COPD

Patterns of Healthcare Utilization by COPD Severity: A Pilot Study

Min J. Joo · Todd A. Lee · Brian Bartle · William B. van de Graaff · Kevin B. Weiss

Received: 28 February 2008/Accepted: 14 April 2008/Published online: 8 May 2008 © Springer Science+Business Media, LLC 2008

Abstract Global Initiative on Chronic Obstructive Lung Disease (GOLD) guidelines recently removed stage 0, a group with symptoms but without airways obstruction, from their severity staging. However, in practice this group may still be diagnosed and medically managed. The aim of this study was to characterize healthcare utilization patterns of chronic obstructive pulmonary disease (COPD) patients by disease severity, focusing on the possible unique

M. J. Joo (🖂)

M. J. Joo

Center for the Management of Complex Chronic Care, Jesse Brown VA Hospital, Chicago, IL, USA

M. J. Joo · T. A. Lee · B. Bartle Center for the Management of Complex Chronic Care, Hines VA Hospital, Hines, IL 60141, USA

T. A. Lee

Institute for Healthcare Studies, Division of General Internal Medicine, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL 60611, USA

W. B. van de Graaff

Division of Pulmonary and Critical Care Medicine, Loyola University Chicago Stritch School of Medicine, Maywood, IL 60626, USA

W. B. van de Graaff Division of Pulmonary and Critical Care Medicine, Hines VA Hospital, Hines, IL 60141, USA

K. B. Weiss

American Board of Medical Specialties, Evanston, IL 60201, USA

attributes of patients who would have been classified as GOLD stage 0. This is a prospective cohort pilot study performed at the Hines Veterans Administration Hospital. One hundred twenty patients with a diagnosis of COPD were enrolled. The participants completed quality-of-life questionnaires and a pulmonary function test. Healthcare utilization data were obtained 1 year prior and 2 years after the enrollment date. Three disease severity groups were defined based on GOLD criteria for comparison [GOLD stage 1-2 (GS 1-2), GOLD stage 3-4 (GS 3-4), and formerly GOLD stage 0 ("at risk")]. The "at risk" group had an average of 14.4 (SD = 30.5) outpatient visits/year and 0.3 (SD = 0.8) hospitalizations/year, which were higher than the other groups, but this was not statistically significant. Respiratory medications were used by 6 (26%), 30 (59%), and 40 (91%) patients from "at risk" to GS 3-4, respectively. Patients in the "at risk" group had a decrement in health status, significant utilization of healthcare services, and were often receiving medications not consistent with guidelines.

Keywords Chronic obstructive pulmonary disease · Health status · Healthcare · Health services research

Introduction

Chronic obstructive pulmonary disease (COPD) is a common chronic disease affecting more than 24 million adults in the United States [1]. The Veterans Administration (VA) plays an important part in the care of patients with COPD in the United States as there are nearly 500,000 patients with a COPD diagnosis receiving care in a given year in the VA.

The updated Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines designate four stages of

Section of Pulmonary, Critical Care, and Sleep Medicine, Department of Medicine, University of Illinois at Chicago, 840 S. Wood St., M/C 719, Chicago, IL 60612, USA e-mail: joo@uic.edu

severity based on spirometry values [2]. Unlike the previous classification, this current version does not include stage 0 defined as the "at risk" population with symptoms, exposure to risk factors, and normal spirometry. Previous studies have shown that the diagnosis of COPD is often made without spirometric evidence with only a third of those with a new diagnosis of COPD having spirometry performed [3, 4]. Based on the National Health and Nutrition Examination Survey III (NHANES III) results, only 17.4 percent of adults with a self-reported diagnosis of COPD had 1987 American Thoracic Society-defined low lung function consistent with chronic obstruction [5, 6]. Even without a label within the GOLD staging of COPD, this former stage 0 group, in practice, may represent a considerable number of adults being diagnosed with COPD and managed with pharmacologic therapy.

