Wake Forest™
Baptist Health

Lung Function
Basics of Diagnosis of Obstructive, Restrictive and Mixed Defects

Use of GOLD and ATS Criteria

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Benefits and Limitations of Pulmonary Function Testing

Benefits

- Useful for diagnosing cause of unexplained respiratory symptoms and monitoring patients with known disease
- Can be used to identify the pattern and severity of an abnormality

Limitations

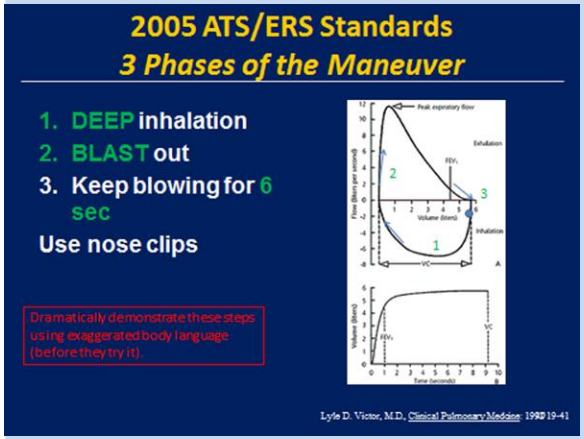
- Generally cannot distinguish among the potential causes of the abnormalities when used alone
- Must be interpreted within the context of a proper history, physical examination, and ancillary diagnostic tests

Indications for Pulmonary Function Testing

- Evaluate symptoms and signs of lung disease (eg, cough, dyspnea, cyanosis, wheezing, hyperinflation, hypoxemia, hypercapnia)
- Assess the progression of lung disease
- Monitor effectiveness of therapy
- Evaluate preoperative patients in selected situations
- Screen at risk individuals for pulmonary disease such as smokers or people with occupational exposure to toxic substances
- Monitor for potentially toxic effects of certain drugs or chemicals (eg, amiodarone, beryllium)

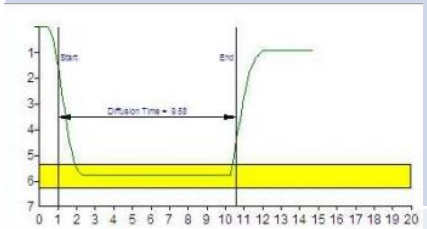
Components of Pulmonary Function Tests

Spirometry



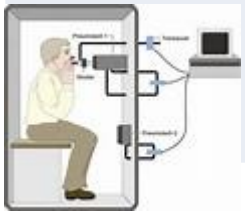
- Measures volume and speed of air movement in and out of lungs during various respiratory maneuvers
- The four most important respiratory parameters are:
  - VC (SVC) – Slow vital capacity – Maximal inhalation or exhalation followed by maximal inhalation/exhalation without regard to time
  - FVC – Maximal inhalation followed by maximal exhalation as long and forcefully as possible
  - FEV1 – Amount of air exhaled during the first second of the FVC maneuver. Tends to be lower in obstructive diseases such as asthma and emphysema
  - FEV1/FVC ratio – Used to determine if the pattern is obstructive, restrictive or normal

Diffusing Capacity (DLCO)



- Measures ability of lung to transfer gas
- Decreased in conditions that minimize the ability of blood to accept and bind the gas that is diffusing (anemia), conditions that decrease surface area of alveolar-capillary membrane (emphysema, pulmonary embolism) and conditions that alter permeability or increase membrane thickness (pulmonary fibrosis)

Residual Volume, Total Lung Capacity



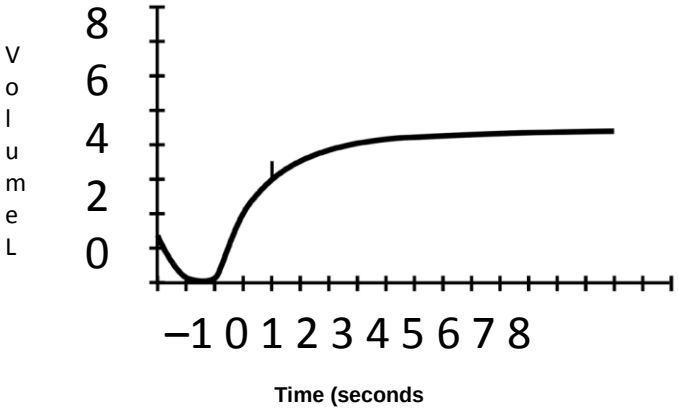
- Must be measured indirectly (inert gas, plethysmography)
- Can demonstrate air trapping and hyperinflation in obstructive diseases and confirm true restriction

Key Measurements

Abbreviation	Characteristic measured
SVC	Slow vital capacity
FVC	Forced vital capacity
FEV_1	Forced expired volume in 1 second
FEV_1 /FVC Ratio	Ratio of the above
PEFR	Peak expiratory flow rate
FEF 25-75%	Forced expiratory flow between 25-75% of the vital capacity

