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# Clinical application of a simple questionnaire for the differentiation of asthma and chronic obstructive pulmonary disease ☆

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**Summary** *Background:* Asthma and chronic obstructive pulmonary disease (COPD) are highly prevalent chronic diseases characterized by airflow limitation. Both diseases have a distinct pathogenesis and require unique treatment approaches. Due to some common characteristic traits, asthma and COPD are often lumped together in clinical practice. We sought to develop a simple questionnaire for the distinction of asthma and COPD.

*Methods:* Clinical discriminants of asthma and COPD were retrospectively identified by multiple logistic regression using files from 547 consecutive adult patients presenting to a pulmonary specialist practice with a diagnosis of asthma or COPD. With these features, we generated a simple quantitative questionnaire supporting a diagnosis of COPD with high scores and asthma with low scores (range 0–15 points). Questionnaire results were compared with physician's diagnosis based on GINA and GOLD guidelines including skin tests, spirometry and reversibility data.

*Results:* 210 patients had COPD and 337 had asthma. Age of onset, smoking history, atopy status, and cough quality were significantly associated with a diagnosis of asthma or COPD. Questionnaire scores for COPD patients were higher than those for asthmatics (mean score $10.5 \pm 0.18$ vs. $4 \pm 0.12$, $P < 0.0001$). Receiver operational characteristics (ROC) analysis revealed a cutoff score of 7 with the highest discriminant power (87.6% sensitivity, 87.2% specificity for COPD, 87.4% correctly classified, area under the ROC curve: 0.954). The overlap between asthma and COPD (score 6–8) comprised about 20% of the total population, these patients included a higher proportion of COPD patients with atopy, and smoking asthmatics.

*Conclusions:* In patients with obstructive airway diseases, a simple questionnaire can support the differentiation of asthma and COPD in everyday clinical practice. Further prospective trials are necessary to confirm these initial observations.


## Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are inflammatory disorders characterized by airway narrowing. Despite some clinical and

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physiological similarities, both diseases represent distinct entities comprising unique features with regard to the underlying inflammatory pattern, the involved mechanisms of airway obstruction, disease progression and prognosis. These differences are also reflected by distinct treatment recommendations, with a clear primacy of anti-inflammatory treatment, e.g. inhaled corticosteroids, in asthma, and bronchodilators in COPD. Moreover, anti-cholinergics are recommended as first-line bronchodilators in COPD,[1] whereas their use in asthma is of minor importance.[2] In view of the critical importance of choosing optimal treatment regimen for both diseases with regard to both efficacy and also health resource utilization, a clear distinction of asthma and COPD in everyday practice would be highly desirable. However, both diseases are often lumped together in clinical practice, possibly due to physician's unawareness and lack or underuse of spirometry.[3–7] Moreover, there is also a considerable degree of overlap between asthma and COPD, as indicated by recent analyses using large databases in the UK and USA.[8] Finally, the fact that "COPD" is an umbrella diagnosis encompassing both chronic bronchitis and/or emphysema may further complicate the differentiation of asthma and COPD. Despite this, it is possible to classify the majority of patients into the two categories of asthma or COPD.

With this as background, we aimed to identify clinical features of asthma and COPD with discriminant power using a large database from a pulmonary specialist located in the inner city of Frankfurt, Germany. Based on such parameters, we hypothesized that it would be possible to generate a simple questionnaire including a scoring system. To evaluate this questionnaire, scores from the questionnaire were retrospectively compared with a "gold standard", i.e. a pulmonary specialist diagnosis of asthma or COPD based on GINA and GOLD recommendations including skin test results and pulmonary function tests.

