Both Pulmonary and Extra-Pulmonary Factors Predict the Development of Disability in Chronic Obstructive Pulmonary Disease

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Key Words

Chronic obstructive pulmonary disease • Disability • Exercise capacity • Functional limitation

Abstract

Background: Although chronic obstructive pulmonary disease (COPD) is a major cause of disability worldwide, its determinants remain poorly defined. **Objective:** We hypothesized that both pulmonary and extra-pulmonary factors would predict prospective disablement across a hierarchy of activities in persons with COPD. **Methods:** Six hundred and nine participants were studied at baseline (T_0) and 2.5 years later (T_1). The Valued Life Activities (VLA) scale quantified disability (10-point scale: 0 = no difficulty and 10 = unable to perform), defining disability as any activity newly rated 'unable to perform' at T_1 . Predictors included pulmonary (lung function, 6-minute walk distance and COPD severity score) and extra-pulmonary (quadriceps strength and lower extremity function) factors. Prospective disability risk was tested by separate logistic regression models for each predictor (baseline value and its change, T_0 – T_1 ; odds ratios were scaled at 1 standard deviation per factor. Incident disability across a hierarchy of obligatory, committed and discretionary VLA subscales was compared. **Results:** Subjects manifested a

40% or greater increased odds of developing disability for each predictor (baseline and change over time). Disability in discretionary activities developed at a rate 2.2-times higher than observed in committed activities, which was in turn 2.5-times higher than the rate observed in obligatory activities ($p < 0.05$ for each level). **Conclusions:** Disability is common in COPD. Both pulmonary and extra-pulmonary factors are important in predicting its development.

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Introduction

Disability among working-aged adults is a critical, yet understudied health outcome that has been identified as a priority for further research [1]. Chronic obstructive pulmonary disease (COPD) currently ranks within the top 5 causes of disability among working-aged adults in the USA and, by 2020, is projected to rank 5th worldwide [2, 3]. Indeed, people with COPD have a 10-fold greater risk of disability than the general population [4]. Despite its importance, however, the pathways leading to COPD-related disability remain poorly characterized.

COPD is particularly relevant to the disablement process because it manifests as a systemic disease with both

pulmonary and extra-pulmonary features [5]. These manifestations include elevations in biomarkers [6] and gene expression [7] related to systemic inflammation, poor muscle function [8] and frailty [9]. Moreover, people with COPD experience a myriad of comorbidities, including atherosclerosis [10], depression [11], osteoporosis [12] and chronic disease anemia [13]. To date, disability in COPD has been predominantly studied from the narrow perspective of activities necessary for survival or basic functioning such as (instrumental) activities of daily living [(I)ADLs] [14–18]. The inability to perform such activities, however, typically develops late, in relatively advanced disease. Not only does this narrow construct of disability underestimate the burden of COPD-related morbidity, but it also provides little insight into the earlier stages of disablement that might be more amenable to intervention.

Nagi [19] advanced disability research by proposing a conceptual model of disablement that was modified by Verbrugge and Jette [20] and that has since been widely adopted. This model proposes that disability begins with alterations in the functioning of a body organ affected by disease, resulting in impairment. Impairment brings about reductions in physical or mental actions conceptualized as functional limitations. Functional limitations, in turn, lead to disability across a hierarchy of activity levels. Findings from our previous work analyzing disablement in COPD are consistent with this model [21].

We conducted a prospective longitudinal study of working-aged adults with COPD to characterize the development of disability. We aimed to determine whether changes over time in pulmonary and extra-pulmonary impairment and functional limitations predicted the prospective development of disability. We further aimed to distinguish the development of such disability across a hierarchy of activity domains: obligatory activities that are required for survival and independence – e.g. (I) ADLs, committed activities that define one's principal social roles – e.g. working for pay or caring for family) and discretionary activities – e.g. involvement in hobbies, socializing or travel).

