (23 patients) was a nonrandomised open-label study of a long-acting β-agonist in a small number of patients [150], while the other study was a retrospective subgroup analysis [151]. By contrast, two randomised, placebo-controlled, multicentre studies could not demonstrate a change in physical activity following therapy with a long-acting bronchodilator [149, 152]. Therefore, it remains currently unknown whether bronchodilator therapies that are known to improve exercise capacity will also either improve physical activity or prevent deterioration of physical activity over time in patients with COPD.

Ambulatory oxygen therapy

Oxygen therapy improves exercise tolerance in hypoxaemic COPD patients, but whether activity levels are also enhanced is unclear. A small, randomised trial of replacing heavier oxygen tanks with lightweight ambulatory oxygen therapy failed to detect improvements in activity monitor assessments of physical activity over a 6-month period [153].

Pulmonary rehabilitation

Pulmonary rehabilitation is a "comprehensive intervention to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours" [154]. Pulmonary rehabilitation has been demonstrated clearly to reduce dyspnoea, increase exercise capacity and improve quality of life in patients with COPD. Increases in exercise capacity in combination with behavioural change may also have the potential to increase physical activity in patients with COPD. Despite this rationale, the 10 studies that evaluated the effect of pulmonary rehabilitation on physical activity [80, 82, 155–162] have yielded inconsistent results; four showed an increase in physical activity [80, 160–162] and six failed to do so [82, 155–159]. In the negative studies, the lack of improvement in physical activity was observed despite a concomitant increase in exercise capacity and quality of life. A systematic review and meta-analysis of single-group and randomised trials of the effect of exercise training (not necessarily pulmonary rehabilitation) on physical activity concluded that this intervention conferred a significant, but small, increase in this outcome [163].

Behaviour changes, feedback, counselling

Solely increasing the exercise capacity of patients with COPD may be insufficient to increase participation in self-directed leisure time activity [47, 80, 82, 155, 157–162, 164]. Widespread acknowledgement of the exercise maintenance problem has led to the identification of behavioural factors related to participation in daily physical activity and to the development of interventions targeting these factors.

Interventions including self-monitoring of activity behaviour using activity monitors in combination with behavioural counselling in patients with COPD might have the potential to change physical activity behaviour [45–47, 165–167]. However, the evidence base is weak since only a few studies have been conducted using small samples [46, 47], often without a control group [45, 165, 166]. Larger studies with long-term follow-up are needed in patients with COPD.

Key components that increase the effectiveness of behavioural interventions have already been summarised in several meta-analyses and international guidelines [168–172], and include mobilising social support, using well-described/established behaviour change and self-regulatory techniques (self-monitoring, stimulus control, problem solving, relapse prevention management, goal setting, self-reinforcement, providing feedback on performance and developing action plans), providing higher contact time or contact frequency, and assessing the readiness/motivation to change [168, 170]. Motivational interviewing techniques have further been recommended as a collaborative communication approach [168].

Summary of treatment strategies to improve physical activity

To date, only a few randomised controlled trials have studied the efficacy of pharmacological or non-pharmacological treatment strategies on daily physical activity in patients with COPD. Therefore, there is an urgent need for additional well-designed trials. Based on the correlates of physical activity, it seems reasonable to focus in future studies on physical, non-physical and environmental factors to improve physical activity in patients with COPD. Moreover, future trials should not only focus on improvements in physical activity but also on the prevention of loss of physical activity.

Moving forward

The scientific foundation regarding the clinical importance of assessing and improving physical activity in patients with COPD has grown considerably in the past decade. Nevertheless, many questions remain unanswered and the methodology of physical activity assessment needs to be further standardised. Therefore, this Task Force identifies the following major areas that need to be further addressed in the coming years.

1) In addition to smoking cessation the disease-modifying potential of increased physical activity in smokers without COPD and in patients with all degrees of airflow limitation should be explored.

2) Further understanding is needed regarding the concepts for optimising the impact of the pharmacological and non-pharmacological interventions that aim to maintain or increase physical activity levels in patients with COPD.

3) Research should be undertaken to understand how improvements in exercise capacity, dyspnoea, and self-efficacy following an intervention (*e.g.* pulmonary rehabilitation or pharmacological therapy) might translate into increased physical activity.

4) The methodology to measure physical activity needs to be further standardised and formal guidance on this should be provided in the future. Such methodologies could rely on objective and accurate assessment of physical activity, patient reported assessment of physical activity experience, or a combination thereof.

