

Undetected chronic obstructive pulmonary disease and asthma in people over 50 years with persistent cough

Berna DL Broekhuizen, Alfred PE Sachs, Arno W Hoes, Karel GM Moons, Jan WK van den Berg, Willem H Dalinghaus, Ernst Lammers and Theo JM Verheij

ABSTRACT

Background

Chronic obstructive pulmonary disease (COPD) and asthma are underdiagnosed in primary care.

Aim

To determine how often COPD or asthma are present in middle-aged and older patients who consult their GP for persistent cough.

Design of study

A cross-sectional study in 353 patients older than 50 years, visiting their GP for persistent cough and not known to have COPD or asthma.

Setting

General practice in the Netherlands.

Method

All participants underwent extensive diagnostic work-up, including symptoms, signs, spirometry, and body plethysmography. All results were studied by an expert panel to diagnose or exclude COPD and/or asthma. The reproducibility of the panel diagnosis was assessed by calculation of Cohen's κ statistic in a sample of 41 participants.

Results

Of the 353 participants, 102 (29%, 95% confidence interval [CI] = 24 to 34%) were diagnosed with COPD. In 14 of these 102 participants, both COPD and asthma were diagnosed (4%, 95% CI = 2 to 7%). Asthma (without COPD) was diagnosed in 23 (7%, 95% CI = 4 to 10%) participants. Mean duration of cough was 93 days (median 40 days). The reproducibility of the expert panel was good (Cohen's κ = 0.90).

Conclusion

In patients aged over 50 years who consult their GP for persistent cough, undetected COPD or asthma is frequently present.

Keywords

asthma; cough; COPD; early diagnosis.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) and asthma are both being underdiagnosed in primary care.¹⁻⁴ This underdiagnosis hampers adequate and timely treatment and patient education. Proper treatment of asthma and COPD, mainly consisting of smoking-cessation interventions and inhalation medication, reduces the number and severity of exacerbations and improves the quality of life of patients.^{5,6} Moreover, informing patients with asthma or COPD about their diagnosis helps those who still smoke to quit.^{7,8}

Complaints of cough are currently often diagnosed as 'acute bronchitis' and subsequently treated with antibiotics,⁹ although trials have failed to show a beneficial effect of this treatment.¹⁰ Awareness of a possible diagnosis of COPD or

BDL Broekhuizen, MD, PhD student; APE Sachs, MD, PhD, associate professor; TJM Verheij, MD, PhD, professor, Department of General Practice; AW Hoes, MD, PhD, professor, Department General Practice and Clinical Epidemiology; KGM Moons, professor, Department of Clinical Epidemiology, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, the Netherlands. JW van den Berg, MD, PhD, lung physician, Department of Pulmonology, Isala Klinieken, Zwolle, the Netherlands. WH Dalinghaus, MD, lung physician, Department of Pulmonology, Meander Medical Center, Amersfoort, the Netherlands. E Lammers, lung physician, Department of Pulmonology, Gelre Hospital, Zutphen, the Netherlands.

Address for correspondence

BDL Broekhuizen, University Medical Center Utrecht, Julius Center for Health Sciences and Primary Care, PO Box 85500 3508 GA Utrecht, the Netherlands.
E-mail: b.d.l.broekhuizen@umcutrecht.nl

Submitted: 1 December 2009; **Editor's response:** 10 February 2010; **final acceptance:** 1 April 2010.

©British Journal of General Practice 2010; 60: 489-494.

DOI: 10.3399/bjgp10X514738

How this fits in

Chronic obstructive pulmonary disease (COPD) and asthma are underdiagnosed in primary care, but the prevalence of these undetected chronic respiratory disorders in patients who present with cough is undetermined. In this cross-sectional study, more than one-third of the 353 patients older than 50 years with persistent cough had unrevealed COPD (29%) or asthma (7%). Considering that adequate treatment of COPD and asthma reduces symptoms and improves the quality of life, these results support diagnostic strategies for asthma and COPD in middle-aged and older primary care patients with persistent cough.

asthma could help GPs to focus more on treating the underlying disorder, and reduce unnecessary prescriptions of antibiotics.