## Methods

### Patients

Data from a database including files from 1434 patients newly admitted to a pulmonary specialist in the city of Frankfurt, Germany, between 1995 and 1996 were reviewed retrospectively.[9] Due to the German health care system, the practice then had approximately 40% of self-referred patients, and 60% of physician referrals, being largely representative for other pulmonary specialist practices in that area. All files included information about patient history, smoking habits, occupation, age at onset of symptoms, atopy status or history of atopic diseases, absence or presence of cough and sputum, and dyspnea variability including triggers. Diagnostic measurements that supported the specialist's diagnosis included pulmonary function tests (spirometry and bodyplethysmography using Masterlab II equipment from Jaeger, Wuerzburg, Germany, with forced expiratory volume in one second [$FEV_1$], forced vital capacity, and bronchodilator reversibility to 400 μg of salbutamol[10]) and skin prick tests with standard allergens[11] (Bencard, Neuss, Germany).

A diagnosis of COPD was based on the criteria proposed by the GOLD guidelines including typical symptoms, exposure to risk factors, and/or characteristic changes in lung function. GOLD staging was based on post-bronchodilator spirometry parameters. In particular, stage 0 COPD was diagnosed in patients exposed to irritants, e.g. active or passive smoking, who presented with chronic symptoms of cough and/or sputum production for at least 3 months.[1]

A diagnosis of asthma was based on the following criteria, that were adopted from GINA guidelines:[12] (1) airflow obstruction ($FEV_1 < 85\%$) with reversibility $> 12\%$ and at least 200 ml from baseline after bronchodilation or (2) positive histamine challenge combined with typical clinical signs like dry cough and wheezing in absence of acute respiratory tract infection and positive atopy status.[13]

Diagnoses of COPD and asthma had been primarily made by a pulmonary specialist (MK) and were subsequently analyzed by another reviewer (KMB) to confirm the initial diagnosis.

### Clinical parameters

Based on availability from patient files, and a presumed discriminant power, five clinical parameters were chosen for multiple regression analysis. These included age at onset of symptoms, atopy status (yes/no), smoking history and packyears, variability of symptoms (constant/diurnal variation and/or triggers), and cough characteristics (none/dry/productive).

### Questionnaire

Building on the results of the regression analysis, a questionnaire including four items (age of onset, smoking history, atopy status and cough quality) was generated. Accordingly, each item was

assigned a quantitative score (age of onset: $<20$ years $=0$ points, 20–40 years $=1$ point, 40–60 years $=2$ points, $>60$ years $=3$ points; atopy: yes $=0$ points, none $=4$ points; smoked packyears: $0=0$ points, $>0<20$ packyears $=1$ point, 20–40 packyears $=2$ points, $>40$ packyears $=4$ points; cough characteristics: dry cough $=0$ points, no cough $=2$, productive cough $=4$ points). Hence, patients had scores ranging from 0 to 15 points. The score was aimed at preferably indicating COPD with high scores and asthma with low scores.

## Statistical analysis

Statistical analysis was performed using the STATA 5.0 intercooled software package (Stata Corp., College Station, TX, USA) for personal computer. Descriptive data are presented as mean values with standard error of mean ($\pm$SEM). Kolmogorov–Smirnov-Test was used to test variables for normal distribution. Group comparisons were performed by Mann–Whitney *U*-test or Student-*t*-test depending on normal distribution. For multiple comparison, repeated analysis of variance followed by Newman–Keuls was used. Categorical data were compared by Fisher–Exact-test. Correlations were calculated by Spearman's correlational analysis (rho).

Clinical parameters associated with a diagnosis of either asthma or COPD were identified by multiple regression analysis controlling for actual age and sex, and presented as odds ratios (OR) with 95% confidence intervals. Age of onset and smoking were also separately analyzed after generating categories for onset age and packyears, to allow a more quantitative assessment of these parameters. Finally, receiver operational characteristics (ROC) were generated to compare discriminant values of single and combined questionnaire items by calculating the ROC area under the curve (AUC) and the corresponding values for sensitivity/specificity. *P*-values of less than 0.05 were considered statistically significant.

