Strategies for Screening for Chronic Obstructive Pulmonary Disease

Paul L Enright MD and David A Kaminsky MD

Chronic obstructive pulmonary disease is easily detected in its preclinical phase, using office spirometry. Successful smoking cessation prevents further disease progression in most patients. Spirometry measures the ratio of the forced expiratory volume in the first second to the forced vital capacity (FEV_1/FVC), which is the most sensitive and specific test for detecting airflow limitation. Primary care practitioners see the majority of adult smokers, but few primary care practitioners currently have spirometers or regularly order spirometry for their smoker patients. Improvements in spirometry software have made it much easier to obtain good quality spirometry test sessions, thereby reducing the misclassification rate. Respiratory therapists and pulmonary function technologists can help primary care practitioners select good office spirometers for identifying chronic obstructive pulmonary disease and teach staff how to use spirometers correctly. *Key words: spirometry, chronic obstructive pulmonary disease, COPD, screening* [Respir Care 2003;48(12):1194–1201. © 2003 Daedalus Enterprises]

Introduction

Undiagnosed airflow limitation (airway obstruction) is common in the general population and is associated with impaired health and functional status.[1,2] In adults without a diagnosis of asthma the cause of about 90% of airflow limitation is chronic obstructive pulmonary disease (COPD) due to cigarette smoking. COPD is easily detected in its preclinical phase, using office spirometry. Successful

Paul L Enright MD is affiliated with the Department of Medicine, The University of Arizona, Tucson, Arizona. David A Kaminsky is affiliated with the Department of Medicine, University of Vermont, Burlington, Vermont.

Paul L Enright MD presented a version of this report at the 32nd RESPIRATORY CARE Journal Conference, Chronic Obstructive Pulmonary Disease: Translating New Understanding Into Improved Patient Care, held July 11–13, 2003, in Los Cabos, Mexico.

Correspondence: Paul L Enright MD, 4460 East Ina Rd, Tucson, Arizona 85718. E-mail: lungguy@aol.com.

Table 1. Screening vs Case-Finding

Screening	Case-Finding
A "man on the street"	Patient being seen by a physician
May not have symptoms	Has respiratory symptoms
May be a cigarette smoker	Has COPD risk factors
No cost and no reimbursement	Medicare will pay $20 for the test

COPD = chronic obstructive pulmonary disease

smoking cessation (a cost-effective intervention) prevents further disease progression in most patients. Though almost all hospitals have a pulmonary function testing (PFT) laboratory, and almost all allergy and pulmonary specialists have spirometers, less than half of primary care practitioners use spirometry in their practices.[3] The American Association for Respiratory Care supports the National Lung Health Education Program (NLHEP) to promote the appropriate use of spirometry by primary care practitioners for the detection of COPD in adult smokers.[4] However, screening for COPD remains controversial,[5–7] since it has not yet been proven that the staff in primary care offices can attain the same low misclassification rate as can experienced and certified pulmonary function technologists who perform spirometry in PFT laboratories.[8] A recent COPD workshop summary stated that "there are no data to indicate that screening spirometry is effective in directing management decisions or in improving COPD outcomes."[9]

Criteria for Using Screening Tests

There is a big difference between using medical tests for screening versus *case-finding* (Table 1). An example of screening is a respiratory therapist (RT) setting up a booth at a county fair and offering spirometry to anyone who walks by and is interested.[10] An example of case-finding is a family physician performing spirometry during an office visit for a 50-year-old smoker because the patient complains of a chronic morning cough. The physician then discusses the results with the patient and refers him or her to a local smoking-cessation program.

Several well-recognized criteria have been established for medical tests proposed for the early detection of disease:[11,12]

1. The disease would progress and cause substantial morbidity or mortality.

2. Treatment is available that is more effective when used at the early stage, before the development of symptoms, than when used after the symptoms develop.

3. There is a feasible, affordable, safe, and relatively simple testing method that is accurate enough to avoid producing large numbers of false-positive or false-negative results.

4. There is an action plan that minimizes adverse effects.

Case-finding spirometry for COPD among adult smokers fulfills all of those criteria.[4] However, the evidence for two of the criteria remains weak. Though spirometry is accurate (has a low misclassification rate) in the PFT laboratory setting, what little is published[13] suggests that this may not be true in the primary care setting. Also, it has not been conclusively demonstrated that adding spirometry to a smoking-cessation program substantially increases the 12-month smoking-cessation rate.

A Comparison of Tests for Detecting COPD

Several tests other than the spirometrically-measured ratio of forced expiratory volume in the first second to forced vital capacity (FEV_1/FVC) have been advocated for detecting COPD. Airflow limitation also prolongs the forced expiratory time, which can be measured during the physical examination simply by using a stethoscope and timing the expiration. It is likely that the patient has airflow limitation if the forced expiratory time substantially exceeds 6 seconds. However, there is a high misclassification rate.[9]

Peak expiratory flow (PEF) is low in patients who have airflow limitation. Current clinical practice guidelines recommend PEF measurements for asthma management but not for helping to make the diagnosis of asthma.[14] Advantages of the PEF test include that it requires only a simple, safe, hand-held device that typically costs less than $30, and the required exhalation maneuver is less than half a second. On the other hand, PEF is relatively insensitive to mild airflow limitation; PEF is very dependent on patient effort; PEF has about twice as much intersubject and intrasubject variability as FEV_1[15]; and PEF meters are much less accurate than spirometers.[16]

Airway obstruction increases airway resistance, which can be measured using a body plethysmograph or a forced oscillator or interrupter. However, these instruments are much more expensive than spirometers, and the results (airway resistance, specific conductance of the airways, and total respiratory resistance) are much more variable than the FEV_1/FVC, resulting in a higher misclassification rate for airflow limitation.