References

1   Buist AS, McBurnie MA, Vollmer WM, *et al.* International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet* 2007; 370: 741–750.

2   Vestbo J, Hurd SS, Agustí AG, *et al.* Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2013; 187: 347–365.

3   Decramer M, Janssens W, Miravitlles M. Chronic obstructive pulmonary disease. *Lancet* 2012; 379: 1341–1351.

4   Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 1985; 100: 126–131.

5   Howley ET. Type of activity: resistance, aerobic and leisure *versus* occupational physical activity. *Med Sci Sports Exerc* 2001; 33: Supp. l, S364–S369.

6   Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. *J Am Geriatr Soc* 1983; 31: 721–727.

7   Fricke J. Activities of Daily Living. *In*: Stone JH, Blouin M, eds. International Encyclopedia of Rehabilitation. Center for International Rehabilitation Research Information and Exchange (CIRRIE) 2013. http://cirrie.buffalo.edu/encyclopedia/en/

8   World Health Organization. Global Recommendations on Physical Activity for Health. Geneva, WHO Press 2010.

9   Wen CP, Wai JP, Tsai MK, *et al.* Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet* 2011; 378: 1244–1253.

10   Haskell WL, Lee IM, Pate RR, *et al.* Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation* 2007; 116: 1081–1093.

11   Hallal PC, Andersen LB, Bull FC, *et al.* Global physical activity levels: surveillance progress, pitfalls, and prospects. *Lancet* 2012; 380: 247–257.

12   Nelson ME, Rejeski WJ, Blair SN, *et al.* Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc* 2007; 39: 1435–1445.

13   Owen N, Healy GN, Matthews CE, *et al.* Too much sitting: the population health science of sedentary behavior. *Exerc Sport Sci Rev* 2010; 38: 105–113.

14   Pate RR, O'Neill JR, Lobelo F. The evolving definition of "sedentary". *Exerc Sport Sci Rev* 2008; 36: 173–178.

15   Bernstein MS, Morabia A, Sloutskis D. Definition and prevalence of sedentarism in an urban population. *Am J Public Health* 1999; 89: 862–867.

16   Li TY, Rana JS, Manson JE, *et al.* Obesity as compared with physical activity in predicting risk of coronary heart disease in women. *Circulation* 2006; 113: 499–506.

17   Mora S, Cook N, Buring JE, *et al.* Physical activity and reduced risk of cardiovascular events: potential mediating mechanisms. *Circulation* 2007; 116: 2110–2118.

18   Li S, Zhao JH, Luan J, *et al.* Physical activity attenuates the genetic predisposition to obesity in 20,000 men and women from EPIC-Norfolk prospective population study. *PLoS Med* 2010; 7: e1000332.

19   Sieverdes JC, Sui X, Lee DC, *et al.* Physical activity, cardiorespiratory fitness and the incidence of type 2 diabetes in a prospective study of men. *Br J Sports Med* 2010; 44: 238–244.

20   Jefferis BJ, Whincup PH, Lennon L, *et al.* Longitudinal associations between changes in physical activity and onset of type 2 diabetes in older British men: the influence of adiposity. *Diabetes Care* 2012; 35: 1876–1883.

21   Friedenreich CM, Neilson HK, Lynch BM. State of the epidemiological evidence on physical activity and cancer prevention. *Eur J Cancer* 2010; 46: 2593–2604.

22   Rovio S, Kåreholt I, Helkala EL, *et al.* Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease. *Lancet Neurol* 2005; 4: 705–711.

23   Gill TM, Allore HG, Gahbauer EA, *et al.* Change in disability after hospitalization or restricted activity in older persons. *JAMA* 2010; 304: 1919–1928.

24   Manini TM, Everhart JE, Patel KV, *et al.* Daily activity energy expenditure and mortality among older adults. *JAMA* 2006; 296: 171–179.

25   Matthews CE, George SM, Moore SC, *et al.* Amount of time spent in sedentary behaviors and cause-specific mortality in US adults. *Am J Clin Nutr* 2012; 95: 437–445.

26   Jakes RW, Day NE, Patel B, *et al.* Physical inactivity is associated with lower forced expiratory volume in 1 second: European Prospective Investigation into Cancer-Norfolk Prospective Population Study. *Am J Epidemiol* 2002; 156: 139–147.

27   Pelkonen M, Notkola IL, Lakka T, *et al.* Delaying decline in pulmonary function with physical activity: a 25-year follow-up. *Am J Respir Crit Care Med* 2003; 168: 494–499.