Methods

Subjects and Design

We used data from the Function, Living, Outcomes and Work (FLOW) study, an ongoing prospective longitudinal cohort study of working-aged adults (age: 40–65 years at baseline) recruited from an integrated health care delivery system. The FLOW cohort consists of 1,202 Kaiser Permanente Medical Care Program

(KPMCP) members with COPD recruited using a validated algorithm based both on recent health care utilization linked to a COPD diagnostic code and pharmacy dispensing for COPD-related medications; recruitment methods have been described previously [22]. At baseline study Wave 1 (T_0), we conducted structured telephone interviews that ascertained sociodemographic characteristics, COPD clinical history and health status. We also conducted a clinic visit to perform spirometry and other physical assessments. Approximately 2.5 years later (T_1), we successfully conducted Wave 2 follow-up interviews on 1,051 (90%) of those subjects studied at baseline (fig. 1). After exclusions for ineligibility for or inability to follow-up with clinic visits, we performed repeat clinic visits on 677 (69%) of 987 participants. For this study, we excluded 68 subjects (10%) because of unacceptable spirometric data at either T_0 or T_1 .

At the time of baseline assessments, we recruited 302 age- and gender-matched referents who were KPMCP members without a COPD diagnosis or obstruction on spirometry. We used these referent data to derive normative values for quadriceps strength [9], but did not otherwise include them in the analyses we present here.

Protocols were approved by the UC San Francisco Committee on Human Research and the Kaiser Foundation Research Institutional Review Board.

Independent Predictor Variables

Respiratory Impairment

Pulmonary Function. We assessed respiratory function by spirometry according to American Thoracic Society (ATS) guidelines [23]. Spirometry was performed with the EasyOne™ Front-line spirometer (ndd Medical Technologies, Chelmsford, Mass., USA). We applied percent predicted FEV₁ values from the regression equations developed from the National Health and Nutrition Examination Survey III [24].

COPD Severity Score. This is a novel, validated survey-based disease severity instrument that does not require physiologic measures of respiratory function or exercise capacity [25]. This feature makes it useful for epidemiologic studies and telephone administration. The COPD severity score is based on items spanning five domains: (1) severity of respiratory symptoms, (2) prior use of systemic corticosteroids, (3) use of other COPD medications, (4) previous hospitalization or intubation for respiratory causes and (5) use of long-term oxygen therapy. It ranges from 0–35; higher scores reflect greater disease severity and correlate with FEV₁, BODE Index, exercise capacity and health-related quality of life [26, 27].

Nonrespiratory Impairment

Exercise Capacity. Exercise capacity was measured using the 6-minute walk test (6MWT) [28]. We used a standardized flat, straight course of 30 m in accordance with American Thoracic Society guidelines. Every 2 min, a technician used standardized phrases to encourage effort.

Quadriceps Strength. Decreased quadriceps strength is associated with poorer exercise capacity and lower extremity functioning across a spectrum of COPD severity [9, 29]. Isometric quadriceps strength was assessed by standard manual muscle testing procedures using a hand-held dynamometer (MicroFet2 dynamometer, Saemmons Preston, Bolingbrook, Ill., USA) [30]. Examiners trained in manual muscle testing by the same experienced

Fig. 1. FLOW study recruitment and retention.

physical therapist practised testing until there was agreement between the raters 90% of the time within 2.3 kg of force. We focused on quadriceps strength because these muscles are considered essential for walking and previous studies have suggested the importance of quadriceps weakness as a predictor of reduced exercise capacity in COPD [31].

Lower Extremity Functioning. This was quantified using the validated Short Physical Performance Battery (SPPB) [32]. Poorer SPPB performance is predictive of incident disability, institutionalization and mortality in older people, independent of comorbidity or socioeconomic factors [32, 33]. This battery includes 3 performance measures of balance, chair stands and a 4-meter walk, each scored from 0 to 4 points. A summary score ranges from 0 to 12.

Outcome Variables

Disability was measured by the Valued Life Activities disability scale (VLA) [34]. The VLA scale makes operational the broad conceptual hierarchy of disability proposed by Verbrugge and Jette [20]. Originally developed for rheumatoid arthritis, the VLA scale measures complex functioning in daily life and has subsequently been validated in asthma and COPD [35]. Originally comprising 32 items, refinements over the past decade have resulted in shorter scales. For this study, a 22-item scale was employed; respondents rated on a 10-point scale how difficult, due to their breathing problems, activity performance was across 22 obligatory, committed and discretionary domains (0 = no difficulty and 10 = unable to perform the activity). The VLA scale was administered at T_0 and T_1 and change scores were derived. Incident disability was defined in two ways: (1) a new rating of 'unable' in any activity domain from T_0 to T_1 or (2) a 1/2 standard deviation increase in the mean difficulty rating across all rated items, which we defined as a 'meaningful change' in mean disability, consistent with prior definitions [35]. We evaluated the overall scale in this manner as well as within the hierarchy of obligatory, committed and discretionary subscales.

