

Quality of life in smokers: focus on functional limitations rather than on lung function?

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ABSTRACT

Background

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification of severity of chronic obstructive pulmonary disease (COPD) is based solely on obstruction and does not capture physical functioning. The hypothesis that the Medical Research Council (MRC) dyspnoea scale would correlate better with quality of life than the level of airflow limitation was examined.

Aim

To study the associations between quality of life in smokers and limitations in physical functioning (MRC dyspnoea scale) and, quality of life and airflow limitation (GOLD COPD stages).

Design

Cross-sectional study.

Setting

The city of IJsselstein, a small town in the centre of The Netherlands.

Method

Male smokers aged 40–65 years without a prior diagnosis of COPD and enlisted with a general practice, participated in this study. Quality of life was assessed by means of a generic (SF-36) and a disease-specific, questionnaire (QOLRIQ).

Results

A total of 395 subjects (mean age 55.4 years, pack years 27.1) performed adequate spirometry and completed the questionnaires. Limitations of physical functioning according to the MRC dyspnoea scale were found in 25.1% (99/395) of the participants and airflow limitation in 40.2% (159/395). The correlations of limitations of physical functioning with all quality-of-life components were stronger than the correlations of all quality-of-life subscales with the severity of airflow limitation.

Conclusion

In middle-aged smokers the correlation of limitations of physical functioning (MRC dyspnoea scale) with quality of life was stronger than the correlation of the severity of airflow limitation with quality of life. Future staging systems of severity of COPD should capture this and not rely on forced expiratory volume in one second (FEV1) alone.

Keywords

dyspnoea; FEV1; middle-aged; FEV1; quality of life; smokers.

INTRODUCTION

There are several ways to assess the severity of chronic obstructive pulmonary disease (COPD). In almost all guidelines the classification of the severity of COPD is based on airflow limitation alone, that is, the level of forced expiratory volume in one second (FEV1) without reference, for instance, to the severity of respiratory symptoms.^{1,2} Importantly, the correlation between airflow limitation and health-related quality of life, that is, an individual's satisfaction or happiness with domains of life insofar as these affect or are affected by health, is modest.^{3–8}

Dyspnoea is the main symptom limiting functional status in patients with chronic obstructive pulmonary disease (COPD). Functional status is the individuals' ability to perform normal daily activities in the different domains of life.³ Limitations of the functional status measured on a dyspnoea-scale seem to be more strongly correlated with quality of life than pulmonary function.⁹ In addition, patients usually attend the physician because of worsening of respiratory symptoms and not because of lung function decline. Therefore, some authors have criticised the one-dimensional grading of COPD severity based on pulmonary function alone, as proposed by the Global Initiative for Chronic

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How this fits in

In patients with moderate and severe chronic obstructive pulmonary disease (COPD) quality of life is more strongly associated with the level of dyspnoea than with disease severity based on lung function. Little is known about these relations in patients with mild COPD. In middle-aged smokers correlation of limitations of physical functioning, as measured by the MRC dyspnoea scale, with quality of life was stronger than correlation of the severity of airflow limitation with quality of life.

Obstructive Lung Disease (GOLD) Guidelines.⁷ In the daily management of smokers, including those with early phases of COPD, there is a need for a simple and standardised instrument to assess health-related quality of life to guide interventions. The Medical Research Council (MRC) dyspnoea scale could represent a useful instrument, because of its ability to categorise patients with severe COPD in terms of their disability.⁶ However, the relationship of the MRC dyspnoea scale with quality of life in smokers at risk of developing COPD or with early stages of COPD, is unknown, as is the correlation of airflow limitation with quality of life in this large population. The aim of this study was to study these relations.