28   Cheng YJ, Macera CA, Addy CL, *et al.* Effects of physical activity on exercise tests and respiratory function. *Br J Sports Med* 2003; 37: 521–528.

29   Garcia-Aymerich J, Lange P, Benet M, *et al.* Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a population-based cohort study. *Am J Respir Crit Care Med* 2007; 175: 458–463.

30   Garcia-Aymerich J, Lange P, Serra I, *et al.* Time-dependent confounding in the study of the effects of regular physical activity in chronic obstructive pulmonary disease: an application of the marginal structural model. *Ann Epidemiol* 2008; 18: 775–783.

31   Pitta F, Troosters T, Probst VS, *et al.* Quantifying physical activity in daily life with questionnaires and motion sensors in COPD. *Eur Respir J* 2006; 27: 1040–1055.

32   Terwee CB, Mokkink LB, van Poppel MN, *et al.* Qualitative attributes and measurement properties of physical activity questionnaires: a checklist. *Sports Med* 2010; 40: 525–537.

33   Forsén L, Loland NW, Vuillemin A, *et al.* Self-administered physical activity questionnaires for the elderly: a systematic review of measurement properties. *Sports Med* 2010; 40: 601–623.

34   Dinger MK, Oman RF, Taylor EL, *et al.* Stability and convergent validity of the Physical Activity Scale for the Elderly (PASE). *J Sports Med Phys Fitness* 2004; 44: 186–192.

35   Frei A, Williams K, Vetsch A, *et al.* A comprehensive systematic review of the development process of 104 patient-reported outcomes (PROs) for physical activity in chronically ill and elderly people. *Health Qual Life Outcomes* 2011; 9: 116.

36   Williams K, Frei A, Vetsch A, *et al.* Patient-reported physical activity questionnaires: a systematic review of content and format. *Health Qual Life Outcomes* 2012; 10: 28.

37   Gimeno-Santos E, Frei A, Dobbels F, *et al.* Validity of instruments to measure physical activity may be questionable due to a lack of conceptual frameworks: a systematic review. *Health Qual Life Outcomes* 2011; 9: 86.

38   Garfield BE, Canavan JL, Smith CJ, *et al.* Stanford Seven-Day Physical Activity Recall questionnaire in COPD. *Eur Respir J* 2012; 40: 356–362.

39   Steele BG, Holt L, Belza B, *et al.* Quantitating physical activity in COPD using a triaxial accelerometer. *Chest* 2000; 117: 1359–1367.

40   van Gestel AJ, Clarenbach CF, Stöwhas AC, *et al.* Predicting daily physical activity in patients with chronic obstructive pulmonary disease. *PLoS One* 2012; 7: e48081.

41   Schneider PL, Crouter SE, Lukajic O, *et al.* Accuracy and reliability of 10 pedometers for measuring steps over a 400-m walk. *Med Sci Sports Exerc* 2003; 35: 1779–1784.

42   Cavalheri V, Donária L, Ferreira T, *et al.* Energy expenditure during daily activities as measured by two motion sensors in patients with COPD. *Respir Med* 2011; 105: 922–929.

43   Furlanetto KC, Bisca GW, Oldemberg N, *et al.* Step counting and energy expenditure estimation in patients with chronic obstructive pulmonary disease and healthy elderly: accuracy of 2 motion sensors. *Arch Phys Med Rehabil* 2010; 91: 261–267.

44   Turner LJ, Houchen L, Williams J, *et al.* Reliability of pedometers to measure step counts in patients with chronic respiratory disease. *J Cardiopulm Rehabil Prev* 2012; 32: 284–291.

45   Moy ML, Weston NA, Wilson EJ, *et al.* A pilot study of an Internet walking program and pedometer in COPD. *Respir Med* 2012; 106: 1342–1350.

46   Hospes G, Bossenbroek L, ten Hacken NH, *et al.* Enhancement of daily physical activity increases physical fitness of outclinic COPD patients: results of an exercise counseling program. *Patient Educ Couns* 2009; 75: 274–278.

47   de Blok BM, de Greef MH, ten Hacken NH, *et al.* The effects of a lifestyle physical activity counseling program with feedback of a pedometer during pulmonary rehabilitation in patients with COPD: a pilot study. *Patient Educ Couns* 2006; 61: 48–55.

