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. 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. Moreover, informing patients with asthma or COPD about their diagnosis helps those who still smoke to quit.

Complaints of cough are currently often diagnosed as ‘acute bronchitis’ and subsequently treated with antibiotics, although trials have failed to show a beneficial effect of this treatment. Awareness of a possible diagnosis of COPD or
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.10,13 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 FEV\textsubscript{1}/FVC ratio physiologically decreases with age, COPD was not diagnosed in every participant with an FEV\textsubscript{1}/FVC ratio below 70%. For the same reason, diagnosis of COPD was accepted without this index being below 70% in young people.\textsuperscript{14} 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 FEV\textsubscript{1}/FVC ratio of 0.71 and an FEV\textsubscript{1} 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.\textsuperscript{10-12}

For a diagnosis of asthma, recurrent episodes of wheezing, cough, or dyspnoea were obligatory, as well as an increase of FEV\textsubscript{1} after bronchodilation of more than 200 ml, or more than 12% of the baseline FEV\textsubscript{1}.\textsuperscript{5} Allergy for pollen or house dust mite and eczema were supportive for asthma. Both asthma and COPD could be diagnosed when FEV\textsubscript{1} increased with more than 12% or 200 ml and the post-bronchodilator FEV\textsubscript{1}/FVC ratio was below 70%, combined with complaints suggestive of both disorders, according to the Dutch guidelines for GPs.\textsuperscript{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 $\kappa$ was calculated.\textsuperscript{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.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total, n = 353</th>
<th>COPD, n = 102\textsuperscript{a}</th>
<th>Asthma, n = 23</th>
<th>No COPD or asthma, n = 228</th>
</tr>
</thead>
<tbody>
<tr>
<td>History and physical examination (day 1)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Age in years, mean (SD)</td>
<td>63 (9)</td>
<td>65 (10)</td>
<td>61 (8)</td>
<td>62 (8)</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>45</td>
<td>61</td>
<td>44</td>
<td>38</td>
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<tr>
<td>Current smoking, %</td>
<td>26</td>
<td>50</td>
<td>22</td>
<td>16</td>
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<tr>
<td>Cardiovascular disease, %</td>
<td>19</td>
<td>34</td>
<td>9</td>
<td>14</td>
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<tr>
<td>Allergy for pollen or house dust mite, %</td>
<td>13</td>
<td>8</td>
<td>35</td>
<td>13</td>
</tr>
<tr>
<td>Duration of cough in days, mean (median, SD)</td>
<td>93 (40, 169)</td>
<td>84 (30, 181)</td>
<td>178 (90, 230)</td>
<td>88 (40, 154)</td>
</tr>
<tr>
<td>Previous GP consultation for cough, %</td>
<td>43</td>
<td>30</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>Complaints of phlegm, %</td>
<td>75</td>
<td>83</td>
<td>91</td>
<td>70</td>
</tr>
<tr>
<td>Complaints of wheezing, %</td>
<td>47</td>
<td>62</td>
<td>39</td>
<td>42</td>
</tr>
<tr>
<td>MRC dyspnoea score, mean (SD)</td>
<td>3 (1.4)</td>
<td>3.1 (1.4)</td>
<td>2.9 (1.1)</td>
<td>3.0 (1.5)</td>
</tr>
<tr>
<td>Asthma in first-degree family member, %</td>
<td>24</td>
<td>22</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>COPD in first-degree family member, %</td>
<td>39</td>
<td>46</td>
<td>48</td>
<td>34</td>
</tr>
<tr>
<td>Body mass index (kg/m\textsuperscript{2}), mean (SD)</td>
<td>28 (5)</td>
<td>27 (5)</td>
<td>29 (5)</td>
<td>29 (5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Spirometry results\textsuperscript{d} day 90</th>
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<tbody>
<tr>
<td>FEV\textsubscript{1} in litres, mean (SD)</td>
</tr>
<tr>
<td>FEV\textsubscript{1} % predicted, mean (SD)</td>
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<tr>
<td>FEV\textsubscript{1} % after bronchodilation, mean (SD)</td>
</tr>
<tr>
<td>FVC in litres, mean (SD)</td>
</tr>
<tr>
<td>FVC % predicted, mean (SD)</td>
</tr>
<tr>
<td>FEV\textsubscript{1}/FVC mean (SD)</td>
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</table>

\textsuperscript{14} of the 102 patients with COPD also had asthma, not included in the n = 23 patients with asthma. \textsuperscript{a}Physician diagnosed. \textsuperscript{b}Medical 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’. \textsuperscript{d}Post-bronchodilator results. FEV\textsubscript{1} = forced expiratory volume in 1 second. FVC = forced vital capacity.
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. Therefore, 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.

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

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

*Pack-years = (number of cigarettes smoked per day/20) × number of years smoking.*
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.\textsuperscript{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.\textsuperscript{1,6}

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.\textsuperscript{3,5} 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.\textsuperscript{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. With regard to the severity of COPD, other authors also found (although in different study populations) that undetected COPD was mainly mild or moderate.\textsuperscript{4,9,6}

Regarding asthma, it has been reported that its development is not rare at higher age and that underdiagnosis is substantial in older people.\textsuperscript{7,14}

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**

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**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.

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**REFERENCES**


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