Other Covariates

We included variables that might confound the relationships between the predictor and outcomes measures of interest. These included sociodemographic characteristics (age, sex and race) as well as cigarette-smoking history using questions refined from the National Health Interview Survey and second-hand smoke exposure using items we had originally developed [36, 37].

Statistical Analysis

Categorical variables were analyzed with the χ^2 test. Continuous variables were analyzed with the Student t test (by follow-up status) or the paired t test (for change T_0 – T_1). We examined the impact of baseline (T_0) and change (T_0 – T_1) in 5 respiratory and nonrespiratory predictors on the prospective risk of VLA disability. Predictors, including FEV₁, 6MWT, COPD severity score, quadriceps strength and SPPB were tested in separate multivariable logistic regression models that included the baseline value of the predictor as well as its change over time. We tested the impact of each predictor on the two definitions of VLA disability. Odds ratios (ORs) were expressed per Z unit [1 standard deviation (SD)] change in each predictor. Each model was tested for two prospective VLA outcomes: incident disability and a meaningful (0.5 SD) increase in mean difficulty rating. All models included gender,

age (continuous variable), race [categorized as white/non-Hispanic (referent), black or all others], BMI (continuous variable), change in BMI from T_0 to T_1 , smoking (packs per day), and second-hand smoke exposure (hours per week). Since they were the most consistent predictors of VLA disability, we used multivariable logistic regression to test the impact of 6MWT and COPD severity score on the risk of disability in the obligatory (e.g. ADLs), committed (e.g. working for pay) and discretionary (e.g. socializing or travel) VLA subscales controlling for gender, age, BMI, race, smoking status and second-hand smoke exposure. Given the ubiquitous use of spirometric measures as a measure of COPD severity, we also tested the impact of percent predicted FEV₁ on the VLA subscales, controlling for the same covariates used in the 6MWT and COPD severity score models. In sensitivity analyses, we defined BMI dichotomously as obese (BMI >30) versus not and change in BMI categorically as a $\geq 10\%$ gain, $\geq 10\%$ loss or other (referent). We also repeated analyses replacing the baseline value of each predictor with its average between T_0 and T_1 .

Lastly, we hypothesized that discretionary activities would be more vulnerable to the development of incident disability than committed activities and, likewise, committed activities would be more vulnerable to disablement than obligatory activities. We compared the rates of disability in each activity domain as a ratio of a Poisson variable to its expected value based on the denominator rate [38].

Analysis was conducted using STATA/ICv11.2 (StataCorp, College Station, Tex., USA).

Results

Among 609 study participants analyzed (table 1), 367 (60%) were female with a mean age of 59.3 ± 6.1 years, and mean baseline FEV₁ was 1.79 ± 0.74 liters ($64\% \pm 23$ predicted). Most subjects (85%) were either current or former smokers. The mean time between study visits was 2.4 ± 0.5 years. Compared to subjects included in the analysis, reinterviewed subjects without follow-up research clinical data ($n = 310$) were more likely ($p < 0.05$) to be current smokers and have lower baseline 6MWT distances, but did not otherwise differ by any of the other variables shown in table 1 (data not shown).

Changes in the independent predictors from T_0 to T_1 are presented in table 2. FEV₁ and percent predicted FEV₁ declined by 0.10 ± 0.25 liters and $1.9 \pm 8.7\%$, respectively (both $p < 0.0001$). These declines, however, were not consistently observed. Over the follow-up period, 40% of subjects manifested essentially stable lung function.

Strong, consistent associations were identified between each physical performance measure (FEV₁, 6MWT, quadriceps strength and SPPB) and the development of incident disability, defined as any VLA activity newly reported as 'unable to perform' (table 3). These predictive

Table 1. Baseline subject characteristics of the FLOW cohort study (n = 609)