48   Hikihara Y, Tanaka S, Ohkawara K, *et al.* Validation and comparison of 3 accelerometers for measuring physical activity intensity during nonlocomotive activities and locomotive movements. *J Phys Act Health* 2012; 9: 935–943.

49   Patel SA, Benzo RP, Slivka WA, *et al.* Activity monitoring and energy expenditure in COPD patients: a validation study. *COPD* 2007; 4: 107–112.

50   Theou O, Jakobi JM, Vandervoort AA, *et al.* A comparison of physical activity (PA) assessment tools across levels of frailty. *Arch Gerontol Geriatr* 2012; 54: e307–e314.

51   Troped PJ, Oliveira MS, Matthews CE, *et al.* Prediction of activity mode with global positioning system and accelerometer data. *Med Sci Sports Exerc* 2008; 40: 972–978.

52   Pitta F, Troosters T, Spruit MA, *et al.* Activity monitoring for assessment of physical activities in daily life in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil* 2005; 86: 1979–1985.

53   Moy ML, Garshick E, Matthess KR, *et al.* Accuracy of uniaxial accelerometer in chronic obstructive pulmonary disease. *J Rehabil Res Dev* 2008; 45: 611–617.

54   Langer D, Gosselink R, Sena R, *et al.* Validation of two activity monitors in patients with COPD. *Thorax* 2009; 64: 641–642.

55   Hill K, Dolmage TE, Woon L, *et al.* Measurement properties of the SenseWear armband in adults with chronic obstructive pulmonary disease. *Thorax* 2010; 65: 486–491.

56   Cohen MD, Cutaia M. A novel approach to measuring activity in chronic obstructive pulmonary disease: using 2 activity monitors to classify daily activity. *J Cardiopulm Rehabil Prev* 2010; 30: 186–194.

57   Sant'Anna T, Escobar VC, Fontana AD, *et al.* Evaluation of a new motion sensor in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil* 2012; 93: 2319–2325.

58   Bauldoff GS, Ryan-Wenger NA, Diaz PT. Wrist actigraphy validation of exercise movement in COPD. *West J Nurs Res* 2007; 29: 789–802.

59   Sugino A, Minakata Y, Kanda M, *et al.* Validation of a compact motion sensor for the measurement of physical activity in patients with chronic obstructive pulmonary disease. *Respiration* 2012; 83: 300–307.

60   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.

61   Van Remoortel H, Giavedoni S, Raste Y, *et al.* Validity of activity monitors in health and chronic disease: a systematic review. *Int J Behav Nutr Phys Act* 2012; 9: 84.

62   Van Remoortel H, Raste Y, Louvaris Z, *et al.* Validity of six activity monitors in chronic obstructive pulmonary disease: a comparison with indirect calorimetry. *PLoS One* 2012; 7: e39198.

63   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.

64   Cohen MD, Cutaia M, Brehm R, *et al.* Detecting motor vehicle travel in accelerometer data. *COPD* 2012; 9: 102–110.

65   Watz H, Waschki B, Meyer T, *et al.* Physical activity in patients with COPD. *Eur Respir J* 2009; 33: 262–272.

66   Hecht A, Ma S, Porszasz J, *et al.* Methodology for using long-term accelerometry monitoring to describe daily activity patterns in COPD. *COPD* 2009; 6: 121–129.

67   Demeyer H, Burtin C, Van Remoortel H, *et al.* Standardizing the analysis of physical activity in patients with COPD following a pulmonary rehabilitation program. *Chest* 2014; 146: 318–327.

68   Butte NF, Ekelund U, Westerterp KR. Assessing physical activity using wearable monitors: measures of physical activity. *Med Sci Sports Exerc* 2012; 44: Suppl. 1, S5–S12.

69   Strath SJ, Pfeiffer KA, Whitt-Glover MC. Accelerometer use with children, older adults, and adults with functional limitations. *Med Sci Sports Exerc* 2012; 44: Suppl. 1, S77–S85.

70   Westerterp KR, Wouters L, van Marken Lichtenbelt WD. The Maastricht protocol for the measurement of body composition and energy expenditure with labeled water. *Obes Res* 1995; 3: Suppl. 1, 49–57.

71   Schoeller DA. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 1999; 129: 1765–1768.

72   Baarends EM, Schols AM, Pannemans DL, *et al.* Total free living energy expenditure in patients with severe chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1997; 155: 549–554.

73   Arvidsson D, Slinde F, Nordenson A, *et al.* Validity of the ActiReg system in assessing energy requirement in chronic obstructive pulmonary disease patients. *Clin Nutr* 2006; 25: 68–74.