Chronic airflow limitation also causes hyperinflation (high functional residual capacity, residual volume, and ratio of residual volume to total lung capacity). Hyperinflation can be measured by helium dilution, nitrogen washout, body plethysmography, and lung imaging techniques (chest radiographs and computed tomography scans). The pulmonary function instruments used to measure hyperinflation are expensive, large, and require specialized train-

ing, and are thus impractical for the primary care setting. The presence of hyperinflation can be noted from a simple chest radiograph, by counting ribs and noting an increase in the retrosternal air space. Chest radiographs are relatively inexpensive and widely available but are very insensitive, compared to spirometry, for detecting airflow limitation. Thomas L Petty used to say that "by the time a patient's chest radiograph shows evidence of COPD, his neighbors already know it." Planimetry of posteroanterior and lateral lung fields yields more accurate estimates of lung volumes, and perhaps hyperinflation, but is rarely done outside of research studies. Lung computed tomography scans are more than 10 times as expensive as spirometry tests and expose the patient to risk from radiation. High-resolution computed tomography can accurately measure another aspect of COPD—emphysema—as detected by reduced lung tissue density and inhomogeneity of lung tissue, such as that caused by blebs and bullae,[17] but high-resolution computed tomography is cost-prohibitive for screening purposes and its availability is limited.

COPD causes maldistribution of ventilation, as measured by closing volume, the slope of phase III of the nitrogen washout curve, or aerosol dispersion tests.[18] However, maldistribution of ventilation is poorly associated with airflow limitation, and nitrogen meters are relatively expensive and notoriously difficult to maintain. And the aerosol dispersion test is currently an unproven technology that does not have adequate clinical validation.

COPD also reduces gas transfer and thus lowers diffusing capacity (D_{LCO}) and blood oxygen levels during exercise (oxygen desaturation). D_{LCO} is an excellent test for differentiating COPD from asthma (D_{LCO} is low in moderate-to-severe COPD, whereas D_{LCO} is normal-to-high in asthma). However, D_{LCO} instruments cost $20,000–30,000 and often have problems with accuracy and repeatability, and thus are rarely found in the out-patient setting. In our experience, blood oxygen saturation measured via pulse oximetry during exercise may be more sensitive to gas exchange abnormalities than is a resting D_{LCO} measurement, but oximetry is plagued by false-positive readings due to motion artifact, even with the latest pulse oximeters. Oximetry is also less specific and less sensitive than FEV_1/FVC for detecting airflow limitation.

The mechanism by which smoking and other noxious particles and gases cause COPD is inflammation of the airways and lung parenchyma. Various aspects of airway inflammation can now be measured noninvasively and with little patient effort or risk, via induced sputum (cell counts and cytokine levels) and tests of exhaled gas and vapors. However, collection of induced sputum requires 12 min of breathing ultrasonically nebulized hypertonic saline, followed by 20 min of preparation of the sputum sample and (currently expensive) cytokine analyses in a specialized laboratory. The relationship between the short-term degree of inflammation and the degree of airflow limitation and COPD morbidity and mortality is unknown, making these new tests currently unsuitable for COPD case-finding. These tests remain research tools at present.

The GOLD Standard

An accepted reference standard—a gold standard—must be available to distinguish between true positive and false positive results from a new test. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) report authoritatively states: "COPD is a disease state characterized by airflow limitation that is not fully reversible. . . . Airflow limitation is measured by spirometry, as this is the most widely available, reproducible test of lung function."[19] Airflow limitation (also known as airway obstruction) in adult ever-smokers is defined by the GOLD document as an FEV_1/FVC of $< 70\%$. The severity of COPD is classified (in stages I–IV) according to the patient's percent-of-predicted FEV_1.

Spirometric measurement of FEV_1/FVC (or FEV_1/FEV_6) will probably remain the best test for COPD case-finding for at least the next 5 years, so the remainder of this review will discuss how to minimize the misclassification rate in COPD case-finding among adult patients when using spirometry.

Minimizing Misclassification Is an Important Goal

The accuracy of a test for screening or case-finding is measured in terms of 2 indices: sensitivity and specificity. A test with poor sensitivity will miss cases, producing false negative results, whereas a test with poor specificity will result in healthy persons being told that they have the disease (a false positive result). The sum of the false negative rate and the false positive rate is the overall misclassification rate. Five percent is usually considered an acceptable misclassification rate for most medical tests; thus 1 in 20 patients will get an inaccurate test result. The American Thoracic Society (ATS) recommends using the fifth percentile of the distribution of lung function as the lower limit of the normal range (LLN).[20] This means that from a group of 100 people with healthy lungs, 5 will get a false positive spirometry result. Ideally, however, the LLN threshold should be chosen to produce a false-positive rate and false-negative rate that is acceptable after considering the physical, psychological, social, and economic consequences of both types of errors.

