Published in final edited form as:

Am J Med. 2008 September ; 121(9): 789–796. doi:10.1016/j.amjmed.2008.04.030.

COPD as a Systemic Disease: Impact on Physical Functional Limitations

Mark D. Eisner, MD, MPH^{1,2}, Paul D. Blanc, MD, MSPH¹, Edward H. Yelin, PhD³, Stephen Sidney, MD, MPH², Patricia P. Katz, PhD³, Lynn Ackerson, PhD², Phenius Lathon, BS², Irina Tolstykh, MS², Theodore Omachi, MD, MPH¹, Nancy Byl, PhD⁴, and Carlos Iribarren, MD, MPH, PhD²

1Division of Occupational and Environmental Medicine and Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of California, San Francisco, USA

2Division of Research, Kaiser Permanente, Oakland, CA, USA

3Institute for Health Policy Studies, Department of Medicine, University of California, San Francisco, USA

4Department of Physical Therapy and Rehabilitation, University of California, San Francisco

Abstract

Purpose—Although chronic obstructive pulmonary disease (COPD) has a major impact on physical health, the specific impact of COPD on physical functional limitations has not been clearly characterized. We aimed to elucidate the physical functional limitations that are directly attributable to COPD compared to a matched referent group without the condition.

Methods—We used the FLOW (Function, Living, Outcomes, and Work) cohort study of adults with COPD (n=1,202) and referent subjects matched by age, sex, and race (n=302) to study the impact of COPD on the risk of a broad array of functional limitations using validated measures: lower extremity function (Short Physical Performance Battery, SPPB), submaximal exercise performance (Six Minute Walk Test, SMWT), standing balance (Functional Reach Test), skeletal muscle strength (manual muscle testing with dynamometry), and self-reported functional limitation (standardized item battery). Multivariate analysis was used to control for confounding by age, sex, race, height, educational attainment, and cigarette smoking.

Results—COPD was associated with poorer lower extremity function (mean SPPB score decrement for COPD vs. referent -1.0 points; 95% CI -1.25 to -0.73 pts) and less distance walked during the SMWT (-334 feet; 95% CI -384 to -282 ft). COPD was also associated with weaker muscle strength

Corresponding Author: Mark D. Eisner, MD, MPH, University of California, San Francisco, 505 Parnassus Avenue, M-1097, San Francisco, CA 94143-0111, Telephone (415) 476-7351, Fax (415) 476-6426, email: mark.eisner@ucsf.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Clinical Relevance

- COPD is related to a broad array of physical functional limitations: lower extremity functioning, exercise performance, skeletal muscle strength, and self-reported limitation in basic physical actions.
- COPD has impacts on diverse body systems remote from the lung.
- The COPD-related decrement in walking amounted to more than the length of a football field.
- Treatment strategies to prevent disability in COPD should target functional limitations.

in every muscle group tested, including both the upper and lower extremities ($p < 0.0001$ in all cases) and with a greater risk of self-reported functional limitation (OR 6.4; 95% CI 3.7 to 10.9).

Conclusions—A broad array of physical functional limitations were specifically attributable to COPD. COPD affects a multitude of body systems remote from the lung.

Keywords

pulmonary disease, chronic obstructive; disability evaluation; outcomes assessment

Chronic obstructive pulmonary disease (COPD) is being increasingly recognized as a multi-system disease.¹ Although pulmonary function decrement is the central physiologic limitation, it does not adequately explain who will become limited or disabled from the condition.²⁻⁴ Efforts to prevent COPD-related disability will not succeed until we understand how the disease affects distant body systems. Unfortunately, the impact of COPD on diverse non-pulmonary organ systems has not been well characterized.

Physical functional limitations are central decrements in basic physical actions such as mobility or strength.⁵ To understand how COPD produces disability, it is important to first determine the disease's impact on a broad array of physical functional limitations. These functional limitations, which represent effects of the disease on body systems distant from the lung, may mediate the disablement process. In a large cohort of adults with well-characterized COPD and a matched referent group recruited from a managed care organization, we elucidated the degree of physical functional limitation directly attributable to COPD.

Methods

Overview

The FLOW (Function, Living, Outcomes, and Work) study of COPD is an ongoing prospective cohort study of adult members of an integrated health care delivery system with a physician's diagnosis of COPD and a matched referent group without COPD. At baseline assessment, we conducted structured telephone interviews that ascertained COPD status, health status, self-reported functional limitations, sociodemographic characteristics, and physician-diagnosed comorbidities. Subjects then underwent a research clinic visit that included spirometry and other physical assessments. Using these baseline data, we evaluated the functional limitations directly attributable to COPD. The study was approved both by the University of California, San Francisco Committee on Human Research and the Kaiser Foundation Research Institute's institutional review board and all participants provided written informed consent.