74   Pitta F, Troosters T, Spruit MA, *et al.* Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005; 171: 972–977.

75   Schönhofer B, Ardes P, Geibel M, *et al.* Evaluation of a movement detector to measure daily activity in patients with chronic lung disease. *Eur Respir J* 1997; 10: 2814–2819.

76   Singh S, Morgan MD. Activity monitors can detect brisk walking in patients with chronic obstructive pulmonary disease. *J Cardiopulm Rehabil* 2001; 21: 143–148.

77   Hernandes NA, Teixeira DC, 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.

78   Troosters T, Sciurba F, Battaglia S, *et al.* Physical inactivity in patients with COPD, a controlled multi-center pilot-study. *Respir Med* 2010; 104: 1005–1011.

79   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.

80   Walker PP, Burnett A, Flavahan PW, *et al.* Lower limb activity and its determinants in COPD. *Thorax* 2008; 63: 683–689.

81   Vorrink SN, Kort HS, Troosters T, *et al.* Level of daily physical activity in individuals with COPD compared with healthy controls. *Respir Res* 2011; 12: 33.

82   Coronado M, Janssens JP, de Muralt B, *et al.* Walking activity measured by accelerometry during respiratory rehabilitation. *J Cardiopulm Rehabil* 2003; 23: 357–364.

83   Van Remoortel H, Hornikx M, Demeyer H, *et al.* Daily physical activity in subjects with newly diagnosed COPD. *Thorax* 2013; 68: 962–963.

84   Gouzi F, Préfaut C, Abdellaoui A, *et al.* Evidence of an early physical activity reduction in chronic obstructive pulmonary disease patients. *Arch Phys Med Rehabil* 2011; 92: 1611–1617.

85   Shrikrishna D, Patel M, Tanner RJ, *et al.* Quadriceps wasting and physical inactivity in patients with COPD. *Eur Respir J* 2012; 40: 1115–1122.

86   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.

87   Vitorasso R, Camillo CA, Cavalheri V, *et al.* Is walking in daily life a moderate intensity activity in patients with chronic obstructive pulmonary disease? *Eur J Phys Rehabil Med* 2012; 48: 587–592.

88   van Remoortel H, Camillo CA, Langer D, *et al.* Moderate intense physical activity depends on selected Metabolic Equivalent of Task (MET) cut-off and type of data analysis. *PLoS One* 2013; 8: e84365.

89   Gimeno-Santos E, Frei A, Steurer-Stey C, *et al.* Determinants and outcomes of physical activity in patients with COPD: a systematic review. *Thorax* 2014; 69: 731–739.

90   Bauman AE, Reis RS, Sallis JF, *et al.* Correlates of physical activity: why are some people physically active and others not? *Lancet* 2012; 380: 258–271.

91   Belza B, Steele BG, Hunziker J, *et al.* Correlates of physical activity in chronic obstructive pulmonary disease. *Nurs Res* 2001; 50: 195–202.

92   Pitta F, Takaki MY, Oliveira NH, *et al.* Relationship between pulmonary function and physical activity in daily life in patients with COPD. *Respir Med* 2008; 102: 1203–1207.

93   Langer D, Cebrià i Iranzo MA, Burtin C, *et al.* Determinants of physical activity in daily life in candidates for lung transplantation. *Respir Med* 2012; 106: 747–754.

94   Garcia-Aymerich J, Serra I, Gómez FP, *et al.* Physical activity and clinical and functional status in COPD. *Chest* 2009; 136: 62–70.

95   Garcia-Rio F, Lores V, Mediano O, *et al.* Daily physical activity in patients with chronic obstructive pulmonary disease is mainly associated with dynamic hyperinflation. *Am J Respir Crit Care Med* 2009; 180: 506–512.

96   Eliason G, Zakrisson AB, Piehl-Aulin K, *et al.* Physical activity patterns in patients in different stages of chronic obstructive pulmonary disease. *COPD* 2011; 8: 369–374.

97   Strecher VJ, DeVellis BM, Becker MH, *et al.* The role of self-efficacy in achieving health behavior change. *Health Educ Q* 1986; 13: 73–92.

98   DePew ZS, Garofoli AC, Novotny PJ, *et al.* 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.

99   Marshall SJ, Jones DA, Ainsworth BE, *et al.* Race/ethnicity, social class, and leisure-time physical inactivity. *Med Sci Sports Exerc* 2007; 39: 44–51.