It has therefore been suggested that early detection should be implemented in patients who present with respiratory complaints in primary care.⁶ Developing improved diagnostic strategies should be based on valid estimations of the prevalence of chronic obstructive lung disorders in symptomatic primary care patients. Until now, only one study has assessed the prevalence of both COPD and asthma in patients who consult their GP with coughing complaints.¹¹ However, the mean age of the patients in the Thiadens *et al* study was relatively low (44 years), while primary care studies suggest that underdiagnosis is more prominent in middle-aged and older individuals.¹⁻³

The aim of the present study was to determine the prevalence of undetected COPD and asthma in middle-aged and older patients who consult their GP for complaints of persistent cough.

METHOD

Study population

Seventy-three GPs in the eastern part of the Netherlands were included in a cross-sectional diagnostic accuracy study: the FRESCO-study (From REspiratory Symptoms to COPD). Inclusion criteria for the participants were being older than 50 years and consulting their GP for cough lasting 14 days or longer. Exclusion criteria were physician-diagnosed COPD or asthma, pneumonia suspected by the GP, severe psychiatric symptoms, and terminal illness. Inclusion started in January 2006 and continued during three winter periods, until April 2009. All patients gave written informed consent and the study was approved by the ethics committee of the University Medical Centre Utrecht.

Diagnostic work-up

During the first visit, participants underwent standardised history taking regarding smoking

habits, dyspnoea, cough, phlegm, medical disorders and use of medication, and physical examination which comprised lung auscultation and measurement of body temperature and breathing frequency.

Extensive lung function tests, including spirometry, body plethysmography, and diffusing capacity of the lung for carbon monoxide (DLCO) by the single-breath method were performed in a secondary care lung function laboratory. These were performed on day 90 rather than day 1, because lung function tests are probably more reliable in a stable phase.^{12,13} Results were obtained before and after bronchodilation with 400 µg salbutamol, and expressed as a percentage of predicted for age, sex, and height.¹⁴ Finally, clinical follow-up information, like new diagnoses or hospital admissions, was provided by the participants' GPs.

Throughout the whole study, the GP treated the patient as usual, in the sense that any necessary diagnostic test or treatment was undertaken as part of routine care.

Panel diagnosis (diagnostic outcome)

For COPD and asthma there is no diagnostic 'gold standard'. Spirometry is an important tool, but without information on symptoms and signs, results are insufficient.^{5,6} In the absence of a single reference test, it is advisable to use a consensus (panel) decision as reference test.¹⁵⁻¹⁷ An outcome panel of two physicians was used to determine whether COPD or asthma was present or not. The panel made the diagnoses in consensus, using (inter)national guidelines, during a meeting in which all available patient information was presented. The outcome panel comprised one GP with expertise in COPD and one of the eight pulmonologists contributing to the study (the pulmonologists attended the panel meetings in turn). In case of doubt, a third physician was consulted. The severity of COPD was determined according to the GOLD criteria (Global initiative for chronic Obstructive Lung Disease): mild (forced expiratory volume in 1 s [FEV₁] >80% of predicted), moderate (FEV₁ 50–80% of predicted), severe (FEV₁ 30–50% of predicted), and very severe (FEV₁ <30% of predicted).

For a diagnosis of COPD, recurrent complaints of cough, sputum, or breathlessness were obligatory, as well as a post-bronchodilator obstruction. Obstruction was defined as a lowered FEV₁/FVC (forced vital capacity; FVC) ratio, and a concave dip in the second part of the curve. According to the GOLD guidelines, a post-bronchodilator FEV₁/FVC ratio below 70% confirms airflow limitation.⁶

However, because the FEV₁/FVC ratio physiologically decreases with age, COPD was not diagnosed in every participant with an FEV₁/FVC ratio below 70%. For the same reason, diagnosis of COPD was accepted without this index being below 70% in young people.¹⁸ A history of smoking was supportive but not obligatory for COPD. As an illustration, a 52-year-old woman with recurrent cough and dyspnoea who had smoked 25 pack-years, with a post-bronchodilator FEV₁/FVC ratio of 0.71 and an FEV₁ of 80% of predicted value, was diagnosed with COPD because DLCO was lowered (70% of predicted value) and the residual volume was increased (160% of predicted value), which both supported this diagnosis.^{19,20}

For a diagnosis of asthma, recurrent episodes of wheezing, cough, or dyspnoea were obligatory, as well as an increase of FEV₁ after bronchodilation of more than 200 ml, or more than 12% of the baseline FEV₁.⁵ Allergy for pollen or house dust mite and eczema were supportive for asthma. Both asthma and COPD could be diagnosed when FEV₁ increased with more than 12% or 200 ml and the post-bronchodilator FEV₁/FVC ratio was below 70%, combined with complaints suggestive of both disorders, according to the Dutch guidelines for GPs.^{21,22}

When detected, other disorders than asthma or COPD were diagnosed.

