Incidence and determinants of moderate COPD (GOLD II) in male smokers aged 40–65 years: 5-year follow up

Roeland MM Geijer, Alfred PE Sachs, Theo JM Verheij, Philippe L Salomé, Jan-Willem J Lammers and Arno W Hoes

ABSTRACT

Background

Chronic obstructive pulmonary disease (COPD) is a major health problem with an estimated prevalence of 10–15% among smokers. The incidence of moderate COPD, as defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD), is largely unknown.

Aim

To determine the cumulative incidence of moderate COPD (forced expiratory volume in 1 second/forced vital capacity ratio [FEV1/FVC] <0.7 and FEV1 <80% predicted) and its association with patient characteristics in a cohort of male smokers.

Design

Prospective cohort study.

Setting

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

Method

Smokers aged 40–65 years who were registered with local GPs, participated in a study to identify undetected COPD. Baseline measurements were taken in 1998 of 399 smokers with normal spirometry (*n* = 292) or mild COPD (FEV1/FVC <0.7 and FEV1 ≥80% predicted, *n* = 107) and follow-up measurements were conducted in 2003.

Results

After a mean follow-up of 5.2 years, 33 participants developed moderate COPD (GOLD II). This showed an estimated cumulative incidence of 8.3% (95% CI = 5.8 to 11.4) and a mean annual incidence of 1.6%. No participant developed severe airflow obstruction. The risk of developing moderate COPD in smokers with baseline mild COPD (GOLD I) was five times higher than in those with baseline normal spirometry (one in five versus one in 25).

Conclusions

In a cohort of middle-aged male smokers, the estimated cumulative incidence of moderate COPD (GOLD II) over 5 years was relatively high (8.3%). Age, childhood smoking, cough, and one or more GP contacts for lower respiratory tract problems were independently associated with incident moderate COPD.

Keywords

incidence; middle-age; moderate COPD; patient characteristics; smokers.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major health problem. Tobacco smoking is its major cause and about 10–15% of all smokers develop COPD.[1] Adult smokers who were exposed to tobacco smoke or other air pollutants during childhood are at increased risk of developing COPD.[1–3] Susceptibility to developing COPD is thought to be influenced by unknown genetic factors.[1] Lifelong smokers die on average about 10 years earlier than lifelong non-smokers.[4] About 25% of the excess mortality among smokers is accounted for by lung cancer and COPD. Smoking cessation at an early stage of COPD is the only intervention that substantially improves the prognosis by normalising lung function decline and decreasing morbidity and all-cause mortality.[4–6] Therefore, early detection of unrecognised airflow obstruction is advocated.[7] Some authors recommend screening spirometry in all smokers who are 45 years or older and attending a GP,[8] while others recommend case-finding among symptomatic smokers attending a GP.[7] However, the optimal cost-effective strategy, which would target all or specific subgroups of smokers, and

***RMM Geijer**, MD, GP; **APE Sachs**, MD, PhD, GP; **TJM Verheij**, MD, PhD, professor of general practice; **PL Salomé**, MD, GP; **Arno W Hoes**, MD, PhD, professor of clinical epidemiology, Julius Centre for Health Sciences and Primary Care; **J-WJ Lammers**, MD, PhD, professor of pulmonary medicine, Department of Pulmonary Diseases, Heart Lung Centre, University Medical Centre Utrecht, the Netherlands.*

Address for correspondence
RMM Geijer, Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, PO Box 85060, 3508 BA Utrecht, the Netherlands.
E-mail: r.geijer@umcutrecht.nl

Submitted: 15 September 2005; **Editor's response:** 31 October 2004; **final acceptance:** 1 March 2005.

optimal screening frequency have not been established.

Knowledge of the prevalence, incidence, and determinants of COPD is needed to assess whether targeted screening in a subgroup of smokers could be useful. In a recent study the prevalence of COPD in smokers has been assessed.[9] However, few studies have examined the incidence of COPD and only one study has used criteria from the Global Initiative for Chronic Obstructive Lung Disease (GOLD).[1] The current 5-year follow-up study of male smokers was designed to determine the cumulative incidence of moderate COPD, defined according to GOLD criteria, and to investigate its associations with patient characteristics.