There is limited information about this population with respect to their health status, healthcare utilization, and progression of disease. One of the studies to focus on this group showed that progression of COPD disease severity from GOLD stage 0 to stage II did not correspond to meaningful differences in health status although a worsening of health status was noted [7]. Whether the presence of chronic cough and sputum without airway obstruction (formerly GOLD stage 0) really identifies individuals at risk to develop future bronchial obstruction is still debatable [8-11]. However, studies have found that this population may have an increased mortality risk compared with asymptomatic smokers with normal lung function [12–15]. To ultimately understand the outcomes associated with the COPD disease severity groups, including the previously defined GOLD stage 0 group, an important step is to better understand the similarities and differences by group with respect to health status and healthcare utilization. We conducted a pilot study at a single institution to characterize health status and healthcare utilization patterns of COPD patients seeking care in the VA by disease severity, focusing on the possible unique attributes of patients who would have been classified as GOLD stage 0 due to presence of symptoms in the absence of airway obstruction.

Methods

This was an observational pilot study approved by the Human Studies Subcommittee of the Hines VA Hospital.

Study Sample

We identified patients who had made an inpatient or outpatient visit and who had a diagnosis of COPD [International Classification of Diseases, ninth revision (ICD-9) 491.x, 492.x, 496.x] during a 12-month period from a Hines VA facility (hospital or outpatient clinics). Eligible patients identified were contacted by letter inviting them to participate; up to two letters were mailed to each individual. Each letter contained a copy of the consent form, the Health Insurance Portability and Accountability Act form, and a one-page description detailing the protocol for the study and contact numbers for study personnel. Mailings were sent until 120 patients were enrolled in the study and informed consent was obtained. The first participant enrolled on May 12, 2003, and the last patient enrolled on September 1, 2004. A total of 1338 unique patients were contacted by letters to recruit 120 patients. Participants were required to attend a single study visit to the Hines Pulmonary Function Lab. Participants completed the St. George's Respiratory Questionnaire followed by a pulmonary function test (PFT) and a 6-minute walk test (6MWT). All participants also completed a smoking history questionnaire, including a self report of current status as a current smoker, ex-smoker, or having never smoked. All spirometries were performed in the Hines VA Hospital Pulmonary Function Lab using a Morgan Scientific PFT system according to ATS standards. Each patient underwent a minimum of three maneuvers and if not reproducible additional maneuvers were performed.

St. George's Respiratory Questionnaire (SGRQ)

The SGRQ is a disease-specific measure of quality of life and well being in patients with obstructive lung disease [16]. The instrument has been shown to be a valid and reliable measure of COPD-related quality of life [16–19]. The questionnaire provides an overall score as well as scores for symptoms, activity, and impact domains. The results from the instrument are measured from 0% (no impairment) to 100% (maximum impairment). A difference in scores of 4% has been shown to be a minimally important difference [16].

Healthcare Utilization

Healthcare utilization, including inpatient visits, outpatient visits, and outpatient respiratory medication utilization was obtained from VA encounter data for 12 months before and 24 months after each patient's study visit. All-cause and COPD-related inpatient and outpatient encounters were analyzed for each group. COPD-related visits were defined as an outpatient or inpatient visit with any diagnosis for COPD. For medication utilization, each patient had to have more than one prescription for each drug category in a single year to be considered a regular user of that medication for that year. The aggregate of all medications for each disease category was obtained as a surrogate for healthcare consumption in relation to disease severity.

Severity of COPD

Three disease severity groups were defined based on GOLD criteria: formerly GOLD stage 0 ("at risk") includes diagnosis of COPD without airway obstruction, GOLD stage 1–2 (GS 1–2) includes GOLD stages I and II (mild-moderate), and GOLD stage 3–4 (GS 3–4) includes GOLD stages III and IV (severe-very severe). The previous classification of GOLD stage 0 required chronic symptoms (cough, sputum production) and normal spirometry. The prebronchodilator values were used.

