regards his or her disease status disabling is an example of subjective stressor. Therefore, those who perceive their present illness condition as more disabling have a tendency to amplify the stressor experience and this can lead to higher severity of depression in these subjects as reflected by the current study as well as other past studies.

Conclusions

The findings of the present study suggest that every asthma patient should be evaluated for depression as it is a common co-morbid condition. Co-existence of asthma and depression increases the severity of each other. Presence of depression in a patient with bronchial asthma leads to poor asthma control and quality of life. Early diagnosis and management of depression in asthma patients will break this vicious cycle and will lead to better outcome of both the diseases. It will also reduce social burden and economic burden in a developing country like India. Therefore, evaluation and management of depression as a co-morbidity should be incorporated in every asthma management guidelines.

Our study has some limitations. As the study was done in a single tertiary care institution, the results might not be generalisable to other places. Being an observational study, it limits the ability to conclude the definite causative relationship between asthma control and depression. The study was done with a relatively smaller cohort of patients. Study duration was one year and we could make only one follow-up after three months. The present investigators suggest a bigger cohort of asthma patients with a longer follow-up to explore such questions.

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Review Article

Interpretation of Spirometry: Selection of Predicted Values and Defining Abnormality

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Abstract

Spirometry is the most frequently performed investigation to evaluate pulmonary function. It provides clinically useful information on the mechanical properties of the lung and the thoracic cage and aids in taking management-related decisions in a wide spectrum of diseases and disorders. Few measurements in medicine are so dependent on factors related to equipment, operator and the patient. Good spirometry requires quality assured measurements and a systematic approach to interpretation. Standard guidelines on the technical aspects of equipment and their calibration as well as the test procedure have been developed and revised from time-to-time. Strict compliance with standardisation guidelines ensures quality control. Interpretation of spirometry data is based only on two basic measurements — the forced vital capacity (FVC) and the forced expiratory volume in 1 second (FEV_1) and their ratio, FEV_1/FVC. A meaningful and clinically useful interpretation of the measured data requires a systematic approach and consideration of several important issues. Central to interpretation is the understanding of the development and application of prediction equations. Selection of prediction equations that are appropriate for the ethnic origin of the patient is vital to avoid erroneous interpretation. Defining abnormal values is a debatable but critical aspect of spirometry. A statistically valid definition of the lower limits of normal has been advocated as the better method over the more commonly used approach of defining abnormality as a fixed percentage of the predicted value. Spirometry rarely provides a specific diagnosis. Examination of the flow-volume curve and the measured data provides information to define patterns of ventilatory impairment. Spirometry must be interpreted in conjunction with clinical information including results of other investigations. **[Indian J Chest Dis Allied Sci 2015;57:91-105]**

Key words: Pulmonary function, Spirometry, Normals, Prediction equations.

Introduction

Spirometry is by far the most frequently performed investigation to evaluate pulmonary function. It provides clinically useful information for management-related decisions in a wide spectrum of diseases and disorders, ranging from those of the airways and parenchyma to pleura and the chest wall. A physician may order spirometry for any of the several indications including evaluation of functional impairment, confirmation of diagnosis, assessment of therapeutic response, monitoring for lung damage in persons engaged in potentially harmful occupations or on certain drugs, pre-operative assessment as well as for following the natural history of diseases. It also finds application in studies on public health as well as in settling legal claims for lung injuries. Being non-invasive and affordable, and almost entirely without any adverse consequences, it may be repeated as often as necessary. An overwhelming majority of patients with chest diseases require only spirometry and only a small proportion of patients have an indication for other tests including measurement of airway resistance, lung volumes and diffusion capacity.

The utility of spirometry as an invaluable aid in the management of several diseases is well-established and its application improves the standard of care. Yet, it remains under-utilised especially at the primary and secondary levels of health-care and even in non-pulmonary tertiary care centers. This is largely due to an almost negligible exposure at the undergraduate level and inadequate training at the postgraduate level of medical education even in pulmonary medicine, a dearth of trained medical personnel in lung function testing as well as the existence of very few training centers and courses for technicians. This lends it an unjustified aura of a difficult science to understand and a complex technique to master. The above barriers to its wider use notwithstanding, its undeniable value in management of chest diseases makes it imperative for a physician, especially a pulmonologist to understand the science and the art underlying spirometry.

Few measurements in medicine are so dependent on factors related to equipment, operator and the patient. In addition, few measurements in medicine have the kind of inherent variability and uncertainty in accuracy that characterises spirometry and other lung function tests. The technical aspects of equipment and the performance of the test require a very meticulous attention to ensure quality control and to limit inter-

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and intra-laboratory differences. These aspects have been well-standardised and revised from time-to-time. Beginning with the Snowbird workshop in 1977, several statements on standardisation of methodology and guidelines on test performance and quality control have been published and revised.[1-5] These guidelines have been developed with the objective to promote quality-assurance in spirometry and to ensure a uniform approach so that inter-laboratory differences are minimised. These guidelines have dealt extensively with issues related to equipment selection, maintenance and calibration, test performance as well as interpretation. Criteria for acceptable and repeatable maneuvers have been described. These have also set technical standards for manufacturers of lung function equipment. The latest effort on standardisation of spirometry published in 2005 by the task force of the American Thoracic Society (ATS) and the European Respiratory Society (ERS).[5] The medical directors of lung function laboratories must be familiar with these guidelines so that quality control can be ensured and deviations can be minimised to avoid errors in measurements and interpretation. A trained technician is essential to maintain the equipment and supervise the test. This review assumes that spirometry has been carried out with full quality assurance of equipment selection and calibration and meets the acceptability criteria and repeatability criteria as described in the standardised methodology guidelines[5] and shown in table 1. It focuses on the next step, i.e. interpretation.

Interpretation of spirometry data is more than a straight-forward and simple matter of reading the printed report. Apart from knowledge of the pathophysiology of lung diseases, it also requires a reasonable familiarity with the science of statistics. Central to interpretation is the understanding of several issues related to the development and application of prediction equations. Interpretation of measured spirometric parameters involves a comparison with normal values. Defining what is abnormal is itself a debatable issue. Interpretation further requires a comparison with any previous test as well as a comparison with known patterns of abnormality.

Prediction Equations

Whether the measured value of a biological parameter is normal or abnormal requires a comparison with values in the population in people who are considered 'healthy'. In most instances, this normal range, for example of blood urea, is universal, i.e. similar in all populations irrespective of ethnicity and gender, and usually over a broad age range. However, lung function parameters are unique as there is no constant or single 'normal' value or range. These parameters vary among different populations globally and by gender and other factors and even in an individual with every year of age and changing anthropometric characteristics. Thus, every person will have a different 'normal' or expected value and that too is not fixed or constant but ever-changing with growth and aging.

