They can’t bury you while you’re still moving

A review of the European Respiratory Society statement on physical activity in chronic obstructive pulmonary disease

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ABSTRACT
Physical activity (PA) and exercise are interrelated but separate concepts. PA refers to bodily movement produced by skeletal muscles that results in energy expenditure. Exercise is a subset of PA, in which generally higher levels of muscular activity are performed for a purpose, such as achieving physical fitness or winning a sporting contest. Higher exercise capacity is considered to be permissive of greater PA in the home and community settings. Individuals with chronic obstructive pulmonary disease (COPD) are physically inactive when compared with healthy age-matched control subjects. Furthermore, physical inactivity is independently associated with adverse outcome in patients with COPD, including more rapid disease progression, impaired health status, and increased health care utilization and mortality risk. While there are several methods to objectively measure PA, recent scientific studies have commonly utilized questionnaires and activity monitors. The latter include simple pedometers and complex accelerometers, which can measure and record movement in up to 3 planes. In COPD, multiple patient characteristics and disease severity markers are related to activity level, including pulmonary physiological abnormalities such as airway obstruction and hyperinflation; exercise capacity such as the 6-minute walking distance; exacerbations of respiratory disease; and comorbid conditions. Clinical trials of bronchodilators, supplemental oxygen therapy, exercise training or pulmonary rehabilitation, or PA counseling have provided inconsistent results in demonstrating increased PA from the interaction. This is probably because the phenomenon of physical inactivity is complex, resulting not only from physiological impairments, but symptoms, cultural, motivational, and environmental factors.
COPD. Our paper will summarize important aspects of this document, including: 1) definition and concept of PA; 2) objective measurement of activity; 3) prevalence of inactivity; 4) clinical relevance of activity disorder; and 5) potential interventions that might improve activity in COPD patients.

Definitions and concepts: physical activity and exercise
The concepts “physical activity” and “exercise”, although overlapping, are distinct. PA can be defined as “any bodily movement produced by skeletal muscles that results in energy expenditure.” Using similar reasoning, physical inactivity is defined as “an absence of physical activity or exercise.” PA is strongly influenced by individual attitudes and social, cultural, seasonal, and environmental factors. PA can be characterized in several ways, including type, context, intensity, duration, bouts, and patterns. Basic activities of daily living are those activities that involve everyday tasks centering on self-care and independent living; this subset traditionally has its own assessment methods. Since the complete absence of PA in living persons is unusual, physical inactivity is often operationally defined using threshold activity values. One such classification places healthy individuals in an inactive category by not meeting any of the following 3 criteria: 1) 30 minutes of moderate-intensity PA on at least 5 days every week; 2) 20 minutes of vigorous-intensity PA on at least 3 days every week; 3) an equivalent combination achieving 600 MET-minutes per week. While these criteria are appropriate for healthy adults and adolescents, they are too stringent for most patients with symptomatic COPD. In other words, most COPD patients with moderate or severe disease (by spirometry) would fall into the inactive category, making this categorization less useful for predicting outcome within this group.

Physical exercise is not synonymous with PA. Rather, exercise is a subset of PA, in which generally higher levels of muscular activity are performed for a purpose, such as achieving physical fitness or winning a sporting contest. Similarly, exercise capacity and PA level, although interrelated, are different constructs: higher exercise capacity, often attained after prolonged exercise training, is permissive of greater PA (intensity and duration) in the home and community settings. However, achieving a greater level of exercise capacity does not necessarily mean that higher PA will follow, since the latter is modified by other factors such as motivation, leisure time, occupation, etc. There is, therefore, a sizeable gap between what individuals can do in the laboratory setting and what they actually do once they leave this environment. This has obvious implications if the PA level is predictive of an outcome, independent of exercise capacity: successful efforts at increasing exercise capacity may not automatically lead to increases in PA.

Measuring physical activity
“If a measurement matters at all, it is because it must have some conceivable effect on decisions and behaviour. If we can’t identify a decision that could be affected by a proposed measurement and how it could change those decisions, then the measurement simply has no value.” PA can be measured either directly (using video techniques) or indirectly (with questionnaires and diaries, doubly labeled water techniques, and activity sensors). These methods are summarized in a 2006 review by Pitta et al.