Reproducibility of the expert panel

The reproducibility of the panel diagnosis with regard to asthma or COPD was estimated by a second diagnosis by a panel after more than a year, of a random sample of 41 patients (12%), without information on the original diagnosis.

Data analysis

Prevalences (with 95% confidence intervals [CIs]) of COPD, asthma, and 'COPD and asthma' were calculated in the total study population, and in subgroups of sex, age, and pack-years of smoking. In the subgroups, participants with both asthma and COPD were included in the group of patients with COPD. Missing data were imputed using single regression techniques.

With the results of the first and second panel diagnosis of the 41 cases that had been reassessed, Cohen's κ was calculated.²³ Analyses were performed using SPSS (version 15.0).

RESULTS

In total, 400 participants were included. In 18 participants the presence of asthma or COPD could not be determined because of missing spirometry results, and 29 participants were already known to have asthma. These 47 participants were excluded from the analysis. In the resulting 353 participants, results were missing in a mean of 5% per patient

Table 1. Characteristics of participants with persistent cough and those diagnosed with chronic obstructive pulmonary disease (COPD), asthma, and neither of these.

Characteristic	Total, n = 353	COPD, n = 102 ^a	Asthma, n = 23	No COPD or asthma, n = 228
History and physical examination (day 1)				
Age in years, mean (SD)	63 (9)	65 (10)	61 (8)	62 (8)
Male sex, %	45	61	44	38
Current smoking, %	26	50	22	16
Cardiovascular disease, ^b %	19	34	9	14
Allergy for pollen or house dust mite, ^b %	13	8	35	13
Duration of cough in days, mean (median, SD)	93 (40, 169)	84 (30, 181)	178 (90, 230)	88 (40, 154)
Previous GP consultation for cough, %	43	30	48	48
Complaints of phlegm, %	75	83	91	70
Complaints of wheezing, %	47	62	39	42
MRC dyspnoea score, ^c mean (SD)	3 (1.4)	3.1 (1.4)	2.9 (1.1)	3.0 (1.5)
Asthma in first-degree family member, %	24	22	26	24
COPD in first-degree family member, %	39	46	48	34
Body mass index (kg/m ²), mean (SD)	28 (5)	27 (5)	29 (5)	29 (5)
Spirometry results ^d day 90				
FEV ₁ in litres, mean (SD)	2.8 (0.8)	2.4 (0.7)	3.0 (0.8)	2.9 (0.8)
FEV ₁ % predicted, mean (SD)	101 (18)	84 (20)	107 (13)	107 (16)
FEV ₁ % after bronchodilation, mean (SD)	6 (12)	8 (12)	10 (8)	4 (12)
FVC in litres, mean (SD)	3.7 (1.0)	3.7 (1.0)	4.0 (1.1)	3.6 (1.0)
FVC % predicted, mean (SD)	110 (18)	107 (19)	113 (15)	111 (17)
FEV ₁ /FVC mean (SD)	0.73 (0.1)	0.62 (0.1)	0.76 (0.1)	0.78 (0.1)

^a14 of the 102 patients with COPD also had asthma, not included in the n = 23 patients with asthma. ^bPhysician diagnosed.

^cMedical Research Council (MRC) dyspnoea score: 1 = 'never'; 2 = 'only during strenuous exercise'; 3 = 'walking fast or uphill'; 4 = 'walking with people of same age'; 5 = 'walking flat'; 6 = 'in rest'. ^dPost-bronchodilator results. FEV₁ = forced expiratory volume in 1 second. FVC = forced vital capacity.

Table 2. Prevalence of COPD and asthma in subgroups of patients with persistent cough according to sex, age, and smoking history.

