Office Spirometry in Primary Care for the Diagnosis and Management of COPD: National Lung Health Education Program Update

Gregg L Ruppel MEd RRT RPFT FAARC, Brian W Carlin MD FAARC, Mary Hart MSc RRT AE-C, and Dennis E Doherty MD

The use of office spirometry was recommended by the National Lung Health Education Program (NLHEP) consensus conference in 1999 for detection and management of COPD. Since that time, spirometry utilization has increased, but its role in the diagnosis of COPD is still evolving. This update reviews the role of spirometry for screening and case finding in COPD as well as for asthma. Spirometry has been used for disease management in patients with airway obstruction, with varying results. The diagnostic criteria for COPD using spirometry have also evolved in the past 17 years, with differences arising between the Global Initiative for Chronic Obstructive Lung Disease and NLHEP recommendations. More sophisticated spirometers as well as new reference equations are widely available. Standardization guidelines from the American Thoracic Society/European Respiratory Society published in 2005 provide a robust framework for performing and interpreting spirometry in the office setting. *Key words: COPD; spirometry; primary care.* [Respir Care 2018;63(2):242–252. © 2018 Daedalus Enterprises]

Introduction

In 1999, a dedicated group of clinicians and researchers met under the auspices of the National Lung Health Edu-

DOI: 10.4187/respcare.05710

cation Program (NLHEP), led by Thomas L Petty MD, to formulate a consensus statement describing office spirometry. This consensus statement was published a year later as the basis for recommending spirometry to identify COPD and to better manage patients who were diagnosed with airway obstruction.¹ The consensus statement was directed at primary care practitioners as the first line of detection in the growing population of those suffering from COPD. Since the consensus statement was published, COPD has advanced to the third leading cause of death in the United States, with >15 million adults reporting a diagnosis of COPD.² Current estimates suggest that 70% of patients diagnosed with COPD have not had diagnostic spirometry.³ Despite the recommendations put forth by NLHEP in the consensus statement, the application of spirometry for detecting and managing COPD in primary care has improved but is still suboptimal. This update proposes to review the use of spirometry in primary care in the context of the original consensus document and to update the recommendations where appropriate.

A literature review was conducted using PubMed for papers published in English between 2000 and 2015, using the primary search term "spirometry," AND each of the

Mr Ruppel is affiliated with the Pulmonary Function Testing Laboratory, St Louis University Hospital, St Louis, Missouri. Dr Carlin is affiliated with Sleep Medicine and Lung Health Consultants, Pittsburgh, Pennsylvania. Ms Hart is affiliated with Baylor Scott & White Health, Dallas, Texas. Dr Doherty is affiliated with the Department of Pulmonary, Critical Care, and Sleep Medicine, Lexington Veterans Affairs Medical Center, Lexington, Kentucky.

Mr Ruppel has disclosed relationships with MGC Diagnostics, Biomedical Systems, ndd Medical, and BioMarin Pharma. Dr Carlin has disclosed relationships with Sunovion, Monaghan, Astra Zeneca, and Nonin. Ms Hart has disclosed relationships with the CHEST foundation, GSK, and Monaghan Medical. Dr Doherty has disclosed relationships with Boehringer Ingelheim and Astra Zeneca.

Correspondence: Brian W Carlin MD FAARC, Sleep Medicine and Lung Health Consultants, PO Box 174, Ingomar, PA 15127. E-mail: bwcmd@yahoo.com.



Fig. 1. Flow chart. NLHEP = National Lung Health Education Program.

following: "primary care"; "COPD, case finding"; "COPD, screening"; "COPD, FEV₁, FEV₆"; "COPD management"; "smoking cessation"; "asthma"; "asthma management"; and "spirometers".

This literature search yielded 2,294 citations (Fig. 1). We (GLR and BWC) reviewed these for studies with direct relevance to the recommendations of the original consensus statement (Table 1). Most of the references from the initial search dealt with spirometry and COPD or asthma diagnosis but were not related to its use in primary care. The primary question used to select references was: Are the original recommendations still appropriate? A secondary criterion was: Have new applications for spirometry in primary care been described? A list of 138 papers (including 6 published following our original search) related to these questions. When one or more papers addressed the same topic and reached similar conclusions, we (GLR, BWC, and DED) selected the most appropriate for the references listed. The authors make up the NLHEP Board of Directors, and this review and the recommendations represent their consensus. This methodology was a simple literature review and did not use any formalized protocol (such as GRADE).

Case Finding and Screening for COPD

Spirometry screening for adults *without* persistent respiratory symptoms has not been shown to be accurate or cost-effective and is not recommended.⁴ A recent review by the United States Preventive Services Task Force reconfirmed that screening asymptomatic persons for COPD has little benefit for improving quality of life, morbidity, or mortality.⁵ The United States Preventive Services Task Force statement does say "[this recommendation] ... does not apply to at-risk persons who present to clinicians with symptoms such as chronic cough, sputum production, dyspnea, or wheezing." Spirometry has been repeatedly identified as the standard for detecting air-flow obstruction as the primary physiological feature of COPD. The National Quality Forum Pulmonary Project (NQF #0577) endorses the use of spirometry to confirm the diagnosis of COPD in those ≥ 40 y of age.⁶ The National Committee for Quality Assurance has deemed the use of spirometry in COPD as a Healthcare Effectiveness Data and Information Set measure for over a decade and a half "... to assess adults 40 years of age or older who have a new diagnosis of COPD or newly active COPD and have received spirometry testing to confirm the diagnosis."7 As such, spirometry is one, but not the only, component of case finding for COPD. Use of questionnaires, peak flow meters (peak expiratory flow; PEF), and diagnostic spirometry have been evaluated in the context of case finding, but it is unclear which approach is optimal. Any effort that targets specific groups (eg, smokers) tends to produce a higher yield of positive findings, but most studies comparing case-finding methods are hampered by different definitions of COPD, lack of randomized trials, and limited evaluation of the impact of case finding on patient care and outcomes.8

Multiple studies have attempted to quantify the prevalence of COPD by employing various case-finding strategies. Although the methodologies are difficult to compare, most studies suggest that COPD prevalence rates between 9 and 25% can be detected with spirometrically determined airway obstruction as the standard.9,10 Most reports have used the Global Initiative for Chronic Obstructive Lung Disease (GOLD)¹¹ criteria of an FEV₁/FVC < 0.70(see "Diagnostic Criteria for Spirometry"). Some of the reported case-finding protocols utilized pre- and postbronchodilator spirometry, whereas many used only prebronchodilator testing. There does not appear to be conclusive evidence that post-bronchodilator measurements are superior for detecting COPD,12 although they are required to discriminate between asthma and COPD. This is probably the result of significant overlap between asthma and COPD.13 Targeting of current or former smokers is almost universal in case-finding studies, with greater numbers of smokers being confirmed with COPD. Few studies have included non-smokers, although a significant proportion of COPD can be attributed to other causes. One small study of non-smokers meeting post-bronchodilator criteria for COPD found asthma to be almost universal.14 A common finding in all of the case-finding analyses is that COPD is underdiagnosed,¹⁵ and in some cases patients labeled with COPD do not meet the criteria for airway obstruction when spirometry is performed.6 Similarly, overdiagnosis of COPD, frequently resulting in unnecessary treatment, also results when spirometry is not performed.16