Statistical Analysis

Characteristics of the patients were summarized using counts and percentages to describe categorical variables and means and standard deviations to describe continuous variables. Comparisons of the means between the severity groups were made with an analysis of variance (ANOVA) model. Covariates that had a significant relationship to severity means or that changed the point estimates more than 10% were included in the adjusted model. Based on this criterion, the model was adjusted for age and smoking status and performed using the analysis of covariance (ANCOVA) model. Post hoc differences between groups were assessed by the Scheffè test [20]. For variables lacking normal distribution and/or homogeneous variance and could not be transformed, the Kruskal-Wallis test was used. Comparisons of means were performed if each group had a sample size greater than six, otherwise only percentages and means were used. A p value less than 0.05 was considered statistically significant.

Results

We recruited 120 patients for participation in the study; four patients were ultimately excluded due to inadequate spirometry based on ATS criteria. Approximately 94% of the patients were white and 98% were male. A total of 23 (19.8%) of the participants were classified as "at risk," 49 (42.2%) as GS 1-2, and 44 (37.9%) as GS 3-4. Comparison of means for the subject characteristics and other laboratory values are shown in Table 1. The average body mass index (BMI) was significantly different between "at risk" and GS 3–4 only (ANOVA p = 0.033), with the "at risk" group having the highest BMI [31.2 (SD = 5.4) kg/ cm²] and the GS 3–4 group having the lowest BMI [27.7 $(SD = 5.5) \text{ kg/cm}^2$]. The 6MWT was statistically different between GS 1-2 and GS 3-4. In the "at risk" group, the prevalence of diabetes mellitus was 26.1%, hypertension was 56.5%, and heart disease was 39.1%. The prevalence of these comorbid conditions was similar in the other groups.

The SGRQ scores by disease severity are seen in Table 2. After adjusting for age and smoking status, the SGRQ total scores were lowest for the "at risk" group and highest for the GS 3–4 group. Most of the differences in scores between groups reached statistical significance. The exceptions were the total, activity, and impact scores, which were not different between the "at risk" group and GS 1–2, and the symptom domain, which showed a difference only between the "at risk" group and GS 3–4 [41.9 (SD = 22.7) vs. 57.9 (SD = 23.9)].

Healthcare visits are summarized in Table 3. The "at risk" group had the highest proportion and most all-cause

Table 1 Subject characteristics

	"At risk" $(n = 23)$	GS 1–2 $(n = 49)$	GS 3–4 $(n = 44)$	p value	Total $(n = 116)$
Age (years)	68.5 (12.9)	72.9 (10.7)	71.5 (7.2)	0.247	71.5 (range = $25-87$) (10.4)
Smoking status					
Current	3	8	8		19 (16.4%)
Past	15	37	34		86 (74.1%)
Never	5	4	2		11 (9.5%)
Smoke-years (years)	20.4 (11.0)	35.9 (14.4)	36.4 (14.8)	< 0.001	33.4 (15.1)
Packs per day	1.54 (1.08)	1.53 (0.87)	1.56 (0.64)	0.986	1.54 (0.82)
Pack-years	31.1 (26.4)	57.4 (43.2)	55.9 (28.5)	0.044	52.6 (range = 0-200) (36.4)
BMI (kg/cm ²)	31.2 (5.4)	29.2 (4.6)	27.7 (5.5)	0.033	29.0 (5.3)
6MWT (m)	337.1 (137.0)	338.6 (86.9)	272.1 (111.7)	0.007	313.1 (111.6)
FEV ₁ /FVC (%)	77.7 (5.5)	56.5 (7.9)	39.9 (11.3)	< 0.001	54.4 (16.5)

Data are presented as mean and standard deviation (SD) in parentheses unless otherwise stated. The ANOVA model was used to determine significance

Smoke-years = number of years of tobacco smoking; Pack-years = packs per day multiplied by the number of years of tobacco smoking; BMI = body mass index; $FEV_1 = forced expiratory volume in one second$; FVC = forced vital capacity; 6MWT = 6 minute walk test