METHOD

In 1998 702 male smokers (aged 40–65 years) enlisted with a general practice in IJsselstein, a town in the centre of the Netherlands, participated in a screening study to identify undetected airflow limitation. Only men were included because of the higher prevalence of COPD in males than in females and due to limited study resources.¹⁰ In 2003, a follow-up survey was performed in this sample of relatively healthy middle-aged smokers to examine the quality of life and to assess the incidence of moderate COPD. A total of 601 subjects (86% of 702) were still eligible, the lower number being mainly due to non-participation of one of the GPs ($n = 65$) and to a minor extent due to removal of the

practice list ($n = 30$) or severe illness or death ($n = 6$). Eventually, 436 of the 601 eligible individuals (73%) participated in the second survey.

Spirometry was performed by means of a hand-held Jaeger spirometer. Details of the procedure are described elsewhere.¹⁰ Briefly, each subject had to perform at least three acceptable forced vital capacity (FVC) manoeuvres while seated. The results were shown on a computer screen and the procedure was supported by computer software. If the FEV1 was less than 85% of the predicted value, the bronchodilator response was tested 15 minutes after inhalation of four 'puffs' of salbutamol [100 mcg] through an inhalation chamber. In subjects aged 60 years or over, the bronchodilator response was tested 30 minutes after inhalation of two puffs of ipratropium bromide [20 mcg]. Experienced and specially trained lung function assistants employed by a primary care diagnostic centre performed all measurements. The spirometer was calibrated daily with a 1-litre syringe at the start of a series of measurements. Two investigators independently assessed the quality of the flow-volume curves and time-volume curves according to the criteria of the American Thoracic Society.¹¹

Predicted values of FVC and FEV1 were computed using the regression equations of the European Coal and Steel Community (ECSC).¹²

According to the GOLD guidelines COPD is defined by a postbronchodilator FEV1/FVC ratio <0.7 .¹² The severity of COPD can be distinguished in four stages according to postbronchodilator FEV1 values (Table 1).

Before each lung function test, height and weight were measured and the body mass index (kg/m^2) was calculated. The number of pack years was computed as the number of cigarettes smoked per day divided by 20 and multiplied by the number of years of smoking.

Limitations of physical functioning were assessed by a Dutch language version of the MRC dyspnoea scale.¹³ The MRC dyspnoea scale measures limitations caused by dyspnoea graded at five levels from grade 1; 'Not troubled with breathlessness except with strenuous exercise' to grade 5, 'Too breathless to leave the house' (Supplementary Table 1). The scale has been used for many years and is simple to administer.¹⁴

Generic quality of life was assessed by means of the Short Form Health Survey questionnaire (SF-36) and disease-specific quality of life by means of the Quality Of Life in Respiratory Illness Questionnaire (QOLRIQ).^{15,16} Both self-administered questionnaires were completed at home in the 4 weeks before the survey. The SF-36 is composed of 36 questions, organised into eight multi-item scales: physical

Table 1. COPD by severity according to the GOLD criteria.

Stage	FEV1/FVC	FEV1 predicted %
Mild (GOLD I)	<0.7	≥ 80
Moderate (GOLD II)	<0.7	50–80
Severe (GOLD III)	<0.7	30–50
Very severe (GOLD IV)	<0.7	<30

FEV1 = forced expiratory volume in one second; FVC = forced vital manoeuvres; COPD = chronic obstructive pulmonary disease; GOLD = global initiative for chronic obstructive lung disease guidelines.

functioning, role limitations due to physical functioning, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. The scores were linearly transformed to a 0–100 scale, with higher scores indicating a better quality of life. The SF-36 is broadly used and validated.^{15,17,18} The disease-specific quality of life questionnaire was developed and validated for patients with mild to moderate asthma or COPD treated primarily in general practice. It comprises 55 items classified into a total score and seven subscales: breathing problems, physical problems, emotions, general activities, situations triggering or enhancing breathing problems, daily and domestic activities and social activities, relationships and sexuality. For every item, patients were asked to answer, on a 7-point Likert-type scale, to what degree they were troubled due to pulmonary complaints. The response categories of all items ranged from 1 (not troubled at all) to 7 (very much troubled). In case of missing data, less than 50% of missing items were allowed per subscale, and one missing subscale was allowed for the calculation of the total score. The total score of the QOLRIQ and subscales scores of both questionnaires were computed by adding the item scores and dividing the sum by the number of valid items. The scores of the QOLRIQ were transformed in such a way that a lower score indicates a reduced quality of life in order to facilitate the comparison of the scores of the QOLRIQ with the scores of the SF-36.

