REVIEW

Improving the Differential Diagnosis of Chronic Obstructive Pulmonary Disease in Primary Care

David B. Price, MBBChir, MA, FRCGP; Barbara P. Yawn, MD, MSPH, MSc; and Rupert C. M. Jones, MBBS, MD

Chronic obstructive pulmonary disease (COPD) and asthma represent a substantial portion of primary care practice. In adults, differentiating asthma from COPD can be difficult but is important because of the marked differences in treatment, disease progression, and outcomes between the 2 conditions. Currently, clinical COPD is often misdiagnosed or undiagnosed until late in the disease. Earlier diagnosis could markedly reduce morbidity and improve quality of life. Establishing a diagnosis of COPD requires spirometry testing, interpreted in the context of the patient's symptoms, smoking status, age, and comorbidities. Additional tests and tools may be helpful in the differential diagnosis, including questionnaires specifically developed to discriminate between COPD and asthma and, in special cases, imaging studies. Follow-up and monitoring of asthma and COPD are always necessary and provide additional benefit in patients in whom only continued care and reassessment can confirm the final diagnosis, such as younger individuals with fixed airway obstruction, smokers with asthma, and patients with both disorders. Key areas for improvement include enhanced case identification, improved quality and interpretation of findings on spirometry, and increased use of tools such as differential diagnosis questionnaires and algorithms to guide the diagnostic and monitoring process. To achieve optimal outcomes, the primary care team should make every effort to establish a firm diagnosis. For this review, we conducted a PubMed search with no time limits using the Medical Subject Headings *chronic obstructive pulmonary disease or COPD* and *asthma*, in association with the following search terms: *diagnosis*, *differential diagnosis*, *mixed or comorbid disease*, *diagnostic techniques*, *spirometry*, *questionnaires*, and *primary care*.

Mayo Clin Proc. 2010;85(12):1122-1129

COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in the first second of expiration; FVC = forced vital capacity; ICS = inhaled corticosteroid

Asthma and chronic obstructive pulmonary disease (COPD) are the most frequent causes of respiratory illness worldwide.[1,2] About 9% of the population in North America and Western Europe have clinical asthma,[3] and 7.7% of adults have COPD.[4] Although prevalence and mortality rates for asthma have reached a plateau or declined in recent years,[5] COPD is currently the fourth leading cause of death in the United States and, globally, is projected to be the third leading cause of death and fifth leading cause of disability by 2030.[6,7] Since 2000, more US women than US men have died each year of COPD.[6] This represents an important and growing burden for primary care, the setting in which most patients with respiratory disease are treated.[8]

Both asthma and COPD have inflammatory characteristics and a reduced rate of pulmonary airflow, but most evidence suggests that they are separate diseases with different etiologies, pathophysiology, and outcomes. Asthma tends to develop earlier in life and is associated with variable but largely reversible airflow limitation and with airway hyperresponsiveness. Airway narrowing is caused by factors including inflammatory mediators, airway edema, and airway remodeling.[9] In contrast, COPD is a progressive disease of declining lung function, developing primarily in adults with a history of smoking and predominantly involving the small airways (obstructive bronchiolitis) and lung parenchyma (emphysema). Typical physiologic changes include gas exchange abnormalities, mucus hypersecretion, and airflow limitation, resulting in air trapping, dynamic hyperinflation, and dyspnea that do not reverse to normal functioning even with treatment.[1,10,11]

Despite some similarities in presentation, distinguishing between COPD and asthma is important because the therapy for and expected progression and outcomes of the 2 conditions are different. Earlier and more accurate diagnosis of both asthma and COPD may prevent substantial morbidity. Up to 80% of COPD cases remain undiagnosed until the disease is advanced and substantial end-organ damage is present,[12-15] unlike other common abnormalities, such as hypertension and hypercholesterolemia, which are identified with regular assessments. Fur-

From the Center of Academic Primary Care, University of Aberdeen, Foresterhill Health Center, Aberdeen, Scotland (D.B.P.); Olmsted Medical Center, Department of Research, Rochester, MN (B.P.Y.); Primary Care, Peninsula Medical School, University of Plymouth, Plymouth, UK (R.C.M.J.).

Dr Price has consultant arrangements with Boehringer Ingelheim, GlaxoSmithKline, Merck, Novartis, and Teva. He or his research team have received grants and support for research in respiratory disease from the following organizations in the past 5 years: UK National Health Service, Aerocrine, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Merck, Novartis, Nycomed, Pfizer, and Teva. He has spoken for Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Merck, Pfizer, and Teva. He has shares in AKL International, which produces phytopharmaceuticals. He is the sole owner of Research in Real-Life. Dr Yawn has received investigator-initiated research grants from Novartis, Boehringer Ingelheim, and GlaxoSmithKline related to studies of screening for chronic obstructive pulmonary disease (COPD). She has been paid to take part in advisory boards related to COPD for Boehringer Ingelheim, GlaxoSmithKline, and Novartis and for asthma by GlaxoSmithKline, Merck, and AstraZeneca. Dr Jones has been paid to take part in advisory boards related to COPD for Boehringer Ingelheim, GlaxoSmithKline, Novartis, Nutricia, Pfizer, and Teva in the past 3 years. He has spoken at scientific/educational meetings financed by Altana, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Merck Sharp & Dohme, Pfizer, Teijin, and Trinity-Chiesi in the past 3 years. He is a consultant for the global emPOWER educational program supported by Pfizer and Boehringer Ingelheim.

Individual reprints of this article are not available. Address correspondence to David B. Price, MBBChir, Center of Academic Primary Care, University of Aberdeen, Foresterhill Health Center, Westburn Road, Aberdeen AB25 2AY, Scotland (david@respiratoryresearch.org).

thermore, respiratory disease misdiagnosis is common; up to 25% of patients older than 40 years who are labeled as having asthma actually have COPD.[16,17] Conversely, many patients in primary care are labeled as having COPD when they in fact have asthma.[18]

The current review focuses on the importance of establishing the correct diagnosis of COPD. It discusses the tools available to primary care physicians to make and confirm an initial diagnosis, highlights confounders of diagnosis and the importance of ongoing monitoring, and identifies areas for improvement.