Subject Recruitment

We identified all adult members of Kaiser Permanente Medical Care Program (KPMCP) who were recently treated for COPD using a previously described approach.⁶ The age range was restricted to 40-65 years because a key study outcome includes work disability.⁷ Using KPMCP computerized databases, we identified all subjects who met each of two criteria: one based on health care utilization and the second based on medication prescribing. The health care utilization criterion was one or more ambulatory visits, emergency department visits, or hospitalizations with a principal International Classification of Disease (ICD-9) diagnosis code for COPD (chronic bronchitis [491], emphysema [492], or COPD [496] during a recent 12 month time period. The medication criterion was two or more prescriptions for a COPD-related medication during a 12 month window beginning 6 months before the index utilization date and ending 6 months after index date. Based on medical record review, we demonstrated that this algorithm is a valid method for identifying adults with COPD.⁷

A total of 5,800 subjects were initially identified using the computerized algorithm. Of these, 298 died before they could be recruited into the study. Another 1,011 did not meet study inclusion criteria. Among the 2,181 non-respondents, 464 declined by prepaid postcard, 934 declined by telephone, and 783 were not reachable by telephone despite numerous attempts (>10). The completion rate for structured telephone interviews was 2,310 out of a remaining eligible group of 4,419 (51%). This is comparable to our earlier cohort study of adult asthma conducted at KPMCP and compares favorably for other survey-based epidemiologic studies conducted in the U.S.^{8, 9} Among the 2,310 respondents, 112 were not eligible for the clinic visit (8 were subsequently deceased, 10 were no longer Kaiser members, 85 were physically unable to attend, and 9 moved out of the area). Of the 2,198 eligible subjects, 1,216 completed the research clinic visit (55% of those interviewed and eligible). An additional 10 subjects were excluded because they did not meet the GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria for COPD after interviews and spirometry were performed.¹⁰ Four additional subjects were excluded from this analysis because they could not perform spirometry due to previous tracheostomy placement. Ultimately, there were 1,202 subjects with COPD who completed both interviews and research clinic visits.

Demographic information was available for non-interviewed subjects from Kaiser computerized databases. Compared to subjects who were eligible but not interviewed, interviewed subjects were slightly older (mean 0.7 years), more likely to be female (59 vs. 51%), and more likely to be white (69 vs. 56%). In terms of race-ethnicity, the two largest minority subgroups were slightly over-represented among those who completed interviews: (African American 14% vs. 11%, Hispanic 9% vs. 4%). Most of the differences in race were driven by limitations inherent in the Kaiser computerized databases: the prevalence of unknown race was much higher among those who did not complete interviews (17% vs 0.3%).

We aimed to recruit 300 referent subjects without COPD. Recruitment methods were identical to those used to recruit the COPD group, except that we excluded subjects with any history of utilization for COPD (i.e., no ambulatory visits, emergency department visits, or hospitalizations with any ICD-9 diagnosis code for COPD). We initially identified 373 referent subjects with no history of utilization for COPD who were matched to subjects with COPD by age, sex, and race. By design, we subsequently excluded 71 subjects who had evidence of airway obstruction ($FEV_1/FVC < 0.70$) at the time of research clinic evaluation leaving 302 referent subjects. Referent subjects were similar to COPD cases in terms of age, sex, and race ($p > 0.20$) (Table 1).

Assessment of Pulmonary Function Impairment

To assess respiratory impairment, we conducted spirometry according to American Thoracic Society (ATS) Guidelines.^{11, 12} We used the EasyOne™ Frontline spirometer (ndd Medical Technologies, Chelmsford, MA), which meets ATS criteria. To calculate percent predicted pulmonary function values, we used predictive equations derived from NHANES III.¹³ Based on FEV_1 , FEV_1/FVC ratio, and respiratory symptoms, COPD severity was staged based on National Heart, Lung, and Blood Institute / World Health Organization Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (stage 0 to IV).^{10, 14} Because research clinic examinations were conducted by trained non-medical personnel, we did not administer bronchodilators for study purposes. However, 90% of subjects had taken their own short-acting bronchodilator within 4 hours of spirometry or had taken a long-acting bronchodilator earlier in the same day.