Factors to Confirm Before Interpreting PFTs

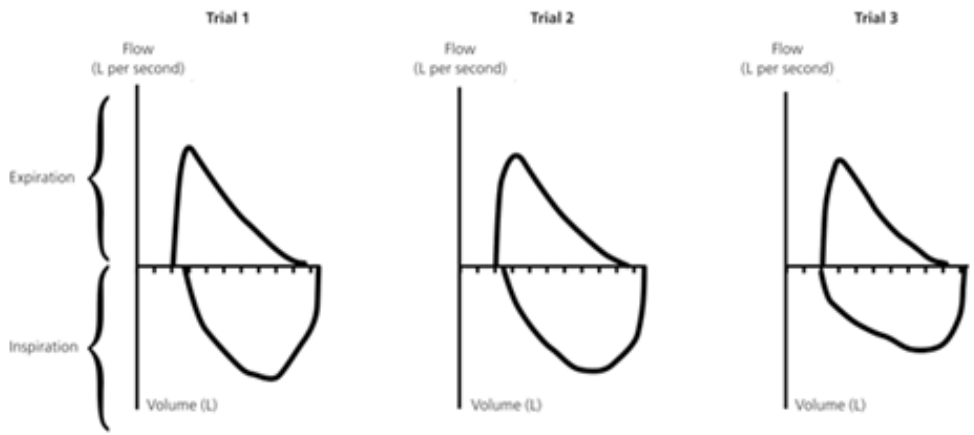
1. The volume-time curve reaches a plateau, and expiration lasts at least six seconds



Factors to Confirm Before Interpreting PFTs

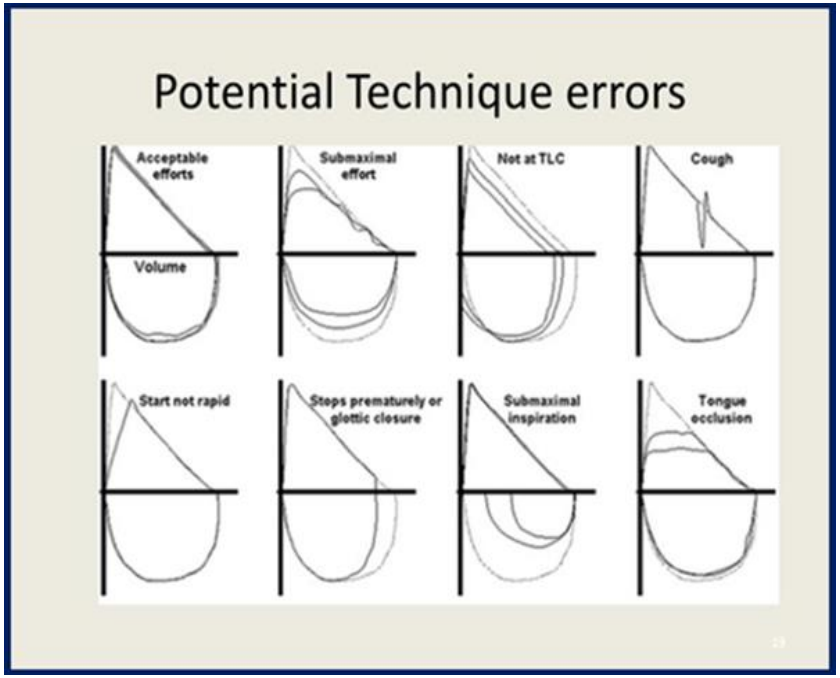
2. Results of the 2 best efforts on the FVC are within 0.2 L. of each other

	Predicted	*Best*	*% of predicted*	*1*	*2*	*3*
FVC (L)	3.66	3.04	83	2.93	3.04	2.94
FEV_1 (L)	2.96	2.12	72	2.09	2.12	2.02
FEV_1/FVC (%)	83	70	84	71	70	69
$FEF_{25\%-75\%}$ (L per second)	3.36	1.36	40	1.44	1.36	1.23
PEF	6.65	4.71	71	5.07	4.71	4.67



Factors to Confirm Before Interpreting PFTs

3. The flow-volume loops are free of artifacts and abnormalities
   - If the patient's efforts yield flattened flow-volume loops, submaximal effort is most likely; however, central or upper airway obstruction should be considered.



Step 1: Determine If the FEV1/FVC Ratio Is Low

- Low FEV1/FVC Ratio indicates an obstructive defect
- Two options:
  - **Follow GOLD Criteria** – Uses a cutoff of less than 70%
    - For patients five to 18 years of age, the National Asthma Education and Prevention Program guideline says that a ratio of less than 85% is consistent with an obstructive defect as long as the patient has symptoms consistent with obstructive lung disease.
  - **Follow the ATS criteria**, which use the lower limit of normal (LLN) as the cutoff for adults.
    - The LLN is a measurement less than the fifth percentile of spirometry data obtained from the Third National Health and Nutrition Examination Survey (NHANES III).