For each lung function parameter, the expected normal value is calculated using 'prediction' or 'regression' or 'reference' equations that take into account the known and unknown predictors or determinants of the parameter of interest. These equations are developed by studying lung function of a large sample of carefully selected and well-defined 'normal' subjects. The criteria for normalcy are rigid to exclude diseased individuals.[6] Once a subject is selected after application of inclusion criteria for normalcy, he/she should not be excluded if the measured values are subsequently found to be lower than what one expects. Otherwise, a bias shifting the normal values upwards will creep in. Usually, only

Table 1. Acceptability and repeatability criteria for spirometry

Criteria for Acceptability
Maneuver performed with maximal effort, starting instantaneously from the level of maximum inspiration, with the effort sustained until the end of the expiration without early termination or cut-off
Lack of artifacts induced by coughing in the initial 1 second, obstruction by tongue, glottic closure, extra breaths or equipment problems (e.g. leak)
Satisfactory instantaneous start to the test without hesitation (back extrapolation volume ≤150mL or 5% of FVC whichever is greater) with quick rise and sharp peak
Satisfactory end-of-test
Exhalation with 6 seconds of smooth continuous exhalation (3-4 s in children) and/or
a plateau (change <25 mL) in the volume time curve of at least one second
when the subject cannot or should not exhale (signs of distress, syncope)
Criteria for Repeatability
Largest FVC within 0.15L of the next largest FVC
Largest FEV_1 within 0.15L of the next largest FEV_1

Adapted from ATS update[4] and Miller *et al*[5]
Definitions of abbreviations: FVC=Forced vital capacity; FEV_1=Forced expiratory volume in 1 second; ATS=American Thoracic Society

non-smokers are included. In studies such as the United States National Health and Nutritional Examination Survey III (NHANES III), the sample of normal subjects was selected from the whole population.[7] This may, however, be difficult for logistic and operational reasons in most populations. Therefore, more often, normal subjects are selected from volunteers who are considered to be 'representative' of the population. This method is acceptable as an alternative to random population sampling so far as the selection criteria and the distribution of anthropometric characteristics remain adequate.[5] Van Ganser *et al*[8] observed that for lung function measurements, the method of selection does not impact mean values or their ranges. For the development of regression equations, a minimum sample size of 150 men and 150 women has been recommended.[6] Prediction models for a parameter are then developed using standard statistical techniques of multivariate regression analysis. Prediction equations have been developed in several countries from time-to-time and also been revised with changes in the methodology. These include equations for Caucasians[7,9,10], African-Americans[7,11,12] and Asians[13,14] besides others. Many of these equations are incorporated in the spirometry softwares providing the user an option to select an appropriate one.

Some studies have pooled data from similar populations to develop equations with a larger sample size. One of the most widely used set of equations, that of the European Community for Steel and Coal, were developed with such an approach.[15] The Global Lungs Initiative (GLI), commissioned by the ERS, is a unique effort to develop reference equations applicable to all ages for major ethnic groups all across the globe by re-analysis of pooled data from several already published or completed studies carried out from time to time.[16]

In India, most of the available equations in children and adults were developed in different regions several decades back using protocols that have since been revised and with equipment that has undergone substantial technological changes and automation.[17-28] These studies have varied in sample size, instrumentation, data analysis and results. Their current validity may be further questionable as the lung health of the population is likely to have changed over time. These older equations may be of limited utility now.

Nevertheless, the Indian studies have provided some information on lung function in children and adults, and their determinants. In children, in general, boys have been found to have larger vital capacities and height is the most important determinant with variable contribution from age, weight and sometimes, other physical measurements. These observations are consistent with those in studies in the pediatric age groups in other populations.[29,30] Similarly, in adults, males have been found to have greater vital capacities than females. In general, lung function parameters have a positive correlation with height and negative with age. Usually, the contribution of weight is very small. These observations also corroborate those reported in adults from other countries.[7,9-16]

Recently, regression equations for spirometry variables for children of north Indian plains have been developed using the 2005 ATS/ERS spirometry standardisation protocol. The linear models that are simple to use were published in a brief communication.[31] Better fitting but more complex equations have also been developed for 6 to 17 years old north Indian children and are under publication. Similarly, validated prediction equations for spirometry variables in adults of north Indian plains have also been published recently using the current standardised methodology.[32] These equations suggest an improvement in the lung health of the population in the middle-aged and the elderly compared to that about five decades ago. In another study, prediction equations have been developed for adult Kashmiri population in India.[33] These recently developed equations in adult north Indian subjects in the plains are presented in table 2. The most commonly used equations for Caucasians (NHANES III) are also shown.

Statistical Issues in the Development of Prediction Equations

The parameter to be predicted is called the 'dependent' variable while the variables that significantly influence and determine its values are called the 'independent' variables. The forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), their ratio and flow rates are the dependent variables. The linear or straight line model of prediction equation shown below has been most often used:

FVC = constant + coefficient x age + coefficient x height

The constant and the coefficients of the independent variables are derived from the regression analysis usually by the least squares method. Entering the age and height into the equation provides the value of the FVC in the above example. A residual standard deviation (RSD) or the standard error of estimate (SEE) are also reported with the equation to provide information about the scatter of data points around the predicted value. The conditions and assumptions of the regression analysis must be satisfied. Usually, several variations of the model including transformations, such as logarithmic of the dependent or the independent variables to achieve linearisation as well as non-linear models are examined to obtain one that best fits the data and predicts the dependent variable. The relationship between the dependent variable (Y) and the independent variable (X) may be logarithmic curve ($Y = a + b\ \mathrm{Log}(X)$), exponential curve

Table 2. Prediction equations for major spirometry parameters for North Indians and Caucasians

Authors and Population	Parameter	Equation	SEE
Chhabra *et al* 2014[32] North Indian plains	*Males*		
	FVC	-5.048-0.014×age+0.054×ht+0.006×wt	0.479
	FEV_1	-3.682-0.024×age+0.046×ht	0.402
	FEV_1/FVC	74.866-0.233×age+0.107×ht-0.075×wt	5.58
	Females		
	FVC	20.07-0.010×age-0.261×ht+0.000972×ht^2	0.315
	FEV_1	-2.267-0.019×age+0.033×ht	0.286
	FEV_1/FVC	73.539-0.330×age+0.151×ht-0.074×wt	5.08
Hankinson *et al* 1999[7] Caucasians NHANES III	*Males*		
	FVC	-0.1933+ 0.00064×age-0.000269×age^2+0.00018642×ht2 (use 0.00015695×ht^2 to compute LLN)	
	FEV_1	0.5536- 0.01303×age-0.000172×age^2+0.00014098×ht^2 (use 0.00011607×ht^2 to compute LLN)	
	FEV_1/FVC	88.066-0.2066×age (use 78.388 as constant to compute LLN)	
	Females		
	FVC	-0.3560+0.1870×age-0.000382×age^2+0.00014815×ht2 (use 0.00012198×ht^2 to compute LLN)	
	FEV_1	0.4333-0.00361×age-0.000194×age^2+0.00011496×ht^2 (use 0.000009283×ht^2 to compute LLN)	
	FEV_1/FVC	90.107-0.1563×age (use 81.307 as constant to compute LLN)	