Case finding in primary care is often limited to symptoms consistent with COPD (dyspnea, cough, wheezing). Patients often do not self-report symptoms, such as dyspnea, until their COPD has advanced. They may modify

 Table 1.
 Recommendations of the Original National Lung Health Education Program Consensus Statement and Updated Recommendations, in Boldface Type

1. Office spirometry is recommended for early detection and management of COPD.

Spirometry for screening and case finding should be available in primary care settings and be used for patients at risk for COPD or asthma. Spirometry is recommended in patients \geq 40 y of age who are current or former smokers and have one or more of the following signs/symptoms: chronic cough, excess sputum production, wheezing, or dyspnea out of proportion to age or activity performed. Use of validated questionnaires alone or in conjunction with PEF can be used to decide which patients need diagnostic spirometry.

2. Spirometry enhances smoking cessation.

Spirometry (with or without lung age) as an adjunct to smoking cessation may be of limited value. All patients should be advised and assisted to stop smoking.

3. Office spirometry is simple and affordable.

Spirometry in primary care used in conjunction with PEF is cost-effective.

- 4. Office spirometry is indicated for those with respiratory symptoms, for health assessments (better than peak flow), or for tracking changes in lung function.
 - Pre- and post-bronchodilator spirometry should be used in primary care to identify patients with COPD and to guide therapy following published guidelines. High-quality spirometry and accurate interpretation of results are necessary components for diagnosis and management of COPD. Spirometry pre- and post-bronchodilator is essential for confirming a diagnosis of asthma and categorizing severity. Whether spirometry results are useful for ongoing management of patients who have asthma is unclear, and further research is needed.
- 5. Office spirometers should report FEV₁, FEV₆, and FEV₁/FEV₆ using NHANES III predicted values.

Either NHANES III or GLI-2012 reference equations may be used for spirometry.

6. Airway obstruction should be interpreted using lower limits of normal for FEV₁ and FEV₁/FEV₆.

Spirometry should be interpreted using the lower limit of normal (defined as the lowest fifth percentile of healthy non-smokers) for both the FEV_1/FVC and for the FEV_1 (as well as for the FEV_1/FEV_6 and FEV_6 , if used). The use of the 0.70 fixed ratio is not recommended. Postbronchodilator spirometry should be performed if a patient meets the criteria for airway obstruction pre-bronchodilator OR if the patient presents with signs/symptoms suggestive of asthma. The goal of pre- and post-bronchodilator testing is to identify asthma vs COPD or an overlap between the two. A single negative response to bronchodilators (suggesting a COPD diagnosis) does not preclude a trial of bronchodilators if clinically indicated.

- 7. Office spirometers should display quality of spirometric efforts, be sold with easy-to-understand instructions, and be easy to calibrate. Personnel performing spirometry in the primary care setting should receive formal training (hands-on) that includes set-up and operation of the spirometer, knowledge and application of standards for acceptable and repeatable maneuvers, and the ability to identify obstructive and restrictive disease patterns. Ongoing feedback regarding the quality of spirometry is recommended. Physicians and others interpreting spirometry results should be able to grade the quality of each test, ensure that appropriate reference values are selected, and identify obstruction and restrictive ventilatory patterns. Interpreters should be able to identify bronchial responsiveness from post-bronchodilator testing.
- 8. Recommended further research includes sensitivity and specificity of office spirometry as well as overall impact on patient care, quality of life, and cost-benefit for pulmonary disease management.

(No additional recommendation).

Adapted from Reference 1. PEF = peak expiratory flow

their lifestyle and avoid performing activities that cause shortness of breath. They may not complain of dyspnea because their activities of daily living are at a low level. A detailed history is needed to be certain that they are truly asymptomatic and are not avoiding activities they used to perform because dyspnea causes them to be uncomfortable. Formal questionnaires designed to improve the efficiency and accuracy of a COPD diagnosis have been shown to perform well when used to select patients for diagnostic spirometry.¹⁷ The COPD Diagnostic Questionnaire,¹⁸ the Lung Function Questionnaire,19 and the COPD Assessment Test²⁰ are 3 examples in which specific cut points (based on questionnaire score) identified patients whose subsequent spirometry confirmed a diagnosis of COPD. Some patients have symptoms that result in questionnaire scores consistent with COPD, although their spirometry values are above the usual thresholds for airway obstruction.²¹

Combining questionnaires and PEF measurements to select patients for diagnostic spirometry has been demonstrated to be an efficient and cost-effective approach for COPD case finding.²² In the Burden of Obstructive Lung Disease (BOLD) study, use of PEF reduced the number of subjects at risk as determined by questionnaire alone, and PEF was highly sensitive in detecting subjects with severe COPD.²³ Both the BOLD and TargetCOPD²⁴ studies demonstrated that spirometry in primary care is cost-effective. Other investigations have found similar results using a combination of questionnaires and PEF measurements.²⁵

Screening for COPD has taken on an additional role in the last 5 y. Lung cancer screening with annual chest computed tomography is recommended for current and former smokers with a \geq 30-pack-year smoking history.²⁶ Patients with COPD are at increased risk of developing lung cancer, and identifying those patients with airway obstruction has the potential to improve detection and reduce overdiagnosis in lung cancer screening.²⁷ Zurawska et al²⁸ have proposed using a low FEV₁ combined with computed tomography-determined emphysema as a reasonable filter for targeting those individuals most likely to benefit from annual screening.

Recommendations

Spirometry for screening and case finding should be available in primary care settings and be used for patients at risk for COPD or asthma. Spirometry is recommended in patients \geq 40 y of age who are current or former smokers and have one or more of the following signs/symptoms: chronic cough, excess sputum production, wheezing, and dyspnea out of proportion to age or activity performed. Use of validated questionnaires alone or in conjunction with PEF can be used to decide which patients need diagnostic spirometry. Spirometry in primary care used in conjunction with PEF is cost-effective.

Spirometry and Disease Management

There is a significant overlap between the use of spirometry for detecting COPD and its utility in helping primary care practitioners make informed decisions regarding patient management. Yawn et al²⁹ found that primary care practitioners were able to perform spirometry that met American Thoracic Society/European Respiratory Society (ATS/ERS) acceptability and repeatability recommendations in 71% of subjects, with appropriate changes in treatment in almost half of the cases. Mapel et al³⁰ report that disease severity was underestimated in about 40% of subjects before spirometry and that treatment changes occurred in 37% of cases when the primary care practitioner had spirometry results. Walker et al³¹ reported that reversibility testing in primary care subjects resulted in 19% no longer obstructed after bronchodilator, and that those patients with post-bronchodilator obstruction had significant and appropriate changes in therapy.