Defining Normal - Lower Limit of Normal (LLN)

- Obtained by analyzing some measure (FVC, FEV1, etc.) in healthy subjects, then determining the variability of that measurement.
- 5th percentile is often defined as the lower limit of normal in clinical medicine because it represents the segment of normal subjects farthest below the average

Defining Normal – Fixed Percentage

- Uses the measured value divided by the reference value X 100
- 80% is often used as the limit of normal
- This method leads to errors because the variability around the predicted value is relatively constant in adults (scatter of normal values does not vary with the size of the predicted value

GOLD VS. ATS Criteria

Eur Respir J 2005; 26: 948–968

DOI: 10.1183/09031936.05.00035205

SERIES "ATS/ERS TASK FORCE: STANDARDISATION OF LUNG FUNCTION TESTING"

Edited by V. Brusasco, R. Crapo and G. Viegi

Number 5 in this Series

Interpretative strategies for lung function tests

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2017

UPDATED

GOLD RECOMMENDATION FOR

COPD

From

The Global Initiative for
Chronic Obstructive Lung Disease (GOLD)

Am J Respir Crit Care Med.

Published January 27, 2017

GOLD VS. ATS CRITERIA

- A large cohort study found that using the GOLD criteria (FEV_1/FVC less than 70%) for diagnosis of chronic obstructive pulmonary disease (COPD) in U.S. adults 65 years and older was more sensitive for COPD-related obstructive lung disease than using the ATS criteria (FEV_1/FVC less than the LLN).
  - Adults who met the GOLD criteria but not the ATS criteria (FEV_1/FVC less than 70% but greater than the LLN) had greater risk of COPD-related hospitalization (hazard ratio = 2.6; 95% confidence interval, 2.0 to 3.3) and mortality (hazard ratio = 1.3; 95% confidence interval, 1.1 to 1.5).
- Another cohort study looking at adults 65 years and older found that, compared with the ATS criteria, the GOLD criteria had higher clinical agreement with an expert panel diagnosis for COPD and better identified patients with clinically relevant events (e.g., COPD exacerbation, hospitalization, mortality).
- Until better criteria for the diagnosis of COPD are found, physicians should use the **GOLD criteria to diagnose obstructive lung disease in patients 65 years and older with respiratory symptoms who are at risk of COPD (i.e., current or previous smoker)**.
- Other studies have found that using the GOLD criteria can miss up to 50% of young adults with obstructive lung disease and leads to overdiagnosis in healthy non-smokers.
- Based on these studies, physicians should use the **ATS criteria to diagnose obstructive lung disease in patients younger than 65 years regardless of smoking status, and in nonsmokers who are 65 years and older.**

Summary of the usage of reference values

Item

Reference values

General

Predicted values should be obtained from studies of ‘‘normal’’ or ‘‘healthy’’ subjects with the same anthropometric (e.g. sex, age and height) and ethnic characteristics of the patient being tested.

Height and weight should be measured for each patient at the time of testing

If possible, all parameters should be taken from the same reference source

When comparing selected reference equations with measurements performed on a sample of healthy subjects in a laboratory, it is suggested to choose the reference equation that provides the sum of residuals (observed – predicted computed for each adult subject, or log observed – log predicted for each subject in the paediatric age range) closest to zero

When using a set of reference equations, extrapolation beyond the size and age of the investigated subjects should be avoided

For each lung function index, values below the 5th percentile of the frequency distribution of values measured in the reference population are considered to be below the expected ‘‘normal range’’

Spirometry

In the USA, ethnically appropriate NHANES III reference equations published in 1999 for those aged 8–80 yrs, and the equations of WANG et al. [29] for children aged 8 yrs are recommended

In Europe, the ECCS combined reference equations published in 1993 [8] are often used for 18–70-yr-old people, and those from QUANJER et al. [30] for paediatric ages.

Currently, a specific set of equations is not recommendable for use in Europe. A new Europe-wide study to derive updated reference equations for lung function is needed Table 1 includes reference equations published from 1995 to August 2004

Lung volumes

No specific set of equations can be recommended

In practice, many USA and European laboratories use the reference equations for TLC, FRC and RV recommended by the 1995 ATS/ERS workshop [7] or by the ECCS in 1993 [8]

Diffusing capacity

No specific set of equations is generally recommended

Commonly used equations appear to be those by the ECCS in 1993 [38] and those of CRAPO and MORRIS [40].

In Europe, equations from COTES et al. [41], PAOLETTI et al. [42] and ROCA et al. [43] are also used

Step 2: Determine If the FVC Is Low

- An FVC less than the LLN for adults or less than 80% of predicted for those five to 18 years of age, indicates a restrictive pattern

- A restrictive pattern can indicate restrictive lung disease, a mixed pattern (if a patient has an obstructive defect and a restrictive pattern), or pure obstructive lung disease with air trapping

Pulmonary Function Test Interpretation

Test results based on age		*Suggested diagnosis*
FVC	*FEV1/FVC ratio**	
5 to 18 years: ≥ 80% Adults: ≥ LLN	5 to 18 years: ≥ 85% Adults: ≥ LLN or ≥ 70%	Normal
5 to 18 years: ≥ 80% Adults: ≥ LLN	5 to 18 years: < 85% Adults: < LLN or < 70%	Obstructive defect
5 to 18 years: < 80% Adults: < LLN	5 to 18 years: ≥ 85% Adults: ≥ LLN or ≥ 70%	Restrictive pattern
5 to 18 years: < 80% Adults: < LLN	5 to 18 years: < 85% Adults: < LLN or < 70%	Mixed pattern

FEV1 = forced expiratory volume in one second; FVC = forced vital capacity; LLN = lower limit of normal (defined as below the fifth percentile of spirometry data obtained from the Third National Health and Nutrition Examination Survey).