Assessment of Functional Limitations at Research Clinic Visit

We assessed functional limitations, which are decrements in basic physical actions, using a multifaceted evaluation that combined a survey-based measure (self-reported functional

limitation as described below) and physical assessment. Submaximal exercise performance was measured using the Six Minute Walk Test, which was developed by Guyatt and has been widely used in studies of COPD.^{15, 16} We used the American Thoracic Society protocol.¹⁷

Lower extremity function was measured using the validated Short Physical Performance Battery (SPPB).¹⁸⁻²⁰ This battery includes 3 performance measures, each scored from 0 to 4 points. The standing balance test asks subjects to maintain their feet in a side-by-side, semi-tandem stand, or tandem stand for 10 seconds. A test of walking speed requires subjects to walk 4 meters at their normal pace. Participants are assigned a score from 1 to 4 based on the quartile of length of time needed to complete the test. The chair stand test, which reflects lower extremity extensor muscle strength, measures the time required for the subject to stand up and sit down from a chair 5 times with arms folded across the chest. Scores from 1 to 4 are assigned based on quartile of length of time to complete the task. A summary performance score integrates the 3 performance measures, ranging from 0 to 12. Previous work indicates that the battery has excellent inter-observer reliability, test-retest reliability, and predictive validity.¹⁸⁻²⁰

In addition to the balance component of the SPPB, we measured balance with the functional reach test. This test measures how far a subject can reach forward beyond arm's length while maintaining a fixed base of support in the standing position, without losing balance.²¹ The functional reach test has excellent test-retest reliability and validity.²¹⁻²⁴

Isometric skeletal muscle strength was evaluated following standard manual muscle testing procedures.²⁵ A hand-held dynamometer was used to improve the objectivity of the force estimates (MicroFet2 dynamometer (Saemmons Preston, Bolingbrook, IL)).²⁵ The examiners were trained in manual muscle testing by the same experienced physical therapist. Each of the examiners practiced testing control subjects until there was agreement between the raters 90% of the time within 5 pounds of force. Power grip strength was measured using a Jamar Hydraulic Hand Dynamometer (Stoelting, Wood Dale, IL) according to the protocol of the American Society of Hand Therapists.^{26, 27} Three trials were performed of each muscle group in alternating fashion. The maximum of three trials on the dominant side was selected for analysis.

Assessment of Self-reported Functional Limitation

Self-reported functional limitation was measured during interviews using a previously validated approach used by Sternfeld and colleagues, which was based on questions from the Framingham Disability Study, Established Populations for Epidemiologic Studies of the Elderly, the Nagle scale, and Rosow and Breslau scales.²⁸ The scale is comprised of 10 questions that assess the degree of difficulty in multiple domains of basic physical functioning such as pushing, stooping, kneeling, getting up from a standing position, lifting lighter or heavier objects, standing, sitting, standing from a seated position, walking up stairs, and walking in the neighborhood (see Appendix). Subjects who indicate "a lot of difficulty" with one or more functions or not doing a function because they were unable or they were told by a doctor not to do so are defined by this measure as having a self-reported functional limitation.²⁸

In addition, two additional questions were derived from the SF-36 scale to measure functional limitation.²⁹ These items ask whether the respondent's health limits him or her a lot, a little, or not at all in moderate activities (e.g., moving a table, pushing a vacuum cleaner, bowling, or playing golf) or climbing several flights of stairs. Subjects who indicated "a lot" of limitation were defined as having functional limitation on each item.

Statistical Analysis

Statistical analysis was conducted using SAS software, version 9.1 (SAS Institute, Inc, Cary, NC). We used linear regression analysis to elucidate the association between COPD status (vs. referent group) and performance on the SPPB, SMWT, functional reach test, and skeletal muscle strength tests. To examine potential confounding we controlled for age, sex, height, race (white, non-hispanic vs. other), educational attainment, and smoking status (current or past vs. never). Logistic regression was used to analyze the relationship between COPD status and the risk of self-reported functional limitations in analogous fashion. Income was not included as a covariate because it may be the outcome of COPD health status (i.e., COPD may lead to work disability and diminished income). We calculated the population attributable fraction (PAR%) for the impact of COPD on self-reported functional limitations.³⁰

To evaluate the more severe spectrum of COPD, we repeated the analysis after redefining COPD as an FEV₁/FVC ratio <0.70 and FEV₁ < 80% predicted (i.e., GOLD stage II or greater) which is consistent with the Burden of Lung Disease (BOLD) Study approach.³¹

The relationship between cardiovascular disease, COPD, and functional limitation is complex. Smoking is a major risk factor for both cardiovascular disease and COPD. COPD itself appears to be a risk factor for cardiovascular disease.⁷ Moreover, pulmonary function impairment is associated with cardiovascular disease even among lifelong never smokers.³² Because the causal pathway is complex, controlling for cardiovascular disease in the analyses would likely “overadjust” the estimates for COPD as a risk factor for functional limitation. Nonetheless, we performed an additional analysis in which we additionally controlled for cardiovascular disease (congestive heart failure, coronary artery disease, myocardial infarction, or stroke) and diabetes.