# Results

## Patients

### Demographics

Among 1434 consecutive patients newly admitted to the practice in 1995, 580 subjects (40%) had a diagnosis of asthma or COPD and were eligible for analysis. Of these, 33 subjects were aged under 18 and therefore excluded from the analysis, since COPD does not occur in children or adolescents. Of the remaining 547 patients, 210 had COPD and 337 asthma (Table 1). In COPD, 37% of patients had stage 0 (''at risk''), 5% stage 1 (mild COPD), 46% stage 2 (moderate COPD) and finally, 12% stage 3 disease (severe COPD). Using the GINA classification of 1994,[12] 56% of asthmatics had intermittent or mild persistent asthma, 27% moderate persistent, and 17% severe asthma.

Other frequent diagnoses in the database were acute upper respiratory tract infections (25%), sole allergic rhinitis (6%), lung cancer (4%), interstitial lung diseases (2%), and pneumonia (2%). About 15%

**Table 1** Characteristics of patients with asthma and COPD.

| | Asthma $N=337$ | COPD $N=210$ | *P* value |
|---|---|---|---|
| Age (median, range) | 33 (18–76) | 55 (20–82) | $<0.0001$ |
| Age at onset (median, range) | 31 (8–73) | 54 (20–82) | $<0.0001$ |
| Sex (male, %) | 43 | 60 | 0.0008 |
| Atopy (%) | 75 | 14 | $<0.0001$ |
| Current smokers (%) | 28 | 68 | $<0.0001$ |
| Packyears (median, range) | 0 (0–40) | 30 (0–150) | $<0.0001$ |
| Cough quality | | | |
| None (%) | 13 | 18 | NS |
| Dry (%) | 65 | 37 | $<0.0001$ |
| Productive (%) | 10 | 45 | $<0.0001$ |
| Symptom variability | | | |
| Diurnal variation (%) | 66 | 58 | NS |
| Constant (%) | 34 | 42 | NS |

of all patients had no medical diagnosis (check-up consultation or non-specific symptoms).

### Multiple logistic regression analysis

All items primarily chosen for the analysis were significantly associated with a diagnosis of COPD or asthma, except for symptom quality (Table 2). AUC (ROC) values for each item were highest for smoked packyears (0.93), followed by age of onset (0.84), atopy status (0.80), cough characteristics (0.68) and symptom quality (0.58).

After adjustment for sex in a separate regression analysis, smoked packyears and age of onset showed an increasing likelihood (OR) of being diagnosed COPD with increasing age and packyears (Figs. 1(a) and (b)). Accordingly, early onset of symptoms (age $<20$) and never smoking dramatically increased the likelihood of an asthma diagnosis.

### Questionnaire scores

Based on the results of the regression analysis indicating no discriminant value, symptom quality was deleted from the questionnaire. Using the remaining four items, COPD patients had significantly higher mean questionnaire scores than patients with asthma ($10.5 \pm 0.19$ vs. $4 \pm 0.12$, $P < 0.0001$) as indicated in (Fig. 2). Questionnaire scores also tended to increase with increasing severity of COPD, but this observation did not reach statistical significance ($P > 0.2$, all comparisons). Moreover, scores were not linked to pre-bronchodilator airway obstruction in asthma patients ($\text{rho} = -0.09$, $P = 0.09$). ROC analysis revealed a high discriminative power of the questionnaire (AUC-ROC: 0.954, 87.4% correctly classified) as shown in (Fig. 3) with 87.6% sensitivity and 87.2% specificity for a diagnosis of COPD using a cutoff of 7 points. However, there was a considerable group of patients with scores between 6 and 8, indicating an overlap population with no clear distinction between asthma and COPD. In particular, this group included COPD patients with positive skin tests (44% vs. 9% in "pure" COPD, $P < 0.001$) and increased bronchodilator reversibility, as shown in Fig. 4(a). This group also included predominantly non-allergic asthmatics (10% positive skin tests vs. 98% in "pure" asthma, $P < 0.001$) with heavier smoking as indicated in Fig. 4(b).