100   Crespo CJ, Ainsworth BE, Keteyian SJ, *et al.* Prevalence of physical inactivity and its relation to social class in U.S. adults: results from the Third National Health and Nutrition Examination Survey, 1988–1994. *Med Sci Sports Exerc* 1999; 31: 1821–1827.

101   Parks SE, Housemann RA, Brownson RC. Differential correlates of physical activity in urban and rural adults of various socioeconomic backgrounds in the United States. *J Epidemiol Community Health* 2003; 57: 29–35.

102   Garcia-Aymerich J, Félez MA, Escarrabill J, *et al.* Physical activity and its determinants in severe chronic obstructive pulmonary disease. *Med Sci Sports Exerc* 2004; 36: 1667–1673.

103   Pitta F, Breyer MK, Hernandes NA, *et al.* Comparison of daily physical activity between COPD patients from Central Europe and South America. *Respir Med* 2009; 103: 421–426.

104   Koskela HO, Koskela AK, Tukiaineu HO. Bronchoconstriction due to cold weather in COPD. The roles of direct airway effects and cutaneous reflex mechanisms. *Chest* 1996; 110: 632–636.

105   Wedzicha JA. Mechanisms of exacerbations. *Novartis Found Symp* 2001; 234: 84–93.

106   Atkinson RW, Anderson HR, Sunyer J, *et al.* Acute effects of particulate air pollution on respiratory admissions: results from APHEA 2 project. Air Pollution and Health: a European Approach. *Am J Respir Crit Care Med* 2001; 164: 1860–1866.

107   O'Shea SD, Taylor NF, Paratz JD. But watch out for the weather: factors affecting adherence to progressive resistance exercise for persons with COPD. *J Cardiopulm Rehabil Prev* 2007; 27: 166–174.

108   Kosatsky T, Dufresne J, Richard L, *et al.* Heat awareness and response among Montreal residents with chronic cardiac and pulmonary disease. *Can J Public Health* 2009; 100: 237–240.

109   Moy ML, Danilack VA, Weston NA, *et al.* Daily step counts in a US cohort with COPD. *Respir Med* 2012; 106: 962–969.

110   Katajisto M, Kupiainen H, Rantanen P, *et al.* Physical inactivity in COPD and increased patient perception of dyspnea. *Int J Chron Obstruct Pulmon Dis* 2012; 7: 743–755.

111   Sewell L, Singh SJ, Williams JE, *et al.* Seasonal variations affect physical activity and pulmonary rehabilitation outcomes. *J Cardiopulm Rehabil Prev* 2010; 30: 329–333.

112   Kelly PT, Swanney MP, Stanton JD, *et al.* Resting and exercise response to altitude in patients with chronic obstructive pulmonary disease. *Aviat Space Environ Med* 2009; 80: 102–107.

113   Pitta F, Troosters T, Probst VS, *et al.* Physical activity and hospitalization for exacerbation of COPD. *Chest* 2006; 129: 536–544.

114   Borges RC, Carvalho CR. Physical activity in daily life in Brazilian COPD patients during and after exacerbation. *COPD* 2012; 9: 596–602.

115   Donaldson GC, Wilkinson TM, Hurst JR, *et al.* Exacerbations and time spent outdoors in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005; 171: 446–452.

116   Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. *Eur Respir J* 2009; 33: 1165–1185.

117   Nussbaumer-Ochsner Y, Rabe KF. Systemic manifestations of COPD. *Chest* 2011; 139: 165–173.

118 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.

119 Watz H, Waschki B, Boehme C, *et al.* Extrapulmonary effects of chronic obstructive pulmonary disease on physical activity: a cross-sectional study. *Am J Respir Crit Care Med* 2008; 177: 743–751.

120 Watz H, Waschki B, Kirsten A, *et al.* The metabolic syndrome in patients with chronic bronchitis and COPD: frequency and associated consequences for systemic inflammation and physical inactivity. *Chest* 2009; 136: 1039–1046.

121 Monteiro F, Camillo CA, Vitorasso R, *et al.* Obesity and physical activity in the daily life of patients with COPD. *Lung* 2012; 190: 403–410.

122 Vozoris NT, O'Donnell DE. Prevalence, risk factors, activity limitation and health care utilization of an obese, population-based sample with chronic obstructive pulmonary disease. *Can Respir J* 2012; 19: e18–e24.