Direct observation
Quantification of PA through direct observation is typically performed in real time by observers or by review of video output. Because it is time-consuming, it cannot be practically used if the required sample size for the study is too large.

Doubly labeled water
Doubly labeled water provides an indirect assessment of total energy expenditure, not PA per se. For this testing, deuterium and $^{18}$O are ingested; the deuterium washes out of the body via renal excretion, while the $^{18}$O washes out as water and carbon dioxide. The difference in washout can be used to estimate global carbon dioxide production, which can then be converted into an estimate of energy expenditure. This technique estimates energy expenditure over long periods of free living conditions, which has obvious advantages and disadvantages. It does not permit the separation of PA-associated energy expenditure from the basal metabolic rate or diet-induced energy expenditure. Also, because of its “broad strokes” assessment, it cannot assess temporal patterns or bouts. The technique is perhaps more suited to obesity research, where global energy expenditure is more relevant.

Questionnaires and activity diaries
Activity assessment via questionnaires and activity diaries are forms of subjective, patient-reported outcomes that involve self-reporting of activities. Being inexpensive and (usually) easy to complete, they are most useful for large clinical or epidemiologic studies. As is generally the case, validated questionnaires and diaries should be used for estimation of activity. Diary information is usually entered daily or several times daily; questionnaires are usually completed much less frequently. Self-reporting has the advantage of incorporating the patient’s perspective and relevance; however, it has potential disadvantages, including perceptual deficiencies and recall errors due to patient-related factors (including age, cultural background, occupational status, and cognitive ability) as well as reliance on the design and psychometric properties of the instrument.

Activity monitors
Activity monitors designed for measuring PA are, in essence, motion sensors. These include pedometers, which estimate...
steps, and accelerometers, which detect acceleration. The increasing interest in motion detectors reflects the recognized limitations of self-reported instruments measures in quantifying PA.

Pedometers estimate the number of steps an individual takes and, indirectly, can be used to provide an estimate of active energy expenditure. Steps per day, unlike most other PA parameters, are intuitive, being grounded in everyday experience. Additionally, this allows clinicians to provide feedback information on steps that can be used to motivate individuals to walk more.73-25 However, a pedometer assessment of activity has limitations. Pedometer devices worn on the waist are relatively insensitive to movements of the upper extremity, and thereby miss some potentially important activity information. Additionally, they may not be sensitive enough to detect walking activity in slow-moving individuals, which is often the case with COPD patients. For example, a study by Dallas et al,26 using pedometers in COPD to detect changes in PA after pulmonary rehabilitation, failed to show any significant associations—a negative finding that was blamed on the insensitivity of the devices.

For the purpose of activity measurement in humans, accelerometers are electronic devices worn on the body that detect acceleration. Being more sophisticated (and more expensive) than pedometers, they are more sensitive to movements in in-active or slowly-moving individuals and, theoretically, would be more suitable to assessing PA in patients with COPD. They are better at detecting motions over a wider range of activities, and can be even responsive to detecting movements in the upper extremities, although the clinical relevance of the latter measurement is not clear. Acceleration can be measured in 1, 2, or 3 planes, (uniaxial, biaxial or triaxial accelerometers, respectively). Practically, they are, at times, too sensitive in detecting movements. For instance, they can demonstrate considerable physical “activity” in someone driving an automobile on a bumpy road.