**Table 2** Multiple logistic regression analysis and odd ratios (OR) with 95% confidence intervals for a diagnosis of COPD.

| | OR | 95% CI |
|---|---|---|
| Age at onset | 1.13 | 1.1–1.6 |
| Male sex | 2.6 | 1.4–5.1 |
| Current smoking | 19.5 | 8.6–44.2 |
| Atopy | 0.04 | 0.02–0.08 |
| Productive cough | 6.2 | 4–23 |
| Lack of symptom variability | 1.5 | 0.8–2.8 |

## Discussion

The results from our study clearly indicate that by means of a simple questionnaire the majority of patients presenting to a practice with a suspected or established diagnosis of obstructive airway diseases can reliably be labelled as asthmatic or COPD patient. Both asthma and COPD are highly prevalent chronic airway diseases with increasing global burden, and although proper discrimination

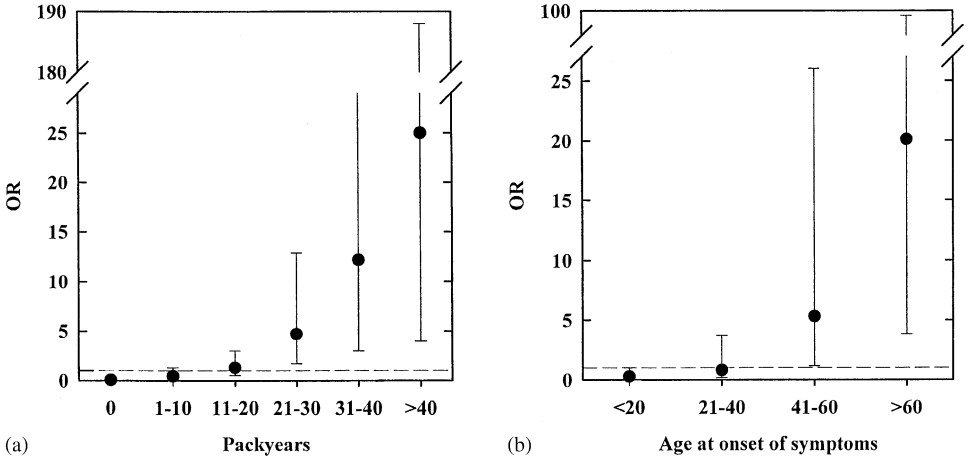


**Figure 1** (a)–(b) ORs and 95% confidence intervals (adjusted for gender) for a diagnosis of COPD with increasing packyears (a), or age at onset of symptoms (b).