Use of the GOLD recommendation of 70% as the LLN for FEV_1/FVC will increase the misclassification rate when testing for airflow limitation. Instead, the LLN should be age-specific and gender-specific, per 1991 ATS recommendations. All published population-based studies of spirometry show that FEV_1/FVC decreases with age in the

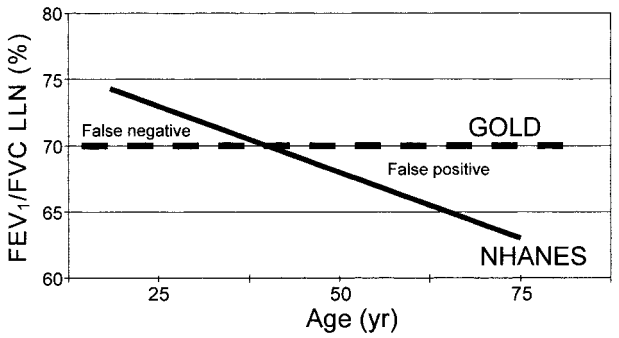

Fig. 1. The lower limit of the normal range (LLN) of the ratio of forced expiratory volume in the first second to forced vital capacity (FEV_1/FVC) normally decreases with age, as shown by the National Health and Nutrition Examination Survey (NHANES III)[21] and other spirometry reference studies of healthy people. The solid, downward sloping line is the LLN for a 6-foot-tall white man, as calculated from the NHANES III reference equations. Values below the solid line indicate airflow limitation. The Global Initiative for Chronic Obstructive Lung Disease (GOLD)[19] states that airflow limitation is indicated whenever FEV_1/FVC is $< 70\%$ in adults of any age, as shown by the dashed horizontal line. The use of such a *fixed* cut-point causes considerable misclassification (false positives and false negatives) for the presence or absence of COPD, especially in older folks.

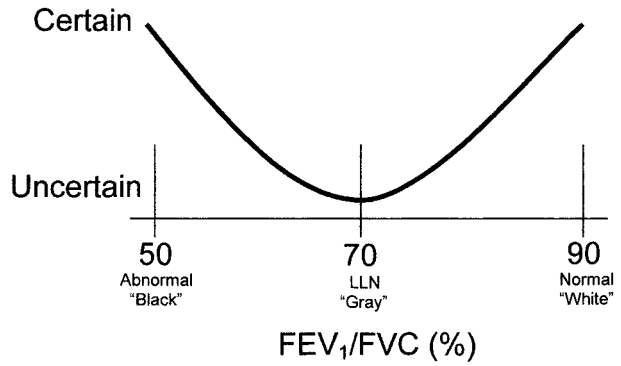

Fig. 2. You should accept uncertainty when spirometry results fall near the lower limit of the normal range (LLN). For example, if a 40-year-old smoker has a ratio of forced expiratory volume in the first second to forced vital capacity (FEV_1/FVC) of around 50%, you can be very certain that she has airflow limitation (airway obstruction and probably chronic obstructive pulmonary disease [COPD]). If her FEV_1/FVC is around 90%, you can be very certain that she has normal airflow and does *not* have COPD. If her FEV_1/FVC is near the LLN of 70% (in the borderline or "gray" area), you should express uncertainty regarding whether she has COPD. Remember that the LLN varies by the age of the individual (see Fig. 1).

Table 2. Factors to Consider During Interpretation of Spirometry Results to Minimize Misclassification

The pre-test probability of disease
The patient's risk factors (eg, age, sex, symptoms)
The quality of the test session (often graded A-F)
The distance from the lower limit of the normal range (percent of predicted)
The consequences of a false-positive interpretation
The consequences of a false-negative interpretation

healthy subset of the population, suggesting that aging alone causes slightly progressive airflow limitation. Whereas 70% is about right for a 50 year-old man, the 5th percentile LLN for a 20-year-old is about 75%, and for an 80-year-old it is 65% (Fig. 1). The use of a fixed 70% threshold causes considerable misclassification when applied to either young adults (among whom the false-negative rate would be high) or elderly adults (among whom the false-positive rate would be high).[22–24] The GOLD committee probably chose 70% for simplicity, as an easy-to-remember "rule of thumb." It does reduce the need for calculations (regression equations, nomograms, or look-up tables) to determine whether a patient has airflow limitation. The 70% LLN perhaps has some merit for third-world countries, where most doctors cannot afford a spirometer with a microprocessor or personal computer.

Accept Uncertainty

Clinicians much prefer to view test results as black-or-white, abnormal or normal, but such a stubborn stance increases the misclassification rate. Results that are near the rather arbitrary threshold (the LLN) should instead be interpreted with uncertainty (Fig. 2 and Table 2). For instance, if the LLN for the FEV_1/FVC is 73% and the patient's FEV_1/FVC is 72%, it should not be stated with confidence that the patient has airflow limitation and COPD. On the other hand, if the patient's FEV_1/FVC is 55% and FEV_1 is 60% of predicted, then even if the quality of the spirometry test was suboptimal, one can state with confidence that the patient has COPD.

Spirometers Need Improvements for Use by Primary Care Practitioners

The 2003 GOLD document correctly emphasized that "maximal patient effort in performing the test is required to avoid errors in diagnosis and management" and that "the supervisor of the test needs training in its effective performance."[9] The NLHEP document goes much further, requiring that office spirometers incorporate software that automatically checks maneuver acceptability and then checks for repeatable FEV_1 and FVC before the test session is considered complete.[4] It also recommends that manufacturers take an active role enabling office staff to learn how to use spirometers by providing easy-to-understand educational materials such as audiovisual instructional aids.