The analysis of accelerometer output can be extrapolated to provide a variety of activity outcomes, such as summed movements in 3 planes per minute (vector magnitude units); estimated steps per day; estimated energy expenditure; and time spent above or below an activity threshold. The threshold cut-off can be used to estimate time spent in sedentary behavior (which, in general, may independently predict poor outcome)27 or time spent above a moderate intensity threshold.28 Estimating time above an activity intensity threshold can eliminate “noise” from minor motions detected by the ultra-sensitive devices. Some devices also have positioning systems that can determine time spent in supine or upright activities, the latter including walking activity.5 Unfortunately, the differing designs of the accelerometer devices make it difficult to compare their output.29

**Physical inactivity and patient-related outcomes in chronic obstructive pulmonary disease**

Physical inactivity in patients with COPD is associated with several clinically-important adverse outcomes. It should be noted, however, that the often-strong associations described below do not necessarily imply a causal link.30 For example, the presence of a particular chronic disease may increase mortality risk and may independently reduce functional status. In this situation, reduced functional status may simply be an epiphenomenon, and not directly related to the risk of death. However, the link between inactivity in COPD, and in healthy subjects as well, to poor outcomes is so pervasive that a strong case can be made for causal inference.

**Exercise performance**

Sustained physical inactivity over years appears to be associated with accelerated reductions in exercise tolerance and decreased fat-free mass, the latter being a marker for muscle depletion.31

**Mortality**

The association between physical inactivity and increased all-cause mortality has been demonstrated in prospective analyses. In 2006, Garcia-Rio et al32 showed a relationship between objectively-measured PA and mortality in 173 patients with COPD. Their activity assessment came from a triaxial accelerometer worn on the waist over 5 consecutive days, recording 1-minute epochs of movement as vector magnitude units (movements in 3 planes summed over each minute). After an initial activity assessment, patients were followed up for 5 to 8 years. Even when the investigators entered potential confounders in their multivariate statistical modeling, lower activity remained a significant predictor of increased all-cause mortality, along with comorbidity and exercise endurance time.

In what would become a landmark study, Garcia-Aymerich et al33 in 2006 reported on their study relating physical inactivity to health care utilization and mortality. They studied data from over 2000 individuals who had participated in the Copenhagen City Heart Study and had demonstrated airway obstruction, relating questionnaire-derived PA information to subsequent outcome.33 For this analysis, they divided baseline, self-reported activity into 4 categories: very low, low, moderate, and high. Very-low, low, moderate, and high levels of PA were present at baseline in 9%, 12%, 46%, and 33% of participants, respectively. The dates and causes of subsequent hospital admissions and mortality were then obtained from Danish registries. After adjustment for relevant confounders (such as age, sex, severity of airflow obstruction, or the presence of ischemic heart disease), those individuals above the very-low PA category had a lower risk of all-cause and respiratory-related mortality (hazard ratios, 0.76 and 0.70, respectively) than those in the very-low category over the mean follow-up of 12 years. The authors concluded that there was a link between
inactivity and this adverse outcome in COPD. Indeed, not only do low baseline levels of PA predict mortality, but decline in PA over years also predicts outcome. In a re-analysis of the Copenhagen City data, Vaez et al demonstrated that a decline from higher to low PA at follow-up was associated with an increased mortality risk in subjects with and without COPD. The authors concluded that this suggests that PA should be encouraged in the earliest stages of COPD in order to maintain a PA level that is as high as possible, and thus effect a better long-term prognosis.

Health care utilization Lower PA is associated with a higher risk of hospitalization in COPD. In the above-cited study by Garcia-Aymerich, those with very low baseline self-reported PA had a higher rate of subsequent hospitalization for COPD by approximately 25% over the follow-up period than those with higher activity levels. Additionally, decline in PA over time predicts this increased health care utilization (as well as mortality, even after adjustment for relevant potential confounders, including age, forced expiratory volume in 1 second (FEV1), and prior hospitalizations. Some variables, such as extreme weather, probably affect PA in the COPD patient in similar ways to the healthy individual. Other influential factors are perhaps unique to patients with chronic disease in general. Others are related to COPD patients in particular. The following will discuss some of the latter activity-modifying variables.