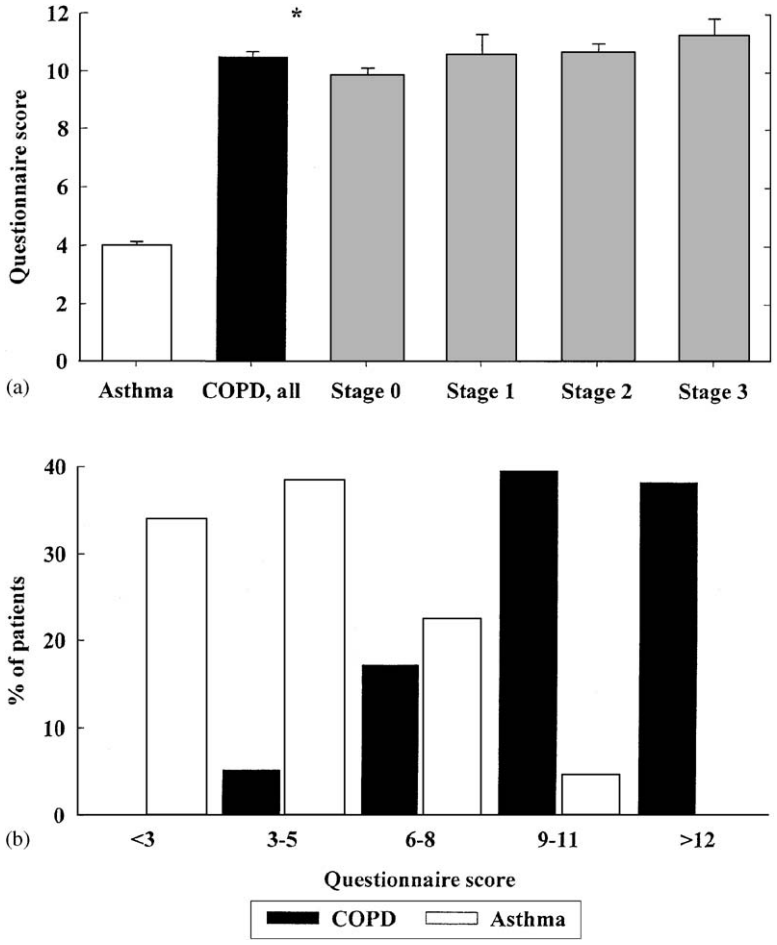


**Figure 2** (a)–(b) Questionnaire mean scores (a) in patients with asthma and COPD, and frequency distribution (b) of score categories. $^{*}P<0.001$ vs. asthmatics.

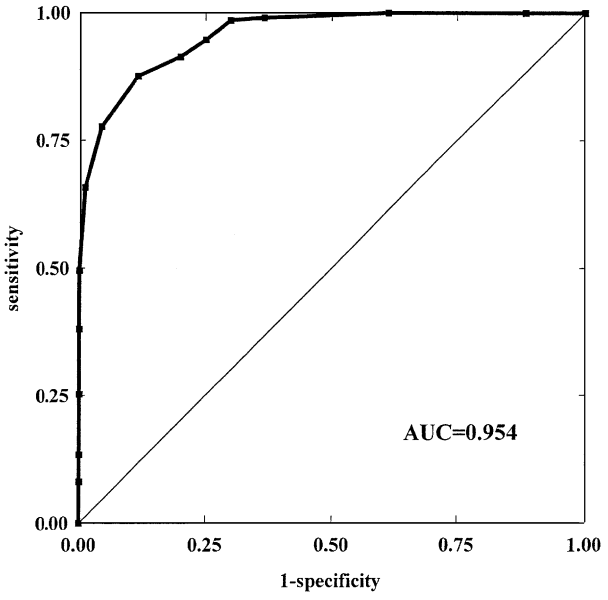


**Figure 3** ROC for questionnaire scores indicating a diagnosis of asthma or COPD. AUC-ROC = 0.954, cutoff >7 points.

is important for the optimal treatment choice, both diseases are often lumped together in everyday practice. The use of such a simple questionnaire may therefore aid practitioners when distinguishing between asthma and COPD.

Clearly, there are several limitations of our study. Firstly, data were analyzed in a retrospective fashion. Secondly, the setting of this study does not fully preclude the possibility of a selectional or referral bias, since it was performed in a pulmonary specialist practice. Hence, the results may not necessarily apply to a GP's practice, thus limiting the generalizability of our findings. However, our approach also offers several advantages for a pilot study. A substantial number of patients was analyzed in a short period of time, and the setting of a pulmonary specialist practice also allowed a reliable diagnosis of asthma and COPD, that was as close as possible to a "gold standard", i.e. the diagnosis was supported by history, spirometry including bronchodilator response and skin test results for nearly all patients under survey.

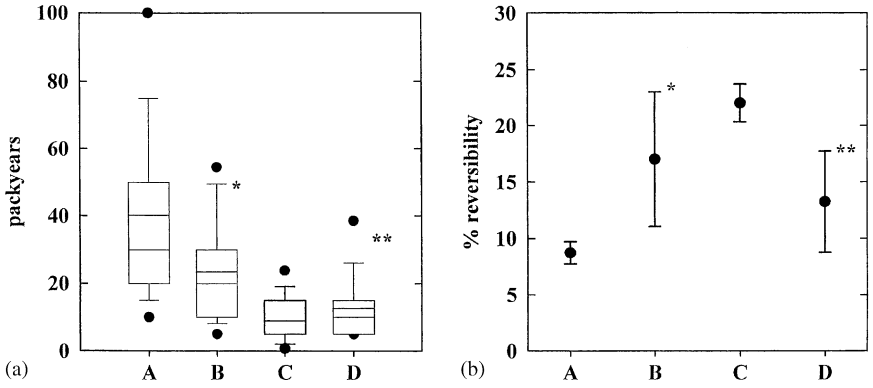


**Figure 4** (a)–(b) Cigarette consumption (packyears) (a), and bronchodilator responses (b) in COPD and asthma. (A) "pure" COPD (score $\geqslant 9$); (B) COPD (score $<9$); (C) "pure" asthma (score $<6$); (D) asthma (score $\geqslant 6$). $^{*}P<0.02$ vs. (A), $^{**}P<0.05$ vs. (C).