Significant (p < 0.05) differences between severity groups were as follows: Smoke-years: "at risk" and 1–2, "at risk" and 3–4; Pack-years: "at risk" and 3–4; BMI: "at risk" and 3–4; PaO₂: "at risk" and 3–4, 1–2 and 3–4; 6MWT: 1–2 and 3–4

 Table 2
 St. George's Respiratory Questionnaire scores by disease severity

Index	"At risk" $(n = 23)$	GS 1–2 (<i>n</i> = 49)	GS 3–4 (<i>n</i> = 44)	p value
SGRQ Symptom	41.88 (22.69)	46.40 (24.01)	57.86 (23.88)	0.023
SGRQ Activity	37.55 (25.33)	52.01 (27.31)	72.35 (20.55)	< 0.001
SGRQ Impact	20.39 (14.10)	24.72 (17.22)	40.31 (18.92)	< 0.001
SGRQ Total	29.14 (16.75)	36.00 (18.25)	52.92 (17.31)	< 0.001

Data are presented as mean and standard deviation (SD) in parentheses unless otherwise stated. The ANCOVA model adjusted for age and smoking status was used. Significant (p < 0.05) differences between severity groups were as follows: SGRQ symptom score: "at risk" and 3–4; SGRQ activity, impact, and total scores: "at risk" and 3–4, 1–2, and 3–4

inpatient visits with 30.4% of the group, averaging 1.89 (SD = 1.36) visits per patient-year. The "at risk" group also had the most all-cause outpatient visits, averaging 14.40 (SD = 30.79) visits per patient-year, while GS 1–2 and GS 3–4 had 10.50 (SD = 13.53) and 10.73 (SD = 14.24) visits per patient-year, respectively. This was not statistically significant.

Medication utilization for each severity group is summarized in Table 4. The proportions in each group receiving medications were 26.1, 59.2, and 90.9% in the "at risk" group, GS 1-2, and GS 3–4, respectively. The means days supplied for the proportion of each group receiving medications were follows: "at risk" was 205.6 (SD = 120.6), GS 1–2 was 331.8 (SD = 240.7), and GS

 Table 3 Inpatient and outpatient visits

3–4 was 501.8 (SD = 328.1) days supplied per patientyear. For individual drug categories, the largest proportions of users for all groups were noted for inhaled anticholinergics, followed by inhaled short-acting β -agonists.

Discussion

Approximately one fifth of our cohort with an existing diagnosis of COPD had no bronchial obstruction noted on spirometry. As expected, GS 3-4 had the most COPDrelated outpatient visits per patient-year and the largest proportion utilizing COPD-related inpatient care. However, the "at risk" group had the most all-cause inpatient and outpatient visits per patient per year, although not statistically significant. Also as expected, the proportion of patients in each group utilizing medications increased with increasing disease severity. About 25% of the "at risk" patients received respiratory medications on a regular basis, while more than 40% in GS 1-2 did not receive any respiratory medications, suggesting a pattern of care not consistent with GOLD guidelines. Because the "at risk" group has no comparison group in the American Thoracic Society and European Respiratory Society, no prior recommendations for treatment exist for this group.

Consistent with previous findings, in this VA population sample, categorizing patients based on the GOLD staging system resulted in differences in health status in the SGRQ between mild-moderate disease (GS 1–2) and severe-very severe disease stages (GS 3–4) [7, 21]. Our findings also indicate that the "at risk" patients have health status deterioration similar to patients with mild-moderate disease