Despite published guidelines for management of COPD,⁹ significant inconsistencies persist when disease management is associated with spirometry. Price et al³² evaluated a large cohort of subjects with spirometry results supporting a diagnosis of COPD. They found overuse of inhaled corticosteroids across all GOLD stages, as well as subjects with symptoms receiving no treatment. The combined problems of not performing spirometry to confirm the diagnosis or of using inappropriate pharmacologic management even with results from spirometry are not unusual in primary care.³³ Lack of training in spirometry interpretation for primary care practitioners may be partially responsible for this disconnect.³⁴

Spirometry is underutilized in both the diagnosis and management of airway obstruction.35 Salinas et al36 found that primary care practitioners familiar with spirometry and pharmacologic guidelines were more likely to adhere to recommended practices but also observed that poor familiarity with guidelines, low confidence in spirometry, and low expectations for treatment limit patient outcomes. Kaminsky et al³⁷ reported that the most common reasons that primary care practitioners do not perform spirometry are uncertainty about the impact of the test, physician/staff unfamiliarity, and lack of training. Primary care practitioners may not consider spirometry necessary to diagnose and treat COPD,³⁸ or they may have negative attitudes about the effectiveness of COPD management.³⁹ There is no evidence to support the use of periodic spirometry to assess disease status or monitor therapy in symptomatic COPD patients after initiation of therapy.⁴⁰ Improvement in clinical symptoms does not necessarily correlate with spirometric findings.

Recommendations

Pre- and post-bronchodilator spirometry should be used in primary care to identify patients with COPD and to guide therapy following published guidelines. Good quality spirometry and accurate interpretation of results are necessary components for diagnosis and management of COPD.

Spirometry has also become an important tool in the management of asthma. Because patients' perceptions of air-flow obstruction are variable and medical history and physical examination are not always reliable for excluding other diagnoses, spirometry is required to establish the diagnosis of asthma. Both the Global Initiative for Asthma⁴¹ and the National Asthma Education and Prevention Program⁴² recommend spirometry for diagnosing and managing asthma in children and adults. The American Academy of Allergy, Asthma, and Immunology, as part of the Choosing Wisely initiative, recommends: "Don't diagnose or manage asthma without spirometry."43 However, Schneider et al44 found that whereas office spirometry performed under optimum conditions had good sensitivity and specificity for detecting COPD, it had a low sensitivity (29%) for detecting asthma.

Sokol et al⁴⁵ reported that in a large cohort of subjects with an asthma diagnosis, <50% had spirometry performed within 1 y. The same study noted that even without spirometry, 78% of subjects were prescribed controller medications. Schifano et al⁴⁶ found poor concordance between spirometry and asthma symptoms for determining severity even when guideline-based clinical assessment tools were used. Use of spirometry for asthma diagnosis in children is

Table 2.	Comparison of Original National Lung Health Education Program and Global Initiative for Chronic Obstructive Lung Disease
	Spirometric Criteria for Diagnosing and Categorizing Airway Obstruction

	NLHEP	GOLD			
Classification	Description	Classification	Description		
Obstruction	$FEV_1/FEV_6 < lower limit of normal (5th percentile)$	Obstruction	$FEV_1/FVC < 0.70$ post-bronchodilator		
		Stage 0*	$FEV_I/FVC > 0.70$, $FEV_I > 80\%$, symptoms only		
Mild	$\text{FEV}_1 < \text{lower limit of normal} \ge 60\%$	Stage I	$\text{FEV}_1 \ge 80\%$		
Moderate	$\text{FEV}_1 \le 59\%, \ge 40\%$	Stage II	$\text{FEV}_1 < 80\%, \ge 50\%$		
Severe	$\text{FEV}_1 < 40\%$	Stage III	$\text{FEV}_1 < 50\%, \ge 30\%$		
Very Severe		Stage IV	$\mathrm{FEV}_1 < 30\%$ or $\mathrm{FEV}_1 < 50\%$ with chronic respiratory failure		
* Stage 0 dropped NLHEP = Nationa	 in later update. I Lung Health Education Program				
GOLD = Global Ir	nitiative for Chronic Obstructive Lung Disease				

variable in primary care,⁴⁷ with physicians unfamiliar with spirometry interpretation.⁴⁸

The clinical utility of spirometry in the management of asthma is unclear. Abramson et al⁴⁹ found that quality of life, everyday activities, and interventions for acute asthma attacks were not different in subjects for whom spirometry was used as opposed to usual care. Holton et al⁵⁰ reported that staff training and use of spirometry in a general practice setting did significantly improve asthma management or patient outcomes. Other studies have found that without spirometry resulted in improved control in general practice patients.^{51,52} Some of these discrepancies may be related to how spirometry is interpreted or the differing criteria used to define asthma control.⁵³

Recommendations

Spirometry pre- and post-bronchodilator is essential for confirming a diagnosis of asthma and categorizing severity. Whether spirometry results are useful for ongoing management of patients who have asthma is unclear, and further research is needed.

The original NLHEP Consensus Statement encouraged the use of spirometry as an adjunct to smoking cessation as the single most effective way to prevent or reduce progression in COPD. Some studies have shown marginal improvements in quit rates when counseling is augmented with spirometry results.⁵⁴ However, two meta-analyses reviewing multiple studies found little evidence to support using spirometry to predict or improve smoking cessation.^{55,56} The concept of using lung age (age of a healthy subject with similar FEV₁) to motivate smoking cessation has been largely ineffective.⁵⁷ Parkes et al⁵⁸ found a small improvement in quit rates when lung age was included, but subjects with worse lung function were no more likely to quit than those with normal lung age. Spirometry does not appear to improve quit rates in smokers with normal lung function at the time of testing.⁵⁹

Recommendations

Spirometry (with or without lung age) as an adjunct to smoking cessation may be of limited value. All patients should be advised and assisted to stop smoking.