Age in cm, height (Ht) in cm, weight (wt) in Kg; For Indian equations, subtract (1.645×SEE) from the predicted value to compute the LLN
Definitions of abbreviations: SEE=Standard error of estimate; FVC=Forced vital capacity; FEV_1=Forced expiratory volume in 1 second; LLN=Lower limit of normal

(Log(Y) = *a* + *b* X), geometric curve (Log(Y) = *a* + *b* Log(X)), quadratic regression (Y = *a* + *b* X + *c* X^2) or nonlinear (Y = 1/(1+exp(a+b X), where a = constant and b or c = coefficient of variable X.

Manual calculations of the spirometry parameters from such transformed or non-linear equations are difficult but conveniently done by spirometry softwares or calculators. The predictive ability of an equation is described in terms of the R^2, that is, the 'explained variance'. The selection of the best model takes into account the R^2, simplicity and ease of use of the, as well as the compliance with the requirements of the regression analysis.

Sources of Variation in Spirometry

Ethnicity

Ethnic differences in lung function were documented between African blacks and European-American whites (Caucasians) several decades back.[34-39] Such differences in lung function have also been reported in many other ethnic groups including Asians.[35,36,40] These studies have shown that generally 'whites' or Caucasians have lung volumes that are 10%–15% higher than the 'blacks', including Africans and Asians, for a given standing height. Among the possible reasons for these observations are the anthropometric differences between these ethnic groups, with whites having larger chest volumes and shorter leg length (i.e. larger trunk-to-leg ratio) at a given height.[38,41] The multi-ethnic all-age equations developed under the GLI also yield the highest FEV_1 and FVC in the Caucasians.[16]

Most of these studies evaluating pulmonary function differences between Asians or Africans and whites of European or American origin have based their conclusions on a comparison of prediction equations rather than a head-to-head comparison in a prospective study. However, methodologies used in different studies have not been uniform, and most of these studies have not defined ethnic groups adequately. There have also been variations in the definitions of health and smoking status of subjects. Testing of subjects with different equipment and testing protocols compound the ethnic diversity in lung function measurements and make quantitative comparisons difficult. Circumventing these confounding factors, direct comparison studies have also confirmed ethnic differences in lung function. Oscherwitz *et al*[35] found the highest values of FVC and FEV_1 in Europeans, intermediate values in Asians, and lowest values in blacks for the same height, age, and sex. Seltzer *et al*[36], in a population of more than 65,000 subjects (82% whites, 14% blacks, and 4% Asians), found FVC and FEV_1 to be

the highest in Europeans-Americans and lowest in blacks. In a study using the same instrument, Asian values for FVC and FEV_1 were significantly lower by 6%-7% than for Europeans.[42]

The ethnic differences are evident even in children.[41-43] This has been confirmed not only in studies comparing prediction equations but also in studies directly comparing lung function in children of different ethnic origins. In 11- to 13-year-olds from London, white children had about 11% to 13% higher FVC and FEV_1 compared to Indian children. The lowest values were observed for black Caribbean / African children, being upto 17% less.[44] Comparison of lung function between UK-born white children and UK-born South Asian children showed substantial differences in age- and height- and gender-adjusted spirometric values. The FVC and FEV_1 were lower in South Asian children by a mean of 11% and 9%, respectively. However, peak expiratory flow (PEF) and force expiratory flow at 50% vital capacity were similar. These persisted after adjustments for cultural and socio-economic factors, and intrauterine growth, and were also not explained by differences in environmental exposures or a personal or family history of wheeze. This suggests that differences in lung function may be mainly genetic in origin.[45]

The difficulty in establishing the magnitude of differences between Caucasians and Africans or Asians accurately notwithstanding, it is certain that ethnicity is a major determinant of lung function.[46] Therefore, it is now a standard practice to develop separate equations for multi-ethnic populations. The most widely used equations in the United States are based on the NHANES III data.[7] The study describes separate equations for Caucasians, African-Americans and Mexican-Americans. The GLI has published separate reference equations for Caucasians, African-Americans and North and South-East Asians.[16]

It, however, needs to be noted that ethnic differences are most consistent for FVC and FEV_1 but marginal or are not significant for FEV_1/FVC ratio and even less so for flow rates. Nevertheless, it is recommended to apply prediction equations for all spirometry parameters from the same study.

Gender

Gender is the other major independent variable that is a major source of variation in lung function.[38] Males in general have 10% to 15% higher FVC and FEV_1 compared to females of matched age and heights. On the other hand, the FEV_1/FVC ratio is usually similar or even slightly higher in females as are the expiratory flow rates apart from the peak expiratory flow rate, which again is higher in males. Thus, in each population, usually separate equations are developed for males and females.

Age

Variation of lung function with age is a well-known physiological fact of lung health. Although number of alveoli increases after birth, especially up to the age of eight years, there is further linear growth of the airway dimensions and lung surface. Thus, the FVC and FEV_1 typically increase upto 18 to 20 years and then maintain a plateau till about 40 years followed by a steady decline thereafter due to a progressive loss of elastic recoil and increasing closing volume. While the exact age at which the peak is reached and when the decline begins differs among studies, and may also differ by ethnicity and gender, the broad pattern of growth and decline is a physiological characteristic. Capturing a complex change such as this in a single all-ages equation is difficult. In most populations, therefore, separate equations have been developed for pediatric age groups[29-31] and adults.[7,9-15,17-28,32,33] Age is included in all models for spirometry variables with a positive coefficient in the pediatric age group and negative in adults. The GLI equations are unique because these have re-analysed previous studies using a generalised additive model for location, scale and shape technique (GAMLSS) and reported single equations valid for 3 to 95 years.[16]

Other Sources of Variability

Several directly measured or derived anthropometric variables may theoretically influence lung function including standing height, trunk-leg ratio, weight, body surface area, and body mass index. Among these, height explains the maximum variance. Height usually has a positive relationship with spirometry variables and is included in most equations. For some parameters, weight may improve the R^2 or the predictive capability of the equation but only marginally. Obese subjects, even if otherwise healthy are invariably excluded from the study population because it is known to reduce the FVC. Usually, inclusion of other predictors does not improve the predictive capability of the equation or only makes it more complex.