Results

Characteristics of Subjects With and Without COPD

By design, subjects with and without COPD were similar in age, sex, and race-ethnicity ($p > 0.20$ in all cases) (Table 1). The prevalence of lifetime smoking was much higher among those with COPD (87%) than in the referent group (48%) ($p < 0.0001$). Persons with COPD also had lower social class, as evidenced by lower educational attainment and household income. As expected, pulmonary function was markedly poorer in the COPD group (Table 2). The prevalence of cardiovascular disease (22 vs. 3%) and diabetes (21 vs 14%) were higher in the COPD group than among referents ($p < 0.05$ in both cases). Among subjects with COPD, the distribution of GOLD stages was stage 0 (31%), stage 1 (7%), stage 2 (32%), stage 3 (21%), AND stage 4 (9%)

Impact of COPD on Functional Limitation

Compared to the matched referent group, a diagnosis of COPD was associated with substantively poorer lower extremity function after controlling for age, sex, race, height, smoking history, and educational attainment (mean score decrement on SPPB -1.0 points; 95% CI -1.25 to -0.73) (Table 3). COPD was also related to much worse performance on the SMWT (-334 feet; 95% CI -384 to -282 feet) and standing balance (-3.0 cm in functional reach; 95% CI -4.2 to -1.8 cm). These COPD-related decrements in physical function correspond to a 9% reduction in mean lower extremity function, 20% reduction in SMWT performance, and 9% decrease in functional reach compared to the referent group.

COPD was related to weaker skeletal muscle strength in all muscle groups tested (Table 4). Both upper and lower extremity strength were affected. Compared to the referent group, the

decrement in mean muscle strength was 18% for quadriceps, 18% for hip flexors, 15% for hip abductors, 17% for elbow flexion, and 10% for grip strength.

COPD was also associated with a greater risk of self-reported functional limitation (OR 6.4; 95% CI 3.7 to 10.9), moderate activity limitation (OR 7.6; 95% CI 4.0 to 14.4), and limitation in stair climbing (OR 11.7; 95% CI 7.3 to 18.6) compared to those without COPD.

When COPD was redefined as GOLD stage II or greater, the results were highly similar for all analyses (Tables 3, 4, and 5). For both COPD definitions, the population attributable fraction for self-reported functional limitations was 82%. In addition, controlling for cardiovascular disease and diabetes slightly attenuated the risk estimates, but the overall pattern of results was very similar.

Discussion

COPD was related to a broad array of physical functional limitations compared to a matched referent group without the disease, including lower extremity functioning, exercise performance, skeletal muscle strength, and self-reported limitation in basic physical actions. These physical functional limitations are directly attributable to COPD, because patients with and without COPD were recruited from the same source population of managed care patients and were matched by age, sex, and race. For distance walked in 6 minutes, the COPD-related decrement amounted to more than the length of a football field.

These findings are important because they indicate that COPD has impacts on diverse body systems remote from the lung. Although previous studies have characterized physical function in COPD patients, they have not been able to estimate a broad array of decrements specifically attributable to the disease. Prior studies have either evaluated a limited spectrum of function or lacked an appropriate referent group.^{16, 33-46} Moreover, many of these studies included a highly selected group of persons with COPD, often on the severe end of the disease spectrum. These results from the FLOW study advance the field by establishing the multiple physical functional decrements that are directly attributable to COPD among persons with a broad range of disease severity.

In our theoretical framework, which is based on the work of Verbrugge and Jette, the development of functional limitations is the first step in the pathway to developing disability in COPD.⁵ Poorer lower extremity function, submaximal exercise performance, and muscle strength may result in disability from the disease. We are prospectively following the matched cohort of patients with and without COPD to determine the eventual impact of functional limitations on disability.

The role of cardiovascular comorbidities in the development of functional limitations in COPD is complex, because both conditions share risk factors (e.g., smoking) and COPD itself appears to predispose to adverse cardiovascular outcomes.⁷³² When we controlled for cardiovascular comorbidities and diabetes, the estimates for functional limitation attributable to COPD were only slightly attenuated. It is likely that these analyses overadjusted the risk estimates. Future longitudinal analyses may better elucidate this complex inter-relationship.

A study strength is the large sample of COPD patients who have a broad spectrum of disease severity, ranging from mild to severe. Our study is, to our knowledge, the largest prospective COPD cohort study to systematically evaluate a broad range of functional limitations compared to an appropriate matched control group. Recruitment from a large health plan should also help ensure generalizability to patients who are being treated for COPD in clinical practice. Availability of interview data, pulmonary function tests, and extensive physical characterization allows robust conclusions about physical functioning.