123 Van Remoortel H, Hornikx M, Langer D, *et al.* Risk factors and comorbidities in the preclinical stages of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2014; 189: 30–38.

124 von Leupoldt A, Taube K, Lehmann K, *et al.* The impact of anxiety and depression on outcomes of pulmonary rehabilitation in patients with COPD. *Chest* 2011; 140: 730–736.

125 Moy ML, Matthess K, Stolzmann K, *et al.* Free-living physical activity in COPD: assessment with accelerometer and activity checklist. *J Rehabil Res Dev* 2009; 46: 277–286.

126 Venkata A, DeDios A, ZuWallack R, *et al.* Are depressive symptoms related to physical inactivity in chronic obstructive pulmonary disease? *J Cardiopulm Rehabil Prev* 2012; 32: 405–409.

127 Nguyen HQ, Fan VS, Herting J, *et al.* Patients with COPD with higher levels of anxiety are more physically active. *Chest* 2013; 144: 145–151.

128 Handschin C, Spiegelman BM. The role of exercise and PGC1α in inflammation and chronic disease. *Nature* 2008; 454: 463–469.

129 Febbraio MA. Exercise and inflammation. *J Appl Physiol* 2007; 103: 376–377.

130 Gleeson M. Immune function in sport and exercise. *J Appl Physiol* 2007; 103: 693–699.

131 Pedersen BK, Febbraio MA. Muscles, exercise and obesity: skeletal muscle as a secretory organ. *Nat Rev Endocrinol* 2012; 8: 457–465.

132 Pedersen BK. Exercise-induced myokines and their role in chronic diseases. *Brain Behav Immun* 2011; 25: 811–816.

133 Moy ML, Teylan M, Weston NA, *et al.* Daily step count is associated with plasma C-reactive protein and IL-6 in a US cohort with COPD. *Chest* 2014; 145: 542–550.

134 Magnussen H, Watz H. Systemic inflammation in chronic obstructive pulmonary disease and asthma: relation with comorbidities. *Proc Am Thorac Soc* 2009; 6: 648–651.

135 McGlone S, Venn A, Walters EH, *et al.* Physical activity, spirometry and quality-of-life in chronic obstructive pulmonary disease. *COPD* 2006; 3: 83–88.

136 Jehn M, Schindler C, Meyer A, *et al.* Daily walking intensity as a predictor of quality of life in patients with chronic obstructive pulmonary disease. *Med Sci Sports Exerc* 2012; 44: 1212–1218.

137 Esteban C, Quintana JM, Aburto M, *et al.* Impact of changes in physical activity on health-related quality of life among patients with COPD. *Eur Respir J* 2010; 36: 292–300.

138 O'Donnell DE. Hyperinflation, dyspnea, and exercise intolerance in chronic obstructive pulmonary disease. *Proc Am Thorac Soc* 2006; 3: 180–184.

139 Bestall JC, Paul EA, Garrod R, *et al.* Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999; 54: 581–586.

140 Todt K, Skargren E, Kentson M, *et al.* Experience of fatigue, and its relationship to physical capacity and disease severity in men and women with COPD. *Int J Chron Obstruct Pulmon Dis* 2014; 9: 17–25.

141 Benzo RP, Chang CC, Farrell MH, *et al.* Physical activity, health status and risk of hospitalization in patients with severe chronic obstructive pulmonary disease. *Respiration* 2010; 80: 10–18.

142 Chen YJ, Narsavage GL. Factors related to chronic obstructive pulmonary disease readmission in Taiwan. *West J Nurs Res* 2006; 28: 105–124.

143 Garcia-Aymerich J, Farrero E, Felez MA, *et al.* Risk factors of readmission to hospital for a COPD exacerbation: a prospective study. *Thorax* 2003; 58: 100–105.

144 Garcia-Aymerich J, Lange P, Benet M, *et al.* Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population based cohort study. *Thorax* 2006; 61: 772–778.

145 Garcia-Rio F, Rojo B, Casitas R, *et al.* Prognostic value of the objective measurement of daily physical activity in patients with COPD. *Chest* 2012; 142: 338–346.

146 Garcia-Aymerich J, Serra Pons I, Mannino DM, *et al.* Lung function impairment, COPD hospitalisations and subsequent mortality. *Thorax* 2011; 66: 585–590.

147 Waschki B, Kirsten A, Holz O, *et al.* Physical activity is the strongest predictor of all-cause mortality in patients with COPD: a prospective cohort study. *Chest* 2011; 140: 331–342.