Diagnostic Criteria for Spirometry

The NLHEP consensus statement recommended using the lowest fifth percentile of healthy, never-smoking subjects as the lower limit of normal for diagnostic spirometry as well as using FEV_1 and FEV_6 , together with their ratio, FEV₁/FEV₆, to diagnose and categorize airway obstruction.¹ FEV₆ was suggested as an alternative to the FVC because it was easier to perform for both the patient and technician and because it obviated some of the repeatability problems with FVC (which can vary with expiratory time). Since publication of the consensus statement, other recommendations regarding spirometry for detecting COPD have been promulgated. The GOLD guidelines (published in 2002, with major updates in 2007, 2011, and 2016) recommend spirometry as a required component for confirming a diagnosis of COPD. However, GOLD recommended a post-bronchodilator $FEV_1/FVC < 0.70$ as diagnostic of airway obstruction, whereas the NLHEP guidelines suggested an FEV₁/FEV₆ less than the lower limit of normal (as defined by the fifth percentile of a healthy non-smoking reference population) as consistent with obstruction. Table 2 compares criteria for spirometry interpretations as originally proposed by NLHEP and GOLD. In 2005, the ATS/ERS jointly published updated guidelines for spirometry and its interpretation, reiterating their previous recommendations to use the lowest fifth percentile to define airway obstruction.⁶⁰ There has been



Fig. 2. Comparison of the lower limit of normal (based on the fifth percentile for healthy non-smoking adult males) with a fixed ratio of 70% for FEV₁/FVC. LLN = lower limit of normal.

vigorous discussion and disagreement regarding the use of fixed thresholds for the FEV_1/FVC as well as for FEV_1 percent of predicted.

 FEV_1 and FVC (and FEV_6) fall with advancing age in adults, with FEV_1 declining at a faster rate. The FEV_1/FVC , which is the primary variable used to diagnose airway obstruction, also decreases with age and differs between men and women as well as in subjects of different ethnicities. The fifth percentile for the ratio falls below 0.70 at about age 45 in white males and slightly later in white females.⁶¹ As a result, older patients may be misdiagnosed as having airway obstruction if their FEV₁/FVC falls below 0.70 (Fig. 2). Numerous studies have described this dilemma and its potential implications.62-64 Cerveri et al65 also found misclassification of young adults whose fifth percentile falls above the fixed threshold of 0.70, subjects who have asthma or early COPD. Although it appears that the fixed ratio detects patients at greater risk of death from COPD, these subjects are typically older male smokers, and development of symptoms is more closely associated with an FEV₁/FVC less than the lower limit of normal.66,67 For patients whose FEV₁/FVC falls between 0.70 and the lower limit of normal, care is necessary when establishing a COPD diagnosis because of the common presence of comorbidities.⁶⁸ An additional issue related to confirming a diagnosis of COPD is the use of FEV₁ percent of predicted to categorize airway obstruction. GOLD guidelines define an FEV₁ < 80% of predicted to classify a patient with obstruction as having "moderate" COPD (Table 2). Miller et al⁶⁹ reported that using 80% along with the fixed ratio for FEV₁/FVC can misclassify as many as 20% of patients. van Dijk et al⁷⁰ found that subjects with COPD diagnosed by either the fixed ratio or lower limit of normal were

more likely to have adverse outcomes (exacerbations, etc) only when their FEV₁ values were <80%.

Recommendations

Spirometry should be interpreted using the lower limit of normal (defined as the lowest fifth percentile of healthy non-smokers) for both the FEV_1/FVC and for the FEV_1 (as well as for the FEV_1/FEV_6 and FEV_6 , if used). The use of the 0.70 fixed ratio is NOT recommended.

The use of the fixed ratio may be associated with issues of misclassification and underdiagnosis. The office spirometry consensus statement from NLHEP recommended spirometry for detecting COPD without utilizing a bronchodilator, unless the test was used to identify asthma.¹ GOLD recommends post-bronchodilator spirometry to define air-flow obstruction that is not responsive to inhaled β -agonists to separate asthma from COPD. Spirometry data from the National Health and Nutrition Examination Survey (NHANES) 2007-2010 showed significantly different prevalence rates for COPD, depending on whether pre- or post-bronchodilator values were used. The overall prevalence decreased by approximately 33% when airflow limitation was based on post-bronchodilator as compared with pre-bronchodilator spirometry, regardless of whether a fixed ratio (0.70) or lower limit of normal was used.71 The PLATINO study found similar differences in COPD prevalence (32-39%) when post-bronchodilator spirometry was used.⁷² Recognition that many patients who meet the spirometric criteria for COPD also meet criteria for significant bronchodilator reversibility has resulted in a new designation: asthma-COPD overlap syndrome.73 Although the syndrome is not well defined, it may be present in as many as 15–25% of obstructed patients.74 The picture of how asthma-COPD overlap syndrome compares with COPD is still evolving, with some studies suggesting that these patients are typically younger and have less smoking history, poorer disease-related quality of life, and increased health-care utilization, whereas others show no significant difference.75,76

Recommendations

Post-bronchodilator spirometry should be performed if a patient meets the criteria for airway obstruction prebronchodilator *or* if the patient presents with signs/symptoms suggestive of asthma. The goal of pre- and postbronchodilator testing is to identify asthma versus COPD or an overlap between the two (asthma-COPD overlap syndrome). A single negative response to bronchodilators (suggesting a COPD diagnosis) does not preclude a trial of bronchodilators if clinically indicated.

The original NLHEP consensus statement encouraged the use of reference equations, which included statistically

Comparison of Spirometry Predicted and Lower Limit of
Normal Values for African-Americans Based on 2
Comparable Reference Sets

	NHAN	ES III	GLI-2012	
Characteristics	Predicted	Lower Limit of Normal	Predicted	Lower Limit of Normal
African-American male,				
175 cm, 60 y				
FEV ₁ , L	3.00	2.19	2.95	2.14
FVC, L/s	3.85	2.94	3.78	2.81
FEV ₁ /FVC	0.78	0.68	0.78	0.67
African-American female, 165 cm, 60 y				
FEV ₁ , L	2.18	1.55	2.22	1.62
FVC, L/s	2.77	2.04	2.80	2.07
FEV ₁ /FVC	0.79	0.69	0.80	0.68

NHANES = National Health and Nutrition Examination Survey

GLI = Global Lung Function Initiative

 Table 4.
 Comparison of Spirometry Predicted and Lower Limit of Normal Values for Caucasians Based on 2 Comparable Reference Sets

	NHAN	ES III	GLI-	GLI-2012		
	Predicted	Lower Limit of Normal	Predicted	Lower Limit of Normal		
Caucasian male,						
175 cm, 60 y						
FEV ₁ , L	3.47	2.71	3.46	2.61		
FVC, L/s	4.59	3.68	4.47	3.41		
FEV ₁ /FVC	0.76	0.66	0.78	0.66		
Caucasian female,						
165 cm, 60 y						
FEV ₁ , L	2.65	2.05	2.58	1.95		
FVC, L/s	3.42	2.71	3.28	2.48		
FEV ₁ /FVC	0.78	0.68	0.79	0.67		

NHANES = National Health and Nutrition Examination Survey

GLI = Global Lung Function Initiative

valid lower limits of normal. The NHANES III predicted set meets this requirement and provides race-specific predicted values for whites, African-Americans, and Mexican-Americans, ages 8–80 y.⁶⁵ In 2012, the Global Lung Function Initiative (GLI) published spline tables allowing predicted values to be calculated for whites, African-Americans, and Northeast and Southeast Asians.⁷⁷ Tables 3 and 4 compare predicted values for an average male and female (African-American and white) using NHANES III and GLI equations. NHANES III provides reference values for FEV₆ and FEV₁/FEV₆, whereas GLI does not. However, GLI provides a wider age range (3–95 y) with a seamless transition between adolescence and adulthood. Stanojevic et al,⁷⁸ using the same methodology as GLI, expanded the NHANES III reference equations to include children as young as 4 y old. Although there are no race-specific reference values for Asian-Americans, Hankinson et al⁷⁹ suggest that a correction factor of 0.88 applied to white values (NHANES III) can be used for both predicted and lower limit of normal.