METHODS

We conducted a literature search with no date limitations for all relevant articles using PubMed, a bibliographic database providing access to citations for biomedical articles from MEDLINE (1950s to present) and life science journals. We used the Medical Subject Headings *chronic obstructive pulmonary disease or COPD* and *asthma*, in association with the following search terms: *diagnosis*, *differential diagnosis*, *mixed or comorbid disease*, *diagnostic techniques*, *spirometry*, *questionnaires*, and *primary care*. Results were limited to clinical studies or reviews in humans. Articles were selected for inclusion on the basis of the relevance of their abstracts.

IMPORTANCE OF DIFFERENTIAL DIAGNOSIS

Differentiation between asthma and COPD is extremely important because treatment strategies differ for the 2 conditions, although smoking cessation is vital irrespective of disease.[10,19] Treatment of asthma includes the use of inhaled corticosteroids (ICSs) in patients with persistent disease[9,20] to suppress eosinophilia-based airway inflammation, leading to symptom control and restoration of pulmonary function.[9,21] However, responsiveness to ICSs is reduced in smokers with asthma, who may have neutrophil-predominant inflammation.[22,23] In contrast, inflammation in COPD is largely unresponsive to ICSs, which are introduced later in the treatment pathway. In COPD, ICSs are deployed in higher doses than for asthma and in patients with more severe COPD and a history of exacerbations.[10,13] Bronchodilators are the cornerstone of therapy for COPD.[10]

An incorrect diagnosis of COPD in an asthmatic patient could lead to denial of appropriate anti-inflammatory and other preventive treatments, which could have serious adverse consequences in terms of asthma burden and risk of future exacerbations. Further, some evidence suggests that long-acting β_2-agonist use in the absence of ICSs could lead to a slight increase in the risk of respiratory death in patients with asthma.[24] Conversely, misdiagnosis of asthma as COPD could lead to inappropriate treatment with ICSs, potentially increasing the risk for pneumonia, undertreatment with long-acting bronchodilators, and denial of access to pulmonary rehabilitation.

Prognoses for patients with the 2 disorders also differ: patients with well-controlled asthma should have normal activity levels and life expectancy,[25] but COPD is usually a progressive disease, meaning that patients' lung function can be expected to worsen over time, even with the best available care, limiting longevity and activity.[10] These issues make it imperative to distinguish between COPD and asthma when possible. The stages of diagnosis for patients presenting in the primary care setting are discussed in the next section. Three case studies highlighting typical presenting symptoms and suggested approaches to diagnosis are summarized in the eAppendix (a link to which is provided in Supporting Online Material at the end of this article).

DIAGNOSING COPD

Initial Diagnosis

A typical patient with COPD is likely to be 35 years or older and have a history of risk factors such as smoking or extended occupational exposures to toxins.[10,26] It is usually unrecognized until patients are in their sixties. Although COPD was once considered a disease of men, a higher prevalence of chronic bronchitis and emphysema has been reported in US women than US men in 2010.[27] Furthermore, women's smaller lung size and differing lung geometry appear to increase their susceptibility to development of COPD.[28] Ethnicity may also be important; in the United States, COPD prevalence is lower in Hispanics than non-Hispanic whites.[27]

Despite experiencing such symptoms as dyspnea, chronic cough, or sputum production for months or years, patients fail to recognize or report them, believing such symptoms to be a normal consequence of smoking, aging, or deconditioning.[29,30] Consequently, an acute exacerbation may be the first time COPD is noted, when the disease may already be advanced. Even with an exacerbation, COPD should be confirmed by spirometry testing, which can be done during the recovery phase but should be repeated 6 to 8 weeks later. Spirometry is the best standardized, most reproducible, and most objective measurement of airflow limitation available.[10] Peak flow meters have limited predictive value and poor specificity for COPD diagnosis.[10]

A single spirometry assessment cannot be counted on to differentiate COPD from all other respiratory conditions. Factors such as the patient's age, smoking status,

TABLE 1. **Clinical Features Differentiating COPD and Asthma**

Feature	COPD	Asthma
Smoker or exsmoker	Nearly all	Possibly
Symptoms before age 35 y	Rare	Often
Chronic productive cough	Common	Uncommon
Breathlessness	Persistent and progressive	Variable
Nighttime waking with breathlessness and/or wheeze	Uncommon	Common
Substantial diurnal or day-to-day variability of symptoms	Uncommon	Common

COPD = chronic obstructive pulmonary disease.
From *Thorax*,[31] with permission.

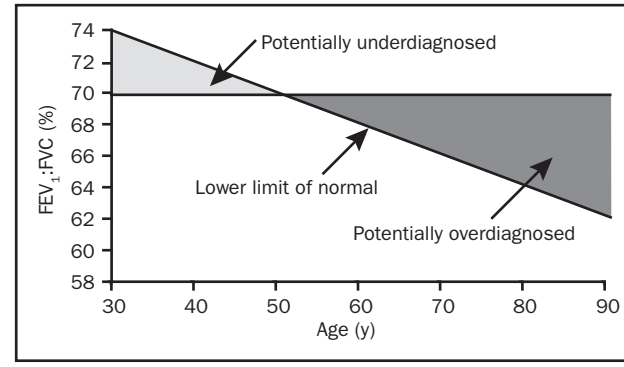

FIGURE 1. The potential for underdiagnosis and overdiagnosis of chronic obstructive pulmonary disease (COPD) with use of a fixed forced expiratory volume in the first second of expiration (FEV_1) to forced vital capacity (FVC) ratio.
From *Thorax*,[50] with permission.

symptoms, other chronic conditions, and family history should be considered when establishing disease severity and distinguishing between asthma and COPD (Table 1).[31] Smoking and age are both strong independent predictors of COPD.[32,33] In screening questionnaires, dyspnea (particularly on exertion) and cough have been found to positively predict airflow obstruction.[32,34,35] Although similar symptoms may be present in asthma and COPD, those associated with COPD are usually persistent and worsen with disease severity, whereas those associated with asthma are variable and may even improve over time with removal of triggers.[8,10] Patients with COPD are also more likely to have other chronic conditions, such as coronary artery disease, lung cancer, cor pulmonale, osteoporosis, and depression,[36] whereas the common coexisting conditions in asthma are more likely to be related to allergy.