—The 70% criteria should be used only for patients 65 years and older who have respiratory symptoms and are at risk of chronic obstructive pulmonary disease (i.e., current or previous smoker)

Step 3: Confirm the Restrictive Pattern

- If the patient's initial PFT results indicate a restrictive pattern or a mixed pattern that is not corrected with bronchodilators, the patient should be referred for full PFTs with DLCO testing

- DLCO is a quantitative measurement of gas transfer in the lungs

- Diseases that decrease blood flow to the lungs or damage alveoli will cause less efficient gas exchange, resulting in a lower DLCO measurement

Step 4: Grade the Severity of the Abnormality

- If an obstructive defect, a restrictive pattern, or a mixed pattern is present, as defined by steps 1 and 2, the physician should grade the severity of the abnormality based on the FEV1 percentage of predicted

Table 3. American Thoracic Society Grades for Severity of a Pulmonary Function Test Abnormality

Severity	*FEV1 percentage of predicted*
Mild	> 70
Moderate	60 to 69
Moderately severe	50 to 59
Severe	35 to 49
Very severe	< 35

FEV1 = forced expiratory volume in one second.

Adapted with permission from Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. Eur Respir J. *2005; 26(5):957.*

Step 5: Determine Reversibility of the Obstructive Defect

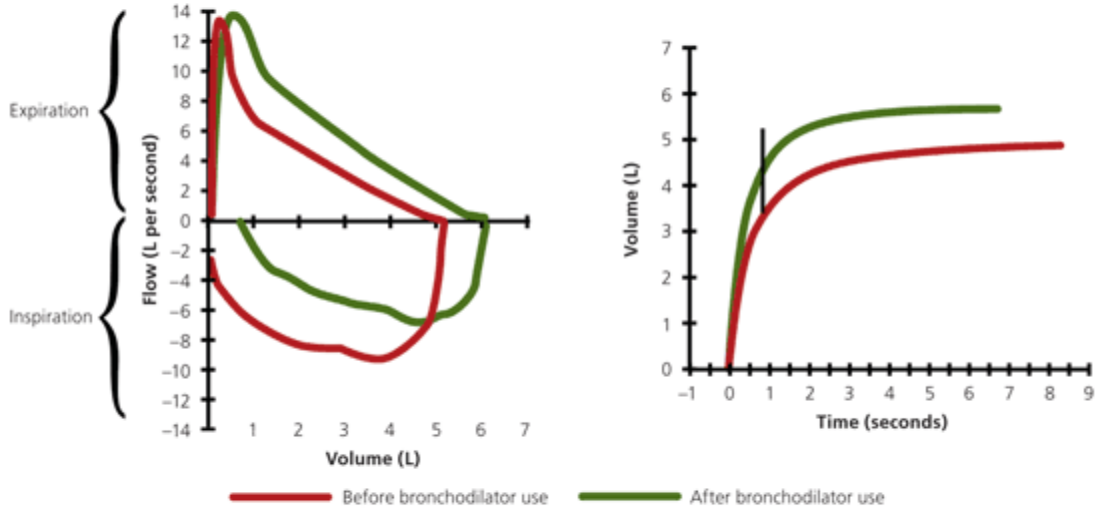
- Is defect reversible based on the increase in FEV1 or FVC after administration of a bronchodilator
  - Increase of more than12% in patients five to 18 years of age
  - More than 12% and more than 200 ml in adults

- Obstructive defects in asthma are usually fully reversible, whereas defects in COPD are not fully reversible

- If PFTs show a mixed pattern, and FVC corrects to ≥80% patients five to 18 or to the LLN or more in adults, patient is likely to have pure obstructive lung disease with air trapping

Age: 26 years **Height:** 5 ft, 8 in **Weight:** 197 lb **Sex:** Male **Race:** Hispanic

	Prebronchodilators				*Postbronchodilators*		
Spirometry	*Predicted*	*LLN*	*Actual*	*% of predicted*	*Actual*	*% of predicted*	*% change*
FVC (L)	5.20	4.34	5.18[A]	99[D]	6.06[F]	116	+16[I]
FEV_1 (L)	4.37	3.64	3.55[B]	81[E]	4.64[G]	106	+30[J]
FEV_1/FVC (%)	84	75	68[C]	81	77[H]	91	+11
$FEF_{25\%-75\%}$ (L per second)	4.74	3.11	2.41	50	3.84	80	+59



A = FVC (before bronchodilators), this is > LLN and thus does not show a restrictive pattern
B = FEV_1 (before bronchodilators)
C = FEV_1/FVC ratio (before bronchodilators), this is < LLN and thus shows an obstructive defect
D = FVC percentage of predicted (before bronchodilators)
E = FEV_1 percentage of predicted (before bronchodilators)
F = FVC (after bronchodilators)
G = FEV_1 (after bronchodilators)
H = FEV_1/FVC ratio (after bronchodilators)
I = A 0.88-L increase in FVC is a 16% increase
J = A 1.09-L increase in FEV_1 is a 30% increase

The above indicates reversibility because at least one of the two (FVC or FEV_1) increased by at least 0.2 L and by at least 12%