Our study is also subject to several limitations. Although the inclusion criteria required health care utilization for COPD, misclassification of asthma could have occurred. Our COPD definition required concomitant treatment with COPD medications to increase the specificity of the definition. In addition, all patients had a physician diagnosis of COPD and reported having the condition. The observed lifetime smoking prevalence was similar to that in other population-based epidemiologic studies of COPD, supporting the diagnosis of COPD rather than asthma.^{47, 48} We also previously demonstrated the validity of our approach using medical record review.⁷ When we limited the definition of COPD to more severe disease (GOLD Stage II or greater), however, the results were not substantively affected. In sum, we have a high degree of confidence that our results are not affected by misclassification bias.

Because our ultimate focus is on disability prevention, we intentionally sampled younger adults with COPD. Therefore, these results may underestimate the impact of COPD on functional limitation among older patients. In addition, Kaiser Permanente members, because they have health care access, may also be different than the general population of adults with COPD. Mitigating these limitations, the sociodemographic characteristics of Northern California Kaiser Permanente members are similar to those of the regional population, with some under-representation of income extremes.^{49, 50} Moreover, selection bias could have been introduced by non-participation in the study. There were some differences among subjects who did and did not participate in the interviews, but they were modest in scope and not likely to affect the results.

In conclusion, a broad array of physical functional limitations could be attributed directly to COPD. Prospective follow-up will determine the impact of these functional limitations on the risk of disability. Strategies to prevent COPD, or to treat it effectively, have potential to reduce physical functional limitation, and perhaps disability, in the general population.

Acknowledgements

Funded by: NHLBI / NIH R01HL077618

Appendix: Assessment of self-reported functional limitations (by structured telephone interview)

The next questions ask about difficulties that you might have with common activities. For the next items, please tell me what level of difficulty you have had during the past month: a lot of difficulty, some difficulty, a little difficulty, or no difficulty.

During the past month, how much difficulty have you had....

In pushing objects, like a living room chair?

In stooping, crouching, or kneeling?

In getting up from a stooping, crouching, or kneeling position?

In lifting or carrying items under 10 pounds, like a bag of potatoes?

In lifting or carrying items over 10 pounds, like a bag of groceries?

In standing in place for 15 minutes or longer?

In sitting for long periods, say 1 hour?

In standing up after sitting in a chair?

In walking alone up and down a flight of stairs?

In walking two or three neighborhood blocks?

References

1. Fabbri LM, Rabe KF. From COPD to chronic systemic inflammatory syndrome? *Lancet* Sep 1;2007 370(9589):797–799. [PubMed: 17765529]
2. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* Jul;1999 54(7):581–586. [PubMed: 10377201]
3. Jette DU, Manago D, Medved E, Nickerson A, Warzycha T, Bourgeois MC. The disablement process in patients with pulmonary disease. *Phys Ther* Apr;1997 77(4):385–394. [PubMed: 9105341]
4. Williams SJ, Bury MR. ‘Breathtaking’: the consequences of chronic respiratory disorder. *Int Disabil Stud* Jul-Sep;1989 11(3):114–120. [PubMed: 2634677]
5. Verbrugge LM, Jette AM. The disablement process. *Soc Sci Med* Jan;1994 38(1):1–14. [PubMed: 8146699]
6. Eisner MD, Blanc PD, Sidney S, et al. Body composition and functional limitation in COPD. *Respir Res* 2007;8:7. [PubMed: 17261190]
7. Sidney S, Sorel M, Quesenberry CP Jr, DeLuise C, Lanes S, Eisner MD. COPD and incident cardiovascular disease hospitalizations and mortality: Kaiser Permanente Medical Care Program. *Chest* Oct;2005 128(4):2068–2075. [PubMed: 16236856]
8. Calfee CS, Katz PP, Yelin EH, Iribarren C, Eisner MD. The influence of perceived control of asthma on health outcomes. *Chest* Nov;2006 130(5):1312–1318. [PubMed: 17099005]
9. Eisner MD, Yelin EH, Katz PP, Lactao G, Iribarren C, Blanc PD. Risk factors for work disability in severe adult asthma. *Am J Med* Oct;2006 119(10):884–891. [PubMed: 17000221]
10. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care Med* Apr;2001 163(5):1256–1276. [PubMed: 11316667]
11. American Thoracic Society. Standardization of spirometry--1987 update. Statement of the American Thoracic Society. *American Review of Respiratory Disease* 1987;136(5):1285–1298. [PubMed: 3674589]
12. American Thoracic Society. Standardization of Spirometry, 1994 Update. *Am J Respir Crit Care Med* Sep;1995 152(3):1107–1136. [PubMed: 7663792]
13. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *American Journal of Respiratory and Critical Care Medicine* 1999;159(1):179–187. [PubMed: 9872837]
14. Fabbri LM, Hurd SS. Global Strategy for the Diagnosis, Management and Prevention of COPD: 2003 update. *Eur Respir J* Jul;2003 22(1):1–2. [PubMed: 12882441]
15. Guyatt GH, Sullivan MJ, Thompson PJ, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. *Can Med Assoc J* 1985;132(8):919–923. [PubMed: 3978515]
16. Sciurba F, Criner GJ, Lee SM, et al. Six-minute walk distance in chronic obstructive pulmonary disease: reproducibility and effect of walking course layout and length. *Am J Respir Crit Care Med* Jun 1;2003 167(11):1522–1527. [PubMed: 12615634]
17. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* Jul 1;2002 166(1):111–117. [PubMed: 12091180]
18. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med* Mar 2;1995 332(9):556–561. [PubMed: 7838189]
19. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci* Apr;2000 55(4):M221–231. [PubMed: 10811152]

20. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* Mar;1994 49(2):M85–94. [PubMed: 8126356]
21. Duncan PW, Weiner DK, Chandler J, Studenski S. Functional reach: a new clinical measure of balance. *J Gerontol* Nov;1990 45(6):M192–197. [PubMed: 2229941]
22. Duncan PW, Studenski S, Chandler J, Prescott B. Functional reach: predictive validity in a sample of elderly male veterans. *J Gerontol* May;1992 47(3):M93–98. [PubMed: 1573190]
23. Weiner DK, Duncan PW, Chandler J, Studenski SA. Functional reach: a marker of physical frailty. *J Am Geriatr Soc* Mar;1992 40(3):203–207. [PubMed: 1538035]
24. Weiner DK, Bongiorno DR, Studenski SA, Duncan PW, Kochersberger GG. Does functional reach improve with rehabilitation? *Arch Phys Med Rehabil* Aug;1993 74(8):796–800. [PubMed: 8347063]
25. Kendall, FP.; McReary, EK.; Provance, PG. *Muscles Testing and Function*. Fourth. Baltimore: Williams & Wilkins; 1993.
26. Adams, LS.; Greene, LW.; Topoozian, E. *American Association of Hand Therapists Clinical Assessment Recommendations*. 7. New York: Churchill Livingstone; 1999.
27. Mathiowetz V, Weber K, Volland G, Kashman N. Reliability and validity of grip and pinch strength evaluations. *J Hand Surg [Am]* Mar;1984 9(2):222–226.
28. Sternfeld B, Ngo L, Satariano WA, Tager IB. Associations of body composition with physical performance and self-reported functional limitation in elderly men and women. *Am J Epidemiol* Jul 15;2002 156(2):110–121. [PubMed: 12117699]
29. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical Care* 1992;30(6):473–483. [PubMed: 1593914]
30. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. *American Journal of Public Health* 1998;88(1):15–19. [PubMed: 9584027]
31. Buist AS, McBurnie MA, Vollmer WM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet* Sep 1;2007 370(9589):741–750. [PubMed: 17765523]
32. Eisner MD, Wang Y, Haight TJ, Balmes J, Hammond SK, Tager IB. Secondhand smoke exposure, pulmonary function, and cardiovascular mortality. *Ann Epidemiol* May;2007 17(5):364–373. [PubMed: 17300955]
33. Mannino DM, Ford ES, Redd SC. Obstructive and restrictive lung disease and functional limitation: data from the Third National Health and Nutrition Examination. *J Intern Med* Dec;2003 254(6):540–547. [PubMed: 14641794]
34. Skeletal muscle dysfunction in chronic obstructive pulmonary disease. A statement of the American Thoracic Society and European Respiratory Society. *Am J Respir Crit Care Med* Apr;1999 159(4 Pt 2):S1–40. [PubMed: 10194189]
35. Hamilton AL, Killian KJ, Summers E, Jones NL. Muscle strength, symptom intensity, and exercise capacity in patients with cardiorespiratory disorders. *Am J Respir Crit Care Med* Dec;1995 152(6 Pt 1):2021–2031. [PubMed: 8520771]
36. Bernard S, LeBlanc P, Whittom F, et al. Peripheral muscle weakness in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* Aug;1998 158(2):629–634. [PubMed: 9700144]
37. Gosker HR, Lencer NH, Franssen FM, van der Vusse GJ, Wouters EF, Schols AM. Striking similarities in systemic factors contributing to decreased exercise capacity in patients with severe chronic heart failure or COPD. *Chest* May;2003 123(5):1416–1424. [PubMed: 12740256]
38. Gosselink R, Troosters T, Decramer M. Peripheral muscle weakness contributes to exercise limitation in COPD. *Am J Respir Crit Care Med* Mar;1996 153(3):976–980. [PubMed: 8630582]
39. Decramer M, Lacquet LM, Fagard R, Rogiers P. Corticosteroids contribute to muscle weakness in chronic airflow obstruction. *Am J Respir Crit Care Med* Jul;1994 150(1):11–16. [PubMed: 8025735]
40. Gosselink R, Decramer M. Peripheral skeletal muscles and exercise performance in patients with chronic obstructive pulmonary disease. *Monaldi Arch Chest Dis* Aug;1998 53(4):419–423. [PubMed: 9828598]