	"At risk" $(n = 23)$	GS 1–2 ($n = 49$)	GS 3–4 ($n = 44$)	p value
Inpatient visits (All) [mean (SD)]	0.25 (0.79)	0.14 (0.50)	0.17 (0.60)	0.308
Proportion of group with an inpatient visit (%)	30.4	18.4	22.0	
Inpatient visits in proportion of group with an inpatient visit [mean (SD)]	1.89 (1.36)	1.62 (0.65)	1.64 (1.20)	0.691
Outpatient visits (All) (mean) [22]	14.4 (30.47)	10.50 (13.53)	10.73 (14.24)	0.903
Proportion of group with an outpatient visit (%)	100	100	100	
Outpatient visits in proportion of group with an outpatient visit [mean (SD)]	14.4 (30.47)	10.50 (13.53)	10.73 (14.24)	0.903
COPD-related outpatient visits (All) [mean (SD)]	0.59 (0.81)	1.59 (2.41)	2.62 (3.24)	< 0.001
Proportion of group with a COPD-related outpatient visit (%)	100	95.9	97.7	
COPD-related outpatient visits in proportion of group with a COPD-related outpatient visit [mean (SD)]	0.59 (0.81)	1.65 (2.44)	2.68 (3.26)	< 0.001
COPD-related inpatient visits (All) [mean (SD)]	0.04 (0.21)	0.09 (0.38)	0.11 (0.49)	N/A ^a
Proportion of group with a COPD-related inpatient visit (%)	13.0	12.2	15.9	
COPD-related inpatient visits in proportion of group with a COPD-related inpatient visit [mean (SD)]	1.00 (0.00)	1.40 (0.52)	1.50 (1.08)	N/A ^a

The mean and standard deviation (SD) in parentheses are visits per patient-year

p value was obtained from the Kruskal-Wallis test

^a N/A = not available due to small sample size

Table 4 Medication utilization

	"At risk" $(n = 23)$	GS 1–2 $(n = 49)$	GS 3–4 $(n = 44)$
Total medications (All) [mean (SD)]	19.4 (53.0)	155.0 (251.7)	366.5 (353.2)
Proportion of group receiving medications (%)	26.1	59.2	90.9
Total medications in proportion of group receiving medications [mean (SD)]	205.6 (120.6)	331.8 (240.7)	501.8 (328.1)
Anticholinergics (All) [mean (SD)]	5.6 (20.9)	38.7 (69.2)	96.7 (97.7)
Proportion of group receiving anticholinergics (%)	26.1	57.1	86.4
Anticholinergics in proportion of group receiving anticholinergics [mean (SD)]	77.0 (22.8)	129.3 (65.3)	161.6 (73.5)
Short-acting β -agonist (All) [mean (SD)]	5.94 (21.2)	51.1 (85.2)	137.3 (156.6)
Proportion of group receiving short-acting β -agonist (%)	21.7	57.1	84.1
Short-acting β -agonist in proportion of group receiving short-acting β -agonist [mean (SD)]	68.3 (31.3)	147.4 (81.9)	221.0 (144.7)
Long-acting β -agonist (All) [mean (SD)]	3.5 (16.7)	33.3 (76.6)	50.0 (89.1)
Proportion of group receiving long-acting β -agonist (%)	8.7	32.7	45.5
Long-acting β -agonist in proportion of group receiving long-acting β -agonist [mean (SD)]	80.0 (17.3)	163.0 (87.6)	161.0 (87.7)
Inhaled corticosteroids (All) [mean (SD)]	4.4 (24.0)	32.0 (72.3)	82.4 (103.7)
Proportion of group receiving inhaled corticosteroids (%)	13.0	30.6	70.5
Inhaled corticosteroids in proportion of group receiving inhaled corticosteroids [mean (SD)]	101.7 (69.0)	156.6 (78.5)	178.4 (78.0)

Mean (SD) are days supplied per patient-year

[7]. This deterioration in health status may be attributable to symptoms and/or other coexisting illnesses, as indicated by the healthcare utilization patterns. Our study did not find differences in the proportion of each group having common comorbidities; however, we are limited by the relatively small sample included in this study. Interestingly, the average BMI of the "at risk" group is classifiable as obese according to Center for Disease Control criteria. Perhaps, the higher prevalence of obesity in the "at risk" group is a factor in these patients being diagnosed as having COPD. They may have symptoms consistent with mild COPD, such as increased dyspnea, while they do not meet criteria for diagnosis of COPD based on lung function testing. Whether these patients truly represent early COPD and optimal treatment are questions that need to be addressed.