Airway obstruction In general, FEV1 shows only a weak-to-moderate relationship with PA in COPD, underscoring the importance of other factors in determining this variable. The association between dynamic hyperinflation (increases in end-expiratory lung volumes with exercise or increased respiratory rate—an important factor in exertional dyspnea in COPD) and PA is somewhat stronger. In a study by Garcia-Rio et al., directly measured PA (vector magnitude units from a triaxial accelerometer worn on the waist) was lower in those 89 study patients with demonstrated dynamic hyperinflation than in those 21 patients who did not hyperinflate. This factor, along with the 6-minute walking distance (see below), remained in a multivariate model predicting PA. Since the associations between these physiological variables and PA are not particularly robust, other factors influencing activity must also be important.

Exercise endurance capacity Higher exercise capacity may be considered permissive of higher PA intensity and duration in the COPD patient: those stopping exercise in the laboratory at low PA intensity and duration in the COPD patient: those stopping exercise in the laboratory at low levels because of dyspnea or leg fatigue (or both) cannot be expected to be very physically active outside of this setting. Thus, it should be no surprise that exercise performance does relate to a what stronger. pulmonary physiological abnormality and exercise capacity limitation appear to independently predict low PA. To illustrate this, a study by Pitta et al demonstrated that COPD patients spent less time walking and standing and more time lying than healthy people of approximately the same age. Furthermore, these COPD patients were less likely to walk 30 minutes per day, and their movement intensity was lower. Of considerable interest, a subsequent study demonstrated that physical inactivity was observed in COPD patients with mild airway obstruction, even appearing to precede the onset of breathlessness. The findings of decreased activity early in the course of COPD suggest that maladaptive behavior, not just symptom-limitation, also plays a role in inactivity in these patients.

Factors associated with physical activity in patients with chronic obstructive pulmonary disease PA in all individuals is a complex phenomenon that is undoubtedly influenced by multiple factors. Some variables, such as extreme weather, probably affect PA in the COPD patient in similar ways to the healthy individual. Other influential factors are perhaps unique to patients with chronic disease in general. Others are related to COPD patients in particular. The following will discuss some of the latter activity-modifying variables.
Chronic obstructive pulmonary disease: exacerbations The exacerbation of COPD can be defined as “… a sustained worsening of the patient’s condition, from the stable state and beyond normal day-to-day variations that is acute in onset and may warrant additional treatment in a patient with underlying COPD.”\textsuperscript{64} Exacerbations cause a substantial increase in symptoms and a decrease in health status lasting for weeks after onset.\textsuperscript{53} Therefore, PA would be expected to decrease in this setting as well. One longitudinal study addressed this issue by evaluating PA (with a triaxial accelerometer worn on the wrist) over about 6 consecutive months in a small number of patients with COPD.\textsuperscript{51} Exacerbations (onset and termination) over this time period were defined using the 14-item Exacerbations of Chronic Pulmonary Disease Tool (EXACT) daily dairy.\textsuperscript{52} Patients spent fewer minutes per day in higher level PA during exacerbation days than non-exacerbation days, with the greatest reduction occurring in the first week. Following the termination of the exacerbation, activity remained low for approximately more 2 weeks.

Comorbid conditions COPD patients frequently have clinically-significant comorbid conditions; these almost certainly add to the physical inactivity problem in this disease. Comorbid states that have been demonstrated to be associated with decreased PA in COPD patients include quadricep dysfunction from deconditioning, systemic inflammation, metabolic syndrome, and left heart dysfunction.\textsuperscript{53,54} Undoubtedly more exist. The relationship between PA and anxiety and depression has been inconsistent, with most studies failing to demonstrate significant associations. In one study, anxiety and depression had opposite effects: higher anxiety levels were associated with lower PA, while higher depression scores were associated with higher PA.\textsuperscript{55}

Chronic obstructive pulmonary disease: symptoms and health status Symptoms common to COPD, dyspnea, and fatigue are associated with lower PA levels in patients.\textsuperscript{6,48,56} However, the relationship between symptoms and activity is probably complex. For example, a longitudinal study by Lareau et al\textsuperscript{57} in a small number of COPD patients did not show changes in exertional dyspnea over the years of follow-up despite progressive declines in the FEV\textsubscript{1}. However, self-reported physical activities also declined over this interval, suggesting that if patients ratchet down their PA, exertional dyspnea will not increase.