Recommendations

Either NHANES III or GLI-2012 reference equations may be used for spirometry.

Performance of Spirometry in Primary Care

Performance of spirometric maneuvers has changed since the NLHEP consensus was published. The 2005 ATS/ERS guidelines reduced the within-session repeatability criteria for FVC and FEV₁ to 150 mL (from 200 mL). The 6-s end-of-test criterion for adults remained the same but was relaxed to 3 s for children <10 y old.⁵³ Several investigators have found that the most common problem affecting office spirometry is failure to meet the 6-s threshold for a plateau in forced exhalation. Hankinson et al⁸⁰ found that computerized spirometers reject FVC maneuvers in which a plateau is reached before 6 s and recommended that end-of-test criteria should be applied during testing to avoid rejecting valid data. Personnel performing spirometry should be able to distinguish between an acceptable blow and one in which the patient stops prematurely.

Correct interpretation of spirometry depends on acceptable and repeatable spirometry, performed according to established guidelines.⁸¹ Despite user training and novel approaches implementing spirometry, COPD is frequently misdiagnosed and often confused with asthma. Walters et al⁸² found, when using trained nurses to perform spirometry versus usual care, that patients with an FEV₁/FVC > 0.70 were misdiagnosed regardless of the model used. Raghunath et al⁸³ compared the diagnostic accuracy of primary care practitioners with that of pulmonary specialists in a cohort of subjects with COPD or asthma and found only 20% agreement. These studies suggest that spirometry interpretation skills are less than optimal for managing patients who have COPD and/or asthma. Interpretation of spirometry in pediatric patients with asthma is similarly problematic. Dombrowski et al47 surveyed a national sample of family practitioners and pediatricians treating children with asthma and found that only 50% of the respondents correctly interpreted a standardized clinical vignette and that asthma severity was frequently underrated.

Table 5 lists steps for interpretation of office spirometry that update the previous NLHEP recommendations.¹ Ei-

Table 5. Interpretation of Office Spirometry Results

- 1. Check the acceptability and repeatability to see if ATS/ERS criteria have been met. Pay special attention to the EOT; was a plateau reached before 6 s?
- 2. Use NHANES III or GLI reference values to calculate predicted values and lower limits of normal for FEV₁, FVC, and FEV₁/FVC; FEV₆ may be substituted for FVC if NHANES III is used.
- 3. If the FEV₁/FVC (FEV₁/FEV₆) and FEV₁ are both below the lower limit of normal in a test with good quality, airway obstruction is present. Use of the 0.70 fixed ratio is NOT recommended.
- 4. Grade the severity of obstruction using the FEV_1 lower limit of normal and percent predicted:
- Lower limit of normal > $FEV_1 \ge 60\%$ = mild obstruction

 $60\% > \text{FEV}_1 \ge 40\% = \text{moderate obstruction}$

 $\text{FEV}_1 < 40\% = \text{severe obstruction}$

5. If the FEV₁/FVC (FEV₁/FEV₆) is great than the lower limit of normal but the FVC (FEV₆) is less than the lower limit of normal, the patient may have a restrictive disease; consider lung volumes.

6. If the patient has airway obstruction, post-bronchodilator testing should be performed.

- If the FEV₁/FVC (FEV₁/FEV₆) and FEV₁ both improve above their respective lower limits of normal, a significant asthmatic component is probably present.
- If the FEV₁ increases by 12% or more, but the FEV₁/FVC (FEV₁/FEV₆) remains below the lower limit of normal, the patient may have combined COPD and asthma.

ATS/ERS = American Thoracic Society/European Respiratory Society

EOT = end of test

NHANES = National Health and Nutrition Examination Survey

GLI = Global Lung Function Initiative

ther FVC or FEV₆ may be used for calculating the ratio with FEV₁. In addition, either the NHANES III or GLI reference values and lower limits of normal may be used for interpretive purposes. Adopting the GLI predicted values in place of older reference equations (not NHANES III) may result in some patients being reclassified into milder severity stages.⁸⁴ Figure 3 shows a sample spirometry report for pre- and post-bronchodilator studies, as suggested by the Canadian Thoracic Society.85 Only the FEV₁, FVC, and FEV₁/FVC are reported. Both the lower limit of normal and percent of predicted are displayed for pre-bronchodilator measurements. For post-bronchodilator studies, the percent of predicted, absolute volume change, and percentage change are reported. A bar graph displays the patient's best values in relation to the predicted value and lower limit of normal. The bar graph is scaled in SD values so that the results can be interpreted visually. Spirometry values that fall on or near the patient's lower limit of normal should be interpreted cautiously, taking into account the pre-test probability of disease.

As noted, the quality of spirometry is of key importance in the use of this as both a diagnostic and management tool. A recent study⁸⁶ evaluated the accuracy and quality of spirometry in primary care offices. In this study, 17 spirometers used in primary care offices with a waveform generator were assessed for accuracy and precision using ATS criteria. Only 1 of 17 spirometers met the accuracy criteria with mean errors for FVC, FEV₁, and FEV₁/FVC ranging from 1.7 to 3.1%. Thus, greater attention to qual-



Fig. 3. Sample format for an office-based spirometry report as recommended by the Canadian Thoracic Society. In addition to the 3 primary spirometry values reported using the lower limit of normal and percentage of the reference value, a pictographic representation of the values is included. The patient's spirometry values are graphed on a scale that displays the reference (predicted) value, and the lower limit of normal is scaled using the SD (Z scores). LLN = lower limit of normal. From Reference 85, with permission.

ity assurance and training is necessary regarding the use of spirometry in primary care offices.

Recommendations

Personnel performing spirometry in the primary care setting should receive formal training (hands on) that includes set-up and operation of the spirometer, knowledge and application of standards for acceptable and repeatable maneuvers, and ability to identify obstructive and restrictive disease patterns. Ongoing feedback regarding the quality of spirometry is recommended. Physicians and others interpreting spirometry results should be able to grade the quality of each test, ensure that appropriate reference values are selected, and identify obstruction and restrictive ventilatory patterns. Interpreters should be able to identify bronchial responsiveness from post-bronchodilator testing.