How this fits in

Chronic obstructive pulmonary disease (COPD) is a major health problem with an estimated prevalence of 10–15% among smokers. Incidence of COPD is largely unknown. This study estimates that the 5-year incidence of moderate COPD is approximately 8% in a population of middle-aged male smokers. Age, childhood smoking (≤15 years of age), cough, and one or more GP contact for lower respiratory tract problems are independently associated with incident moderate COPD.

METHOD

This study was part of the IJsselstein cohort study to assess the prevalence, incidence, and determinants of undetected airflow obstruction in middle-aged smokers. The study was conducted between 1998 and 2003.

Study population

In 1998, all men aged 40–65 years registered with a GP in IJsselstein (*n* = 3985), a town in the centre of the Netherlands, were sent a form by post and asked if they had smoked one or more cigarettes per day during the previous 12 months, and if so whether they were willing to participate in a study to identify undetected airflow obstruction. Participants with documented lung disease (*n* = 222, 5.6%) were excluded. A total of 2596 of the 3763 men without previously documented lung disease returned the form (69%). Of the 2596 responders, 978 (37.7%) were current smokers. Sixty smokers were excluded at the first examination because of smoking cessation of more than 12 months before the study (*n* = 33), smoking only pipe or cigars (*n* = 17), or reporting lung disease (*n* = 10). Thus the eligible population consisted of 918 (35.4%) current cigarette smokers without known lung disease. Of the 918 eligible smokers, 805 (87.7%) attended the first survey, of whom 702 performed adequate spirometry. Details of the first part of the study have been previously published.[9]

In 2003, a follow-up survey was conducted. A total of 101 participants (14%) were ineligible due to removal from the practice list: that is, due to death or severe illness (*n* = 36), or because of non-participation of one of the GPs (*n* = 65). Follow-up measurements were refused by 165 of the 601 eligible participants (27%). The final number of individuals participating in the follow-up study were 436 of the 601 eligible participants (73%). The incidence of moderate COPD (GOLD II) was calculated for 399 participants with normal spirometry or mild COPD (GOLD I) at baseline, excluding 10 participants with baseline GOLD II and 27 participants not performing an acceptable lung function test at the follow-up survey.

Spirometry

Spirometry was performed in all participants with a hand-held spirometer. At the baseline survey in 1998 a Vitalograph spirometer (Vitalograph Ltd, Buckingham, UK) was used and at the follow-up survey in 2003 a Jaeger spirometer (VIASYS Healthcare, Höchburg, Germany) was used for logistic reasons. Each participant was required to perform at least three acceptable forced vital capacity (FVC) manoeuvres while sitting. The results were shown on a computer screen and the procedure was supported by computer software. If the forced expiratory volume in 1 second (FEV1) was less than 85% of the predicted volume, the bronchodilator response was tested 15 minutes after inhalation of four puffs of salbutamol [100 μg] through an inhalation chamber. For participants older than 60 years the bronchodilator response was tested 30 minutes after inhalation of two puffs of ipratropium bromide [20 μg]. 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 American Thoracic Society criteria.[10] According to these criteria the manoeuvres with the largest sum of FEV1 and FVC were used in this analysis. Predicted values of FVC and FEV1 were calculated using regression equations of the European Community for Steel and Coal.[11]

Before each lung function test, height and weight were measured and smoking history was assessed. Full details of the procedure have been previously described.[9]

Definition of COPD

After the publication of the GOLD guidelines on

Table 1. Chronic obstructive pulmonary disease by severity according to Global Initiative for Chronic Obstructive Lung Disease (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/FVC = forced expiratory volume in 1 second/forced vital capacity ratio.

COPD in 2001 and subsequent annual updates, a uniform classification has been advocated worldwide.[1,2] According to the GOLD guidelines, COPD is defined by a postbronchodilator FEV1/FVC <0.7. The severity of COPD can be distinguished in four stages according to postbronchodilator FEV1 values (Table 1).