Step 6: Bronchoprovication

- If PFT results are normal but exercise or allergen-induced asthma is suspected consider bronchoprovocation
  - Methacholine (Positive response = Greater than 20% fall in FEV1 at or before administration of 4 mg per ml of inhaled methacholine)
  - Mannitol
  - Exercise testing
  - Eucapnic voluntary hyperpnea
- If FEV1 is <70%, trial of a bronchodilator may be considered

Step 7: Establish the Differential Diagnosis

Obstructive Disease

- **Airflow limitation**
- **Increased lung volumes with air trapping**
- **Normal or increased compliance**

Restrictive Disease

- **Reduced lung volumes**
- **Increase in overall stiffness of lungs (decreased compliance)**

Common Obstructive Lung Diseases

- Asthma
- Asthmatic bronchitis
- Chronic obstructive bronchitis
- Chronic obstructive pulmonary disease (includes asthma, asthmatic bronchitis, chronic bronchitis, emphysema, overlap syndrome)

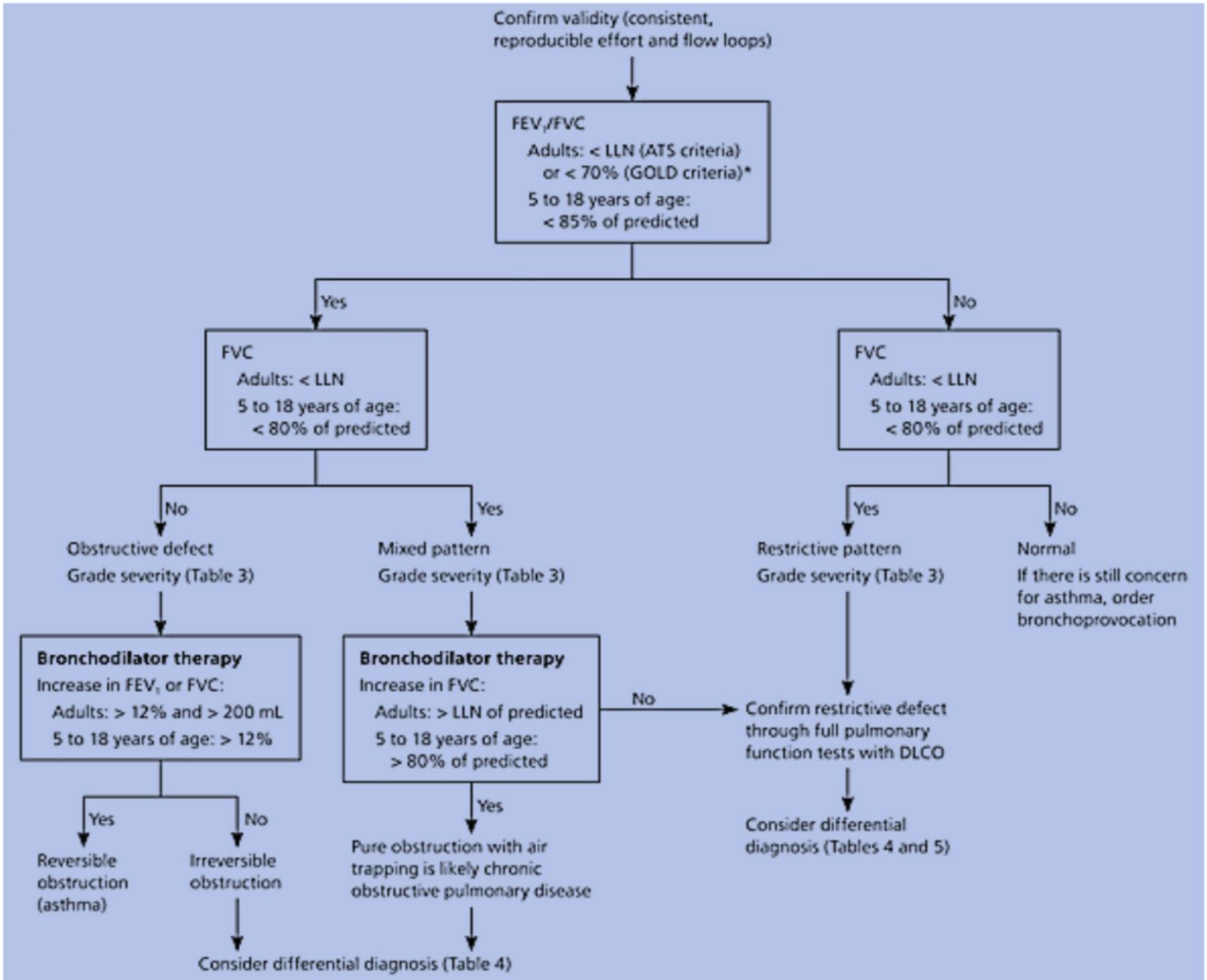
Common Restrictive Lung Diseases

- Beryllium disease
- Congestive heart failure
- Idiopathic pulmonary fibrosis
- Infectious inflammation (histoplasmosis, mycobacterium infection)
- Interstitial pneumonitis
- Neuromuscular diseases
- Sarcoidosis
- Thoracic deformities