41. Engelen MP, Schols AM, Does JD, Wouters EF. Skeletal muscle weakness is associated with wasting of extremity fat-free mass but not with airflow obstruction in patients with chronic obstructive pulmonary disease. *Am J Clin Nutr* Mar;2000 71(3):733–738. [PubMed: 10702166]
42. Rantanen T, Masaki K, Foley D, Izmirlian G, White L, Guralnik JM. Grip strength changes over 27 yr in Japanese-American men. *J Appl Physiol* Dec;1998 85(6):2047–2053. [PubMed: 9843525]
43. Fink G, Moshe S, Goshen J, et al. Functional evaluation in patients with chronic obstructive pulmonary disease: pulmonary function test versus cardiopulmonary exercise test. *J Occup Environ Med* Jan; 2002 44(1):54–58. [PubMed: 11802466]
44. McGavin CR, Gupta SP, McHardy GJ. Twelve-minute walking test for assessing disability in chronic bronchitis. *Br Med J* Apr 3;1976 1(6013):822–823. [PubMed: 1260350]
45. McGavin CR, Artvinli M, Naoe H, McHardy GJ. Dyspnoea, disability, and distance walked: comparison of estimates of exercise performance in respiratory disease. *Br Med J* Jul 22;1978 2 (6132):241–243. [PubMed: 678885]
46. Poulain M, Durand F, Palomba B, et al. 6-minute walk testing is more sensitive than maximal incremental cycle testing for detecting oxygen desaturation in patients with COPD. *Chest* May;2003 123(5):1401–1407. [PubMed: 12740254]
47. Eisner MD, Balmes J, Katz PP, Trupin L, Yelin EH, Blanc PD. Lifetime environmental tobacco smoke exposure and the risk of chronic obstructive pulmonary disease. *Environ Health* May 12;2005 4(1): 7. [PubMed: 15890079]
48. Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance--United States, 1971-2000. *MMWR Surveill Summ* Aug 2;2002 51(6):1–16.
49. Karter AJ, Ferrara A, Liu JY, Moffet HH, Ackerson LM, Selby JV. Ethnic disparities in diabetic complications in an insured population. *JAMA* May 15;2002 287(19):2519–2527. [PubMed: 12020332]
50. Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. *American Journal of Public Health* 1992;82(5):703–710. [PubMed: 1566949]

Table 1

Baseline Characteristics of FLOW Cohort of COPD vs. Referent Subjects

Characteristic	COPD (n=1202)	Referents (n=302)	P value
Age (years)	58.2 (6.2)	58.5 (6.2)	0.50
Sex (female)	691 (57.4%)	185 (61%)	0.23
Race / ethnicity			
White, non-hispanic	810 (67%)	200 (66%)	0.96
African-American	206 (17%)	57 (19%)	
Asian / Pacific Islander	35 (3%)	8 (3%)	
Hispanic	111 (9%)	28 (9%)	
Other	40 (3%)	9 (3%)	
Smoking history			<0.0001
Never smoked	162 (13%)	158 (52%)	
Current smoker	393 (33%)	12 (4%)	
Ex-smoker	644 (54%)	132 (44%)	
Educational attainment			<0.0001
High school or less	352 (29%)	42 (14%)	
Some college	524 (44%)	95 (31%)	
College /graduate degree	326 (27%)	165 (55%)	
Household income			<0.0001
Low (<\$20,000)	129 (11%)	9 (3%)	
Intermediate (\$20 to 80,000)	699 (58%)	137 (45%)	
High (>\$80,000)	276 (23%)	133 (44%)	
Declined to report	98 (8%)	23 (8%)	

Table 2

Pulmonary Function and Stage of COPD in the FLOW Cohort

Measure	COPD (n=1202)	Referents (n=302)	P value for comparison
FEV ₁ (liters)	1.79 (0.78)	2.17 (0.66)	<0.0001
FEV ₁ % predicted	62% (23)	96% (13)	<0.0001
FVC	2.93 (0.98)	3.55 (0.87)	<0.0001
FVC % predicted	79% (20)	96 (14%)	<0.0001
FEV ₁ /FVC	0.61 (0.15)	0.78 (0.04)	<0.0001
Mean (sd)			

Table 3
Impact of COPD on Functional Limitation: Lower Extremity Functioning, Exercise Performance, and Balance