Subject characteristics	n (%) or mean $\pm$ SD
Age, years	59.3 $\pm$ 6.1
Sex, female	367 (60)
BMI	31.8 $\pm$ 8.3
Race/ethnicity	
White, non-Hispanic	421 (69)
Black	105 (17)
Other	83 (14)
Cigarette smoking, packs/day	0.85 $\pm$ 0.35
Second-hand smoke exposure, h/week	1.10 $\pm$ 5.02
Pulmonary function	
FEV ₁ , liters	1.79 $\pm$ 0.74
Percent predicted FEV ₁ ^a	64 $\pm$ 23
FEV ₁ /FVC	0.61 $\pm$ 0.15
6MWT, m	412 $\pm$ 117
Skeletal muscle strength	
Quadriceps, kg of force	27.1 $\pm$ 9.3
Quadriceps % predicted ^b	84.4 $\pm$ 25.6
SPPB	10.6 $\pm$ 1.8
COPD severity score	10.1 $\pm$ 6.0

^a Percent predicted FEV₁ values derived directly from the linear regression equations developed from the National Health and Nutrition Examination Survey (NHANES III) [24].

^b Muscle strength % predicted values generated from 302 age- and sex-matched control subjects without COPD, employing linear regression controlling for age, gender, BMI and height [9].

SPPB = Short Physical Performance Battery.

associations were observed for both baseline measures as well as their change over time. ORs for incident disability per SD decrement in each performance measure were ≥ 1.43 (95% CI: 1.00–3.75; p values < 0.04). Similarly, for each SD decrement in baseline COPD severity score as well as in changes over time, subjects had a 2.19 (95% CI: 1.65–2.89) and 1.94 (95% CI: 1.45–2.58) increased odds of developing incident disability, respectively (p values < 0.01).

For VLA disability, defined alternatively as a meaningful increase (1/2 SD) in the mean difficulty rating across activities, predictive associations of the 6MWT and COPD severity score with VLA disability remained strong, but were less consistent for FEV₁ and SPPB (table 3). Moreover, quadriceps strength did not predict new disability by this definition. Overall, point estimates for the ORs for incident disability were lower when disability was defined as a meaningful increase in mean difficulty compared to previous analyses based on the new rating of ‘unable’ in any activity domain.

Table 2. Changes in characteristics of subjects from baseline to follow-up (n = 609)

Subject characteristics	Mean $\pm$ SD	p value
FEV ₁ , liters	−0.10 $\pm$ 0.25	< 0.0001
Percent predicted FEV ₁ ^a	−1.9 $\pm$ 8.7	< 0.0001
6MWT distance, m	−36.1 $\pm$ 84.1	< 0.0001
Quadriceps, kg of force	0.8 $\pm$ 7.5	0.01
Quadriceps % predicted ^b	1.8 $\pm$ 23.0	0.01
SPPB	0.1 $\pm$ 1.5	0.02
COPD severity score	0.1 $\pm$ 4.7	0.70
BMI	−0.2 $\pm$ 3.2	0.15

^a Percent predicted FEV₁ values derived directly from the linear regression equations developed from the National Health and Nutrition Examination Survey (NHANES III) [24].

^b Muscle strength % predicted values generated from 302 age- and sex-matched control subjects without COPD, employing linear regression controlling for age, gender, BMI and height [9].

SPPB = Short Physical Performance Battery.

We next examined the impact of the COPD severity score and 6MWT, the two most consistent predictors of overall VLA disability, and percent predicted FEV₁ on the development of disability in the obligatory, committed and discretionary VLA subscales (table 4). Both baseline COPD severity score and change in the COPD severity score over time were consistently predictive of incident disability across all subscales: the ORs for incident disability across scales per SD decrement in the COPD severity score were all ≥ 1.90 (p values ≤ 0.01). Additionally, baseline 6MWT and percent predicted FEV₁ predicted incident disability across all VLA subscales with estimated ORs of ≥ 2.6 per SD decrement in 6MWT (p values < 0.01). Change in 6MWT, however, predicted incident disability in only the discretionary subscale. Change in percent predicted FEV₁ predicted incident disability in only the committed and discretionary subscales.

Eleven subjects (2%) developed incident disability in the obligatory subscale, 27 (4%) in the committed subscale and 60 (10%) in the discretionary subscale. Disability in committed activities was 2.5 times more likely than obligatory activities disability, taking that as the expected rate (95% CI: 1.27–4.54). In addition, disability in discretionary activities was 2.2 times more likely to develop than in committed activities (95% CI: 1.5–3.2).

The results of the sensitivity analyses including alternative definitions of BMI and in other analyses replacing T₀ predictor variables with the mean of T₀–T₁ were not substantively different from the results presented (data not shown).