Family history is helpful in that a history of 1 or more parents having asthma increases the risk of asthma 2- to 6-fold,[9,37] whereas a family history of obstructive airway disease increases the likelihood of COPD.[38,39]

Standardized guidelines for obtaining and interpreting spirometry data are available.[10,40-42] Chronic obstructive pulmonary disease is defined by the presence of a postbronchodilator ratio of forced expiratory volume in the first second of expiration to forced vital capacity (FEV_1:FVC) of less than 0.70 (70%), which confirms the presence of airflow limitation that is not fully reversible.[10,42] However, several factors should be taken into account to ensure that accurate and interpretable data are obtained from spirometry.

The use of the postbronchodilator measurement is important and supported by guidelines as a better and more consistent predictor of COPD than the prebronchodilator FEV_1:FVC ratio.[10,26,43] Prebronchodilator spirometry has been shown to lead to overdiagnosis of COPD[44-46] by 11% in primary care[18] and by 27% in screening studies.[47]

Some caution is required in the interpretation of spirometry results. Establishing the presence of obstruction with a fixed cut point of 70% for FEV_1:FVC ratio may underestimate airway obstruction in younger patients and overestimate it in older adults.[48,49] The normal fixed ratio can exceed 0.75 (75%) to 0.80 (80%) in healthy young adults but decline to 0.60 (60%) to 0.65 (65%) in healthy older adults (Figure 1).[50] Alternative cut points, such as the "lower limit of normal" (the bottom 5% of the normal population distribution for FEV_1:FVC or FEV_1:slow vital capacity ratio), which takes age, height, sex, and ethnic group into account, appear to better reflect clinically relevant irreversible airflow limitation.[46,49,51]

Unreliable or inaccurate interpretation of spirometry results may complicate diagnosis.[52] Spirometers used in general practice may provide automated readings that should be reassessed. For example, some automated readings report FEV_{25-75} and incorrectly interpret small changes as early COPD. These findings reinforce the importance of putting spirometry results in the context of the patient.

Despite these issues, studies from a number of countries, including the United States, indicate that office-based spirometry performed by trained health care professionals significantly improves diagnosis and management of COPD and asthma in general practice,[17,53-55] reducing the need for referral to a specialist.[56]

Confirming the Diagnosis

Respiratory symptoms and airflow obstruction may be a result of COPD or other chronic lung or cardiovascular conditions, including bronchiectasis, tuberculosis, bronchiolitis, chronic heart failure, or lung cancer as well as cardiovascular disease (Table 2).[10,57,58] Thus, further investigations and careful follow-up of patients are needed to confirm the initial result.[49]

Physical examination is of limited use in definitively diagnosing COPD but may be useful to identify coexisting conditions, markers of alternative pathologic conditions (such as clubbing and lymphadenopathy), and signs

TABLE 2. **Differential Diagnosis of COPD**

Diagnosis	Suggestive features	Recommended investigations to confirm diagnosis
COPD	Onset in midlife; symptoms slowly progressive; long history of exposure to noxious particles, typically tobacco smoking or air pollution; dyspnea during exercise; airflow limitation that is not fully reversible	Spirometry confirms presence of airflow limitation that is not fully reversible
Asthma	Onset early in life (often childhood); variation in symptoms from day to day; symptoms at night or in early morning; other atopic conditions present (eg, allergy, rhinitis, eczema); family history of asthma; largely reversible airflow limitation	Spirometry confirms presence of airflow limitation
Chronic heart failure	Fine basilar crackles on auscultation	Chest radiography shows dilated heart, pulmonary edema; spirometry confirms restrictive rather than obstructive lung disease
Bronchiectasis	Large volume of purulent sputum; commonly associated with bacterial infection; coarse crackles/clubbing on auscultation	Chest radiography or CT shows bronchial dilation, bronchial wall thickening
Tuberculosis	Onset at all ages; high local prevalence of tuberculosis	Chest radiography shows lung infiltrate; microbiological confirmation
Obliterative bronchiolitis	Onset at younger age in nonsmokers; may have history of rheumatoid arthritis or fume exposure	CT on expiration shows hypodense areas
Diffuse panbronchiolitis	Most patients are men and nonsmokers; almost all have chronic sinusitis	Chest radiography and HRCT show diffuse small centrilobular nodular opacities and hyperinflation
Carcinoma of the bronchus	Symptoms may include dyspnea, hemoptysis, coughing, wheezing, pain in chest or abdomen, cachexia, fatigue, and loss of appetite; history of exposure to carcinogens (such as those in tobacco smoke), ionizing radiation, or viral infection	Chest radiography; CT; bronchoscopy
Goiter	Presence of anterior neck mass; may cause breathing difficulties if particularly large; associated with iodine deficiency; may be related to hyperthyroidism or hypothyroidism	Physical examination; thyroid function tests; ultrasonography

COPD = chronic obstructive pulmonary disease; CT = computed tomography; HRCT = high-resolution CT.
Adapted from the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2009,[10] with permission.

indicative of pleural effusion. Only patients with late-stage COPD are likely to demonstrate an increased expiratory time or the barrel chest of hyperinflation and muscle wasting.[8,59,60]

At the time of initial COPD diagnostic evaluation, all patients should undergo chest radiography to exclude other possible pathologic conditions that may coexist with or be mimicking COPD.[26,61] In addition, all patients with newly diagnosed COPD should have testing for α_1-antitrypsin deficiency, an important predisposing genetic cause of pulmonary emphysema.[10,62] Low-cost or no-cost options are available to facilitate this testing in primary care. The place of trials of treatment in diagnosing asthma and COPD in adults is very limited. Oral corticosteroid trials are rarely indicated and are not recommended by guidelines for diagnosing COPD.[10,26,43,63] Because both COPD and asthma can demonstrate an increase in FEV_1 of 12% or more and 200 mL or more after use of an inhaled bronchodilator, trials of bronchodilator monotherapy are generally not helpful. Serial peak expiratory flow measurements may help identify patterns of variability related to exposure to particular substances, which may be useful, particularly when occupational asthma is suspected.[64]