Our study is unique in characterizing the healthcare utilization patterns of patients with chronic symptoms and no airway obstruction, formerly referred to as the GOLD stage 0 group. Based on the NHANES III results, 82.6% with self-reported obstructive lung disease did not have obstruction according to ATS guidelines [5, 6]. Therefore, many in this group would have been classified as stage 0 based on GOLD guidelines. We found that a significant proportion of these patients are being treated with bronchodilators in the absence of bronchial obstruction. In addition, the fact that these patients are using more healthcare services than the other groups may be an indicator that they are, on average, a sicker group of patients. It is unclear whether treatment in this setting offers any benefits in symptom reduction but there is clearly an added economic burden to the overall costs associated with COPD.

Our study has some limitations. First, the patients were enrolled by sending out letters, therefore, there could be self-selection bias. This bias may have produced a healthier cohort willing to make an extra visit to participate without compensation. However, the final cohort expressed a good distribution of disease severities with no differences in mean age. Second, as expected with a VA population, the cohort was predominantly men, and thus we were unable to assess any gender differences. Third, lack of statistical significance between the early-disease severity stages does not always correlate with clinical significance. Although the SGRQ symptom score from "at risk" to GS 1-2 and from GS 1-2 to GS 3-4 was more than 4%, considered a minimally important difference, there was no statistically significant difference in our study; however, this may not be so in a larger sample. Also, the overall proportions of patients for medication utilization were too small to obtain valid statistical significance. Fourth, we did not have pharmacy data outside of the VA system. However, the majority of our cohort would have been Medicare eligible and at the time of the study there were no Medicare pharmaceutical benefits. Because the "at risk" group is younger, we would expect they would be the group to more likely have supplemental insurance and pharmacy benefits. In that case, our findings would underestimate the percentage of patients in this group receiving medications. Finally, we cannot rule out misclassification due to reversible reactive airways disease. However, our study

emphasizes current practice patterns and classification designated by providers and thus is a reflection of healthcare utilization regardless of misclassification.

In this single-center pilot study, patients with a diagnosis of COPD without airway obstruction, formerly referred to as the GOLD stage 0 "at risk" group, had a decrement in health status, significant utilization of healthcare services not always associated with a diagnosis of COPD, and were likely to be receiving regular medications not consistent with guidelines. Although controversy exists as to whether this group is "at risk" for COPD, in clinical practice a proportion of them are being managed as if they have obstruction. It is unclear whether this group benefits from the observed treatment pattern. In the future, larger studies of this formerly "at risk" group may help to identify the optimal management of these patients to improve and/or better understand outcomes, in particular quality of life, disease progression, and mortality.

Acknowledgments This study was partly funded by an unrestricted research grant from Boehringer-Ingelheim Pharmaceuticals. This material was also based upon work supported by the HSR&D Service, Center for Management of Complex Chronic Care COE, Hines VA Hospital. The funding agency had no role in the design, conduct, or interpretation of the study results. Kevin Weiss was the Director for the Management of Complex Chronic Care, Hines VA Hospital, Hines, IL, and the Institute for Healthcare Studies at Northwestern University Feinberg School of Medicine, Chicago, IL, when this work was performed. This work was performed while all authors were employees of the Hines Veterans Administration Hospital. As U.S. government employees, this article was made in that capacity, thus assignment applies only to the extent allowable by U.S. law.