Summary

Spirometry is essential to establish the diagnosis of COPD and asthma. When diagnostic spirometry is combined with validated questionnaires and the use of peak flow, screening for COPD is enhanced. Spirometry is recommended for the management of COPD and asthma, but application of pharmacotherapy based on test results is inconsistent. The barriers to wider use of spirometry appear to be lack of familiarity with guidelines, inadequate training and feedback for practitioners, and incorrect interpretation of test results, along with time and financial constraints. Spirometry does not appear to be a useful adjunct for smoking cessation.

Airway obstruction is commonly defined using a fixed FEV₁/FVC of 0.70, although NLHEP and ATS/ERS recommend using the lower limit of normal. This document reiterates that the lower limit of normal should be used for the FEV₁/FVC or FEV₁/FEV₆, whichever is used, and that the FEV₁ lower limit of normal should be used to categorize mild obstruction rather than 80% of predicted. Both the NHANES III and GLI predicted sets are appropriate for interpretation of office spirometry.

Interpretation of spirometry results remains problematic because it is closely related to the quality of the results. Spirometry interpretation training for primary care practitioners needs to be standardized and emphasized going forward.

REFERENCES

- 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. Chest 2000;117(4):1146-1161.
- Leading causes of death. Atlanta, Georgia: Centers for Disease Control and Prevention. http://www.cdc.gov/nchs/fastats/leading-causesof-death.htm. Accessed November 17, 2015.
- Martinez CH, Mannino DM, Jaimes FA, Curtis JL, Han MK, Hansel NN, Diaz AA. Undiagnosed obstructive lung disease in the U.S.: associated factors and long-term mortality. Ann Am Thorac Soc 2015;12(12):1788-1795.
- 4. Wilt TJ, Niewoehner D, Kim C, Kane RL, Linabery A, Tacklind J, et al. Use of spirometry for case finding, diagnosis, and management of chronic obstructive pulmonary disease (COPD). summary, evidence report/technology assessment no. 121. AHRQ Publication No.

05-E017-1. Rockville, Maryland: Agency for Healthcare Research and Quality. Aug 2005.

- US Preventive Services Task Force (USPSTF), Siu AL, Bibbins-Domingo K, Grossman DC, Davidson KW, Epling JW Jr, et al. Screening for chronic obstructive pulmonary disease: US Preventive Services Task Force recommendation statement. JAMA 2016; 315(13):1372-1377.
- Use of spirometry testing in the assessment and diagnosis of COPD. National Quality Forum. http://www.qualityforum.org/Projects/n-r/ Pulmonary_Endorsement_Maintenance/0577_Spirometry_Testing_ for_COPD.aspx. Accessed November 8, 2017.
- Use of spirometry testing in the assessment and diagnosis of COPD. National Committee for Quality Assurance. http://www.ncqa.org/ report-cards/health-plans/state-of-health-care-quality/2016-table-ofcontents/spirometry. Accessed August 1, 2017.
- Haroon SM, Jordan RE, O'Beirne-Elliman J, Adab P. Effectiveness of case finding strategies for COPD in primary care: a systematic review and meta-analysis. NPJ Prim Care Respir Med 2015;25:15056.
- Llordés M, Jaén A, Almagro P, Heredia JL, Morera J, Soriano JB, Miravitlles M. Prevalence, risk factors and diagnostic accuracy of COPD among smokers in primary care. COPD 2015;12(4):404-412.
- Sansores RH, Ramírez-Venegas A, Hernández-Zenteno R, Mayar-Maya ME, Pérez-Bautista OG, Velázquez Uncal M. Prevalence and diagnosis of chronic obstructive pulmonary disease among smokers at risk: a comparative study of case-finding vs. screening strategies Respir Med 2013;107(4):580-586.
- 11. Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017: GOLD executive summary. Am J Respir Crit Care Med 2017;195(5):557-582.
- Kjeldgaard P, Dahl R, Løkke A, Ulrik CS. Detection of COPD in a high-risk population: should the diagnostic work-up include bronchodilator reversibility testing? Int J Chron Obstruct Pulmon Dis. 2015;10:407-414.
- Barrecheguren M, Román-Rodríguez M, Miravitlles M. Is a previous diagnosis of asthma a reliable criterion for asthma-COPD overlap syndrome in a patient with COPD? Int J Chron Obstruct Pulmon Dis 2015;10:1745-1752.
- Sexton P, Black P, Wu L, Sommerville F, Hamed M, Milne D, et al. Chronic obstructive pulmonary disease in non-smokers: a case-comparison study. COPD 2014;11(1):2-9.
- Tinkelman DG, Price D, Nordyke RJ, Halbert RJ. COPD screening efforts in primary care: what is the yield? Prim Care Respir J 2007; 16(1):41-48.
- Spyratos D, Chloros D, Michalopoulou D, Sichletidis L. Estimating the extent and economic impact of under and overdiagnosis of chronic obstructive pulmonary disease in primary care. Chron Respir Dis 2016;13(3):240-246.
- Yawn BP, Duvall K, Peabody J, Albers F, Iqbal A, Paden H, et al. The impact of screening tools on diagnosis of chronic obstructive pulmonary disease in primary care. Am J Prev Med 2014;47(5):563-575.
- Stanley AJ, Hasan I, Crockett AJ, van Schayck OC, Zwar NA. COPD Diagnostic Questionnaire (CDQ) for selecting at-risk patients for spirometry: a cross-sectional study in Australian general practice. NPJ Prim Care Respir Med 2014;24:14024.
- Sims EJ, Price D. Spirometry: an essential tool for screening, casefinding, and diagnosis of COPD. Prim Care Respir J 2012;21(2): 128-130.
- Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD Assessment Test. Eur Respir J 2009;34(3):648-654.