Comorbidity, defined as a diagnosis of cardiovascular, musculoskeletal or renal disease, cancer or diabetes mellitus, was extracted from the GP medical records. A disease was classified as present when a diagnosis by a primary or secondary care physician was found in the records or in the medical correspondence. In total 17 of 409 (4.2%) medical records were missing. Chronic cough was considered present if the patient responded 'yes' when asked whether they were coughing almost every day for the previous 3 months.

Statistical analysis

Spearman's correlation coefficients (r_s) were determined to quantify the correlation of the MRC dyspnoea scale and GOLD staging (independent variables) with the components of the quality of life questionnaires (dependent variables). The MRC scores were recoded in value 0 = not troubled by breathlessness, value 1 = MRC grade I–II, and value 2 = MRC grade III–V, while GOLD stages were recoded in value 0 = no airflow limitation, value 1 = GOLD stage I, and value 2 = GOLD stage II (Supplementary Table 1).

There were no participants with GOLD stage III or IV. The component scores of both quality of life questionnaires appeared to be skewed to the right, indicating that a significant proportion of responders had filled in the maximum score. The scores could not be normalised using any form of transformation. Therefore, the SF-36 and QOLRIQ component scores were dichotomised around a cut-off of the maximum score minus the minimal important

Table 2. Patients' characteristics and quality of life scores: 395 middle-aged male smokers.

Characteristics	Mean (SD) or %
Age, (years)	55.4 (6.3)
Smoking history, (pack years)	27.1 (19.3)
No employment/retired	29%
Living alone	9%
Comorbidity ^a	27%
Chronic cough	23%
BMI	26.6 (3.8)
FEV1 (L)	3.5 (0.7)
FEV1 % predicted	98 (16)
Lung function	
No airflow limitation	59.7%
Mild COPD (GOLD I)	29.6%
Moderate COPD (GOLD II)	10.6%
Functional limitations by dyspnoea	
None	74.9%
Mild (MRC I-II)	17.7%
Moderate or severe (MRC III-V)	7.3%
Generic QOL components ^b (range 0–100) SF36	
Physical functioning	86.3 (17.7)
Role functioning (physical)	85.9 (29.5)
Bodily pain	83.3 (22.5)
General health	66.1 (18.8)
Vitality	68.3 (19.2)
Social functioning	87.9 (18.4)
Role functioning (emotional)	88.9 (26.9)
Mental health	78.4 (16.4)
Disease specific QOL components ^b (range 1–7)	
QOLRIQ	
Total score	6.5 (0.5)
Breathing problems	6.1 (0.8)
Physical problems	6.4 (0.7)
Emotions	6.5 (0.7)
General activities	6.6 (0.8)
Situations triggering or enhancing breathing problems	6.7 (0.6)
Daily and domestic activities	6.5 (0.6)
Social activities/relationships/sexuality	6.8 (0.5)

^aComorbidity denotes cardiovascular disease, diabetes mellitus, musculoskeletal disease, cancer, renal disease.

^bHigher scores indicate a better quality of life. BMI = body mass index; FEV1 = forced expiratory volume in one second; COPD = chronic obstructive pulmonary disease; GOLD = global initiative for chronic obstructive lung disease guidelines; (L) = Litres; MRC = Medical Research Council; QOL = quality of life; QOLRIQ = quality of life in respiratory illness questionnaire.

Table 3. Bivariate^a associations of limitations by dyspnoea and airflow limitation with quality of life in middle-aged male smokers.