Almost all spirometers now sold in the United States incorporate an internal microprocessor or are connected to

a personal computer. The primary function of the computer is to measure the spirometry results from each maneuver, calculate the percent-of-predicted values, and format a printed report. The software can be enhanced (quality-control software) to help the spirometry technologist obtain better quality test sessions.[13,25] Each maneuver is checked for acceptability and error messages are displayed. As additional maneuvers are performed, the repeatability of the FEV_1 and FVC are determined and a quality grade (A–F) is computed for the test session. The goal is to obtain an A or B grade by performing additional acceptable FVC maneuvers. Such software may not be necessary for experienced technologists working in a hospital-based PFT laboratory: they have considerable experience coaching patients and recognize unacceptable maneuvers from the flow-volume and volume-time graphs.[26] However, the NLHEP group recognized that quality-control software is essential for those who perform spirometry relatively infrequently in a primary care office setting. An NLHEP committee, composed primarily of RTs, will soon test office spirometers and their quality-control software, using a standardized checklist based on NLHEP and ATS recommendations. The results will be posted on the NLHEP web site as a guide for those planning to purchase an office spirometer.

The NLHEP spirometry document makes office spirometry faster and easier by enabling the use of the 6-second forced expiratory volume maneuver (FEV_6), which is slightly smaller than the FVC or the slow VC among healthy subjects, so the NHANES III reference equations must be used.[21] FEV_6 is more reproducible than the traditional FVC. The FEV_1/FEV_6 is just as good as the traditional FEV_1/FVC for diagnosing airflow limitation and for predicting FEV_1 decline in smokers.[27] The use of FEV_6 reduces technologist and patient fatigue and also has less risk of syncope than the prolonged FVC maneuvers, which often last 20–30 seconds before a volume-time plateau is achieved with a COPD or asthma patient.

The Potential Positive Impact of Widespread Spirometry Screening

Does spirometry testing enhance smoking-cessation rate? Studies of lung function testing in the general population have had mixed results, with some showing no effect and others suggesting that knowledge of an abnormal lung function test doubled the likelihood of quitting smoking, even when no other interventions were applied.[28] A 1997 review[29] concluded that spirometry meets all the criteria for a test for the early detection of COPD, except that there is no conclusive evidence that spirometry adds to the efficacy of standard smoking-cessation advice that is based on current clinical practice guidelines.[30] The single randomized controlled trial that addressed this issue included 923 Italian smokers; the researchers found a 1-year quit rate of 6.5% among those who received counseling with spirometry, 5.5% among those with counseling alone, and 4.5% among those who received only brief physician advice.[31] Those rates do not differ significantly; however, only half of the study participants who were asked to visit a laboratory for spirometry testing ever did so, and there was no evidence that the spirometry results were even discussed with those who performed the test; therefore the study probably had inadequate power to show a difference (a type II error). However, even a 1% improvement in smoking-cessation rate, as was found in the Italian study, would result in a very large number of lives saved each year in the United States.

Potential Adverse Effects of Spirometry Screening

As with any other medical test, there are tangible and intangible costs. Adverse effects may occur (1) due to the procedure itself, (2) due to the investigation of abnormal results, or (3) due to the treatment of detected abnormalities or diseases.[11,12] The economic costs of the spirometry test includes the cost of the instrument and the cost of personnel time (both training and testing). Office spirometers currently cost about $1,000 and about $10 for personnel time (including initial training time) and disposable supplies, per test. We estimate that accurate office spirometers will soon cost less than $500. There are no adverse effects from spirometry testing, other than occasional minor discomfort, which lasts for a few minutes.

Investigation and confirmation of abnormal spirometry results cost both time and money and may result in psychological and social harm to a few. Diagnostic spirometry to confirm airflow obstruction costs $20–$60 in a hospital-based PFT laboratory. The estimated travel time, waiting time, and testing time spent by the patient is 1–3 hours. The possible psychological impact of being labeled as "ill," by self and others, following a positive (including false-positive) test could lead to alterations in lifestyle, work, and seeking medical attention.

Another important potential adverse effect is the unmeasured risk of reinforcing the smoking habit in some of the 4 out of 5 adult smokers who are told they have normal spirometry. However, the clinician should counteract this possibility by telling the patient that normal spirometry does not mean that the patient's high risk of dying from a heart attack, lung cancer, or other smoking related diseases are substantially reduced, and, therefore, smoking cessation remains very important.

Finally, the risk of an adverse effect caused by the intervention for COPD—smoking cessation—is very small. The adverse effects of over-the-counter nicotine replacement therapies are minor. Successful smoking cessation tends to lead to an increase in body weight,[32] but the slight

increase in medical risk from minor weight gain is far exceeded by the benefits of quitting smoking, including reduced morbidity and mortality and savings in cigarette and cleaning costs.

The Action Plan

Early intervention following early identification of lung function abnormalities can lead to improved smoking cessation, work-place or home environmental changes, and increased awareness of and attention to cancer, cardiac health, and nonpulmonary health issues associated with abnormal lung function. Early identification of lung function abnormalities in relatively asymptomatic patients may provide "teachable moments" (ie, moments when the patient has increased awareness of medical risks and a more positive response to medical education and intervention). Such moments may increase the success of smoking cessation efforts and enhance opportunities for other preventive therapies to minimize the patient's risk.