Differential Diagnosis Based on DLCO Results

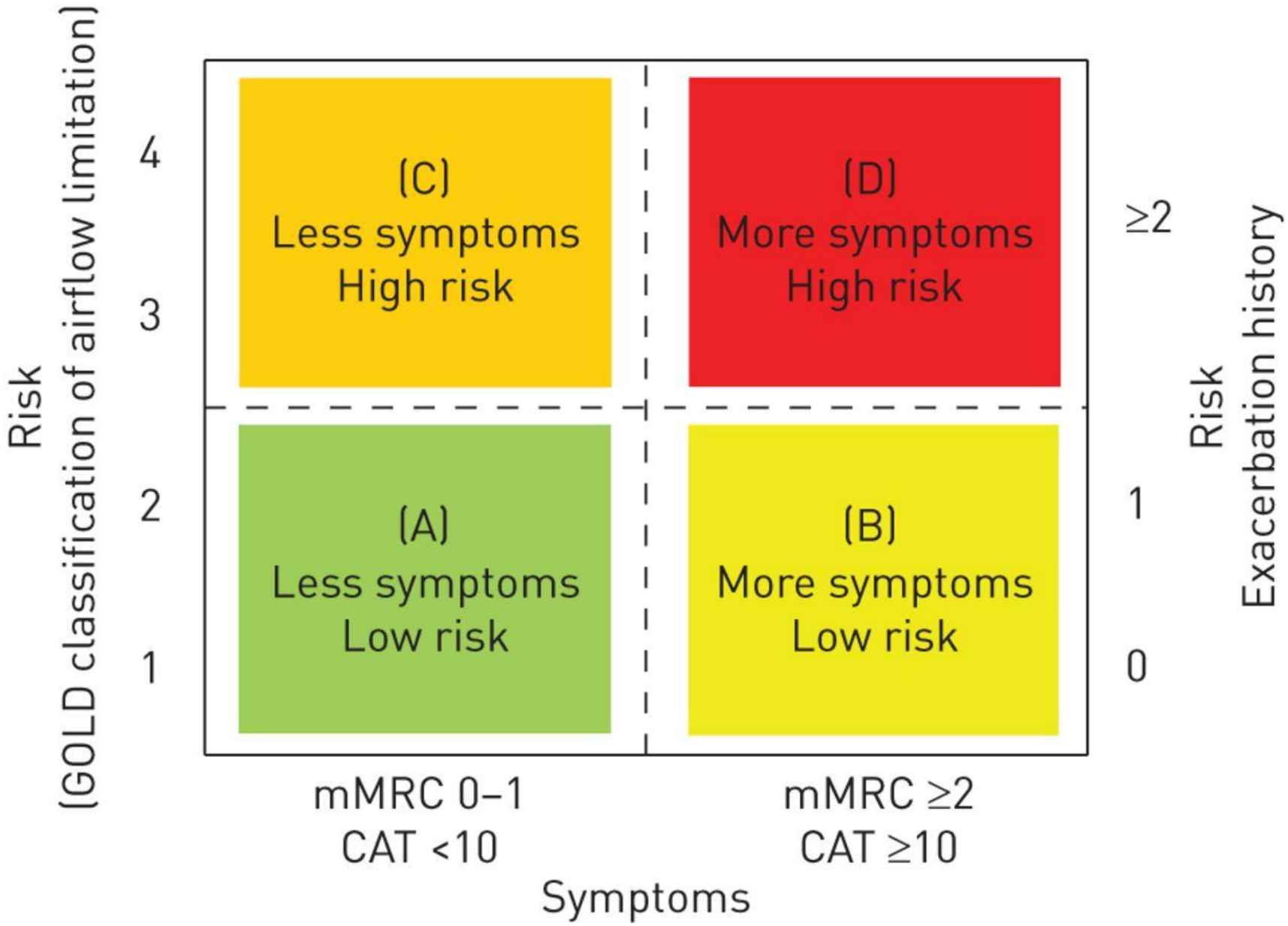
DLCO results	*Differential diagnosis*
High DLCO	Asthma, left-to-right intracardiac shunts, polycythemia, pulmonary hemorrhage
Normal DLCO with restrictive pattern	Kyphoscoliosis, morbid obesity, neuromuscular weakness, pleural effusion
Normal DLCO with obstructive component	α1-antitrypsin deficiency, asthma, bronchiectasis, chronic bronchitis
Low DLCO with restriction	Asbestosis, berylliosis, hypersensitivity pneumonitis, idiopathic pulmonary fibrosis, Langerhans cell histiocytosis (histiocytosis X), lymphangitic spread of tumor, miliary tuberculosis, sarcoidosis, silicosis (late)
Low DLCO with obstruction	Cystic fibrosis, emphysema, silicosis (early)
Low DLCO with normal pulmonary function test results	Chronic pulmonary emboli, congestive heart failure, connective tissue disease with pulmonary involvement, dermatomyositis/polymyositis, inflammatory bowel disease, interstitial lung disease (early), primary pulmonary hypertension, rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, Wegener granulomatosis (also called granulomatosis with polyangiitis)