Besides these, there are several other factors that may also influence the measurements but cannot be adequately quantified, including environmental, genetic, socio-economic, and technical factors.[47] Further, there may be other biological determinants of lung health that have as yet not been identified. Finally, there is an inherent biological variability in lung function measurements. Due to factors that cannot be accounted for, most prediction equations have an explained variance that may only be 50% to 70% for some parameters or sometimes even less for others.

Unexplained variability leads to loss of accuracy and adds to the uncertainty about predictions. Therefore, prediction is a range rather than a single

predicted value. It is a standard practice to report the SEE or the residual standard deviation (RSD) along with the equations. From the SEE, the predicted range of normal values can be calculated, as explained later. The so-called predicted value is only the 50th percentile value or the median in a normal distribution. Usually, the SEE is fairly large, and thus typically, lung function parameters have a wide range of normal values around the predicted. Among spirometry parameters, FVC and FEV_1 have the least variability (even this is quite large) while the flow rates have a wider variability.

Selection of Equations

As interpretation of measured data involves a comparison with predicted values, the selection of prediction equations is a critical step in the interpretative strategy. The spirometry softwares usually offer a wide choice of prediction equations specific for different ethnicities and populations. Selection of equations requires consideration of different sources of variability in lung function as discussed above. The spirometry report should mention the equation used for interpretation. Due to well-known differences in lung function between subjects of different ethnic origins, equations developed in the population with the same ethnicity as the subject being tested must be selected. The equations also need to be gender-specific.

Ideally, the reference population should also be matched for socio-economic and environmental exposures as the subject and should have been developed using similar instruments and lung function protocols in the reference population.[48] Usually, this information is either not available for the reference population or is ignored for practical reasons and because the magnitude of variation due to these factors is not known. All parameters, i.e. the FEV_1 FVC, FEV_1 / FVC and the flow rates should come from the same reference source. An important statistical caveat is that the prediction equations may not be valid for ages and anthropometric characteristics that are beyond those of the reference population sample. That is to say, if the study sample of the reference population in which the equation was developed had an age range of up to 70 years, then the equation is strictly valid only in subjects up to this age. The same applies to height. Extrapolation beyond the range of age and height of the reference sample sometimes produces weird results, and therefore, caution is required. If a patient's age or height is outside the limits of the reference population, a statement in the interpretation should indicate that an extrapolation has been made.[49] However, this information is usually not available in the spirometry softwares.

Directors of lung function laboratories should enquire about the list of equations available in the software before buying a spirometer. The software should preferably have an editing function that allows users to add their own locally developed equations if these are not pre-loaded. With the world increasingly becoming ethnically heterogeneous, a laboratory should have in its software equations for patients with different ethnicities. This is a daunting task even for laboratories that are centers of excellence in pulmonary function testing.

Consequences of Selection of Inappropriate Equations

Selection of the right equations is a surprisingly ignored task. Use of equations that are not matched with the patient for ethnicity or gender or anthropometric characteristics will lead to substantial errors in interpretation. These errors of interpretation are likely to affect management decisions adversely. This has been documented in several studies.[50] Use of prediction equations from the European-American men consistently over-predicted FVC by 0.3 L to 0.4 L and FEV_1 by 0.15 L in Japanese in one study.[51]

In most lung function laboratories in India, Caucasian equations are used, usually because the software does not provide the option of an Indian equation. Aggarwal *et al*[52] showed that the use of Caucasian equations resulted in mis-interpretation of spirometry data in a significant proportion of patients. The Caucasian prediction equations had poor agreement with a north Indian equation in most height and age categories among both men and women. The use of Caucasian prediction equations in interpreting spirometry data in Indian patients is, therefore, neither appropriate nor advisable.

Although most Indian studies from different regions of the country,[17-30] except the recent ones,[31-33] require a re-examination of their current validity, significant regional differences have been found even among these.[53,54] Aggarwal *et al*[53] observed that north, west and south Indian reference equations did not yield equivalent results for spirometry interpretation in north Indian patients. The north and west Indian equations were discordant in 22.1% instances, and the north and south Indian equations in 12.9% instances. Most of the patients with abnormal spirometry using north Indian equations were erroneously interpreted to have normal spirometry using west or south Indian equations. Similarly, Chhabra[54] reported that, in general, old northern and eastern equations on one hand, and, western and southern equations on the other yielded closer values. The 1960s' northern Indian equation gave the highest predicted vital capacity. However, this was true only for lower values of vital capacities and at higher values, this may be less than that predicted by eastern or western equations. The regional differences imply that data of a north Indian patient should be interpreted with an equation for north Indians only. This applies similarly to other regions. The recent Indian equations presented in table 1 were developed

in north Indian subjects and are recommended for this population.

Use of Adjustment Factors

In most developing countries, barring a few, locally developed equations using standardised methodology and rigorous statistical procedures are usually not available. As a practical way out, it has been suggested that a fairly large sample of about 100 normal subjects that is representative for the local population may be tested and the equation that gives the least mean difference between the observed and the predicted values, i.e. closest to zero may be used.[48] However, few laboratories have the resources to do this.

A frequently used practice to circumvent the problem of non-availability of locally-developed equations is the application of adjustment factors with Caucasian equations.[5,6,55] As Caucasians are known to have higher vital capacity than Asians or African-Americans by 10% to 15%, a typical correction factor would be 0.85 or 0.9, i.e. the predicted FVC by the Caucasians equations is multiplied by this factor to obtain the predicted FVC for these populations. Both the ATS and American Medical Association recommend a reduction of 12% in predicted values for disability evaluation of African-Americans.[56,57] Due to absence of Asian-Americans in the NHANES III equations, a correction factor of 0.94 has been suggested while applying Caucasian equations for this population in the United States.[55]

Although this practice is popular, and has even been made available in several softwares by the manufacturers, it is a flawed concept and an over-simplification, and this can lead to substantial errors in interpretation of data. Hankinson *et al*[55] evaluating the performance of correction factors for applying NHANES III Caucasian equations to Asian-Americans have cautioned that a single correction factor may not be valid across all ages. Ip *et al*[58] have also demonstrated that the blanket application of correction factors for Asian populations may not be appropriate. Aggarwal *et al*[52] observed that using a correction factor to reduce Caucasian predicted values to 90% did not improve the agreement with the Indian equations.

If a correction or adjustment factor is used, it must be mentioned in the report. The application of correction factors is not a substitute to development of reference equations in the local populations and is best avoided.

Expression of Data and Defining Abnormality

The measured data (numerator) is most often expressed as a percentage of the predicted value (denominator). It needs to be emphasised that the predicted value calculated from the regression equation represents the 50th percentile value and though normal, is not synonymous with normal value. The usually large standard error of estimate in regression equations implies that there cannot be a single normal value. Instead, normalcy has a range. In a normally distributed data (bell-shaped, — normal or Gaussian distribution), half the sample of normal males of a particular age and height in a population will have values above, and half, below the predicted values. Values beyond this range are abnormal. For spirometry though, there is no upper limit of normal. The lower end of the normal range defines the cut-off between the normal and the abnormal. There are several methods of expressing the results and defining abnormality in spirometry. Consensus on defining the lower end of the normal range is elusive and very often convenience replaces science.