Characteristics	COPD, <i>n</i> (%; 95% CI)	Asthma, <i>n</i> (%; 95% CI)	No COPD or asthma, <i>n</i> (%; 95% CI)
Sex			
Males (<i>n</i> = 158)	62 (39, 32 to 46)	10 (6, 3 to 11)	86 (54, 47 to 62)
Females (<i>n</i> = 195)	40 (21, 15 to 27)	13 (7, 4 to 11)	142 (73, 66 to 79)
Age in years			
50–59 (<i>n</i> = 142)	30 (21, 15 to 29)	10 (7, 4 to 12)	102 (72, 64 to 79)
60–69 (<i>n</i> = 125)	37 (30, 22 to 38)	10 (8, 4 to 14)	78 (62, 54 to 70)
≥70 (<i>n</i> = 86)	35 (41, 31 to 51)	3 (3, 1 to 10)	48 (56, 45 to 66)
Smoking			
Never smoker (<i>n</i> = 92)	3 (3, 1 to 9)	8 (9, 4 to 16)	81 (88, 82 to 95)
1–9 pack-years ^a (<i>n</i> = 97)	17 (18, 11 to 26)	10 (10, 6 to 18)	70 (72, 63 to 80)
10–29 pack-years (<i>n</i> = 93)	44 (47, 37 to 57)	3 (3, 1 to 9)	46 (49, 40 to 59)
≥30 pack-years (<i>n</i> = 71)	38 (54, 42 to 65)	2 (3, 1 to 10)	31 (44, 33 to 55)

^aPack-years = (number of cigarettes smoked per day/20) × number of years smoking.

characteristic. Mean age of the 353 participants was 63 years, and 45% were male (Table 1). Mean duration of cough was 93 days (median 40 days) in all participants, and 178 days (median 90 days) in participants with asthma.

In 102 participants previously unknown COPD was diagnosed (prevalence 29%, 95% CI = 24 to 34%), of whom 71 had mild, 29 moderate, and two severe disease. In 14 of these 102 participants with COPD, both COPD and asthma were diagnosed (prevalence 4%, 95% CI = 2 to 7%). Asthma without COPD was diagnosed in 23 participants (prevalence 7%, 95% CI = 4 to 10%). The prevalence of COPD increased with male sex, higher age, and number of pack-years (Table 2).

In two of the 41 reassessed cases, disagreement occurred concerning the presence of COPD or asthma (Cohen's κ = 0.90).

With regard to other disorders, lung cancer was diagnosed in one, heart failure in three, and pneumonia in one participant. These diagnoses were based mainly on the follow-up information provided by the GPs.

DISCUSSION

Summary of main findings

The prevalence of previously undetected COPD or asthma was determined in a study population of 353 patients who consulted their GP for persistent cough and were older than 50 years. In 29% of the cases, previously unknown COPD was diagnosed, and in 7% previously unknown asthma. Severity of the diagnosed COPD was mainly mild or moderate.

Strengths and limitations of the study

Before drawing conclusions from the results, some issues should be considered. First, it could be

argued that a panel diagnosis is a subjective tool for diagnosis of chronic respiratory disorders. However, the reproducibility of the panel diagnosis of asthma and COPD was good, and therefore it could be concluded that the subjectivity of the panel diagnosis in this study was limited.

Second, it has been recognised that the use of a fixed FEV₁/FVC ratio of 70% may result in overdiagnosis of COPD in older people and in underdiagnosis in younger people. Using the lower limit of normal values for FEV₁/FVC, classifying the lowest 5% of the healthy population as abnormal has been suggested to decrease misclassification.^{6,24} This method was not included in the panel diagnosis because it is currently not incorporated in the guidelines. Moreover, the values of the normal distribution of the Dutch population are unknown. However, it is thought that misclassification by interpreting the FEV₁/FVC ratio in the study was limited because normal ageing of the lungs, as well as all other test results of the participants were taken into account when diagnosing COPD. Hence, in nine participants older than 65 years with an FEV₁/FVC ratio below 70%, COPD was not diagnosed because there was no other sign of COPD except for a single episode of cough. Accordingly, COPD was diagnosed in eight participants in whom FEV₁/FVC index was not below 70% but was 70% or 71%. In these participants, who were all (former) smokers and aged below 55 years, DLCO was below 80% of predicted value and/or the residual volume measured by body plethysmography was above 150% of predicted.

Third, possible selection bias by participating GPs is a shortcoming of the study. Probably, many more patients were eligible during the inclusion period. Of the 73% participating GPs, 22 GPs included more than eight participants, 40 included between two and eight, and 11 GPs included only one or two participants. The eligibility criterion 'cough for 14 days or longer' was used, but the duration of cough of most included participants was much longer, with interquartiles of 21, 40, and 90 days. Therefore, the results are generalisable to patients who present with persistent cough, rather than to patients who present with cough in general. It may be assumed that inclusion of participants was mainly hampered by lack of time of the GPs, considering the comprehensive protocol. Participating GPs were explicitly requested to include all eligible patients, and not only those in whom they suspected asthma or COPD. It is possible that the GPs included or excluded patients on the basis of the GPs' perception of the patients' risk of having or not having a chronic lung disorder.