- Woodruff PG, Barr RG, Bleecker E, Christenson SA, Couper D, Curtis JL, et al. Clinical significance of symptoms in smokers with preserved pulmonary function. N Engl J Med 2016;374(19):1811-1821.
- Perez-Padilla R, Vollmer WM, Vazquez-Garcia JC, Enright PL, Menezes AM, Buist AS, BOLD and PLATINO Study Groups. Can a normal peak expiratory flow exclude severe chronic obstructive pulmonary disease? Int J Tuberc Lung Dis 2009;13(3):387-393.
- Jithoo A, Enright PL, Burney P, Buist AS, Bateman ED, Tan WC, et al. Case-finding options for COPD: results from the Burden of Obstructive Lung Disease study. Eur Respir J 2013;41(3):548-555.
- 24. Jordan RE, Adab P, Sitch A, Enocson A, Blissett D, Jowett S, et al. Targeted case finding for chronic obstructive pulmonary disease versus routine practice in primary care (TargetCOPD): a cluster-randomised controlled trial. Lancet Respir Med 2016;4(9):720-730.
- Nelson SB, LaVange LM, Nie Y, Walsh JW, Enright PL, Martinez FJ, et al. Questionnaires and pocket spirometers provide an alternative approach for COPD screening in the general population. Chest 2012;142(2):358-366.
- National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011;365(5):395-409.
- Young RP, Duan F, Chiles C, Hopkins RJ, Gamble GD, Greco EM, et al. Airflow limitation and histology shift in the national lung screening trial: the NLST-ACRIN cohort substudy. Am J Respir Crit Care Med 2015;192(9):1060-1067.
- Zurawska JH, Jen R, Lam S, Coxson HO, Leipsic J, Sin DD. What to do when a smoker's CT scan is "normal"?: implications for lung cancer screening. Chest 2012;141(5):1147-1152.
- Yawn BP, Enright PL, Lemanske RF Jr, Israel E, Pace W, Wollan P, Boushey H. Spirometry can be done in family physicians' offices and alters clinical decisions in management of asthma and COPD. Chest 2007;132(4):1162-1168.
- Mapel DW, Dalal AA, Johnson P, Becker L, Hunter AG. A clinical study of COPD severity assessment by primary care physicians and their patients compared with spirometry. Am J Med 2015;128(6): 629-637.
- 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.
- 32. Price D, West D, Brusselle G, Gruffydd-Jones K, Jones R, Miravitlles M, et al. Management of COPD in the UK primary-care setting: an analysis of real-life prescribing patterns. Int J Chron Obstruct Pulmon Dis 2014;9:889-904.
- Chavez PC, Shokar NK. Diagnosis and management of chronic obstructive pulmonary disease (COPD) in a primary care clinic. COPD 2009;6(6):446-451.
- Joo MJ, Au DH, Fitzgibbon ML, McKell J, Lee TA. Determinants of spirometry use and accuracy of COPD diagnosis in primary care. J Gen Intern Med 2011;26(11):1272-1277.
- Lamprecht B, Soriano JB, Studnicka M, Kaiser B, Vanfleteren LE, Gnatiuc L, et al. Determinants of underdiagnosis of COPD in national and international surveys. Chest 2015;148(4):971-985.
- 36. Salinas GD, Williamson JC, Kalhan R, Thomashow B, Scheckermann JL, Walsh J, et al. Barriers to adherence to chronic obstructive pulmonary disease guidelines by primary care physicians. Int J Chron Obstruct Pulmon Dis 2011;6:171-179.
- Kaminsky DA, Marcy TW, Bachand M, Irvin CG. Knowledge and use of office spirometry for the detection of chronic obstructive pulmonary disease by primary care physicians. Respir Care 2005; 50(12):1639-1648.

- Joo MJ, Sharp LK, Au DH, Lee TA, Fitzgibbon ML. Use of spirometry in the diagnosis of COPD: a qualitative study in primary care. COPD 2013;10(4):444-449.
- Walters JA, Hansen EC, Walters EH, Wood-Baker R. Under-diagnosis of chronic obstructive pulmonary disease: a qualitative study in primary care. Respir Med 2008;102(5):738-743.
- 40. Qaseem A, Wilt TJ, Weinberger SE; Hanania NA, Criner G, van der Molen T, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. Ann Intern Med 2011;155(3):179-191.
- Global Initiative for Asthma. http://www.ginasthma.org/2017-ginareport-global-strategy-for-asthma-management-and-prevention. Updated 2014. Accessed November 14, 2017.
- 42. Guidelines for the diagnosis and management of asthma. Bethesda, Maryland: National Heart, Lung, and Blood Institute, National Institutes of Health. https://www.nhlbi.nih.gov/files/docs/guidelines/ asthsumm.pdf. Updated 2007. Accessed May 15, 2017.
- 43. Ten things physicians and patients should question. Philadelphia, Pennsylvania: American Academy of Allergy, Asthma, and Immunology. http://www.choosingwisely.org/societies/americanacademy-of-allergy-asthma-immunology/. Updated March 3, 2014. Accessed May 15, 2017.
- Schneider A, Gindner L, Tilemann L, Schermer T, Dinant GJ, Meyer FJ, Szecsenyi J. Diagnostic accuracy of spirometry in primary care. BMC Pulm Med 2009;9:31-41.
- 45. Sokol KC, Sharma G, Lin YL, Goldblum R. Choosing wisely: adherence by physicians to recommended use of spirometry in the diagnosis and management of adult asthma. Am J Med 2015;128(5): 502-508.
- Schifano ED, Hollenbach JP, Cloutier MM. Mismatch between asthma symptoms and spirometry: implications for managing asthma in children. J Pediatr 2014;165(5):997-1002.
- Dombkowski KJ, Hassan F, Wasilevich EA, Clark SJ. Spirometry use among pediatric primary care physicians. Pediatrics 2010;126(4): 682-687.
- Zanconato S, Meneghelli G, Braga R, Zacchello F, Baraldi E. Office spirometry in primary care pediatrics: a pilot study. Pediatrics 2005; 116(6):e792-e797.
- 49. Abramson MJ, Schattner RL, Holton C, Simpson P, Briggs N, Beilby J, et al. Spirometry and regular follow-up do not improve quality of life in children or adolescents with asthma: cluster randomized controlled trials. Pediatr Pulmonol 2015;50(10):947-954.
- Holton C, Crockett A, Nelson M, Ryan P, Wood-Baker R, Stocks N, et al. Does spirometry training in general practice improve quality and outcomes of asthma care? Int J Qual Health Care 2011;23(5): 545-553.
- Dostaler SM, Olajos-Clow JG, Sands TW, Licskai CJ, Minard JP, Lougheed MD. Comparison of asthma control criteria: importance of spirometry. J Asthma 2011;48(10):1069-1075.
- 52. Oei SM, Thien FC, Schattner RL, Sulaiman ND, Birch K, Simpson P, et al. Effect of spirometry and medical review on asthma control in patients in general practice: a randomized controlled trial. Respirology 2011;16(5):803-810.
- He XO, D'Urzo A, Jugovic P, Jhirad R, Sehgal P, Lilly E. Differences in spirometry interpretation algorithms: influence on decision making among primary-care physicians. NPJ Prim Care Respir Med 2015;25:15008.
- 54. Górecka D, Bednarek M, Nowiński A, Puścińska E, Goljan-Geremek A, Zieliński J. Diagnosis of airflow limitation combined with smoking cessation advice increases stop-smoking rate. Chest 2003; 123(6):1916-1923.