Quality of life components	Limitations by dyspnoea graded by MRC scale		Airflow limitation graded by GOLD staging	
	OR	95% CI	OR	95% CI
Generic questionnaire (SF-36)				
Physical functioning	8.4	4.6 to 15.5	1.3	1.0 to 1.5
Role functioning (physical)	2.9	2.0 to 4.3	0.8	0.7 to 1.1
Bodily pain	1.7	1.2 to 2.5	1.0	0.8 to 1.1
General health	7.0	1.0 to 47.5	1.0	0.7 to 1.4
Vitality	8.3	1.2 to 55.8	1.0	0.7 to 1.4
Social functioning	2.1	1.5 to 3.0	1.0	0.8 to 1.2
Role functioning (emotional)	2.5	1.7 to 3.7	0.8	0.6 to 1.0
Mental health	2.6	1.5 to 4.7	1.1	0.9 to 1.4
Disease specific questionnaire (QOLRIQ)				
Total score	6.0	3.8 to 9.4	1.3	1.0 to 1.6
Breathing problems	3.7	2.2 to 6.3	1.5	1.2 to 1.8
Physical problems	4.5	2.9 to 7.0	1.0	0.8 to 1.2
Emotions	4.7	3.1 to 7.1	1.1	0.9 to 1.3
General activities	3.2	2.2 to 4.7	1.0	0.9 to 1.3
Situations triggering or enhancing breathing problems	2.9	2.0 to 4.2	1.2	0.9 to 1.5
Daily and domestic activities	11.1	6.3 to 19.4	1.3	1.0 to 1.6
Social activities, relationships				
sexuality	3.5	2.3 to 5.2	1.2	0.9 to 1.5

^aORs are obtained from logistic regression analysis using MRC scale and GOLD stages as independent variables and dichotomised scores of the QOL components as separate dependent variables. GOLD = Global Initiative for Chronic Obstructive Lung Disease guidelines; MRC = Medical Research Council; OR = odds ratio; QOLRIQ = quality of life in respiratory illness questionnaire.

difference: SF-36 high score (96–100: value 0) versus low score (≤ 95 : value 1) and QOLRIQ high score (6.5–7: value 0) versus low score (≤ 6.5 : value 1). The cut-offs of 95 points (SF-36) and 6.5 points (QOLRIQ) were chosen since the minimal important difference is considered to be 5 points for the SF-36 and 0.5 points for the QOLRIQ.^{19,20} In bivariate logistic regression analysis the association of the MRC scale and the GOLD staging (independent variables) with the separate dichotomised quality-of-life component scores (dependent variable) was assessed. Regression equations were computed with each separate quality-of-life component score being the outcome measure.

RESULTS

A total of 395 male smokers (91% of the 436 participants) performed adequate spirometry and completed the questionnaires. Twenty-seven subjects (6%) did not perform adequate spirometry and 14 participants (3%) did not sufficiently complete the questionnaires. The mean age of the participants was 55.4 years (standard deviation [SD] 6.3) and the mean smoking history was 27.1 pack years (SD 19.3) (Table 2). Airflow limitation was found in 40.2% (159/395) and limitations of physical functioning due to dyspnoea — MRC dyspnoea

scale I to V — in 25.1% (99/395) of the participants. (Table 2) The MRC dyspnoea scale correlated moderately ($r_s = 0.52$) with the overall score of the disease-specific questionnaire while the severity of airflow limitation correlated weakly ($r_s = 0.22$) with this score (data not shown).