Statistically-derived Lower Limit of Normal

Conventionally, the normal ranges of physiological parameters are intended to include 90% of healthy people in the population. The 5th percentile is taken as the lower limit of normal (LLN) and the 95th percentile is taken as the upper limit of normal. For spirometry parameters, very high values are only a physiological variation and not a sign of disease. Only low values are abnormal, and therefore, the 5th percentile defines the LLN. If the data for a parameter is normally distributed, the LLN can be calculated as follows:

LLN = predicted minus (1.645 x SEE)

Thus defined, the LLN has an inherent but acceptable error of wrongly labelling values of healthy persons below the 5th percentile as abnormal, i.e. 5% false positives. If the distribution is not normal but skewed, the 5th percentile value from the distribution also defines the LLN. The 1991 guidelines of the ATS on interpretative strategies recommended that a statistically valid LLN based on the 5th percentile of the reference data of healthy population be used as the cut-off for defining abnormality.[6] The ATS-ERS Task Force statement of 2005 also recommends using the 5th percentile as the LLN to define the cut-off between normal and abnormal.[49]

Using 80% of Predicted and Fixed Values as Cut-offs

A classic example of a practice where convenience and not statistical validity has universally become acceptable as the preferred method of defining the cut-off between normal and abnormal is the use of a fixed value of 80% of predicted. This rule of thumb is firmly entrenched in clinical practice.[59] Most laboratories, software algorithms and physicians continue to define cut-offs as a fixed percentages of the predicted value. Thus, if the measured FVC is less than 80% of the predicted value, it is considered as abnormal.

This practice is not only deeply flawed but also does not have any physiological or statistical validity. The extent to which the 80% rule will deviate from the true cut-off is a function not only of the scatter but also the

steepness of the regression line. The scatter of lung function data found in healthy population is not proportional to the mean value. It is constant or homoscedastic rather than vary with the size of the values, heteroscedastic. Thus, the LLN is parallel to the regression line. On the other hand, a line representing 80% of predicted deviates from it.[60] The LLN expressed as percent predicted is dependent upon age. It is lower in the older people. In other words, the 5th percentile of FVC at 70 years is substantially lower than 80% of predicted. Thus, LLN and 80% of predicted do not equate, with the former progressively falling below 80% with increasing age.[61] This is illustrated in figure 1. The line of LLN of predicted FVC is higher than the line of 80% of predicted FVC at age 18 years (point A) and crosses the latter at around 30 years of age, so that the LLN at age 70 is lower than the 80% of FVC value (point B). This would mean that an 80% cut-off would overdiagnose a normal subject as abnormal or increase the false positives with increasing age.

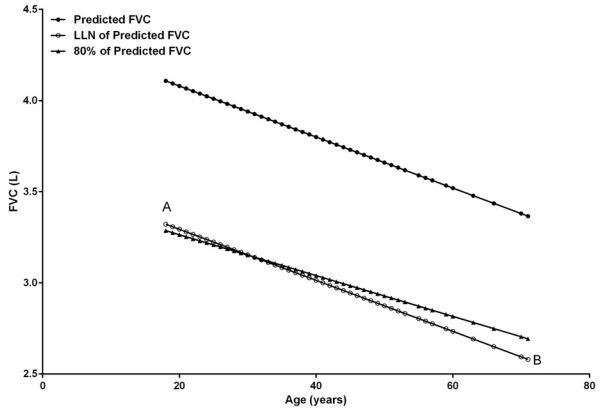

Figure 1. Graph showing lines of predicted FVC, lower limit of normal (LLN) of predicted FVC, and 80% of predicted FVC values in a male subject of height of 167 cm and weight of 67 Kg plotted against age.

Even the most widely adopted Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) guidelines for the management of COPD define airways obstruction as a fixed cut-off, i.e. a post-bronchodilator FEV_1/FVC ratio of less than 70%.[62] This recommendation is also statistically erroneous. The line representing the 70% of predicted is not parallel to the regression line for FEV_1/FVC ratio. The FEV_1/FVC ratio normally falls below 70% in the elderly. Thus, airways obstruction is over-diagnosed in the elderly with the GOLD criteria.[63,64] The ATS/ERS statement on COPD, on the other hand, recommends using the 5th percentile value of the FEV_1/FVC ratio as the cut-off to define airways obstruction.[65] The GOLD guidelines have, however, acknowledged that a fixed cut-off has been retained only for practical rather than statistically valid reasons as good quality regression equations are available only for limited populations, and therefore, it is not possible to base a diagnosis of COPD on the LLN across the globe.

The reason why a fixed percentage method of defining the cut-off is universally popular with physicians is that it is simpler to deal with a single value than to look at different LLNs for different people. However, this convenience comes at a cost of risking substantial errors in decision-making in the management. Studies have shown that the use of 80% of predicted as the cut-off between normal and abnormal leads to substantial misclassification of spirometry data, and thus, wrong management decisions. Miller *et al*[66] determined the discrepancy rates in pulmonary function test interpretation between the GOLD-percent predicted and LLN methods and found that the former could mis-diagnose more than 20% of patients referred for pulmonary function tests. They recommended using the LLN based on the 5th percentile values. Therefore, as good quality equations become available locally, abandoning the fixed cut-offs and switching to a statistically valid LLN to define abnormality is strongly recommended.

Use of Standardised Residuals

Standardised residuals (z-scores) are a validated method for expressing the deviations of lung function parameters from the mean. This method has been endorsed by the ERS for long.[49,67] Residuals are the deviation of the observed value from the predicted. A z-score is the number of standard deviations of the residuals from the mean value (i.e., predicted) in a normal distribution. The standardised residuals yield z-scores as follows:

z-score = (measured minus predicted)/standard deviation

The advantage of the z-score over the percent predicted method is that it is completely independent of age, height and sex. If the z-score for any parameter is –1.64, this signifies that the measured value is at the 5th percentile irrespective of the age and gender. Thus, a z-score of –1.64 is equal to the LLN. An advantage of the z-score is that it permits comparison of values between different populations. Further, it also quantifies the exact deviation from the predicted value even beyond the LLN. Thus, the severity of impairment can also be quantified.

However, this method has not been adopted universally probably because it appears to be too cumbersome and too 'mathematical'. Expression of data as a percentage of predicted values remains the most widely used method for expressing the results in lung function tests inspite of its limitations.