Questionnaires

Symptoms at baseline were assessed by the Airways Questionnaire (AQ20), a short questionnaire to measure health-related quality of life of patients with COPD. The AQ20 consists of 20 items related to the impact of chest problems, such as coughing and dyspnoea during mild to moderate exertion in everyday life.[12] At baseline only the item concerning coughing was used. Family history was assessed using the Dutch translation of the Modified Medical Research Council for Respiratory Symptoms questionnaire.[13]

Table 2. Baseline characteristics of male smokers aged 40–65 years.[a]

	Overall (*n* = 399)	Normal spirometry (*n* = 292)	GOLD I (*n* = 107)
Age (years)	50.0 (6.4)	49.2 (6.2)	52.3 (6.5)
Smoking history (years)	31.3 (8.5)	30.5 (8.2)	33.5 (8.9)
Pack years	24.1 (8.7)	23.2 (8.5)	26.6 (8.7)
BMI (kg/m^2)	25.4 (3.3)	25.5 (3.4)	25.1 (3.2)
Family history of obstructive lung disease	38%	39%	37%
Parental smoking	88%	87%	91%
Childhood smoking	39%	36%	46%
Cough	21%	18%	29%
≥1 GP contact for LRT	17%	16%	23%
FVC % predicted	111 (13)	109 (13)	118 (11)
FEV1 % predicted	102 (12)	104 (12)	97 (10)
FEV1/FVC ratio	0.74 (0.06)	0.77 (0.05)	0.66 (0.03)

[a]*Mean (SD) unless otherwise stated. GOLD I = chronic obstructive pulmonary disease stage I according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. Pack years = number of packs smoked per day times number of years smoked. BMI = body mass index. LRT = lower respiratory tract problems in the previous 12 months. FVC = forced vital capacity. FEV1 = forced expiratory volume in 1 second.*

Medical records

All GPs had computer-based medical records. The number of clinical encounters for lower respiratory tract problems was extracted from medical records retrospectively. A clinical encounter for lower respiratory tract problems was defined as the presence of one of the following items in the medical records: a diagnosis of acute or chronic bronchitis, pneumonia, or lower respiratory tract infection; symptoms such as cough, dyspnoea, phlegm production or wheezing, without a specific diagnosis. In total, 17 of 399 (4.3%) medical records were missing because of removal of the participants from the practice list at the time the medical records were inspected.

Statistics

Patient characteristics that were significantly associated with the incidence of moderate COPD in the univariate analysis were entered in a multivariate logistic regression model. Forward and backward multiple logistic regression analysis was performed to assess patient characteristics independently associated with the incidence of moderate COPD. Odds ratios (OR) and 95% confidence intervals (95% CIs) were calculated. Missing data (4.3%) from the medical records of GP contacts for lower respiratory tract problems were imputed using SPSS software. All statistical analyses were performed using SPSS (version 11.0).

RESULTS

General characteristics

Mean age of participants was 50 years (SD = 6.4), mean pack years (that is, number of packs smoked per day times number of years smoked) was 24.1 (SD = 8.7), and mean smoking history was 31.3 years (SD = 8.5). Mean FVC and FEV1 (% predicted) were 111% (SD = 13) and 102% (SD = 12) respectively (Table 2). Mean follow-up period was 5.2 years. The cumulative incidence of GOLD II (moderate COPD) was estimated at 8.3% (33/399; 95% CI 5.8 to 11.4%). Mean annual incidence was 1.6%. No participant developed GOLD III or IV (severe or very severe COPD).

Determinants of incidence of GOLD II

The cumulative incidence of GOLD II in participants with baseline mild COPD (GOLD I) was approximately five times the incidence among those with baseline normal spirometry (19.6 versus 4.1%) (Table 3). The incidence of GOLD II was significantly associated with older age, heavy

smoking, and starting smoking in childhood (≤15 years of age) (Table 3). The incidence was higher in symptomatic smokers, either reporting cough in the questionnaire or presenting lower respiratory symptoms to the GP. The highest incidence was found in smokers with GOLD I at baseline who reported cough (9/31; 29%) while the lowest incidence was assessed in smokers with normal spirometry at baseline not reporting cough (7/239; 2.9%). Family history of obstructive lung disease (asthma, bronchitis, or emphysema) was not associated with the incidence of GOLD II.

Multivariate analysis showed that age, childhood smoking, cough and one or more GP contacts for lower respiratory tract problems at baseline were independently associated with the incidence of GOLD II. Smoking history was not associated with GOLD II when age and childhood smoking were included (Table 4).

DISCUSSION

Summary of main findings

The 5-year cumulative incidence of moderate COPD (GOLD II) in a cohort of male smokers, either with normal spirometry or mild COPD (GOLD I) at baseline, was 8.3% (95% CI = 5.8 to 11.4%), with a mean annual incidence of 1.6%. The incidence of GOLD II was five times higher in participants with baseline GOLD I than in those with baseline normal spirometry. Patient characteristics that were independently associated with incident GOLD II were increasing age, childhood smoking (≤15 year of age), cough, and one or more GP contacts for lower respiratory tract problems at baseline.