Nevertheless, when using the questionnaire, there was no clear distinction between both entities in a considerable amount of patients, and this observation fits well into clinical experience, where asthma and COPD, or at least their clinical and physiological features, may be present in the same patient,[14,15] in particular in asthmatics who smoke.[16] In our population, COPD patients with lower scores had clinical features of asthma, e.g. some degree of atopy, whereas COPD patients with high scores represented those with lowest reversibility and more severe disease.

The degree of overlap between asthma and COPD in our population was about 20% of all patients. This finding concurs with recent data from the general practice research database and the NHANES III trial in the US,[8] where between 17% and 19.1% of patients had overlapping features. These authors further distinguished between chronic bronchitis and emphysema. However, a diagnosis of emphysema was based solely on the fact, that a patient had "ever been told to have emphysema by his doctor". Given the fact, that the medical term "emphysema" is an anatomical diagnosis that should be ideally confirmed by imaging techniques, e.g. high-resolution CT, we decided rather to use COPD as an umbrella diagnosis for chronic bronchitis and/or emphysema, as proposed by GOLD guidelines. Diffusion capacity has also been proposed as a marker for emphysema, but this procedure was not performed in the majority of our patients (in particular in asthmatics), hence we abstained from further including emphysema as a separate entity. Despite these problems, it is apparent that the distinction of asthma and COPD is not an artificial one for the majority of patients.

Further, it is clear that our analysis only focussed on patients with an established diagnosis of obstructive airway disease. We did not evaluate patients presenting with respiratory symptoms attributable to other respiratory or non-respiratory diseases, e.g. pulmonary fibrosis or cardiac failure. Obviously, it was not intended to use the presented questionnaire as a diagnostic instrument (e.g. for case detection or screening). In contrast, the questionnaire was merely designed to eliviate the differentiation of asthma and COPD, once a chronic obstructive airway disease has been diagnosed.

Finally, the selection of clinical parameters to develop a questionnaire was primarily an arbitrary one grounded on availability, the author's experience and published typical features.[1,17–19] It remains to be determined, whether the addition or substitution of items would improve the discriminative power of our tool. It also remains speculative, whether the addition of reversibility, e.g. assessed by peak flow measurements or spirometry, would further add to diagnostic accuracy. Undoubtedly, spirometry or peak flow measurements are pivotal tools for case detection in general or risk population surveys, as demonstrated previously.[20,21] The combination of spirometry or peak flow with bronchodilator reversibility testing also serves as a guidance to distinguish asthmatics from COPD patients by means of an objective physiological response. However, bronchodilator reversibility is not a categorical variable, and may vary considerably intraindividually when measured at different timepoints.[22] Further, there is a wide distribution of bronchodilator responses even in COPD,[23] and many asthma patients as well as stage 0 COPD patients share the finding of normal spirometry, thus the true diagnostic value of adding reversibility tests remains to be assessed prospectively. Finally, one of our primary aims in this pilot study was simplicity, offering the physician a support in decision making, that is easy to handle and non-time consuming. Thus, in light of the

already high discriminative power of our questionnaire and a given amount of ''true'' overlap, we believe that there is only limited room for improvement by adding spirometry results. Spirometry, however, should nevertheless be always mandatory to support the initial diagnosis of an obstructive airway disease and guide therapy.

In conclusion, the results of our pilot analysis clearly indicate, that a reasonable distinction between asthma and COPD in everyday practice can be done for the majority of patients with obstructive airway diseases, even without taking into account results from spirometry or reversibility testing. Questionnaire-based tools are of valuable assistance and can be easily and readily performed. These initial observations warrant confirmation in prospective trials.