Steps in Interpretation (Table 3)

Most spirometry softwares have built-in algorithms that provide an interpretation of the measured data. Most often, these classify the patients into four

Table 3. Steps in interpretation

- Software interpretation should preferably be turned off
- Review and comment on the test quality for acceptability and repeatability criteria
- Check that the appropriate prediction equation has been selected; if not appropriate or adjustment factors are used, make a note
- Check the reporting format. Range of normal values (5^{th} to 95^{th} percentile) should be reported. Z-scores may also be printed
- Define abnormal values with a statistically valid LLN and not a fixed value, if possible
- Examine the shape of the flow volume curve and the volume-time graph for quality assurance and any obvious abnormality or pattern
- Examine the FVC, FEV_1 and FEV_1/FVC ratio for interpretation according to algorithm in figure 7 using statistically valid LLN to define abnormality
- Comment on the pattern of the ventilatory defect if abnormal (obstructive, suggestive of restrictive, mixed, large airway obstruction) and its severity
- Comment on bronchodilator responsiveness, if tested
- Answer the clinical problem for which the test was ordered
- Examine clinical data and other investigations
- Consider pre-test probability of disease
- Compare with any previous tests, if available
- Advise on further testing, if required

quadrants: normal, obstruction, restriction and mixed. Such a categorisation may be misleading as it does not take into account the normal variability as well as the fact that a reduced FVC may be due to air trapping and not necessarily be due to a parenchymal or any other restrictive disease process. Further, from a physiological perspective, a 'restrictive' label should be used only when the total lung capacity (TLC) is reduced. A reduced FVC may only suggest a restrictive process though it may also be due to air-trapping or may be a physiological variant. Physicians will often find it more rewarding when they use their own knowledge and judgment along with clinical information to arrive at a diagnostic labelling rather than use the software algorithms. Such algorithms may, however, be of some use to primary care physicians. The software usually provides an option to turn the interpretation option off. Table 3 outlines the steps in interpretation.

1. *Review and Comment on the Test Quality*

Meticulous quality control is mandatory to ensure that the patient performs the test maneuver properly and provides three acceptable efforts as defined in the ATS-ERS 2005 statement on standardisation of spirometry and shown in table 1.[5] The technician has a pivotal role in this, and therefore, needs to be trained to recognise the unacceptable efforts and discard these. Further, the repeatability criteria also need to be met. The technician should provide his own short report on the quality of performance and whether the acceptability and repeatability criteria were met. Usually the physician gets to see only the printout with the 'best' effort — one with the highest sum of FVC and FEV_1. An alternative selection method is to select the highest FVC and the highest FEV_1 even if these are from different curves.[4,5] However, reporting formats that print all the curves can also be used by the laboratory director to check conformity with the acceptability and repeatability criteria.

It needs to be pointed out that tests that do not meet the acceptability or repeatability criteria may still contain useful information. For example, patients with severe COPD may not meet the end-of-expiration criteria[5] even though they may have exhaled for 20 seconds or even longer (Figure 2). Such a sustained and forceful expiration may be dangerous as positive intra-thoracic pressure may reduce the cardiac output and cause a black-out. The technician must constantly observe the patient for any signs of distress or dizziness and if noted, terminate the expiration. Even without meeting the end-of-test acceptability criteria,

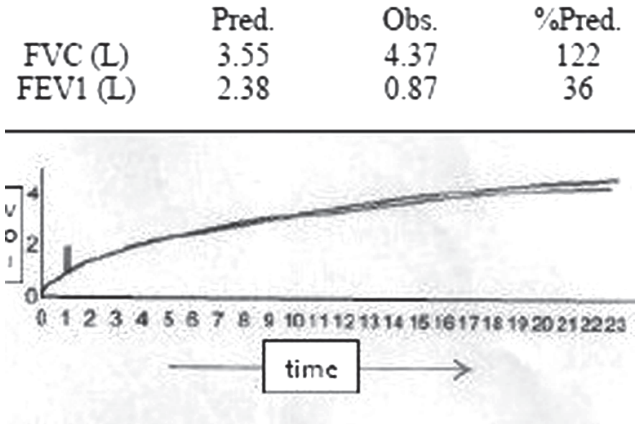

Figure 2. Forced expiratory maneuver in volume-time format showing a failure to attain the end-of-test criteria in a patient with severe COPD even after 23s.

severe airways obstruction can still be diagnosed from the shape of the curve and the data. Many patients with asthma develop bronchospasm with deep inspiration,[68] and therefore, each successive effort may yield progressively lower values of FVC and FEV_1 and thus, repeatability criteria may not be met. Patients with severe pulmonary fibrosis as occurs in advanced idiopathic pulmonary fibrosis (IPF) may complete their expiration much sooner than 6 seconds, and thus, not meet these criteria for end-of-test. In such instances, useful information about the nature and the severity of the ventilatory defect can still be salvaged. However, the physician should make a note about the failure to meet the acceptability or repeatability criteria.

2. *Select Appropriate Prediction Equation*

The importance of selecting appropriate prediction equations was discussed in detail earlier. These should be matched for ethnicity, gender and should be valid for the patient's age and anthropometric characteristics. The prediction equation selected must be clearly mentioned in the report. If equations for the patient's ethnicity are not available, a note must be made warning the physician of a possible error in classification of the ventilatory defect. If any adjustment or correction factors are used, a note must be made. Usually, prediction equations can be changed if required even after the test.

3. *Check the Reporting Format*

Usually, the observed values, predicted values and observed values expressed as percent predicted are displayed in the print-outs. It is desirable that the range of normal values (5^{th} to 95^{th} percentile) should also be presented so that a statistically valid LLN can be used to determine abnormal values. Some manufacturers also provide the z-scores. Figure 3 shows a printout with a preferred format of a report in a patient with IPF. Usually, manufacturers offer a choice of several print formats.

4. *Examine the Shape of the Flow-Volume Curve*

An examination of the shape of the flow-volume curve and the volume-time graph is very informative and recommended before one looks at the data. The graphic print-outs, besides allowing evaluation of quality control for acceptability criteria, also provide a quick insight into the type of abnormality. A triangular expiratory limb that runs close and parallel to the predicted curve suggests a normal spirometry (Figure 4). A quick rise and fall of the expiratory limb suggests a restrictive disease process (Figure 5).

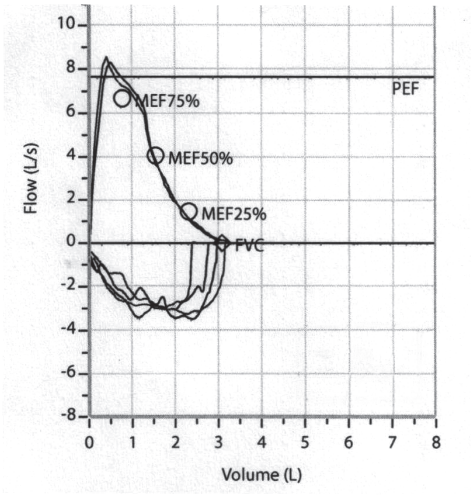

Figure 4. A maximal flow-volume curve showing the characteristic shape in a normal subject.