Impaired health status also mirrors physical inactivity, but the correlation is only weak to moderate.\textsuperscript{48,58-61} Finally, a longitudinal decline in PA is associated with a corresponding decline health status in COPD.\textsuperscript{52} In one study of 346 patients with COPD, very low questionnaire-rated PA (the equivalent of walking less than 15 minutes per day) was associated with worse health status, as measured by a generic instrument.\textsuperscript{59} Adding to this association, changes in leisure time PA are associated with corresponding changes in health status: for example, COPD patients with increases in PA over time had increases in health status scores, and vice versa.\textsuperscript{62} The obvious question deriving from these associations is: what is the horse and what is the cart? In other words, does physical inactivity drive poor health status, does poor health status drive physical inactivity, or is the causality bidirectional?

Increasing physical activity in patients with chronic obstructive pulmonary disease Bronchodilators Compared to the extensive literature on the beneficial effect of bronchodilators in COPD on airway obstruction, hyperinflation, dyspnea, exercise capacity, and health status, their effect on increasing PA has received little attention. One randomized crossover trial comparing the long-acting β-agonist bronchodilator, indacaterol, to placebo showed no effect on directly-measured activity despite demonstrable improvements in exercise capacity.\textsuperscript{63} However, a second, 3-arm, crossover study testing this drug that compared its effect on activity to that of placebo and the long-acting anticholinergic bronchodilator, tiotropium, showed a significant positive effect of the β-agonist on activity.\textsuperscript{64} A large study comparing tiotropium to placebo showed a nonsignificant, numerical increase in activity.\textsuperscript{55} Finally, a crossover trial of the long-acting anticholinergic bronchodilator, aclidinium, to placebo demonstrated a small increase in one (of several) activity parameters.\textsuperscript{65} These studies suggest that simply increasing lung function will have only a marginal effect on PA. Bronchodilators alone are not a panacea when it comes to PA.

Supplemental oxygen therapy Regular use of supplemental oxygen prolongs life in hypoxemic patients with COPD. However, the beneficial effect of oxygen therapy on other outcomes of importance to patients has not been well tested. One very small, randomized study evaluated the effect of adding ambulatory oxygen (as opposed to a stationary system only) on hypoxemic COPD patients receiving continuous oxygen therapy.\textsuperscript{66} The study did not show a beneficial effect of adding supplemental oxygen on activity. Larger studies are needed to better examine this relationship.

Pulmonary rehabilitation With its essential components of exercise training and self-management education, and its proven benefits in exercise capacity, comprehensive pulmonary rehabilitation would be expected to have a positive effect on PA in patients with COPD. Despite this strong rationale, randomized clinical trials testing this outcome\textsuperscript{41,42,68-70} have thus far provided inconsistent results. Somewhat less than one-half of these trials demonstrated increases in PA despite often significant improvements in other outcome areas. Putative reasons for the negative result have included small, underpowered
trials, poor sensitivity of pedometers to detect steps in slow-moving COPD patients, and unfavorable signal-to-noise characteristics of some sensitive accelerometers. It may be that the behavioral program in traditional pulmonary rehabilitation must be modified to focus on this important outcome. For example, many pulmonary rehabilitation programs are of relatively short duration, typically 8–12 weeks, which may not provide enough time to elicit behavior change. To illustrate this potential limitation, one randomized trial of pulmonary rehabilitation demonstrated that, unlike exercise capacity and health status which improved by 3 months, PA took 6 months to significantly increase. This led to the editorial remark that it takes 3 months to train the muscles and 6 months to train the brain.

Physical activity counseling As mentioned earlier, physical inactivity in COPD may be as much the result of maladaptive behavior patterns as symptom-limitation of exercise capacity. This conclusion is based on relatively weak-to-moderate correlations between exercise capacity and PA in cross-sectional studies already discussed. Consequently, a variety of cognitive and behavioral interventions have been offered to increase PA in healthy children and adults. Unfortunately, for patients with COPD, many of these interventions have not been proved successful.