If the diagnosis remains uncertain, referral for more detailed tests should be considered. Computed tomography may be helpful in the differential diagnosis for a small subgroup of specialized cases (eg, for the identification of bronchiectasis or interstitial lung disease and for patients with dyspnea but normal or minor changes in lung function).[65] In such cases, computed tomography can identify emphysema; tests such as diffusing capacity of lung for carbon monoxide may also be indicated.[44,66]

Other potentially useful tests are measurements of airway responsiveness to methacholine, histamine, or exercise challenge; skin testing to establish allergic status; and measurement of inflammatory markers, including total and differential cell count and mediator assays in sputum, blood, urine, and exhaled air.[8,9,20]

Most of these tests are of unproven value in differentiating between COPD and asthma, and in certain patients, an accurate diagnosis may remain problematic. To

address this, questionnaires for use in primary care have been developed by identifying factors significantly related to a diagnosis of COPD.[67,68] Tinkelman et al[68] found that the strongest differential indicators were increasing age and pack-years of smoking, dyspnea that had worsened in recent years, breathing-related hospitalization, phlegm of more than 15 mL/d, and a tendency for "colds to go to the chest." Coughing more in recent years and breathing-related disability suggested a decreased likelihood of COPD vs asthma, but presence of wheezing or productive cough had poor discriminatory value. The final questionnaire demonstrated a sensitivity of 72.0 and a specificity of 82.7 (ability to identify true positives and negatives, respectively), providing good discriminatory evidence of asthma or COPD.

Confounders of Diagnosis

Diagnosis may be particularly problematic in certain patient groups. Fixed airflow limitation in a patient would suggest COPD, but up to 30% of such patients have a history of asthma. These patients tend to be older men with a longer duration of disease and have an increased risk of death from airway disease.[69-71] Conversely, many patients with COPD demonstrate at least some degree of reversibility despite having no clinical features of asthma[72-74] (although these studies included higher doses of short-acting bronchodilators than would be used in normal clinical practice). Further, for both asthma and COPD, reversibility can vary in the same patient between assessments.[9,75]

Distinguishing COPD from asthma is particularly difficult in smokers. A history of smoking suggests COPD but is also a risk factor for nonatopic asthma, which is more common with increasing age.[76] Smokers with asthma have features similar to those found in COPD, including poor response to bronchodilators and oral corticosteroids, reduced sensitivity to ICSs, and accelerated decline in lung function. They may have evidence of mild emphysematous changes and have an inflammatory profile more typical of that seen in COPD than asthma.[77-79] Thus, a smoking history does not always help to discriminate between COPD and asthma, particularly in older patients.

Ultimately, it may not be possible to make an exclusive diagnosis of COPD or asthma because both disorders can coexist in the same patient. Current estimates of patients with both asthma and COPD vary depending on diagnostic criteria, but at least 10% of patients with COPD also could have asthma.[18,80-82] Such patients should be treated as having asthma, but with COPD-expected outcomes.[9,83]

Ongoing Monitoring

Regular reassessment and ongoing monitoring should be undertaken to confirm the initial diagnosis. Hand-held spirometers are user-friendly and may be particularly convenient for medical review in primary care.[15,84] Patients who received their diagnosis after an acute exacerbation should be followed up for 4 to 6 weeks after discharge and their diagnosis kept under review. Such monitoring is also important if any diagnostic uncertainty remains between COPD and asthma or if response to treatment is not as expected, because it helps ensure that patients receive the optimal treatment and enables any necessary adjustments to management to be made.[26,85] In one study, 54% and 14% of patients with an initial diagnosis of asthma or COPD, respectively, had their diagnosis changed after clinical assessment (including a specific smoking history, nighttime and daytime symptoms, respiratory illness and allergy history, medication details, and family history) and spirometry.[86]

Improving Diagnosis in Primary Care

Despite existing tools to support diagnosis, underdiagnosis and misdiagnosis of COPD continue to be a major problem in general practice,[14,87] with differential diagnosis between asthma and COPD being a particular challenge.[15,17] Key areas for improvement include better case identification of patients and improved use of spirometry for diagnosis by trained, evaluated staff using appropriate spirometers.[18,87,88]

International guidelines recommend spirometry to identify airflow obstruction in symptomatic individuals with a history of exposure to risk factors,[10,54,89] but primary care physicians should also be proactive in asking patients about their symptoms.[90] Short questionnaires such as the 5-item patient-completed Lung Function Questionnaire may be useful screening tools to identify patients with a high risk of airflow obstruction.[35] Improving the accuracy of disease registries to allow systematic identification of populations of patients not receiving necessary care would also be valuable.[91]

Use of spirometry in the primary care setting is a major issue. As few as a third of patients with COPD have their diagnosis properly verified with spirometry.[12,92,93] Barriers to spirometry use include lack of time and access to calibrated spirometers, inadequate training and lack of confidence in performing spirometry, lack of quality-control systems to ensure accurate results, and inadequate interpretation skills.[84,87] However, in a recent study in the United States, family physicians who underwent an intensive 2-day training session were able to perform and interpret spirometry results with acceptable levels of technical accuracy and to make appropriate management changes consistent with guidelines.[17]

Confidence in performing spirometry may be increased and standards improved through better involvement of the whole primary care team, including trained practice nurses[94,95]; better access to regional pulmonary function laboratories[96]; availability of visiting teams of trained staff