A concavity in the expiratory limb marks an obstructive defect with its depth increasing with increasing severity (Figure 6). A variable intra-thoracic obstruction produces a flattening of the expiratory limb, a variable extra-thoracic obstruction produces a flattening of the inspiratory limb while a fixed obstruction produces a flattening of both the limbs (Figure 7).

		PRE					POST BD				
		Meas.	Normal Range	Pred	% Pred	z score	Meas.	Change	% Change	% Pred	z score
FVC	L	**1.26**	1.18 - 2.59	1.88	67	-1.46	**1.36**	0.10	8	72	-1.22
FEV1	L	**1.12**	0.93 - 2.18	1.56	72	-1.16	**1.12**	0.00	0	72	-1.16
FEV1/FVC%	%	**88.9**	66.6 - 88.0	77.3	115	1.79	**82.2**	-6.7	-8	106	0.75
PEF	L/s	**5.85**	3.74 - 6.70	5.22	112	0.70	**6.53**	0.68	12	125	1.46
FEF25-75%	L/s	**1.44**	1.27 - 4.07	2.67	54	-1.45	**1.12**	-0.31	-22	42	-1.82
MEF25%	L/s	**0.58**	< 2.26	1.12	52	-0.79	**0.42**	-0.15	-26	38	-1.01
MEF50%	L/s	**1.66**	1.45 - 5.07	3.26	51	-1.45	**1.53**	-0.13	-8	47	-1.57
MEF75%	L/s	**4.46**	2.62 - 7.06	4.84	92	-0.28	**4.25**	-0.21	-5	88	-0.44

BD=Bronchodilator

Figure 3. A printout of pre- and post-bronchodilator spirometry in a patient with idiopathic pulmonary fibrosis; measured data is shown in absolute values and as percent of predicted along with normal range (5^{th} to 95^{th} percentile) and z-scores.

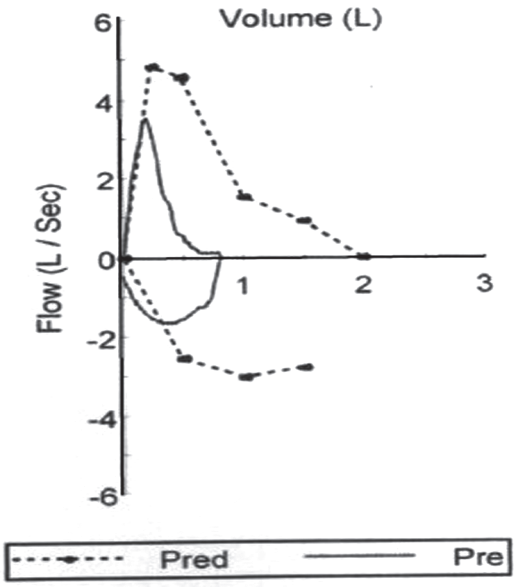

Figure 5. A maximal flow-volume curve showing the characteristic shape (sharp decline in the expiratory limb) in a patient with a restrictive ventilatory impairment.

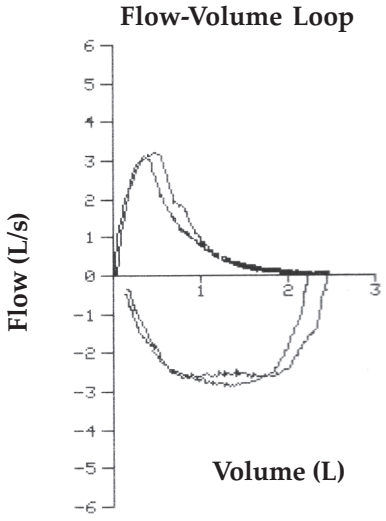

Figure 6. A maximal flow-volume curve showing the characteristic shape (concavity in the expiratory limb) in a patient with airways obstruction.

5. *Examine the Measured Data: FVC, FEV_1 and FEV_1/FVC Ratio and Identify Abnormal Values*

Interpretation of spirometry data is based only on two basic measurements — FVC and FEV_1, and their ratio (FEV_1/FVC). These are the two most repeatable parameters and when examined together provide almost all the information one is seeking from spirometry in most cases. The peak expiratory flow rate (PEFR) may help to corroborate compliance with the acceptability criteria as a reduced reading indicates a submaximal blast. Expiratory flow rates (FEF_{25-75}, FEF_{50}, FEF_{75}) usually do not add any additional information and should be read only with the two basic

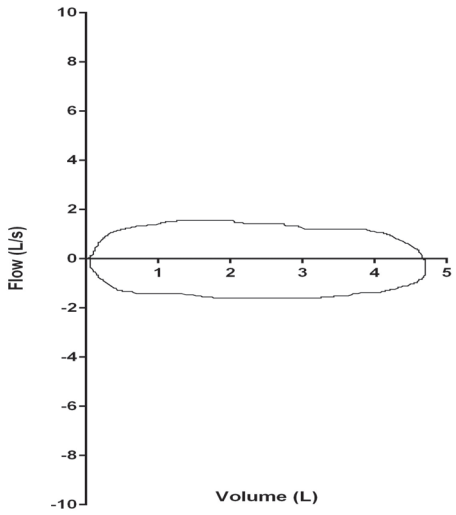

Figure 7. A maximal flow-volume curve showing the characteristic shape (flattened expiratory and inspiratory limbs) in a patient with tracheal stenosis.

measurements and their ratio, and not in isolation because of their greater variability and volume dependence. The FEF_{25-75} should not be used in isolation to make a diagnosis of small airways disease. Usually, inspiratory flow rates are useful only in specific situations, such as extra-thoracic obstructions. A spirometry report contains several other measured and derived parameters. Most of these do not provide any useful information or only corroborate the information obtained from the basic parameters.

Most softwares allow customisation of the reported parameters. Thus, the user can print data only for FVC and FEV_1, and the FEV_1/FVC ratio as the main parameters for interpretation, expiratory flow rates (PEFR, FEF_{25-75}, FEF_{50}, FEF_{75}) as supportive measurements and inspiratory measurements, such as inspiratory vital capacity and flow rates if required for specific indications. It is useful to include the forced expiratory time (FET). Even if limited parameters are printed, others are still computed and can be retrieved later from the stored data.

It is emphasised that defining what is abnormal is a critical step in interpretation. The discussion in the previous sections suggests that a statistically valid LLN rather than a fixed cut-off should be preferred. An interpretation algorithm is shown in figure 8.