Table 3. Impact of change in characteristics on the development of incident disability in VLA

Characteristic	Incident disability in VLA			
	VLA, newly unable to perform ^a (n = 55/609) (9%)		mean VLA rating, meaningful increase ^a (n = 91/619) (15%)	
	OR (95% CI) ^b	p value	OR (95% CI) ^b	p value
Baseline FEV ₁	1.76 (1.21–2.56)	<0.01	1.11 (0.84–1.45)	0.48
Decrement in FEV ₁	1.57 (1.15–2.15)	<0.01	1.58 (1.24–2.00)	<0.01
Baseline 6MWT	2.65 (1.87–3.75)	<0.01	1.46 (1.10–1.92)	<0.01
Decrement in 6MWT	1.43 (1.10–1.85)	<0.01	1.37 (1.11–1.69)	<0.01
Baseline quadriceps strength	1.75 (1.18–2.58)	<0.01	1.08 (0.80–1.46)	0.63
Decrement in quadriceps strength	1.39 (1.00–1.95)	0.05	1.09 (0.85–1.42)	0.49
Baseline SPPB	1.85 (1.42–2.41)	<0.01	1.32 (1.05–1.66)	0.02
Decrement in SPPB	1.43 (1.11–1.84)	<0.01	1.14 (0.91–1.41)	0.26
Baseline COPD severity score	2.19 (1.65–2.90)	<0.01	1.37 (1.09–1.73)	<0.01
Increase in COPD severity score	1.94 (1.45–2.59)	<0.01	1.37 (1.09–1.72)	<0.01

^a Newly unable to perform defined as a new rating of 'unable' in any activity domain from T0 to T1; a meaningful increase defined as a 1/2 SD increase in the mean difficulty in rated items from T0 to T1.

^b ORs expressed per standardized Z unit (1 SD) decrements in FEV₁, 6MWT, quadriceps strength or SPPB or increase in COPD

severity score, all of which were tested in separate multivariable logistic regression models that included the baseline value of the predictor as well as its change over time. All models also include gender, age, BMI, change in BMI, race, smoking status and second-hand smoke exposure.

VLA = Valued Life Activities.

Table 4. Impact of change in 6MWT and COPD severity score on the development of incident disability in subcategories of VLA

Characteristic	Incident disability in newly unable to perform VLA by VLA subcategory ^a					
	Obligatory (n = 11/609) (2%)		Committed (n = 27/609) (4%)		Discretionary (n = 60/609) (10%)	
	OR (95% CI) ^b	p value	OR (95% CI) ^b	p value	OR (95% CI) ^b	p value
Change in 6MWT	1.12 (0.66–1.94)	0.66	1.38 (0.96–1.96)	0.08	1.35 (1.04–1.75)	0.02
Baseline 6MWT	2.68 (1.37–5.23)	<0.01	2.86 (1.80–4.54)	<0.01	2.92 (2.08–4.11)	<0.01
Change in COPD severity score	2.06 (1.16–3.67)	0.01	2.25 (1.51–3.36)	<0.01	1.92 (1.45–2.55)	<0.01
Baseline COPD severity score	2.02 (1.17–3.50)	0.01	1.98 (1.36–2.88)	<0.01	2.44 (1.84–3.23)	<0.01
Change in percent predicted FEV ₁	1.31 (0.69–2.50)	0.41	1.61 (1.05–2.47)	0.03	1.47 (1.10–1.97)	<0.01
Baseline percent predicted FEV ₁	2.18 (1.06–4.44)	0.03	1.70 (1.07–2.68)	0.02	1.66 (1.21–2.27)	<0.01

^a Newly unable to perform defined as a new rating of 'unable' in any activity domain from T0 to T1.

^b ORs expressed per standardized Z unit (1 SD range) decrements in 6MWT and percent predicted FEV₁ or increase in COPD severity score, all of which were tested in separate multivariable

logistic regression models that included the baseline value of the predictor as well as its change over time. All models also include gender, age, BMI, change in BMI, race, smoking status and second-hand smoke exposure.

VLA = Valued Life Activities.