The MRC dyspnoea scale was weakly to moderately correlated to all separate component scores of both questionnaires ($r_s = 0.19$ – 0.58) while airflow limitation was only weakly associated with all component scores of the disease-specific questionnaire ($r_s = 0.12$ – 0.28) and some component scores of the generic questionnaire ($r_s = 0.13$ – 0.20). The MRC dyspnoea scale correlated best with quality of life components measuring impairment in daily activities, that is 'physical functioning' from the generic questionnaire ($r_s = 0.53$) and 'daily and domestic activities' from the disease specific questionnaire ($r_s = 0.58$). In addition, in bivariate logistic regression analysis the correlations of the MRC dyspnoea scale with all quality-of-life components were stronger than the correlations of airflow limitation with all quality-of-life subscales (Table 3). For example, the odds ratio (OR) of having a worse score of the 'physical functioning' component of the SF-36 was approximately eightfold higher in subjects with moderate or severe limitations on the dyspnoea scale than in those with mild limitations on this scale (OR = 8.4; 95% confidence interval [CI] = 4.6–15.5), while the corresponding OR was only slightly higher (1.3; 1.0–1.5) in patients with moderate compared to those with mild COPD according to the GOLD criteria (Table 3).

DISCUSSION

Summary of main findings

In this cohort of male smokers, aged 45–70 years, of whom 40% had mild or moderate COPD (GOLD I or II), quality of life was more strongly related to limitations of physical functioning measured by the MRC dyspnoea scale than to the severity of airflow limitation defined according to the GOLD staging of COPD. This is the first study to show this relationship in a general population of smokers at risk for COPD or with early disease.

Strengths and limitations of the study

One of the strengths of this study is that the survey was performed in a population representative of the whole Dutch population. For example, 35% of those who returned the questionnaire on smoking habits at the baseline survey, were current smokers, a figure similar to the expected proportion of smokers (35–36%) in men, aged 40–65 years, in the Netherlands.²¹

Quality of life was measured with a generic questionnaire (SF-36) as well as with a disease specific questionnaire (QOLRIQ). The SF-36 is commonly used and has been demonstrated to be reliable, responsive and valid in COPD.^{8,18,22} The Dutch version of the SF-36 has proven to be a reliable and valid instrument for use in studies of chronic disease populations in the Netherlands.¹⁵ The SF-36 component scores of this study in middle-age smokers were highly similar to the scores derived from two random samples from the Dutch population, supporting the finding that early COPD does not markedly affect quality of life.¹⁵ Reliability and validity of the QOLRIQ has been tested in stable primary care patients with asthma or COPD.^{16,23} Limitations in physical functioning were measured with the MRC dyspnoea scale. The MRC dyspnoea scale is widely used and has been demonstrated to be valid compared to alternative clinical dyspnoea ratings such as the baseline dyspnoea index, dyspnoea components of the St George's Respiratory Questionnaire (SGRQ) and the Chronic Respiratory Disease Questionnaire (CRQ).²⁴

Some limitations of this study must be addressed. First, the cohort consisted of male smokers only. In general, most, but not all, studies report lower quality of life in females with COPD compared to males with COPD.^{4,5,17,25} In smoking and non-smoking women, higher frequencies of respiratory symptoms are reported than in men. Moreover, women are visiting GPs more frequently for respiratory symptoms.²⁶⁻³⁰ Therefore, it seems likely that the independent relation of the MRC dyspnoea scale with quality of life will be found in female smokers as well. Second, 236 (59.7%) participants did not have airflow limitation. Theoretically, in those with airflow limitation the results could be different compared to those without airflow obstruction. Limiting the analysis to the subjects with airflow obstruction only, however, yielded similar associations. Third, 601 subjects participated in the baseline survey and 436 in the second survey. In subjects only participating in the baseline survey the FEV1 predicted was slightly lower (98% versus 102%) than in those attending both surveys. This may indicate that a slightly higher proportion of subjects with relatively poorer lung function tended to discontinue participation. However, this conclusion is valid for smokers with mild and moderate COPD while its validity for subjects with more severe COPD has already been established in earlier studies.^{9,31} Finally, 9% of the participants did not perform adequate spirometry or did not complete the questionnaires. However, these 41 individuals did not differ from the included

participants with respect to the characteristics presented in Table 2.