148 Esteban C, Quintana JM, Aburto M, *et al.* The health, activity, dyspnea, obstruction, age, and hospitalization: prognostic score for stable COPD patients. *Respir Med* 2011; 105: 1662–1670.

149 O'Donnell DE, Casaburi R, Vincken W, *et al.* Effect of indacaterol on exercise endurance and lung hyperinflation in COPD. *Respir Med* 2011; 105: 1030–1036.

150 Hataji O, Naito M, Ito K, *et al.* Indacaterol improves daily physical activity in patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2013; 8: 1–5.

151 Kesten S, Casaburi R, Kukafka D, *et al.* Improvement in self-reported exercise participation with the combination of tiotropium and rehabilitative exercise training in COPD patients. *Int J Chron Obstruct Pulmon Dis* 2008; 3: 127–136.

152 Troosters T, Sciurba FC, Decramer M, *et al.* Tiotropium in patients with moderate COPD naive to maintenance therapy: a randomised placebo-controlled trial. *NPJ Prim Care Respir Med* 2014; 24: 14003.

153 Casaburi R, Porszasz J, Hecht A, *et al.* Influence of lightweight ambulatory oxygen on oxygen use and activity patterns of COPD patients receiving long-term oxygen therapy. *COPD* 2012; 9: 3–11.

154 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.

155 Steele BG, Belza B, Hunziker J, *et al.* Monitoring daily activity during pulmonary rehabilitation using a triaxial accelerometer. *J Cardiopulm Rehabil* 2003; 23: 139–142.

156   Steele BG, Belza B, Cain KC, *et al.* A randomized clinical trial of an activity and exercise adherence intervention in chronic pulmonary disease. *Arch Phys Med Rehabil* 2008; 89: 404–412.

157   Dallas MI, McCusker C, Haggerty MC, *et al.* Using pedometers to monitor walking activity in outcome assessment for pulmonary rehabilitation. *Chron Respir Dis* 2009; 6: 217–224.

158   Mador MJ, Patel AN, Nadler J. Effects of pulmonary rehabilitation on activity levels in patients with chronic obstructive pulmonary disease. *J Cardiopulm Rehabil Prev* 2011; 31: 52–59.

159   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.

160   Sewell L, Singh SJ, Williams JE, *et al.* Can individualized rehabilitation improve functional independence in elderly patients with COPD? *Chest* 2005; 128: 1194–1200.

161   Mercken EM, Hageman GJ, Schols AM, *et al.* Rehabilitation decreases exercise-induced oxidative stress in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005; 172: 994–1001.

162   Pitta F, Troosters T, Probst VS, *et al.* Are patients with COPD more active after pulmonary rehabilitation? *Chest* 2008; 134: 273–280.

163   Cindy Ng LW, 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.

164   Probst VS, Kovelis D, Hernandes NA, *et al.* Effects of 2 exercise training programs on physical activity in daily life in patients with COPD. *Respir Care* 2011; 56: 1799–1807.

165   Nguyen HQ, Gill DP, Wolpin S, *et al.* Pilot study of a cell phone-based exercise persistence intervention post-rehabilitation for COPD. *Int J Chron Obstruct Pulmon Dis* 2009; 4: 301–313.

166   Wewel AR, Gellermann I, Schwertfeger I, *et al.* Intervention by phone calls raises domiciliary activity and exercise capacity in patients with severe COPD. *Respir Med* 2008; 102: 20–26.

167   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.

168   Greaves CJ, Sheppard KE, Abraham C, *et al.* Systematic review of reviews of intervention components associated with increased effectiveness in dietary and physical activity interventions. *BMC Public Health* 2011; 11: 119.

169   Conn VS, Minor MA, Burks KJ, *et al.* Integrative review of physical activity intervention research with aging adults. *J Am Geriatr Soc* 2003; 51: 1159–1168.

170   Conn VS, Hafdahl AR, Brown SA, *et al.* Meta-analysis of patient education interventions to increase physical activity among chronically ill adults. *Patient Educ Couns* 2008; 70: 157–172.

171   Estabrooks PA, Glasgow RE, Dzewaltowski DA. Physical activity promotion through primary care. *JAMA* 2003; 289: 2913–2916.

172   Ferrier S, Blanchard CM, Vallis M, *et al.* Behavioural interventions to increase the physical activity of cardiac patients: a review. *Eur J Cardiovasc Prev Rehabil* 2011; 18: 15–32.