Once an abnormality has been detected, an action plan must follow. Even when test quality is good, diagnostic spirometry is highly recommended to confirm the initial abnormal spirometry findings prior to initiating an expensive work-up or interventions with negative economic consequences, such as a recommendation to change jobs. When airway obstruction is identified in a smoker, the primary intervention is smoking cessation, since it is currently the only intervention that has been demonstrated to improve the decline in lung function and thereby reduce the risk of disabling COPD.[33] In asymptomatic smokers with airway obstruction, smoking cessation is the only intervention with proven value. Referral to a subspecialist for further diagnostic testing should be considered in some cases. In the event that a patient with airway obstruction continues to smoke, renewed/increased effort to assist with smoking cessation is essential.[30]

Current Spirometry Screening Programs

The Polish national program for early diagnosis and prevention of COPD started in 2001, in 12 cities. Over 11,000 ever-smokers were tested in pulmonary out-patient clinics,[34] and about one fourth of those had airflow limitation (10% mild, 10% moderate, 5% severe). They all received physician advice to stop smoking. About 9% had the nonspecific pattern of low FVC without airway obstruction. Two thirds of the participants returned for a follow-up visit about 12 months later.[35] Half of those who returned had airflow limitation during the baseline examination. The biochemically verified 12-month smoking-cessation rates showed that those with moderate to severe airflow limitation were twice as likely to have quit as those without airway obstruction (17% vs 8.4% quit rates). The independent predictors of success were a late start of smoking, older age, fewer pack-years, and a lower FEV_1. There was no gender difference in quit rates.

A pilot program of COPD screening was recently completed in the Netherlands.[36] In 2 semi-rural general practice offices, 651 adult current smokers underwent spirometry. By ATS criteria 85% had acceptable test session quality, and of those, 18% had an abnormally low FEV_1. Patients reporting a chronic cough were about twice as likely as the other smokers to have abnormal spirometry, and nearly half of the smokers over the age of 60 had abnormal spirometry. The researchers estimated that in each practice when 1 adult smoker was tested every day, 1 case of COPD was found per week.

In Vermont a state-wide COPD case-finding program began in 2001, funded by the American Lung Association of Vermont. Primary care practitioners were surveyed about their knowledge and use of spirometry. Slightly more than half owned spirometers, could correctly diagnose airflow limitation, and were aware of the NLHEP guidelines. Many did not realize the strong association of FEV_1 with cardiovascular disease. Reasons for not performing spirometry included lack of education, logistic barriers, and concerns about cost and reimbursement (unpublished data). A subset of practices participated in 1-hour workshops designed to provide education about and practical instruction on use of spirometers. Preliminary results suggest that knowledge and use of spirometry have improved in the participant practices. The program highlights the importance of continuing spirometry education.

In 2002 the GlaxoSmithKline Respiratory Institute began planning Project Spirometry, a program designed to get primary care practitioners acquainted with office spirometry. The GlaxoSmithKline Respiratory Institute contracted with AlphaMedica (a medical communications firm) to produce 4 different educational materials, which were completed in July 2003: a booklet for primary care practitioners called "Office Spirometry"; a videotape and DVD (with physician continuing-education credit) called "Practice With the Experts"; a booklet with 12 patient vignettes and spirometry results, each followed by questions and answers; and a booklet and videotape (with available nursing continuing-education credit) called "Measurable Differences in Respiratory Care," which was designed to teach nurses, nurse practitioners, physician assistants, and respiratory technologists how to perform spirometry. GlaxoSmithKline Respiratory Institute representatives have identified over 1,500 primary care practitioners in the United States who are interested in the program. The physician and an office staff person designated to perform spirometry will each complete the continuing-education course, and then a spirometer will be provided to them for a 60-day period. Over 1,500 spirometers were purchased for the program, and the spirometer software has been customized

according to NLHEP guidelines. Project Spirometry will be the largest COPD case-finding program ever attempted.

The Value of Respiratory Therapists Working With Local Primary Care Practitioners

RTs and pulmonary function technologists can add value by facilitating COPD case-finding in their own communities. RTs can advise primary care office staff in the purchase of spirometers and help staff learn how to use them correctly.[37] Primary care practitioners can benefit by taking advantage of the many services RTs can provide for their patients with lung disease, such as pulmonary rehabilitation programs, chronic disease management programs (eg, for COPD, asthma, sleep apnea, cystic fibrosis), smoking-cessation programs, and long-term oxygen therapy services.

Summary

COPD case-finding is worthwhile if (1) a currently smoking adult patient seen in a health care setting has any respiratory symptom, (2) good quality spirometry is done, (3) the result is interpreted correctly, and (4) the patient is referred to an effective local smoking-cessation program.