Comparison with existing literature

Several earlier studies addressed the association of the level of dyspnoea and lung function with quality of life. In subjects with moderate and severe COPD – GOLD stage II and over – The one-dimensional grading of COPD severity based on pulmonary function alone has been criticised⁷ since patients do not visit their GP because of a low lung function but because of respiratory complaints and functional limitations. The GOLD classification of COPD lacks an index quantifying the impact of respiratory symptoms on physical functioning such as the New York Heart Association (NYHA) classification in patients with heart disease. Therefore, some authors have proposed a multidimensional severity index for moderate or severe COPD including pulmonary function, BMI, dyspnoea and exercise capacity.³² The current use of the GOLD staging system in patient care is meant not only to diagnose COPD, but also to grade the impact of the disease on functioning of patients, and to guide treatment. From many studies it has become clear that the mono-dimensional grading with FEV1 misses to a large extent the impact of the level of dyspnoea on the individual patient as well as other aspects of the disease.

Implications for future research and clinical practice

Assessing changes in both physical functioning by means of the MRC dyspnoea scale and in lung function is needed in day-to-day practice in order to guide medical treatment, and in particular smoking cessation intervention, of individual patients either at risk for COPD or with diagnosed COPD. In the current study limitations of physical functioning due to breathlessness in middle-aged smokers as measured by the MRC dyspnoea scale, are more strongly related to quality of life than the severity of airflow limitation. Future staging systems of severity of COPD should capture this and not rely on FEV1 alone.

Supplementary information

Additional information accompanies this paper at <http://www.rcgp.org.uk/bjgp-supinfo>