Functional limitation	Test	ALL SUBJECTS Mean change in score for COPD vs. referent (95% CI)	GOLD Stage II+ Mean change in score for COPD vs. referent (95% CI)	GOLD II+ CONTROLLING FOR COMORBIDITIES Mean change in score for COPD vs. referent (95% CI)
Lower extremity function	Short Physical Performance Battery total score (points)	-1.0 (-1.25 to -0.73) P<0.0001	-0.94 (-1.23 to -0.65) P<0.0001	-0.81 (-1.10 to -0.53) P<0.0001
Submaximal exercise performance	Six Minute Walk Test (feet)	-334 (-384 to -282) P<0.0001	-348 (-404 to -291) P<0.0001	-317 (-372 to -262) P<0.0001
Standing balance	Functional Reach Test (cm)	-3.0 (-4.2 to -1.8) P<0.0001	-2.4 (-3.7 to -1.1) P<0.0003	-2.1 (-3.4 to -0.8) P=0.0017

All analyses control for age, sex, height, race, educational attainment, smoking

The third column show results for all subjects. The fourth column shows results for more severe COPD only (GOLD Stage II or greater) vs. referent group (n=742 COPD cases vs. 302 referent subjects)

The fifth column shows results for GOLD Stage II or greater vs. referent group, controlling for baseline covariates plus inclusion of cardiovascular comorbidities (congestive heart failure, coronary artery disease, myocardial infarction, or stroke) and diabetes

Table 4
Impact of COPD on Functional Limitation: Skeletal Muscle Strength

Region	Muscle group	ALL SUBJECTS Mean difference in strength, COPD vs. referents (95% CI)	GOLD Stage II+ Mean difference in strength, COPD vs. referents (95% CI)	GOLD II+ CONTROLLING FOR COMORBIDITIES Mean change in score for COPD vs. referent (95% CI)
LOWER EXTREMITY	Quadriceps	-12.7 (-15.2 to -10.3) P<0.0001	-12.6 (-15.4 to -9.9) P<0.0001	-12.2 (-15.0 to -9.4) P<0.0001
	Hip flexors	-8.3 (-10.4 to -6.3) P<0.0001	-7.9 (-10.1 to -5.7) P<0.0001	-7.2 (-9.4 to -5.0) P<0.0001
	Hip abductors	-6.3 (-7.9 to -4.6) P<0.0001	-6.3 (-8.1 to -4.5) P<0.0001	-6.1 (-7.8 to -4.2) P<0.0001
UPPER EXTREMITY	Elbow flexors	-8.5 (-10.2 to -6.8) P<0.0001	-8.7 (-10.5 to -6.9) P<0.0001	-8.6 (-10.4 to -6.7) P<0.0001
	Grip	-3.6 (-4.5 to -2.6) P<0.0001	-3.6 (-4.7 to -2.5) P<0.0001	-3.5 (-4.5 to -2.4) P<0.0001

Muscle strength is measured in pounds of force; greatest of 3 repetitions on the dominant side

All analyses control for age, sex, race, educational attainment, and smoking history

The fourth column shows results for more severe COPD only (GOLD Stage II or greater) vs. referent group (n=742 COPD cases vs. 302 referent subjects); last column also controls for cardiovascular comorbidities and diabetes

Table 5

Impact of COPD on Self-reported Functional Limitation

Functional limitation measure	ALL SUBJECTS		GOLD Stage II+		GOLD II+ CONTROLLING FOR COMORBIDITIES	
	Odds ratio for COPD vs. referents (95% CI)		Odds ratio for COPD vs. referents (95% CI)		Odds ratio for COPD vs. referents (95% CI)	
Self-reported functional limitation [†]	6.4 (3.7 to 10.9) P<0.0001		7.0 (3.9 to 12.3) P<0.0001		6.0 (3.4 to 10.7) P<0.0001	
Limitation in moderate activities ^{††}	7.6 (4.0 to 14.4) P<0.0001		8.7 (4.5 to 16.9) P<0.0001		7.8 (4.0 to 15.1) P<0.0001	
Limitation in climbing several flights of stairs	11.7 (7.3 to 18.6) P<0.0001		14.0 (8.5 to 23) P<0.0001		13.2 (8.0 to 22) P<0.0001	

Multivariate logistic regression analysis controlling for age, sex, race, height, smoking, education

[†]“Unable to do” or “severe limitation” in a battery of basic physical activities (see Methods)

^{††}Health limits “a lot” in performing moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf

The fourth column shows results for more severe COPD only (GOLD Stage II or greater) vs. referent group (n=742 COPD cases vs. 302 referent subjects). The fifth column shows the same group with additional statistical control for cardiovascular comorbidities and diabetes.