However, as data on eligible patients who were not included were not gathered, it is not possible to determine with certainty the direction of the possible bias caused by selection. Nevertheless, it can be assumed that overestimation of the prevalence by selection is more likely than underestimation.

Fourth, in 14 participants both asthma and COPD were diagnosed according to the Dutch guidelines for COPD and asthma.^{21,22} Internationally, there is no consensus on how to diagnose these people with signs of both disorders. In international guidelines, most cases of asthma with persistent obstruction are defined as COPD.^{5,6}

Finally, in participants with recurrent complaints of cough or wheezing and normal spirometry results, asthma was not diagnosed in the present study. Possibly, some of these patients did, nevertheless, have asthma, which might have been revealed by a histamine or metacholine provocation test.^{5,25} However, these tests were not included for practical reasons. A strong aspect of the study is the use of extensive pulmonary function and other tests to diagnose or exclude asthma and COPD.

Comparison with existing literature

The prevalence of undetected COPD or asthma in a study population of people who consult their GP for cough was, to the authors' knowledge, reported before only once, in 1998.¹¹ In this study by Thiadens *et al*, 74 of the 192 participants had asthma (39%) and 14 had COPD (7%). The lower mean age of the participants of that study was probably the main cause for the high prevalence of asthma and the low prevalence of COPD, compared to the present results. In a study by van Schayck *et al*, cough was found to be a strong predictor for obstructive lung disease in general practice: in 64 smokers with chronic cough, 16 (27%) had obstructive lung disease. However, no distinction was made between asthma and COPD.¹ With regard to the severity of COPD, other authors also found (although in different study populations) that undetected COPD was mainly mild or moderate.^{4,26} Regarding asthma, it has been reported that its development is not rare at higher age and that underdiagnosis is substantial in older people.^{27,28}

The underdiagnosis of relevant chronic respiratory morbidity that was found could have been caused by a doctor or a patient delay. Symptoms of asthma or COPD, like cough, breathlessness, wheezing, and sputum might have been attributed to smoking habits, older age, or poor fitness. Smokers might have been restrained in consulting their GP for their complaints because they felt guilty about smoking. Moreover, a lot of

patients who did visit the GP with cough before had probably been diagnosed with uncomplicated respiratory tract infections, instead of with COPD or asthma.

Implications for future research and clinical practice

This study suggests that COPD and asthma are frequent undetected underlying disorders in middle-aged and older patients who consult the GP for complaints of persistent cough. GP awareness of this high prevalence, as well as new diagnostic strategies, are needed to reduce underdiagnosis of COPD and asthma in order to enhance adequate treatment, education, and follow-up of patients.

Funding body

This work was funded by The Netherlands Organisation for Health Research and Development (grant number 945-04-015) and received research grants from GlaxoSmithKline, Boehringer-Ingelheim, and Pfizer.

Ethical approval

The study was approved by the ethics committee of the University Medical Centre Utrecht.

Competing interests

Alfred Sachs has been speaker on congresses, sponsored by GlaxoSmithKline, Boehringer Ingelheim, Pfizer, or AstraZeneca. Theo Verheij participates in studies that received grants from GlaxoSmithKline and Wyeth. The other authors have stated that there are no competing interests. The study sponsors had no involvement in the study design, the collection, analysis, and interpretation of the data, the writing of the report or in the decision to submit the paper for publication.

Acknowledgements

We gratefully acknowledge all participating patients, GPs and their assistants and the technicians of the pulmonary function laboratories. SAA Chergwandi, R Hage, JWK Lammers, HEJ Sinnighe Damsté, and WJA Wijnands, pulmonologists, facilitated lung function tests and performed, as well as JWK van den Berg, WH Dalinghaus and E Lammers, as experts in the expert panels.