## Conflict of interest

The corresponding author has conducted clinical trials or received grants from AstraZeneca, Altana, Boehringer Ingelheim, GlaxoSmithKline, Merck Sharp&Dohme, Novartis, Pfizer, Schering-Plough, Texas Biotechnologies, Yamanouchi. The corresponding author does not hold shares of any of these companies.

## References


1. Pauwels RA, Buist AS, Calverley PMA, 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**:1256–76.
2. GINA: Global initiative for asthma. *Global strategy for asthma management and prevention*. NIH Publication 2002, No. 02-3659. p. 1–176.
3. Jans MP, Schellevis FG, van Hensbergen W, et al. Management of asthma and COPD patients: feasibility of the application of guidelines in general practice. *Int J Qual Health Care* 1998;**10**(1):27–34.
4. McIvor RA, Tashkin DP. Underdiagnosis of chronic obstructive pulmonary disease: a rationale for spirometry as a screening tool. *Can Respir J* 2001;**8**(3):153–8.
5. Petty TL. Scope of the COPD problem in North America: early studies of prevalence and NHANES III data: basis for early identification and intervention. *Chest* 2000;**117**: 326S–31S.
6. Ryu JH, Scanlon PD. Obstructive lung diseases: COPD, asthma, and many imitators. *Mayo Clin Proc* 2001; **76**(11):1144–53.
7. Voelkel NF. Raising awareness of COPD in primary care. *Chest* 2000;**117**:372S–5S.
8. Soriano JB, Davis KJ, Coleman B, et al. The proportional Venn diagram of obstructive lung disease. *Chest* 2003; **124**:474–81.
9. Kornmann O, Beeh KM, Beier J, et al. Newly diagnosed chronic obstructive pulmonary disease: clinical features and distribution of the novel GOLD stages. *Respiration* 2003; **70**:67–75.
10. American Thoracic Society. Standardization of Spirometry-1987 Update. *Am Rev Respir Dis* 1987;**136**:1285–98.
11. Terr AI. Skin Prick Testing. In: Stites DP, Terr AI, editors. *Basic and clinical immunology*. East Norwalk, Connecticut: Appleton and Lange; 1991. p. 375.
12. GINA. Global strategy for asthma management and prevention. *NHLBI/WHO Workshop Report*. 1995.
13. Toelle BG, Peat JK, Salome CM, et al. Toward a definition of asthma for epidemiology. *Am Rev Respir Dis* 1992;**146**: 633–7.
14. Sluiter HJ, Koeter GH, de Monchy JG, et al. The dutch hypothesis (chronic non-specific lung disease) revisited. *Eur Respir J* 1991;**4**:479–89.
15. Buist AS. Similarities and differences between asthma and chronic obstructive pulmonary disease: treatment and early outcomes. *Eur Respir J* 2003;**21**:30s–5s.
16. Lange P, Parner J, Vestbo J, et al. A 15-year follow-up study of ventilatory function in adults with asthma. *N Engl J Med* 1998;**339**:1194–200.
17. Chen JC, Mannino DM. Worldwide epidemiology of chronic obstructive pulmonary disease. *Curr Opin Pulm Med* 1999; **5**:93–9.
18. Ferguson GT, Cherniack RM. Management of chronic obstructive pulmonary disease. *N Engl J Med* 1993;**328**: 1017–22.
19. Senior RM, Anthonisen NR. Chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998;**157**:S139–47.
20. Jackson H, Hubbard R. Detecting chronic obstructive pulmonary disease using peak flow rate: cross sectional survey. *BMJ* 2003;**327**:653–4.
21. 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**:1370.
22. Calverley PMA, Burge PS, Spencer S, et al. Bronchodilator reversibility testing in chronic obstructive pulmonary disease. *Thorax* 2003;**58**:659–64.
23. Anthonisen NR, Wright EC. Bronchodilator response in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1986;**133**:814–9.