Interpretation: High = greater than 120% of predicted; Normal = LLN to 120% of predicted; Low (mild decrease) = greater than 60% of predicted and less than LLN; Low (moderate decrease) = 40% to 60% of predicted; Low (severe decrease) = less than 40% of predicted. If the laboratory does not report LLN, observational studies indicate that the LLN for men is approximately 80%, and the LLN for women is approximately 76%[11]



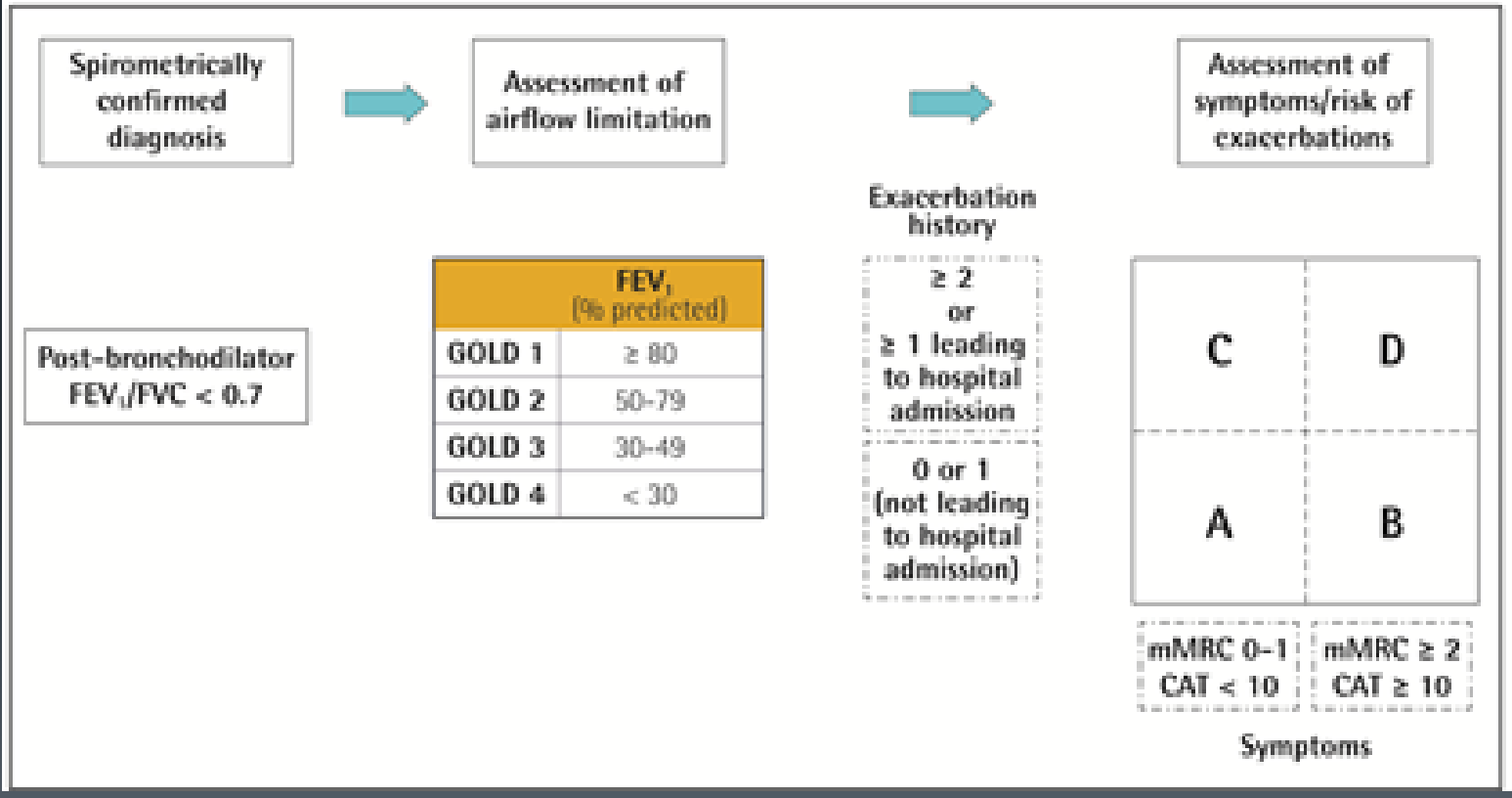
NOTE: *A tool to calculate the LLN in adults up to 75 years of age is available at http://hankconsulting.com/RefCal.html.*

**—The 70% criteria should be used only for patients 65 years and older who have respiratory symptoms and are at risk of chronic obstructive pulmonary disease (i.e., current or previous smoker).*


Risk
(GOLD classification of airflow limitation)
4
3
2
1
(C)
Less symptoms
High risk
(D)
More symptoms
High risk
(A)
Less symptoms
Low risk
(B)
More symptoms
Low risk
≥2
1
0
Risk
Exacerbation history
mMRC 0–1
CAT <10
mMRC ≥2
CAT ≥10
Symptoms

ABCD Assessment Tool

Figure 2.4. The refined ABCD assessment tool



ABCD Assessment Tool

Example

- Consider two patients:
  - Both patients with FEV_1 < 30% of predicted
  - Both with CAT scores of 18
  - But, one with 0 exacerbations in the past year and the other with 3 exacerbations in the past year.