REFERENCES

1. O'Hagan J. Prevention of chronic obstructive pulmonary disease: a challenge for the health professions. N Z Med J 1996;109(1014):1–2.
2. Coultas DB, Mapel D, Gagnon R, Lydick E. The health impact of undiagnosed airflow obstruction in a national sample of United States adults. Am J Respir Crit Care Med 2001;164(3):372–377.
3. Gentry SE, Hodge RH, Kaiser D, Walker FB 4th, Suratt PM. Pulmonary function testing in a general medical practice. J Community Health 1983;8(4):263–268.
4. Ferguson GT, Enright PL, Buist AS, Higgins MW. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. Respir Care 2000;45(5): 513–530.
5. Stoller JK. Pulmonary function testing as a screening technique. Respir Care 1989;34(7):611–623; discussion 623–625.
6. McIvor RA, Tashkin DP. Underdiagnosis of chronic obstructive pulmonary disease: a rationale for spirometry as a screening tool. Can Respir J 2001;8(3):153–158.
7. den Otter JJ, van Dijk B, van Schayck CP, Molema J, van Weel C. How to avoid underdiagnosed asthma/chronic obstructive pulmonary disease? J Asthma 1998;35(4):381–387.
8. Enright PL, Crapo RO. Controversies in the use of spirometry for early recognition and diagnosis of chronic obstructive pulmonary disease in cigarette smokers. Clin Chest Med 2000;21(4):645–652.
9. Fabbri LM, Hurd SS; GOLD Scientific Committee. Global strategy for the diagnosis, management and prevention of COPD: 2003 update (editorial). Eur Respir J 2003;22(1):1–2.
10. Schoh RJ, Fero LJ, Shapiro H, Aslor JP, Kaelin OJ, Rollins DR, Petty TL. Performance of a new screening spirometer at a community health fair. Respir Care 2002;47(10):1150–1157.
11. Marshall KG. Prevention. How much harm? How much benefit? 1. Influence of reporting methods on perception of benefits. CMAJ 1996;154(10):1493–1499.
12. Marshall KG. Prevention. How much harm? How much benefit? 3. Physical, psychological and social harm. CMAJ 1996;155(2):169–176.
13. Eaton T, Withy S, Garrett JE, Mercer J, Whitlock RM, Rea HH. Spirometry in primary care practice: the importance of quality assurance and the impact of spirometry workshops. Chest 1999;116(2): 416–423.
14. NHLBI National Asthma Education and Prevention Program Expert Panel Report 2: Guidelines for the diagnosis and management of asthma. National Institute of Health. Pub No 97–4051, 1997;12–18. Available at http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm (accessed 9/29/03).
15. Gardner RM, Crapo RO, Jackson BR, Jensen RL. Evaluation of accuracy and reproducibility of peak flowmeters at 1, 400 m. Chest 1992;101(4):948–952.
16. American Thoracic Society. Standardization of spirometry, 1994 update. Am J Respir Crit Care Med 1995;152(3):1107–1136.
17. Stern EJ, Frank MS. CT of the lung in patients with pulmonary emphysema: diagnosis, quantification, and correlation with pathologic and physiologic findings. AJR Am J Roentgenol 1994;162(4): 791–798.
18. Buist AS, Van Fleet DL, Ross BB. A comparison of conventional spirometric tests and the test of closing volume in an emphysema screening center. Am Rev Respir Dis 1973;107(5):735–743.
19. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS; GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med 2001;163(5):1256–1276.
20. American Thoracic Society. Lung function testing: selection of reference values and interpretative strategies. Am Rev Respir Dis 1991; 144(5):1202–1218.
21. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U. S. population Am J Respir Crit Care Med 1999;159(1):179–187.
22. Lebowitz MD, Holberg CJ. Comparisons of spirometric reference values and the proportions of abnormal subjects among male smokers and those symptomatic in a community population. Am Rev Respir Dis 1990;141(6):1491–1496.
23. Hardie JA, Buist AS, Vollmer WM, Ellingsen I, Bakke PS, Morkve O. Risk of over-diagnosis of COPD in asymptomatic elderly never-smokers. Eur Respir J 2002;20(5):1117–1122.
24. Lundback B, Lindberg A, Lindstrom M, Ronmark E, Jonsson AC, Jonsson E, et al; Obstructive Lung Disease in Northern Sweden Studies. Not 15 but 50% of smokers develop COPD?—Report from the Obstructive Lung Disease in Northern Sweden Studies. Respir Med 2003;97(2):115–122.
25. Enright PL, Johnson LR, Connett JE, Voelker H, Buist AS. Spirometry in the Lung Health Study. 1. Methods and quality control. Am Rev Respir Dis 1991;143(6):1215–1223.
26. American Association for Respiratory Care. AARC Clinical Practice Guideline: Spirometry, 1996 update. Respir Care 1996;41(7):629–636.
27. Enright RL, Connett JE, Bailey WC. The FEV_1/FEV_6 predicts lung function decline in adult smokers. Respir Med 2002;96(6):444–449.
28. Risser NL, Belcher DW. Adding spirometry, carbon monoxide, and pulmonary symptom results to smoking cessation counseling: a randomized trial. J Gen Intern Med 1990;5(1):16–22.
29. Badgett RG, Tanaka DJ. Is screening for chronic obstructive pulmonary disease justified? Prev Med 1997;26(4):466–472.