Strengths and limitations of the study

Some limitations of the study should be considered. Only men were included. Sex differences in lung vulnerability to tobacco smoking are currently being investigated; therefore, the estimated incidence of moderate COPD in this study of male smokers can not be generalised to female smokers.[14–17] There were 702 participants in the baseline survey and 436 in the second survey. In those only participating in the baseline survey the prevalence of GOLD II at baseline was slightly higher (4.0 versus 2.4%) and FEV1 percentage predicted was slightly lower (98 versus 102%) than in those participating in both surveys. This may indicate that a slightly higher proportion of participants with relatively poorer lung function tended to discontinue participation, and that the incidence rate of GOLD II is possibly slightly underestimated. As non-participation in the baseline survey could have been higher among smokers with poorer lung function, the estimated 8.3% cumulative incidence is likely to be conservative.

Table 3. Five-year cumulative incidence of moderate chronic obstructive pulmonary disease (COPD: GOLD II) in middle-aged smokers.

Characteristic	(Participants/*n*)[a]	GOLD II (%)	*P*-value[b]
Overall incidence	Total (33/399)	8.3	
Baseline spirometry	Normal (12/292)	4.1	<0.001
	GOLD I (21/107)	19.6	
Age (years)	40–44 (3/99)	3.0	0.011
	45–49 (6/97)	6.2	
	50–54 (9/108)	8.3	
	55–65 (15/95)	15.8	
Pack years	<20 (4/109)	3.7	0.011
	20–29 (15/198)	7.6	
	≥30 (14/92)	15.2	
Family history of obstructive lung disease	Absent (20/238)	8.4	0.9
	Present (12/149)	8.1	
Parental smoking	Absent (2/40)	5.0	0.4
	Present (27/292)	9.2	
Childhood smoking	Absent (11/245)	4.5	0.002
	Present (22/154)	14.3	
Cough	Absent (19/315)	6.0	0.002
	Present (14/84)	16.7	
≥1 GP contact for LRT	Absent (21/329)	6.4	0.003
	Present (12/70)	17.1	

[a]Participants/n = number of participants with GOLD II/number of participants positive for the characteristic. [b]χ^2 test for association or trend. GOLD II = chronic obstructive pulmonary disease stage II according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. Pack years = number of packs smoked per day times number of years smoked. LRT = lower respiratory tract problems in the previous 12 months.

To assess potential bias associated with using different spirometers at baseline (Vitalograph) and follow-up (Jaeger), the change in FEV1 in a subset of 171 participants who performed an additional lung function test in 2002 was compared with results from the Vitalograph spirometer. The change in FEV1

Table 4. Association between baseline characteristics and incidence of GOLD II (*n* = 33) in middle-aged smokers (*n* = 399).

Characteristic	Odds ratio unadjusted (95% CI)	Odds ratio adjusted (95% CI)	*P*-value
Age (years)			
40–44	1.0[a]	1.8 (1.2–2.6)	0.002
45–49	2.1 (0.5–8.7)	(per 5 years)	
50–54	2.9 (0.8–11.1)		
55–65	6.0 (1.7–21.5)		
Pack years[b]			
<20	1.0[a]		
20–29	2.1 (0.7–6.6)		
≥30	4.7 (1.5–14.9)		
Childhood smoking (absent/present)	3.5 (1.7–7.5)	3.3 (1.5–7.3)	0.002
Cough (absent/present)	3.1 (1.5–6.5)	2.2 (1.0–4.8)	0.05
≥1 GP contact for LRT	3.0 (1.4–6.5)	2.8 (1.3–6.4)	0.01

[a]Reference category. [b]Not included in multivariate analysis; Pack years = number of packs smoked per day times number of years smoked. LRT = lower respiratory tract problems in the previous 12 months.

between the baseline and additional tests, both performed with the Vitalograph spirometer, was similar to the change in FEV1 between the baseline and the follow-up tests performed with the Vitalograph and Jaeger spirometer, respectively (63.5 versus 60.6 ml/year, *t*-test for difference $P = 0.6$).