Discussion

We found that, in working-aged adults with COPD, greater impairments and poorer pulmonary and extra-pulmonary functioning predicted the development of incident disability. Although spirometric lung function was predictive of disability, so too was 6MWT and an integra-

tive COPD severity score that does not require either lung function or exercise testing. Moreover, measures of extra-pulmonary impairment (quadriceps strength) and function (SPPB) also predicted incident disability. Finally, within a hierarchy of activities, those considered discretionary were the most vulnerable to the development of disability and manifested the most consistent relation-

ship with both baseline and change in the independent predictors studied. Notably, discretionary activities are those least commonly assessed in traditional measures of ADL functioning.

These findings offer important insights into the COPD disablement process. Not only is COPD a respiratory disease, it is also a systemic process with effects on body systems distant from the lungs. Our study provides prospective epidemiological evidence that these effects on extra-pulmonary body systems predict the development of disability in patients with COPD. It is likely, therefore, that interventions aimed exclusively at improving pulmonary function are unlikely to fully mitigate COPD-related disablement.

We also identified a gradient in the development of disability that also has relevance for preventive strategies. Discretionary activities appear to represent a particularly vulnerable and 'sensitive' measure of the impact of COPD on disability. Over a follow-up period of only 2.5 years, 10% of subjects developed disability in discretionary activities. Moreover, this risk of disablement was 5-fold higher than the risk observed in the obligatory category, a category that subsumes (I)ADLs. In addition, in COPD, the disability in discretionary activities is strongly associated with the development of depression [35]. Thus, narrowly defining disability as (I)ADLs substantially underestimates the burden of COPD on daily life [21]. Thus, interventions aimed at COPD disability prevention should measure disability broadly across a spectrum of activities considered important to patients.

Our study builds upon previous work to advance the understanding of the disablement process in COPD; indeed, it reflects the growing appreciation of COPD as a systemic disease process. We systematically quantified the impact on COPD-related disability of both pulmonary and extra-pulmonary body systems at baseline and over time. Most longitudinal studies of disability in COPD have focused on advanced disease [39–41] (for which interventions to prevent disablement may be less effective), the elderly [42], hospitalized subjects [39, 43] or on (I)ADLs [41, 42]. By longitudinally studying a working-aged population with a wide range of disease severity, our findings are particularly relevant to ambulatory COPD populations at early risk for disability. Moreover, most previous studies of COPD have defined disability based on (I)ADLs. Although widely used to study disability in debilitated populations, (I)ADLs have limited utility in ambulatory populations because of a 'floor' effect in which most subjects score rather well and do not appear to change over time. By defining disability across a

broad range of activities, we identified a heretofore unobserved gradient in the prospective development of disability. Finally, we demonstrated that the COPD severity score, a method of disease severity assessment that does not require measuring pulmonary function, is as strong a predictor of disability as laboratory-based measures of pulmonary and extra-pulmonary functioning. This may be useful for epidemiological studies aiming to risk-adjust for disease severity or to identify subjects at higher risk of developing disability.

Our study also faces limitations. Of the 1,051 subjects reinterviewed, 69% completed follow-up clinic visits. Of these, 10% were excluded from this analysis due to inadequate/missing spirometry data. It is possible that death, a refusal to continue to participate or loss to follow-up may have introduced selection bias. The 310 subjects who did decline a follow-up visit were more likely to be current smokers and had worse exercise capacity. Thus, it is likely that any selection bias introduced would have resulted in an underestimation of disability risk. Our method of ascertaining a COPD diagnosis may also have resulted in misclassification, although our algorithm required utilization of COPD services, concomitant treatment with COPD medications and a physician diagnosis of COPD and was validated against a sample chart review [22]. In addition, the primary aim of this longitudinal study was to identify predictors of COPD-related disability; accordingly, subject recruitment was limited to working-aged adults. Thus, while our findings are particularly applicable to this population, our results may not be generalizable to older patients. Finally, there was, on average, little change in lung function over the observation period, even though within the group there were some subjects who declined rapidly; this appears to be consistent, however, with the heterogeneous natural history of COPD [44]. Despite these potential limitations, we identified factors that predict the development of disability over a relatively short period of time in an ambulatory COPD population and across a broad range of activities.

In summary, decrements in lung function as well as in body systems far away from the lungs are important predictors of the development and progression of COPD-related disablement. We also delineated a hierarchy of disablement in which discretionary activities are most vulnerable. Our findings suggest that interventions designed to prevent disability in COPD should comprehensively target both pulmonary and extra-pulmonary factors and should be initiated at the time disability appears in discretionary activities.

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