30. The Agency for Health Care Policy and Research Smoking Cessation Clinical Practice Guideline. JAMA 1996;275(10):1270–1280.
31. Segnan N, Ponti A, Battista RN, Senore C, Rosso S, Shapiro SH, Aimar D. A randomized trial of smoking cessation interventions in general practice in Italy. Cancer Causes Control 1991;2(4):239–246.
32. Wise RA, Enright PL, Connett JE, Anthonisen NR, Kanner RE, Lindgren P, et al. Effect of weight gain on pulmonary function after smoking cessation in the Lung Health Study. Am J Respir Crit Care Med 1998 Mar;157(3 Pt 1):866–872.
33. Anthonisen NR, Connett JE, Kiley JP, Altose MD, Bailey WC, Buist AS, 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.
34. Zielinski J, Bednarek M; Know the Age of Your Lung Study Group. Early detection of COPD in a high-risk population using spirometric screening. Chest 2001;119(3):731–736.
35. Gorecka D, Bednarek M, Nowinski A, Puscinska E, Goljan-Geremek A, Zielinski J. Diagnosis of airflow limitation combined with smoking cessation advice increases stop-smoking rate. Chest 2003; 123(6):1916–1923.
36. Van Schayck CP, Loozen JMC, Wagena E, Akkermans RP, Wesseling GJ. Detecting patients at a high risk of developing chronic obstructive pulmonary disease in general practice: cross-sectional case finding study. BMJ 2002;324(7350):1370–1375.
37. Wanger J, Irvin CG. Office spirometry: equipment selection and training of staff in the private practice setting. J Asthma 1997;34(2): 93–104.

Discussion

MacIntyre: Let me ask you a physiology question. David Mannino described a group of COPD patients who don't have obstruction but do have what I heard you call "restriction," and I want to make sure I understand what that really means. Is it *true* restriction, implying some kind of fibrotic or interstitial process? Or is it what I think may be more likely, a small-airway phenomenon causing a small vital capacity? If that were the case, nitrogen washout lung volumes would probably show an enlarged residual volume encroaching on the vital capacity. So what I'm asking is, is this "restriction" you describe just another manifestation of airway obstruction, or is it a *true* restrictive disease?

Enright: We don't know from the NHANES data because they didn't take chest radiographs or measure lung volumes or D_{LCO} [diffusing capacity of the lung for carbon monoxide], so the term "restriction" in our report[1] means a low FVC with a normal FEV_1/FVC. These are not patients with COPD or airways obstruction; these are persons from a sample of the general population who had low FVC.

REFERENCE

1. Mannino DM, Buist AS, Petty TL, Enright PL, Redd SC. Lung function and mortality in the United States: data from the First National Health and Nutrition Examination Survey follow up study. Thorax 2003; 58(5):388–393.

MacIntyre: So do you believe there's really a *restrictive* process? Restriction in the sense there's not just airway disease but some kind of interstitial or parenchymal process that causes a true restriction in the ability to fill the lung?

Enright: The "restriction" category we created from the NHANES spirometry results includes all people who had a low FVC but no airflow limitation, and *all* of the processes that you just mentioned are included in that category. We don't know the breakdown of the causes for their low vital capacity; it may have been due to obesity, heart failure, or interstitial lung disease.

Stoller: I'm troubled, as you are, by the absence of evidence of efficacy for screening as a smoking intervention, and the question is, given what we know, why doesn't it work? Why is screening not an effective motivator, despite the data you've shown, which are weak, though the other studies are actually weaker? Is it the shortcoming of the smoking-cessation intervention? Is there something else that we're missing? It seems it ought to be a motivator, and I'm troubled as to why it isn't.

Enright: Those of us who were investigators in the Lung Health Study believe that it *is* a very strong motivator. These other studies did not do what we did in the Lung Health Study: a physician did not sit down with the spirometry results and say, "You're *not* like your lucky grandfather who smoked 2 packs a day and died of prostate disease at age 95. *You* are susceptible. You have the disease. It will get worse, and we have the best community resource to help you stop smoking, and we'll do it for free, and it's easy."

I believe that all of the published studies failed in that they did not have a physician deliver a strong message explaining the spirometry results and then refer the patient to an effective, community-based smoking-cessation program. I think that's the reason. Resources for smoking cessation are limited, and I believe they ought to be preferentially directed toward high-risk patients. Funding is unlikely to become available to prescribe bupropion for a year and have weekly counseling sessions for *everyone* who should stop smoking.

Make: I appreciate the limitations you outlined about the use of spirometry and other screening tests; they certainly need further study. Your conclusion was a little different from what I expected. You suggested that for case-finding we should evaluate smok-

ers who have any respiratory symptom. Do you think we could take out "any respiratory symptom" and just use "all smokers"?

Enright: Any respiratory symptom doubles the risk of having airflow limitation. Certainly, we could have set the age threshold at 35-years-or-older rather than 45-years-or-older. There's a continuum of risk in smokers, but because we don't yet have the evidence that spirometry has a low false-positive and false-negative rate in the primary care setting, I think that for now we should only recommend it for the highest-risk patients. The NLHEP document is vague regarding the need for a respiratory symptom.

MacIntyre: Barry [Make], would you do spirometry with all smokers, regardless of symptoms? Probably at least two thirds of them will have normal spirometry. What are you going to tell those normal-spirometry people? The only therapeutic thing they can do is stop smoking. But they should stop smoking anyway. These normal-spirometry people scare me because I'm afraid that they're going to get the wrong message—that their lungs are tough enough to allow continued smoking. They're among those that Sam Giordano calls "leather people," and they'll think they can continue their 2 or 3 packs a day because their lungs have been shown to be "healthy" enough to handle it.

Make: That's a good question, Neil. We should remember that cigarette smokers are at risk for a number of diseases in addition to COPD. To a patient who smokes but has normal spirometry, I would say, "We've evaluated you for one smoking-related illness, and fortunately you don't have COPD. However, you are still at risk for heart disease, lung cancer, and other diseases." Informing patients that their spirometry is normal doesn't stop smoking-cessation efforts and continued monitoring for multiple other diseases the patient is at risk for. In addition, spirometry is only one motivator to inform patients of the need to discontinue smoking.