Discuss this article

Contribute and read comments about this article on the Discussion Forum: <http://www.rcgp.org.uk/bjgp-discuss>

REFERENCES

1. 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): 1370–1374.
2. Stupka E, deShazo R. Asthma in seniors: Part 1. Evidence for underdiagnosis, undertreatment, and increasing morbidity and mortality. *Am J Med* 2009; **122**(1): 6–11.
3. Bednarek M, Maciejewski J, Wozniak M, *et al*. Prevalence, severity and underdiagnosis of COPD in the primary care setting. *Thorax* 2008; **63**(5): 402–407.
4. Geijer RM, Sachs AP, Hoes AW, *et al*. Prevalence of undetected persistent airflow obstruction in male smokers 40–65 years old. *Fam Pract* 2005; **22**(5): 485–489.
5. The Global Initiative for Asthma. *GINA Report, Global Strategy for Asthma Management and Prevention*. Global Initiative for Asthma (GINA) 2008. <http://www.ginasthma.org> (accessed 10 June 2010).
6. Rabe KE, Hurd S, Anzueto A, *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007; **176**(6): 532–555.
7. Bednarek M, Gorecka D, Wielgomas J, *et al*. Smokers with airway obstruction are more likely to quit smoking. *Thorax* 2006; **61**(10):

- 869–873.
8. Parkes G, Greenhalgh T, Griffin M, Dent R. Effect on smoking quit rate of telling patients their lung age: the Step2quit randomised controlled trial. *BMJ* 2008; **336**(7644): 598–600.
 9. Akkerman AE, Kuyvenhoven MM, van der Wouden JC, Verheij TJ. Prescribing antibiotics for respiratory tract infections by GPs: management and prescriber characteristics. *Br J Gen Pract* 2005; **55**(511): 114–118.
 10. Smucny J, Fahey T, Becker L, Glazier R. Antibiotics for acute bronchitis. *Cochrane Database Syst Rev* 2004; (4): CD000245.
 11. Thiadens HA, de Bock GH, Dekker FW, et al. Identifying asthma and chronic obstructive pulmonary disease in patients with persistent cough presenting to general practitioners: descriptive study. *BMJ* 1998; **316**(7140): 1286–1290.
 12. Williamson HA Jr. Pulmonary function tests in acute bronchitis: evidence for reversible airway obstruction. *J Fam Pract* 1987; **25**(3): 251–256.
 13. Boldy DA, Skidmore SJ, Ayres JG. Acute bronchitis in the community: clinical features, infective factors, changes in pulmonary function and bronchial reactivity to histamine. *Respir Med* 1990; **84**(5): 377–385.
 14. 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.
 15. Weller SC, Mann NC. Assessing rater performance without a 'gold standard' using consensus theory. *Med Decis Making* 1997; **17**(1): 71–79.
 16. Moons KG, Grobbee DE. When should we remain blind and when should our eyes remain open in diagnostic studies? *J Clin Epidemiol* 2002; **55**(7): 633–636.
 17. Bossuyt PM, Reitsma JB, Bruns DE, et al. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. *Ann Intern Med* 2003; **138**(1): W1–12.
 18. Roberts SD, Farber MO, Knox KS, et al. FEV₁/FVC ratio of 70% misclassifies patients with obstruction at the extremes of age. *Chest* 2006; **130**(1): 200–206.
 19. McLean A, Warren PM, Gillooly M, et al. Microscopic and macroscopic measurements of emphysema: relation to carbon monoxide gas transfer. *Thorax* 1992; **47**(3): 144–149.
 20. Collard P, Njinou B, Nejadnik B, et al. Single breath diffusing capacity for carbon monoxide in stable asthma. *Chest* 1994; **105**(5): 1426–1429.
 21. Geijer RM, Smeele IJ, Goudswaard AN. [Summary of the practice guideline 'Asthma in adults' (second revision) from the Dutch College of General Practitioners]. *Ned Tijdschr Geneesk* 2008; **152**(20): 1146–1150.
 22. Smeele IJ, van WC, Van Schayck CP, et al. NHG-standaard COPD. *Huisarts en Wetenschap* 2007; **50**(8): 362–379.
 23. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas* 2008; **20**(1): 37–46.
 24. Levy ML, Quanjer PH, Booker R, et al. Diagnostic spirometry in primary care: Proposed standards for general practice compliant with American Thoracic Society and European Respiratory Society recommendations. *Prim Care Respir J* 2009; **18**(3): 130–147.
 25. Cockcroft DW, Murdock KY, Berscheid BA, Gore BP. Sensitivity and specificity of histamine PC20 determination in a random selection of young college students. *J Allergy Clin Immunol* 1992; **89**(1 Pt 1): 23–30.
 26. Miller CE, Jones SF, Bailey WC, Dransfield MT. Underdiagnosis of COPD in the national lung screening trial. *Chest* 2006; **130**(4): 2805–d.
 27. Enright PL, McClelland RL, Newman AB, et al. Underdiagnosis and undertreatment of asthma in the elderly. *Chest* 1999; **116**(3): 603–613.
 28. 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.