- Both would have been labelled GOLD D in the prior classification scheme.
- With the new proposed scheme, the subject with 3 exacerbations in the past year would be labelled GOLD grade 4, group D.
- The other patient, who has had no exacerbations, would be classified as GOLD grade 4, group B.

Choice of thresholds

- COPD Assessment Test (CAT ™)
- Chronic Respiratory Questionnaire (CCQ®)
- St George's Respiratory Questionnaire (SGRQ)
- Chronic Respiratory Questionnaire (CRQ)
- Modified Medical Research Council (mMRC) questionnaire

Figure 2.3. CAT Assessment

For each item below, place a mark (✗) in the box that best describes you currently. Be sure to only select one response for each question.

			SCORE
Example:	I am very happy	(0) (✗) (2) (3) (4) (5) I am very sad	
I never cough	(0) (1) (2) (3) (4) (5)	I cough all the time	
I have no phlegm (mucus) in my chest at all	(0) (1) (2) (3) (4) (5)	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	(0) (1) (2) (3) (4) (5)	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	(0) (1) (2) (3) (4) (5)	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	(0) (1) (2) (3) (4) (5)	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	(0) (1) (2) (3) (4) (5)	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	(0) (1) (2) (3) (4) (5)	I don't sleep soundly because of my lung condition	
I have lots of energy	(0) (1) (2) (3) (4) (5)	I have no energy at all	
		TOTAL SCORE	

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

Table 2.5. Modified MRC dyspnea scale[a]

PLEASE TICK IN THE BOX THAT APPLIES TO YOU (ONE BOX ONLY) (Grades 0–4)	
mMRC Grade 0. I only get breathless with strenuous exercise.	❑
mMRC Grade 1. I get short of breath when hurrying on the level or walking up a slight hill.	❑
mMRC Grade 2. I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	❑
mMRC Grade 3. I stop for breath after walking about 100 meters or after a few minutes on the level.	❑
mMRC Grade 4. I am too breathless to leave the house or I am breathless when dressing or undressing.	❑

[a] Fletcher CM. BMJ 1960; 2: 1662.

1. 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.
2. National Asthma Education and Prevention Program. Expert Panel Report 3 (EPR-3): Guidelines for the diagnosis and management of asthma—summary report 2007 [published correction appears in *J Allergy Clin Immunol.* 2008;121(6):1330]. *J Allergy Clin Immunol*. 2007;120(5 suppl):S94-S138.
3. Vesbo J, Hurd SS, Agustí AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med.* 2013; 187(4):347-365.
4. Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. *Eur Respir J*. 2005;26(5):948-968.
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6. Güder G, Brenner S, Angermann CE, et al. GOLD or lower limit of normal definition? A comparison with expert-based diagnosis of chronic obstructive pulmonary disease in a prospective cohort-study. *Respir Res.* 2012;13(1):13
7. Hansen JE, Sun XG, Wasserman K. Spirometric criteria for airway obstruction: use percentage of FEV1/FVC ratio below the fifth percentile, not < 70%. *Chest*. 2007;131(2):349-355

8. Hansen JE, Sun XG, Wasserman K. Spirometric criteria for airway obstruction: use percentage of FEV1/FVC ratio below the fifth percentile, not < 70%. *Chest*. 2007;131(2):349-355
9. Swanney MP, Ruppel G, Enright PL, 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
10. Crapo RO, Forster RE II. Carbon monoxide diffusing capacity. *Clin Chest Med*. 1989;10(2):187-198.
11. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2017 Report. www.GOLDCOPD.org

Table 2.3. Considerations in performing spirometry
Preparation
• Spirometers need calibration on a regular basis.
• Spirometers should produce hard copy or have a digital display of the expiratory curve to permit detection of technical errors or have an automatic prompt to identify an unsatisfactory test and the reason for it.
• The supervisor of the test needs training in optimal technique and quality performance.
• Maximal patient effort in performing the test is required to avoid underestimation of values and hence errors in diagnosis and management.
Bronchodilation
• Possible dosage protocols are 400 mcg short-acting beta$_2$-agonist, 160 mcg short-acting anticholinergic, or the two combined.[a] FEV_1 should be measured 10-15 minutes after a short-acting beta$_2$-agonist is given, or 30-45 minutes after a short-acting anticholinergic or a combination of both classes of drugs.
Performance
• Spirometry should be performed using techniques that meet published standards.[b]
• The expiratory volume/time traces should be smooth and free from irregularities. The pause between inspiration and expiration should be < 1 second.
• The recording should go on long enough for a volume plateau to be reached, which may take more than 15 seconds in severe disease.
• Both FVC and FEV_1 should be the largest value obtained from any of three technically satisfactory curves and the FVC and FEV_1 values in these three curves should vary by no more than 5% or 150 ml, whichever is greater.
• The FEV_1/FVC ratio should be taken from the technically acceptable curve with the largest sum of FVC and FEV_1.
Evaluation
• Spirometry measurements are evaluated by comparison of the results with appropriate reference values based on age, height, sex, and race.
• The presence of a postbronchodilator FEV_1/FVC < 0.70 confirms the presence of airflow limitation.

[a] Pellegrino et al. Eur Respir J 2005; 26(5): 948-68;

[b] Miller et al. Eur Respir J 2005; 26(2): 319-38.