One of the strengths of the study is that the survey was performed in a population representative of the 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.[18] Moreover, a high proportion (87.7%) of the eligible male smokers participated. Thus, selective response seems unlikely. In addition, all participants with a new diagnosis of moderate COPD performed postbronchodilator lung function measurements as recommend by the GOLD guidelines.

Comparison with existing literature

A limited number of studies have provided incidence rates of COPD.[19–22] In a Finnish study the mean annual incidence of COPD (FEV1/FVC <0.6) among male smokers aged 40–64 years was about 0.5%.[19] In a Polish study the mean annual incidence of COPD (FEV1 <65% predicted) in male smokers aged 41–60 years was 1.2–1.6%.[20] Using different definitions of COPD and prebronchodilator lung function values in those studies, limits comparison of the annual incidence estimates with the current study. A more recent study showed a 10-year cumulative incidence of moderate COPD (GOLD II) in male smokers aged 51–52 years of about 25%,[22] which is comparable to the current study's 5-year incidence in 50–54 year-old male smokers.

Univariate analysis in the current study showed that the incidence of COPD in smokers is associated with age and smoking history, that is, the number of pack years. In the multivariate analysis the number of pack years disappeared when age and childhood smoking were included.

Several determinants of COPD, such as childhood smoking, respiratory symptoms, a family history of obstructive lung disease, and parental smoking, have been implicated to varying degrees.[1,23,24] In one study, childhood smoking was an independent risk factor of obstructive airways disease in women but not in men as diagnosed by a doctor.[23] In contrast, the current study showed that childhood smoking was an independent risk factor of GOLD II, which can possibly be explained using different definitions of airflow obstruction. Support for the increased risk of COPD with childhood smoking in both sexes was given in a prognostic study, which found that cigarette smoking in males and females, 10–18 years of age, is associated with mild airflow obstruction and slowed growth of lung function.[24] A similar incidence of GOLD II in symptomatic and asymptomatic smokers with normal baseline spirometry (7.4 versus 6.7%) has been previously reported,[25] while the current study found that the incidence of GOLD II in symptomatic smokers was three times higher than in asymptomatic smokers (9.3 versus 2.9%).

An association between bronchitic symptoms, such as cough or sputum production, and the incidence of GOLD II is supported by the results of a Swedish study which found a significant association between each bronchitic symptom and the incidence of GOLD II after adjustment for possible confounders.[22]

In the current study, no association between a family history of obstructive lung disease and the incidence of GOLD II was found. An association between positive family history and the development of airflow obstruction may be undetected by poor recall in participants completing questionnaires, or by smaller family size in contemporary generations compared with earlier generations.

In a European study, parental smoking, especially smoking by fathers, was related to a poorer lung function among smoking and non-smoking adults aged 20–44 years.[26,27] However, the current study found no significant association between parental smoking and the incidence of GOLD II. This may be due to lack of contrast, as parental smoking during childhood was reported by almost 90% of the participants in the current study.

Implications for clinical practice

Early identification of COPD is important because smoking cessation at an early stage of COPD is the only intervention that substantially improves the prognosis by normalising lung function decline and decreasing morbidity and all-cause mortality.[4–6] Middle-aged male smokers (40–65 years of age) showed an overall estimated cumulative 5-year incidence of moderate COPD (GOLD II) that was relatively high (8.3%). The incidence was even higher in those who smoked before the age of 16 years or who had lower respiratory tract problems.

Funding body
The Dutch Asthma Foundation (Reference 3.4.01.93)
Ethical approval
Ethics committee of the University Medical Centre Utrecht (Reference 00/212)
Competing interests
The authors have stated that there are none
Acknowledgements
We thank the GPs from IJsselstein who participated in this study.