- Bize R, Burnand B, Mueller Y, Rège-Walther M, Camain JY, Cornuz J. Biomedical risk assessment as an aid for smoking cessation. Cochrane Database Syst Rev. 2012;(12):CD004705.
- Wilt TJ, Niewoehner D, Kane RL, MacDonald R, Joseph AM. Spirometry as a motivational tool to improve smoking cessation rates: a systematic review of the literature. Nicotine Tob Res 2007;9(1):21-32.
- Quanjer PH, Enright P. Should we use "lung age"? Prim Care Respir J 2010;19(3):197-199.
- Parkes G, Greenhalgh T, Griffin M, Dent R. Effect on smoking quit rate of telling patients their lung age: the Step2quit randomised controlled trial. BMJ 2008;336(7644):598-600.
- Kotz D, Wesseling G, Aveyard P, van Schayck OC. Smoking cessation and development of respiratory health in smokers screened with normal spirometry. Respir Med 2011;105(2):243-249.
- Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretive strategies for lung function tests. Eur Respir J 2005;26(5):948-968.
- 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.
- Hardie JA, Buist AS, Vollmer WM, Ellingsen I, Bakke PS, Mørkve O et al. Risk of over-diagnosis of COPD in asymptomatic elderly never-smokers. Eur Respir J 2002;20(5):1117-1122.
- Swanney MP, Ruppel G, Enright PL, Pedersen OF, Crapo RO, Miller MR, et al. Using the lower limit of normal for the FEV1/FVC ratio reduces the misclassification of airway obstruction. Thorax 2008; 63(12):1046-1051.
- 64. Vaz Fragoso CA, Concato J, McAvay G, Van Ness PH, Rochester CL, Yaggi HK, Gill TM. The ratio of FEV1 to FVC as a basis for establishing chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2010;181(5):446-451.
- 65. Cerveri I, Corsico AG, Accordini S, Niniano R, Ansaldo E, Antó JM, et al. Underestimation of airflow obstruction among young adults using FEV1/FVC <70% as a fixed cut-off: a longitudinal evaluation of clinical and functional outcomes. Thorax 2008;63(12):1040-1045.
- Mannino DM, Sonia Buist A, Vollmer WM. Chronic obstructive pulmonary disease in the older adult: what defines abnormal lung function? Thorax 2007;62(3):237-241.
- Mohamed Hoesein FA, Zanen P, Lammers JW. Lower limit of normal or FEV1/FVC <0.70 in diagnosing COPD: an evidence-based review. Respir Med 2011;105(6):907-915.
- Camiciottoli G, Bigazzi F, Magni C, Bonti V, Diciotti S, Bartolucci M, et al. Prevalence of comorbidities according to predominant phenotype and severity of chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2016;11:2229-2236.
- Miller MR, Quanjer PH, Swanney MP, Ruppel G, Enright PL. Interpreting lung function data using 80% predicted and fixed thresholds misclassifies more than 20% of patients. Chest 2011;139(1): 52-59.
- 70. van Dijk W, Tan W, Li P, Guo B, Li S, Benedetti A, Bourbeau J. CanCOLD Study Group: clinical relevance of fixed ratio vs lower limit of normal of fev1/fvc in COPD: patient-reported outcomes from the CanCOLD cohort. Ann Fam Med 2015;13(1):41-48.
- Tilert T, Dillon C, Paulose-Ram R, Hnizdo E, Doney B. Estimating the U.S. prevalence of chronic obstructive pulmonary disease using

pre- and post-bronchodilator spirometry: the National Health and Nutrition Examination Survey (NHANES) 2007-2010. Respir Res 2013;14:103.

- Pérez-Padilla R, Hallal PC, Vázquez-García JC, Muiño A, Máquez M, López MV, et al. Impact of bronchodilator use on the prevalence of COPD in population-based samples. COPD 2007;4(2):113-120.
- Postma DS, Rabe KF. The asthma-COPD overlap syndrome. N Engl J Med 2015;373(13):1241-1249.
- Papaiwannou A, Zarogoulidis P, Porpodis K, Spyratos D, Kioumis I, Pitsiou G, et al. Asthma-chronic obstructive pulmonary disease overlap syndrome (ACOS): current literature review. J Thorac Dis 2014; 6(Suppl 1):S146-S151.
- Braman SS. The chronic obstructive pulmonary disease-asthma overlap syndrome. Allergy Asthma Proc 2015;36(1):11-18.
- Caillaud D, Chanez P, Escamilla R, Burgel PR, Court-Fortune I, Nesme-Meyer P, et al. Asthma-COPD overlap syndrome (ACOS) vs "pure" COPD: a distinct phenotype? Allergy 2017;72(1):137-145.
- Quanjer PH, Stanojevic S, Cole TJ, Baur X. Multi-ethnic reference values for spirometry for the 3-95 year age range: the global lung function 2012 equations. Eur Respir J 2012;40(6):1324-1343.
- Stanojevic S, Wade A, Stocks J, Hankinson J, Coates AL, Pan H, et al. Reference ranges for spirometry across all ages: a new approach. Am J Respir Crit Care Med 2008;177(3):253-260.
- Hankinson JL, Kawut SM, Shahar E, Smith LJ, Stukovsky KH, Barr RG. Performance of American Thoracic Society-recommended spirometry reference values in a multiethnic sample of adults; the multiethnic study of atherosclerosis (MESA) lung study. Chest 2010; 137(1):138-145.
- Hankinson JL, Eschenbacher B, Townsend M, Stocks J, Quanjer PH. Use of forced vital capacity and forced expiratory volume in 1 second quality criteria for determining a valid test. Eur Respir J 2015; 45(5):1283-1292.
- White P, Wong W, Fleming T, Gray B. Primary care spirometry: test quality and the feasibility and usefulness of specialist reporting. Br J Gen Pract 2007;57(542):701-705.
- Walters JA, Hansen EC, Johns DP, Blizzard EL, Walters EH, Wood-Baker R. A mixed methods study to compare models of spirometry delivery in primary care for patients at risk of COPD. Thorax 2008; 63(5):408-414.
- Raghunath AS, Innes A, Norfolk L, Hannant M, Greene T, Greenstone M, Morice AH. Difficulties in the interpretation of lung function tests in the diagnosis of asthma and chronic obstructive pulmonary disease. J Asthma 2006;43(9):657-660.
- 84. Sluga R, Smeele IJ, Lucas AE, Thoonen BP, Grootens-Stekelenburg JG, Heijdra YF, Schermer TR. Impact of switching to new spirometric reference equations on severity staging of airflow obstruction in COPD: a cross sectional observational study in primary care. Prim Care Respir J 2014;23(1):85-91.
- Coates AL, Graham BL, McFadden RG, McParland C, Moosa D, Provencher S, et al. Spirometry in primary care. Can Respir J 2013; 20(1):13-21.
- Hegewald MJ, Gallo HM, Wilson EL. Accuracy and quality of spirometry in primary care offices. Ann Am Thorac Soc 2016;13(12): 2119-2124.