I have a question related to education for health care providers. Are we doing enough education for all health care providers about the role and use of spirometry? NLHEP and other organizations are very interested in educating physicians about spirometry. We have an initiative to develop spirometry education programs for medical students. This year we will develop content, and next year we propose to develop curriculum materials that we will provide free of charge to all medical and osteopathic schools to assist in medical student education about spirometry. No one has previously targeted medical students or thought they are a key population. Hopefully, education during their formative years will translate into routine use of spirometry when they become practicing physicians.

Enright: That's excellent. That's where it needs to start. It's just amazing that during the last 12 months Glaxo (through AlphaMedica, a medical communications firm in New York) has put probably $2 million into similar materials for practicing primary care physicians. This continuing medical education program, a component of "Project Spirometry," recently became available in the United States.

Make: One issue we didn't address is the widespread use of questionnaires to potentially assist in the diagnosis of lung disease. That was a subject of several abstracts at this year's American Thoracic Society meeting, and questionnaires may be a useful screening or case-finding tool that physicians can easily use in their practices. Do you have any sense as to whether non-physiologic measures such as questionnaires are likely to be useful?

Enright: If you have any of the cardinal respiratory symptoms, your COPD risk is doubled as a cigarette smoker. You can also use age and gender to rate the risk and put that into a model. So questionnaires certainly have some place. But I think as soon as a patient sees a physician in a health care setting, it is worthwhile and inexpensive to make an objective measurement of airflow and/or airway obstruction.

Make: That's my bias, too: that questionnaires may be useful when the patient doesn't see the physician. Once the patient sees the physician, they should do the spirometry.

Enright: I agree.

Hansen-Flaschen: I like your idea of recognizing uncertainty in diagnosing COPD within some range of FEV_1/FVC, such as 65 to 75%. That would describe a large, important group of people. When we have an uncertain first-level screening test, we often go to a second-level investigation or confirmatory test. So if we were to rethink the way we do this, and define an uncertain zone, what would be the second-level test for those patients?

Enright: I think the current answer is that they need to go to a pulmonary function lab or pulmonologist or allergist—someone who's experienced with spirometry, to have it confirmed, although that's not practical in most settings, and it's very expensive.

Hansen-Flaschen: But what use is it to confirm the spirometry results? If you have the spirometry re-done in a reference laboratory and they also find borderline spirometry numbers, would you look next to functional residual capacity, residual volume, symptoms, or *what* for second-level confirmation?

Enright: The physician should weigh the consequences of a false-positive versus a false-negative result, and that should push him or her to-

ward the correct action. For instance, our therapies for mild airway obstruction in a cigarette smoker are quite limited right now; I don't think there's currently an indication for Serevent, ipratropium, or tiotropium in that group. There's certainly no evidence that those drugs alter the disease outcome. So I think you have to look at the patients' co-morbidities and the down side of them continuing smoking versus the down side of the cost and likelihood of success in the smoking-cessation program in your community.

Shrake:* One of the deficiencies, I believe, in this whole process is the lack of good local smoking-cessation programs that primary care physicians and pulmonologists can refer smokers to. One of the strategies the American Association for Respiratory Care has looked at is an Internet-based smoking-cessation program that would provide materials that could be tied to the nicotine replacement therapy products, which could be tied to an Internet "chat room" for people to help each other during the cessation process, and then perhaps tie that through the Association's network to some local people who could provide some face-to-face contact. I'd like your thoughts on the appropriateness of that type of program, or challenge the point that there's even a deficiency of programs.

* Kevin L Shrake MSc RRT FAARC, Chief Operating Officer, American Association for Respiratory Care, Dallas, Texas.

Enright: About 5 years ago one of the industry sponsors put together a wonderful professional group called "Professionally Assisted Cessation Therapy" (PACT). An Internet resource would certainly be effective for a certain segment of the population, but not for blue-collar people who don't get on the Internet every night. A toll-free telephone number, for instance, at which a person could enter his zip code and be referred to a local cessation program that follows the World Health Organization guidelines would be very effective but currently does not exist. NLHEP and the American Thoracic Society are working very closely with the American Association for Respiratory Care to encourage respiratory therapists to become resource people for primary care physicians in their community, and this is one of the things they can *definitely* add that we as pulmonologists have failed to do or don't have the time to do.

Hill: Paul, I think your bottom-line conclusion was that screening spirometry is worthwhile, but I'd like to play the devil's advocate. We don't know that spirometry adds anything to smoking cessation, and we don't know that the quality of spirometry done by primary care practitioners is any good; we know that often it *isn't* much good. Thus, the conclusion would be that screening spirometry has not been shown to be worthwhile. Is that fair to say?

Enright: Well, you saw all the caveats. We're working closely with the spirometer manufacturers to get them to improve their software to detect poor spirometry maneuvers and poor test sessions. Poor-quality results should *not* be interpreted by the spirometer as they currently are—they are just tossed out, which increases the number of tests where the patient and the clinician are frustrated by not having a result.

One should realize that there's uncertainty in screening tests, much like in hypertension, hypercholesterolemia, and most other medical conditions with which the health risks are on a continuum. When done inexpensively in a mass marketplace you *should* be uncertain about some results and not worry when your cholesterol bounces 20 points up or down.