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Ethics committee

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Competing interests

The authors have stated that there are none

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REFERENCES

- Pauwels RA, Buist S, Calverley PMA, et al, on behalf of the GOLD Scientific Committee. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease; NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD). *Am J Respir Crit Care Med* 2001; **163**(5): 1256–1276.
- Fabbri LM, Hurd SS, for the GOLD Scientific Committee. Global Strategy for the Diagnosis, Management and Prevention of COPD: 2003 update. *Eur Resp J* 2003; **22**: 1–2.
- Wilson IB, Cleary PD. Linking clinical variables with health related quality of life. A conceptual model of patient outcomes. *JAMA* 1995; **273**(1): 59–65.
- Wijnhoven HAH, Kriegsman DMW, Hesselink AE, et al. Determinants of different dimensions of disease severity in asthma and COPD; pulmonary function and health related quality of life. *Chest* 2001; **119**: 1034–1042.
- Antonell-Incalzi R, Imperiale C, Bellia V, et al. Do GOLD stages of COPD severity really correspond to difference in health status? *Eur Respir J* 2003; **22**(3): 444–449.
- Bestall JC, Garrod PR, Garnham R, et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999; **54**: 581–586.
- Kerstjens HAM. The GOLD classification has not advanced understanding of COPD. *Am J Respir Crit Care Med* 2004; **170**: 212–213.
- Mahler DA, Mackowiak JI. Evaluation of the Short-Form 36-Item questionnaire to measure health-related quality of life in patients with COPD. *Chest* 1995; **107**: 1585–1589.
- Hajiro T, Nishimura K, Tsukoni M, et al. A comparison of the level of dyspnoea vs disease severity in indicating the health-related quality of life of patients with COPD. *Chest* 1999; **116**: 1632–1637.
- Geijer RMM, Sachs APE, Hoes AW, et al. Prevalence of undetected persistent airflow obstruction in male smokers 40–65 years old. *Fam Pract* 2005; **22**(5): 485–489.
- American Thoracic Society. Standardization of spirometry, 1994 update. *Am J Respir Crit Care Med* 1995; **152**(3): 1107–1136.
- Quanjer PH, Tammeling GJ, Cotes JE, et al, on behalf of the working party (Standardization of lung function testing). Lung volumes and forced ventilatory flows. Report working party standardization of lung function tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 1993; **6**(suppl): 5–40.
- Thiaden HA. *Questionnaire. Diagnosing asthma or COPD in patients with persistent cough: variations on a theme*. Leiden: University of Leiden, 1999.
- Fletcher CM (Chairman). Standardized questionnaire on respiratory symptoms: a statement prepared and approved by the MRC Committee on the Aetiology of Chronic Bronchitis (MRC breathlessness score). *BMJ* 1960; **2**: 1665.
- Aaronson NK, Muller M, Cohen PD, et al. Translation, validation, and norming of the Dutch language version of the SF-36 health survey in community and chronic disease populations. *J Clin Epidemiol* 1998; **51**(11): 1055–1068.
- Maille AR, Koning CJ, Zwinderman AH, et al. The development of the 'Quality-of-life for Respiratory Illness Questionnaire (QOLRIQ)': a disease-specific quality-of-life questionnaire for patients with mild to moderate chronic non-specific lung disease. *Respir Med* 1997; **91**(5): 297–309.
- Van Manen JG, Bindels PJE, Dekker FW, et al. The influence of COPD on health-related quality of life independent of the influence of comorbidity. *J Clin Epidemiol* 2003; **56**(12): 1177–1184.
- Curtis, JR, Patrick DL. The assessment of health status among patients with COPD. *Eur Resp J* 2003; **21** Suppl(41): 36S–45S.
- Van Stel HF, Maillé R, Colland VT, Everaerd W. Interpretation of change and longitudinal validity of the quality of life for respiratory illness questionnaire (QOLRIQ) in inpatient pulmonary rehabilitation. *Qual Life Res* 2003; **12**(2): 133–145.
- Hajiro T, Nishimura K, Tsukoni M, et al. Comparison of discriminative properties among disease-specific questionnaires for measuring health-related quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998; **157** (3 Pt 1): 785–790.
- Geijer RMM, Sachs APE, Verheij TJM, et al. Incidence and determinants of moderate COPD (GOLD II) in male smokers aged 40–65 years: 5-year follow up. *Br J Gen Pract* 2006; **56**(530): 656–661.
- Viramontes JL, O'Brien B. Relationships between symptoms and health-related quality of life in chronic lung disease. *Gen Inter Med* 1994; **9**(1): 46–48.
- Maille AR. Quality of life in asthma and COPD. Development of a disease-specific questionnaire (Thesis). Amsterdam: University of Amsterdam, 2000.
- Hajiro T, Nishimura K, Tsukino M, et al. Analysis of clinical methods used to evaluate dyspnoea in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998; **158**(4): 1185–1189.
- Ferrer M, Alonso J, Morera J, et al. Chronic obstructive pulmonary disease and health-related quality of life. *Ann Int Med* 1987; **127**(12): 1072–1079.
- Engström CP, Persson LO, Larsson S, Sullivan M. Health-related quality of life in COPD: why both disease-specific and generic measures should be used. *Eur Respir J* 2001; **18**(1): 69–76.
- Langhammer A, Johnsen R, Gulsvik A, et al. Sex differences in lung vulnerability to tobacco smoking. *Eur Respir J* 2003; **21**(6): 1017–1023.
- Langhammer A, Johnsen R, Holmen J, et al. Cigarette smoking gives more respiratory symptoms among women than among men. *J Epidemiol Comm Health* 2000; **54**(12): 917–922.
- Kerstjens HA, Rijcken B, Schouten JP, Postma DS. Decline of FEV1 by age and smoking status: facts, figures, and fallacies. *Thorax* 1997; **52**: 820–827.
- Braspenning JCC, Schellevis, FG, Grol RPTM (eds). *Second national survey of diseases in primary care*. Utrecht: NIVEL/WOK, 2004.
- Hajiro T, Nishimura K, Tsukino M, et al. Stages of disease severity and factors that affect the health status of patients with chronic obstructive disease. *Resp Medicine* 2000; **94**(9): 841–846.
- Celli BR, Cote CG, Marin JM, et al. The body-mass Index, airflow obstruction, dyspnoea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med* 2004; **350**(10): 1005–1012.