REFERENCES

1. Pauwels RA, Buist AS, Calverley PM, *et al*. 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* 2001; **163(5):** 1256–1276.
2. Fabbri LM, Hurd SS; GOLD Scientific Committee. Global strategy for the diagnosis, management and prevention of COPD: 2003 update. *Eur Respir J* 2003; **22(1):** 1–2.
3. Gauderman, WJ, Avol E, Gilliland F, *et al*. The effect of air pollution on lung development from 10 to 18 years of age. *N Engl J Med* 2004; **351(11):** 1057–1067.
4. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. *BMJ* 2004; **328(7455):** 1519, 1529–1533.
5. Anthonisen NR, Connett JE, Murray RP. Smoking and lung function of Lung Health Study participants after 11 years. *Am J Respir Crit Care Med* 2002; **166(5):** 675–679.
6. Anthonisen NR, Skeans MA, Wise RA, *et al*. The effects of smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. *Ann Intern Med* 2005; **142(4):** 233–239.
7. Van Schayck CP, Loozen JM, Wagena E, *et al*. Detecting patients at a high risk of developing chronic obstructive pulmonary disease in general practice: cross sectional case finding study. *BMJ* 2002; **324(7350):** 1370–1376.
8. Ferguson GT, Enright PL, Buist AS, Higgins MW. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. *Chest* 2000; **117(4):** 1146–1461.
9. Geijer RM, Sachs AP, Hoes AW, Salomé PL, Lammers JW, Verheij TJ. Prevalence of undetected persistent airflow obstruction in male smokers 40–65 years old. *Fam Pract* 2005; **22(5):** 485–459.
10. American Thoracic Society. Standardization of spirometry, 1994 update. *Am J Respir Crit Care Med* 1995; **152(3):** 1107–1136.
11. Quanjer PH, Tammeling GJ, Cotes JE, *et al*. 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; **16:** 5–40.
12. Hajiro T, Nishimura K, Jones PW, *et al*. A novel, short, and simple questionnaire to measure health-related quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1999; **159(6):** 1874–1878.
13. Fletcher CM (Chair.). Standardised 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.
14. Langhammer A, Johnsen R, Gulsvik A, *et al*. Sex differences in lung vulnerability to tobacco smoking. *Eur Respir J* 2003; **21(6):** 1017–1023.
15. Prescott E, Bjerg AM, Andersen PK, *et al*. Gender differences in smoking effects on lung function and risk of hospitalization for COPD: results from a Danish longitudinal population study. *Eur Respir J* 1997; **10(4):** 822–827.
16. Kerstjens HA, Rijcken B, Schouten JP, Postma DS. Decline of FEV1 by age and smoking status: facts, figures, and fallacies. *Thorax* 1997; **52(9):** 820–827.
17. Vollmer WM, Enright PL, Pedula KL, *et al.* Race and gender differences in the effects of smoking on lung function. *Chest* 2000; **117(3):** 764–772.
18. Koolhaas C. Rookgewoonten volwassenen (vanaf 2001) en jongeren (vanaf 1997). [Smoking among adults and young adults]. Amsterdam: TNS/NIPO, 2004.
19. Huhti, E, Ikkala J. A follow-up study on respiratory symptoms and ventilatory function in a middle-aged rural population. *Eur J Resp Dis* 1980: **61:** 33–45.
20. Krzyzanowski M, Jedrychowski W, Wysocki M. Factors associated with the change in ventilatory function and the development of chronic obstructive pulmonary disease in a 13-year follow-up of the Cracow Study. Risk of chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1986; **134(5):** 1011–1019.
21. Lundback B, Gulsvik A, Albers M, *et al.* Epidemiological aspects and early detection of chronic obstructive airway diseases in the elderly. *Eur Respir J Suppl* 2003; **40:** 3s–9s.
22. Lindberg A, Jonsson AC, Rönmark E, *et al.* Ten-year cumulative incidence of COPD and risk factors for incident disease in a symptomatic cohort. *Chest* 2005; **127(5):** 1544–1552.
23. Patel BD, Luben RN, Welch AA, *et al.* Childhood smoking is an independent risk factor for obstructive airways disease in women. *Thorax* 2004; **59(8):** 682–686.
24. Gold DR, Wang X, Wypij D, *et al*. Effects of cigarette smoking on lung function in adolescent boys and girls. *N Engl J Med* 1996; **335(13):** 931–937.
25. Vestbo J, Lange P. Can GOLD Stage 0 provide information of prognostic value in chronic obstructive pulmonary disease? *Am J Respir Crit Care Med* 2002; **166(3):** 329–332.
26. Svanes C, Omenaas E, Jarvis D, *et al*. Parental smoking in childhood and adult obstructive lung disease: results from the European Community Respiratory Health Survey. *Thorax* 2004; **59(4):** 295–302.
27. De Marco, R, Accordini S, Cerveri I, *et al.* An international survey of chronic obstructive pulmonary disease in young adults according to GOLD stages. *Thorax* 2004; **59(2):** 120–125.