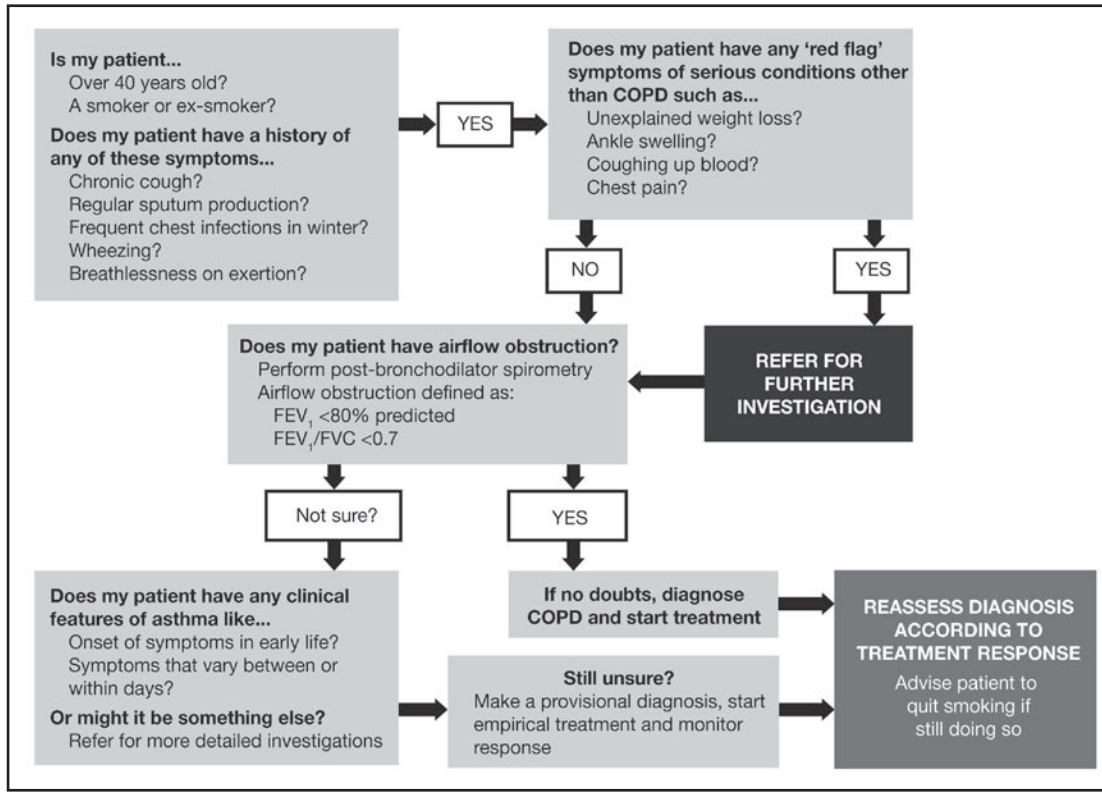

FIGURE 2. An algorithm for the differential diagnosis of chronic obstructive pulmonary disease (COPD).[88] FEV_1 = forced expiratory volume in the first second of expiration; FVC = forced vital capacity.
Adapted from *Pocket Science–COPD*,[99] with permission.

with portable equipment to service the needs of primary care practices[97,98]; and improved cooperation between providers of primary and specialized or hospital-based care.[55] This has been encapsulated by Enright, who stated that what primary care needs is spirometry, not spirometers.[97]

Also desirable would be the wider adoption and more consistent use of management algorithms such as that illustrated in Figure 2[99] and greater use of questionnaires for differential diagnosis[68] or for the identification of specific conditions (eg, bronchial hyperresponsiveness).[100] Some evidence suggests that accurate diagnosis may also be improved by computer-based assessment systems that provide management recommendations on the basis of patient history and characteristics, spirometry results, treatment, and inhaler technique.[18]

Ultimately, the holy grail for differential diagnosis in primary care would be a simple, easy-to-administer test with high specificity and sensitivity, perhaps based on a single biomarker or a genetic profile. The ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points) study[101] is investigating a wide range of end points with the aim of discovering markers that better describe the subtypes of COPD, as well as defining predictive markers of its progression. This study is soon to report and may shed some light on whether there are markers potentially useful for diagnosis.

CONCLUSION

For many years, COPD was deemed to be a disease of fixed airflow obstruction for which no beneficial treatment was available. This led to a largely nihilistic view of COPD among health care professionals, with little incentive to diagnose COPD accurately. However, early detection of airflow limitation and intervention for smoking abstinence can delay lung function decline, reduce the burden of COPD symptoms, and improve patients' quality of life.[19,84,103] Accurate differential diagnosis of asthma and COPD is essential, because these 2 disorders require distinctly different approaches for optimal management. Areas of difficulty remain, particularly in older patients, smokers with asthma, and patients with coexisting COPD and asthma. However, the primary care team must make every effort to establish a firm diagnosis when possible, as well as follow up with ongoing monitoring to assess the benefit of treatment, to achieve the best possible outcomes for patients.

We thank Mary Sayers of ACUMED, who provided medical writing services. This support was funded by Novartis Pharma AG.

REFERENCES

1. Barnes PJ. Against the Dutch hypothesis: asthma and chronic obstructive pulmonary disease are distinct diseases. *Am J Respir Crit Care Med*. 2006;174(3):240-243.

2. Theisen C, Bruckbauer S. Defining global health: who is responsible for the world's burden of disease? *J Natl Cancer Inst*. 2003;95(21):1568-1570.

3. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy*. 2004;59(5):469-478.

4. Halbert RJ, Isonaka S, George D, Iqbal A. Interpreting COPD prevalence estimates*: what is the true burden of disease? *Chest*. 2003;123(5):1684-1692.

5. Moorman JE, Rudd RA, Johnson CA, et al; Centers for Disease Control and Prevention (CDC). National surveillance for asthma–United States, 1980–2004. *MMWR Surveill Summ*. 2007;56(8):1-54.

6. Jemal A, Ward E, Hao Y, Thun M. Trends in the leading causes of death in the United States, 1970–2002. *JAMA*. 2005;294:1255-1259.

7. World Health Organisation. World Health Statistics 2008. http://www.who.int/whosis/whostat/2008/en/index.html. Accessed September 15, 2010.