One promising intervention is feedback information from wearable activity monitors, which has been successfully used to increase daily PA in various populations, including a small (negative) study in COPD. One recent trial of pedometer feedback in COPD patients deserves special comment. Ninety-seven patients were randomized to either PA encouragement alone or a pedometer-based feedback program. Outcome variables included mean step count over 1 week, the 6-minute walk distance, dyspnea, and health status. The pedometer feedback group showed significantly greater improvements in step counts per day, walk distance, and health status, leading the investigators to conclude that this form of intervention may increase PA and quality of life.

Summary and future directions This summary of the European Respiratory Society statement on PA discusses the concepts of PA and exercise which, while interrelated, are not synonymous. Exercise capacity is permissive of PA. However, PA is undoubtedly influenced by multiple factors. Methods by which PA can be measured, their limitations, and potential applications has also been reviewed. COPD patients are generally quite inactive and that this physical inactivity is associated with impairment in other areas, including lung function (airway obstruction and dynamic hyperinflation) exercise capacity, and health status, as well as the presence of certain comorbid conditions. As would be anticipated, PA is reduced during the COPD exacerbation. Importantly, physical inactivity is associated with adverse outcome, including increased health care utilization, increased mortality risk, and (perhaps) an accelerated decline in cigarette smokers with COPD. Efforts to increase PA in patients with COPD have been challenging, and there appears to be no “quick-fix” to this problem.

Increased efforts to better understand the determinants of PA as well as effective strategies to improve this variable must be undertaken if we are to improve the lives of our patients. Future research must include both advancing the science and treating the patient.

REFERENCES
They can’t bury you while you’re still moving…

REFERENCES


Nie mogą cię pochwalić, gdy się ruszasz

Omówienie stanowiska European Respiratory Society dotyczącego aktywności fizycznej u chorych na przewlekłą obturacyjną chorobę płuc

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aktywność fizyczna, przewlekła obturacyjna choroba płuc, stanowisko

STRESZCZENIE
Określenia „aktywność fizyczna” i „ćwiczenia fizyczne” nie są synonimami, ale częściowo się nakładają. Aktywność fizyczna (AF) to ruchy ciała spowodowane przez mięśnie szkieletowe, których wynikiem jest zużycie energii. Ćwiczenia fizyczne stanowią kategorię AF, w której zwiększona aktywność mięśni służy osiągnięciu celu, np. sprawności fizycznej czy wygranej w zawodach sportowych. Większa wydolność wysiłkowa umożliwia większą AF w domu i w społeczności. Chorzy na przewlekłą obturacyjną chorobę płuc (POChP) są mniej aktywni fizycznie w porównaniu z osobami zdrowymi w podobnym wieku. Ponadto u chorych na POChP brak AF wiąże się z niekorzystnymi zdarzeniami zdrowotnymi: szybszą progresją choroby, pogorszeniem stanu zdrowia, większym zużyciem zasobów opieki zdrowotnej i większym ryzykiem zgonu. Pomimo dostępności wielu metod obiektywnej oceny AF, obecnie w badaniach klinicznych stosuje się kwestionariusze i monitory aktywności. Do tych ostatnich należą proste pedometry i skomplikowane akcelerometry, które mogą mierzyć i rejestrować ruchy nawet w 3 płaszczyznach. U chorych na POChP poziom AF wiąże się z parametrami klinicznymi, w tym z zaburzeniami czynności płuc (np. obturacją dróg oddechowych i nadmiernym rozdęciem płuc), wydolnością wysiłkową (ocenianą w teście 6-minutowego marszu) oraz występowaniem zaostrzeń POChP i chorób współistniejących. Wyniki badań klinicznych, w których oceniano wpływ leków rozkurczających oskrzela, tlenoterapii, treningu wysiłkowego i rehabilitacji oddechowej na AF są niejednoznaczne. Jest to prawdopodobnie spowodowane tym, że zjawisko braku AF jest złożone i zależy nie tylko od upośledzenia czynności organizmu, ale i od innych czynników, takich jak występowanie objawów chorobowych, czynniki kulturowe, motywacja i czynniki środowiskowe.