References

- 1. Morbidity & Mortality (2007) Chart book on cardiovascular, lung, and blood diseases. National Institutes of Health, National Heart, Lung, and Blood Institute, Bethesda, MD
- Global Inititiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease (updated 2006). http://www. goldcopd.org/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed 1 December 2007
- Han MK, Kim MG, Mardon R, Renner P, Sullivan S, Diette GB, Martinez FJ (2007) Spirometry utilization for COPD: how do we measure up? Chest 132:403–409
- 4. Lee TA, Bartle B, Weiss KB (2006) Spirometry use in clinical practice following diagnosis of COPD. Chest 129:1509–1515
- Agency for Healthcare Research and Quality (2005) Use of spirometry for case finding, diagnosis and management of chronic obstructive pulmonary disease (COPD). www.ohrq. gov/downloads/pud/evidence/pdf/spirocopd/spiro.pdf. Accessed 1 December 2007

- Mannino DM, Gagnon RC, Petty TL, Lydick E (2000) Obstructive lung disease and low lung function in adults in the United States: data from the National Health and Nutrition Examination Survey, 1988–1994. Arch Intern Med 160:1683–1689
- Antonelli-Incalzi R, Imperiale C, Bellia V, Catalano F, Scichilone N, Pistelli R, Rengo F (2003) Do GOLD stages of COPD severity really correspond to differences in health status? Eur Respir J 22:444–449
- Enright PL, Crapo RO (2000) Controversies in the use of spirometry for early recognition and diagnosis of chronic obstructive pulmonary disease in cigarette smokers. Clin Chest Med 21:645– 652
- Lindberg A, Eriksson B, Larsson LG, Ronmark E, Sandstrom T, Lundback B (2006) Seven-year cumulative incidence of COPD in an age-stratified general population sample. Chest 129:879–885
- Lindberg A, Jonsson AC, Ronmark E, Lundgren R, Larsson LG, Lundback B (2005) Ten-year cumulative incidence of COPD and risk factors for incident disease in a symptomatic cohort. Chest 127:1544–1552
- Vestbo J, Lange P (2002) Can GOLD Stage 0 provide information of prognostic value in chronic obstructive pulmonary disease? Am J Respir Crit Care Med 166:329–332
- Ekberg-Aronsson M, Pehrsson K, Nilsson JA, Nilsson PM, Lofdahl CG (2005) Mortality in GOLD stages of COPD and its dependence on symptoms of chronic bronchitis. Respir Res 6:98
- Ferrer M, Alonso J, Morera J, Marrades RM, Khalaf A, Aguar MC, Plaza V, Prieto L, Anto JM (1997) Chronic obstructive pulmonary disease stage and health-related quality of life. The Quality of Life of Chronic Obstructive Pulmonary Disease Study Group. Ann Intern Med 127:1072–1079
- Mannino DM, Doherty DE, Sonia Buist A (2006) Global Initiative on Obstructive Lung Disease (GOLD) classification of lung disease and mortality: findings from the Atherosclerosis Risk in Communities (ARIC) study. Respir Med 100:115–122
- Stavem K, Sandvik L, Erikssen J (2006) Can global initiative for Chronic Obstructive Lung Disease stage 0 provide prognostic information on long-term mortality in men? Chest 130:318–325
- Jones PW, Quirk FH, Baveystock CM (1991) The St George's Respiratory Questionnaire. Respir Med 85 Suppl B:25–31; discussion 33–27
- Barr JT, Schumacher GE, Freeman S, LeMoine M, Bakst AW, Jones PW (2000) American translation, modification, and validation of the St. George's Respiratory Questionnaire. Clin Ther 22:1121–1145
- Jones PW, Quirk FH, Baveystock CM, Littlejohns P (1992) A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. Am Rev Respir Dis 145:1321–1327
- Rutten-van Molken M, Roos B, Van Noord JA (1999) An empirical comparison of the St. George's Respiratory Questionnaire (SGRQ) and the Chronic Respiratory Disease Questionnaire (CRQ) in a clinical trial setting. Thorax 54:995–1003
- Kleinbaum DG, Kupper LL, Muller KE, Nizam A (1988) Applied Regression Analysis and Other Multivariate Methods. Brooks/ Cole Publishing Company, Pacific Grove, CA, pp 451–457
- 21. Stahl E, Lindberg A, Jansson SA, Ronmark E, Svensson K, Andersson F, Lofdahl CG, Lundback B (2005) Health-related quality of life is related to COPD disease severity. Health Qual Life Outcomes 3:56