8. Levy ML, Fletcher M, Price DB, Hausen T, Halbert RJ, Yawn BP. International Primary Care Respiratory Group guidelines: diagnosis of respiratory diseases in primary care. *Prim Care Respir J*. 2006;15(1):20-34.

9. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. Issued January 1995 (NIH Publication No. 02-3659); updated 2009. www.ginasthma.org. Accessed September 15, 2010.

10. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2009. http://www.goldcopd.com. Accessed September 15, 2010.

11. Kraft M. Asthma and chronic obstructive pulmonary disease exhibit common origins in any country! *Am J Respir Crit Care Med*. 2006;174(3):238-240.

12. Arne M, Lisspers K, Ställberg B, et al. How often is diagnosis of COPD confirmed with spirometry? *Respir Med*. 2009;104(4):550-556.

13. Bellamy D, Bouchard J, Henrichsen S, et al. International primary care and respiratory group (IPCRG) guidelines: management of chronic obstructive pulmonary disease (COPD). *Prim Care Respir J*. 2006;15(1):48-57.

14. Joish VN, Brady E, Stockdale W, Brixner DI, Dirani R. Evaluating diagnosis and treatment patterns of COPD in primary care. *Treat Respir Med*. 2006;5(4):283-293.

15. Soriano JB, Zielinski J, Price D. Screening for and early detection of chronic obstructive pulmonary disease. *Lancet*. 2009;374(9691):721-732.

16. Tinkelman DG, Price DB, Nordyke RJ, Halbert RJ. Misdiagnosis of COPD and asthma in primary care patients 40 years of age and over. *J Asthma*. 2006;43(1):75-80.

17. Yawn BP, Enright PL, Lemanske RF Jr, et al. Spirometry can be done in family physicians' offices and alters clinical decisions in management of asthma and COPD. *Chest*. 2007;132(4):1162-1168.

18. Jones RC, Dickson-Spillmann M, Mather MJ, Marks D, Shackell BS. Accuracy of diagnostic registers and management of chronic obstructive pulmonary disease: the Devon primary care audit. *Respir Res*. 2008;9:62.

19. Anthonisen NR, Connett JE, Kiley JP, et al. Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV_1: the Lung Health Study. *JAMA*. 1994;272(19):1497-1505.

20. National Heart, Lung and Blood Institute/National Asthma Education and Prevention Program. (NHLBI/NAEPP 2007). Expert Panel Report 3: guidelines for the diagnosis and management of asthma. NIH Publication No. 07-4051. Bethesda, MD: US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute, 2007.

21. Humbert M. The right tools at the right time. *Chest*. 2006;130(1, suppl):29S-40S.

22. Chalmers GW, Macleod KJ, Little SA, Thomson LJ, McSharry CP, Thomson NC. Influence of cigarette smoking on inhaled corticosteroid treatment in mild asthma. *Thorax*. 2002;57(3):226-230.

23. Kerstjens HA, Overbeek SE, Schouten JP, Brand PL, Postma DS; Dutch CNSLD Study Group. Airways hyperresponsiveness, bronchodilator response, allergy and smoking predict improvement in FEV_1 during long-term inhaled corticosteroid treatment. *Eur Respir J*. 1993;6(6):868-876.

24. Nelson HS, Weiss ST, Bleecker ER, Yancey SW, Dorinsky PM; SMART Study Group. The Salmeterol Multicenter Asthma Research Trial: a comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. *Chest*. 2006;129(1):15-26.

25. McFadden ER Jr. Natural history of chronic asthma and its long-term effects on pulmonary function. *J Allergy Clin Immunol*. 2000;105(2, part 2):S535-S539.

26. National Clinical Guideline Centre. (2010). Chronic obstructive pulmonary disease: management of chronic obstructive pulmonary disease in adults in primary and secondary care. London: National Clinical Guideline Centre. Available at http://guidance.nice.org.uk/CG101/Guidance/pdf/English.

27. American Lung Association. Trends in COPD (Chronic Bronchitis and Emphysema): Morbidity and Mortality. American Lung Association Epidemiology and Statistics Unit, Research and Program Services Division, February 2010.

28. Chapman KR. Chronic obstructive pulmonary disease: are women more susceptible than men? *Clin Chest Med*. 2004;25(2):331-341.

29. Rodin A, Cote C. Primary care of the patient with chronic obstructive pulmonary disease–part 1: frontline prevention and early diagnosis. *Am J Med*. 2008;121(7 suppl):S3-S12.

30. Yawn BP. Differential assessment and management of asthma vs chronic obstructive pulmonary disease. *Medscape J Med*. 2009;11(1):20.

31. National Institute of Clinical Excellence. Chronic obstructive pulmonary disease: national clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. NICE guideline 12. *Thorax*. 2004;59(suppl 1):i1-i232.

32. Martinez FJ, Raczek AE, Seifer FD, et al. Development and initial validation of a self-scored COPD population screener questionnaire (COPD-PS). *COPD*. 2008;5(2):85-95.

33. Price DB, Tinkelman DG, Nordyke RJ, Isonaka S, Halbert RJ. Scoring system and clinical application of COPD diagnostic questionnaires. *Chest*. 2006;129(6):1531-1539.

34. Freeman D, Nordyke RJ, Isonaka S, et al. Questions for COPD diagnostic screening in a primary care setting. *Respir Med*. 2005;99(10):1311-1318.

35. Yawn BP, Mapel DW, Mannino DM, et al; Lung Function Questionnaire Working Group. Development of the Lung Function Questionnaire (LFQ) to identify airflow obstruction. *Int J Chron Obstruct Pulmon Dis*. 2010;5(1):1-10.

36. Soriano JB, Visick GR, Muellerova H, Payvandi N, Hansell AL. Patterns of comorbidities in newly diagnosed COPD and asthma in primary care. *Chest*. 2005;128(4):2099-2107.

37. Dold S, Wjst M, von Mutius E, Reitmeier P, Stiepel E. Genetic risk for asthma, allergic rhinitis, and atopic dermatitis. *Arch Dis Child*. 1992;67(8):1018-1022.

38. Jyrki-Tapani K, Sovijärvi A, Lundbäck B. Chronic obstructive pulmonary disease in Finland: prevalence and risk factors. *COPD*. 2005;2(3):331-339.

39. Silverman EK. Progress in chronic obstructive pulmonary disease: genetics. *Proc Am Thorac Soc*. 2006;3(5):405-408.

40. Levy ML, Quanjer PH, Booker R, Cooper BG, Holmes S, Small IR. 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.

41. Miller MR, Hankinson J, Brusasco V, et al; ATS/ERS Task Force. Standardisation of spirometry. *Eur Respir J*. 2005;26(2):319-338.

42. Miller MR, Crapo R, Hankinson J, et al. General considerations for lung function testing. *Eur Respir J*. 2005;26(1):153-161.

43. Celli BR, MacNee W, Force AET. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*. 2004;23(6):932-946.

44. McCormack MC, Enright PL. Making the diagnosis of asthma. *Respir Care*. 2008;53(5):583-590.

45. Perez-Padilla R, Hallal PC, Vazquez-Garcia JC, et al. Impact of bronchodilator use on the prevalence of COPD in population-based samples. *COPD*. 2007;4(2):113-120.

46. Vollmer WM, Gíslason T, Burney P, et al; BOLD Collaborative. Research Group. Comparison of spirometry criteria for the diagnosis of COPD: results from the BOLD study. *Eur Respir J*. 2009;34(3):588-597.

47. Johannessen A, Omenaas ER, Bakke PS, Gulsvik A. Implications of reversibility testing on prevalence and risk factors for chronic obstructive pulmonary disease: a community study. *Thorax*. 2005;60(10):842-847.

48. Cerveri I, Corsico AG, Accordini S, et al. Underestimation of airflow obstruction among young adults using FEV_1/FVC, 70% as a fixed cut-off: a longitudinal evaluation of clinical and functional outcomes. *Thorax*. 2008;63(12):1040-1045.

49. Schermer TRJ, Smeele IJM, Thoonen BPA, et al. Current clinical guideline definitions of airflow obstruction and COPD overdiagnosis in primary care. *Eur Respir J*. 2008;32(4):945-952.

50. Mannino DM, Buist AS, Vollmer WM. Chronic obstructive pulmonary disease in the older adult: what defines abnormal lung function? *Thorax*. 2007;62(3):237-241.

51. Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. *Eur Respir J*. 2005;26(5):948-968.

52. Liistro G, Vanwelde C, Vincken W, Vandevoorde J, Verleden G, Buffels J. Technical and functional assessment of 10 office spirometers: a multicenter comparative study. *Chest*. 2006;130(3):657-665.

53. Buffels J, Degryse J, Heyrman J, Decramer M. Office spirometry significantly improves early detection of COPD in general practice: the DIDASCO Study. *Chest*. 2004;125(4):1394-1399.

54. Dales RE, Vandemheen KL, Clinch J, Aaron SD. Spirometry in the primary care setting: influence on clinical diagnosis and management of airflow obstruction. *Chest*. 2005;128(4):2443-2447.

55. Lusuardi M, De Benedetto F, Paggiaro P, et al. A randomized controlled trial on office spirometry in asthma and COPD in standard general practice: data from spirometry in asthma and COPD: a comparative evaluation Italian study. *Chest*. 2006;129(4):844-852.

56. Walker PP, Mitchell P, Diamantea F, Warburton CJ, Davies L. Effect of primary-care spirometry on the diagnosis and management of COPD. *Eur Respir J*. 2006;28(5):945-952.

57. Gharib H, Papini E, Valcavi R, et al; AACE/AME Task Force on Thyroid Nodules. American Association of Clinical Endocrinologists and Associazione Medici Endocrinologi Task Force on Thyroid Nodules. Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. *Endocr Pract*. 2006;12(1):63-102.

58. Alberts WM. Diagnosis and management of lung cancer executive summary. ACCP evidence-based clinical practice guidelines. *Chest*. 2007;132(3):1S-19S.

59. Broekhuizen BDL, Sachs APE, Oostvogels R, Hoes AW, Verheij TJM, Moons KGM. The diagnostic value of history and physical examination for COPD in suspected or known cases: a systematic review. *Fam Pract*. 2009;26(4):260-268.

60. Tokuda Y, Miyagi S. Physical diagnosis of chronic obstructive pulmonary disease. *Intern Med*. 2007;46(23):1885-1891.

61. Wallace GMF, Winter JH, Winter JE, Taylor A, Taylor TW, Cameron RC. Chest X-rays in COPD screening: are they worthwhile? *Respir Med*. 2009;103(12):1862-1865.

62. American Thoracic Society; European Respiratory Society. American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency. *Am J Respir Crit Care Med*. 2003;168(7):818-900.

63. Qaseem A, Snow V, Shekelle P, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2007;147(9):633-638.

64. Fishwick D, Barber CM, Bradshaw LM, et al. Standards of care for occupational asthma. *Thorax*. 2008;63(3):240-250.

65. Washko GR. Diagnostic imaging in COPD. *Semin Respir Crit Care Med*. 2010;31(3):276-285.

66. Mishima M. Physiological differences and similarities in asthma and COPD: based on respiratory function testing. *Allergol Int*. 2009;58(3):333-340.

67. Beeh KM, Kornmann O, Beier J, Ksoll M, Buhl R. Clinical application of a simple questionnaire for the differentiation of asthma and chronic obstructive pulmonary disease. *Respir Med*. 2004;98(7):591-597.

68. Tinkelman DG, Price DB, Nordyke RJ, et al. Symptom-based questionnaire for differentiating COPD and asthma. *Respiration*. 2006;73(3):296-305.

69. Bumbacea D, Campbell D, Nguyen L, et al. Parameters associated with persistent airflow obstruction in chronic severe asthma. *Eur Respir J*. 2004;24(1):122-128.

70. Mannino DM, Gagnon RC, Petty TL, Lydick E. Obstructive lung disease and low lung function in adults in the United States: data from the National Health and Nutrition Examination Survey, 1988-1994. *Arch Intern Med*. 2000;160:1683-1689.

71. Fabbri LM, Romagnoli M, Corbetta L, et al. Differences in airway inflammation in patients with fixed airflow obstruction due to asthma or chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2003;167(3):418-424.

72. Dorinsky PM, Reisner C, Ferguson GT, et al. The combination of ipratropium and albuterol optimizes pulmonary function reversibility testing in patients with COPD. *Chest*. 1999;115(4):966-971.

73. Donohue JF. Therapeutic responses in asthma and COPD: bronchodilators. *Chest*. 2004;126(2 suppl):125S-137S.

74. Tashkin DP, Celli B, Decramer M, et al. Bronchodilator responsiveness in patients with COPD. *Eur Respir J*. 2008;31(4):742-750.

75. Calverley PMA, Burge PS, Spencer S, Anderson JA, Jones PW; ISOLDE Study Investigators. Bronchodilator reversibility testing in chronic obstructive pulmonary disease. *Thorax*. 2003;58(8):659-664.

76. Court CS, Cook DG, Strachan DP. Comparative epidemiology of atopic and non-atopic wheeze and diagnosed asthma in a national sample of English adults. *Thorax*. 2002;57(11):951-957.

77. Thomson NC, Chaudhuri R. Asthma in smokers: challenges and opportunities. *Curr Opin Pulm Med*. 2009;15(1):39-45.

78. Boulet LP, Lemiere C, Archambault F, Carrier G, Descary MC, Deschesnes F. Smoking and asthma: clinical and radiologic features, lung function and airway inflammation. *Chest*. 2006;129(3):661-668.

79. Chalmers GW, MacLeod KJ, Thomson L, Little SA, McSharry C, Thomson NC. Smoking and airway inflammation in patients with mild asthma. *Chest*. 2001;120(6):1917-1922.

80. Gibson PG, Simpson JL. The overlap syndrome of asthma and COPD: what are its features and how important is it? *Thorax*. 2009;64(8):728-735.

81. Guerra S. Overlap of asthma and chronic obstructive pulmonary disease. *Curr Opin Pulm Med*. 2005;11(1):7-13.

82. Shaya FT, Dongyi D, Akazawa MO, et al. Burden of concomitant asthma and COPD in a Medicaid population. *Chest*. 2008;134(1):14-19.

83. Crockett T. Asthma and COPD: chalk and cheese? *The New Generalist*. 2003;1(1):19-22.

84. Price D, Crockett A, Arne M, et al. Spirometry in primary care case-identification, diagnosis and management of COPD. *Prim Care Respir J*. 2009;18(3):216-223.

85. Kardos P, Brutsche M, Buhl R, et al. Combination of asthma and COPD: more frequent as considered to be [in German]? *Pneumologie*. 2006;60(6):366-372.

86. Pearson M, Ayres JG, Sarno M, Massey D, Price D. Diagnosis of airway obstruction in primary care in the UK: the CADRE (COPD and Asthma Diagnostic/management REassessment) programme 1997–2001. *Int J Chron Obstruct Pulmon Dis*. 2006;1(4):435-443.

87. Bolton CE, Ionescu AA, Edwards PH, Faulkner TA, Edwards SM, Shale DJ. Attaining a correct diagnosis of COPD in general practice. *Respir Med*. 2005;99(4):493-500.

88. van Weel C. Underdiagnosis of asthma and COPD: is the general practitioner to blame? *Monaldi Arch Chest Dis*. 2002;57(1):65-68.

89. U.S. Preventive Services Task Force. Screening for chronic obstructive pulmonary disease using spirometry: U.S. preventive services task force recommendation statement. *Ann Intern Med*. 2008;148(7):529-534.

90. Mosenifar Z. Differentiating COPD from asthma in clinical practice. *Postgrad Med*. 2009;121(3):105-112.

91. Joo MJ, Au DH, Lee TA. Use of spirometry in the diagnosis of chronic obstructive pulmonary disease and efforts to improve quality of care. *Transl Res*. 2009;154(3):103-110.

92. Caramori G, Bettoncelli G, Tosatto R, et al. Underuse of spirometry by general practitioners for the diagnosis of COPD in Italy. *Monaldi Arch Chest Dis*. 2005;63(1):6-12.

93. Cazzola M, Bettoncelli G, Sessa E, Cricelli C. Primary care of the patient with chronic obstructive pulmonary disease in Italy. *Respir Med*. 2009;103(4):582-588.

94. Bunker J, Hermiz O, Zwar N, et al. Feasibility and efficacy of COPD case finding by practice nurses. *Aust Fam Physician*. 2009;38(10):826-830.

95. Wallace LD, Troy KE. Office-based spirometry for early detection of obstructive lung disease. *J Am Acad Nurse Pract*. 2006;18(9):414-421.

96. Poels PJP, Schermer TRJ, Thoonen BPA, et al. Spirometry expert support in family practice: a cluster-randomised trial. *Prim Care Respir J*. 2009;18(3):189-197.

97. Enright P. Provide GPs with spirometry, not spirometers. *Thorax*. 2008;63(5):387-388.

98. Miller MR. Spirometry in primary care. *Prim Care Respir J*. 2009;18(4):239-240.

99. Jones R. Pocket science–COPD. 2nd rev. ed. Cheltenham, GLOS, UK: JUST Medical Media Ltd; 2010. http://www.justmedicalmedia.com/downloads/PS_COPD_2e_sheet.pdf. Accessed September 16, 2010.

100. Riemersma R, Postma D, Kerstjens H, et al. Development of a questionnaire for the assessment of bronchial hyperresponsiveness. *Prim Care Respir J*. 2009;18(4):287-293.

101. Vestbo J, Anderson W, Coxson HO, et al; ECLIPSE investigators. Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points (ECLIPSE). *Eur Respir J*. 2008;31(4):869-873.

Online Supporting Material

www.mayoclinicproceedings.com/content/85/12/1122/suppl/DC1eAppendix