6. *Identify the Pattern of Ventilatory Impairment*

Spirometry rarely provides a specific diagnosis. Rather, it allows recognition of patterns of ventilatory impairments that may be produced by different diseases: obstructive pattern, pattern suggestive of restriction, pattern suggestive of a mixed obstructive-cum-restrictive process and, variable and fixed large airway obstruction (Table 4). This categorisation is done by examining the flow volume curve and the measured parameters. An FEV_1/FVC ratio and FVC above the LLN define a normal spirometry. A reduced FEV_1/FVC ratio below the LLN is the hallmark of

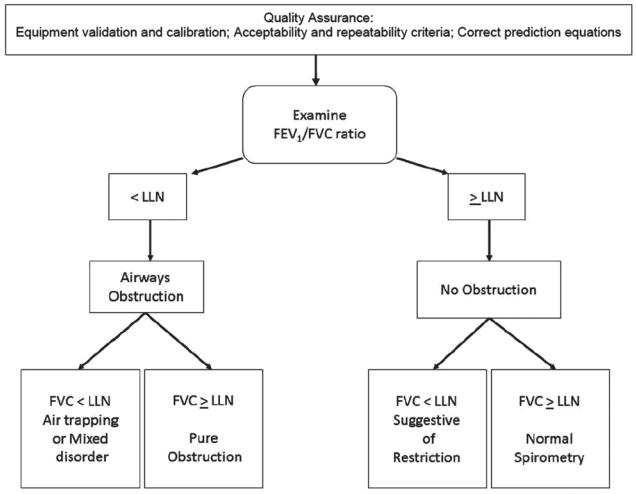

Figure 8. Interpretation algorithm for spirometry.

airways obstruction. A reduced FVC below the LLN with a normal FEV_1/FVC ratio points towards a restrictive ventilatory impairment and is observed in several diseases of the parenchyma, pleura and the chest wall. However, a reduced FVC is also a feature of moderate or severe obstructive diseases that result in air-trapping or increased residual volume. Therefore, though the term 'restrictive' is well-entrenched, it should be avoided as a reduction in FVC is not always due to a restrictive process. Possible causes of a reduced FVC are shown in table 5. Physiologically, only a reduction in total lung capacity defines restriction. The common causes of the disease patterns are shown in table 6.

7. *Grade the Severity of Ventilatory Impairment*

The severity of ventilatory impairment can be graded using arbitrary slabs. The 1991 ATS statement on interpretation used FEV_1 for grading the severity of

Table 4. Characteristics of patterns of ventilatory impairment

Abnormality	Features
Generalised airways obstruction	*Early disease*
	Slowing in terminal part of flow-volume (FV) curve giving a concavity in the tail-end
	$FEF_{75\%}$ or FEF_{25-75} is reduced
	Limited value because of large within-session variations and usually poor prediction capability of equations for these parameters
	Not specific for small airway disease; hence should not be relied upon to make a diagnosis
	Generalised airways obstruction
	Later, FEV_1 decreases out of proportion to FVC leading to reduced FEV_1/FVC ratio <LLN
	Expiratory flow rates are reduced
	Curve becomes more and more concave as the severity of airways obstruction increases
	FET is characteristically increased >6s
	FVC may also be reduced due to air trapping, especially in COPD and moderate-to-severe asthma
	Bronchodilator responsiveness test should be performed at the time of diagnosis
Restriction	Characterised by a reduction in TLC below the LLN
	FVC is reduced with FEV_1/FVC ratio in the normal range
	Expiratory flow rates are normal or even increased
	As spirometry cannot measure TLC, strictly, one should not make a diagnosis of "restriction" but use the phrase "suggestive of restriction" and confirm with TLC measurement
	FV curve is small with straight or convex descending limb
	FET is usually <6s
Mixed	Coexistence of obstruction and restriction
	Both FEV_1/FVC ratio and TLC are <LLN
	FVC may be reduced in both obstruction, and restriction and therefore, a mixed disorder is suggested but cannot be reliably diagnosed by spirometry; consider measurement of TLC
Variable and fixed large airway obstruction	Diagnosed by characteristic changes in the shape of the FV
	The inspiratory limb is flattened in variable extra-thoracic obstruction, the expiratory limb is flattened in variable intra-thoracic obstruction and both limbs are flattened in fixed large airways obstruction
	FEV_1/FVC ratio and FVC data may resemble obstructive or a mixed pattern

Definitions of abbreviations: FEF=Forced expiratory flow; FEV_1=Forced expiratory volume in 1 second; FVC=Forced vital capacity; LLN=Lower limit of normal; FET=Flow expiratory time; TLC=Total lung capacity

Table 5. Possible causes of reduced vital capacity

- Restrictive disorder
- Physiological variant
- Incomplete inhalation
- Incomplete exhalation
- Leak
- Equipment faulty (not validated or calibrated)
- Use of inappropriate prediction equation
- Rare cases of asthma
- Diseases causing air-trapping

Table 6. Examples of diseases causing obstructive and restrictive ventilatory defects

Obstructive Disorders	Restrictive Disorders
Asthma	Scoliosis and other thoracic cage defects
COPD	Obesity
Cystic Fibrosis*	Pregnancy
Bronchiectasis*	Neuromuscular diseases
Post-tubercular sequelae*	Pleural fibrosis
Endobronchial tuberculosis	Lung resection
Bronchiolitis	Cystic fibrosis*
Eosinophilic lung diseases*	Bronchiectasis*
Sarcoidosis*	Interstitial lung disease
Intra- and extra-thoracic localised obstructions due to tumours, stenosis, etc	Post-tubercular sequelae* Lung fibrosis of any aetiology Post-chest surgery (e.g., thoracoplasty) Space occupying lesions (e.g., lung cancer, infections)

*= May cause a pure defect or a mixed pattern

obstructive impairment and FVC (or TLC) for restrictive impairment.[6] The 2005 ATS/ERS guidelines[49] suggest grading both obstructive and restrictive ventilatory impairments solely according to FEV_1 (expressed as percent predicted) as follows: mild: >70%; moderate: 60% to 69%; moderately severe: 50% to 59%; severe: 35% to 49%; very severe: <35%.

The classification is not recommended for variable and fixed large airways obstructions. The GOLD staging of COPD uses a different criteria that is based on post-bronchodilator spirometry.[62]

8. *Evaluate Bronchodilator Responsiveness (if done)*

Bronchodilator responsiveness is assessed by carrying out spirometry before and 20 minutes after inhalation of 400µg of salbutamol from a metered dose inhaler. An increase in FVC or FEV_1 by 200mL and 12% over the baseline indicates a significant response to bronchodilator.[6,49] This is the most commonly used method to assess bronchodilator response. Other methods include expressing absolute change and expressing change as a percentage of predicted value.[2,69]

Except for diagnosing COPD, the interpretation of spirometry data and the inference of pattern of abnormality is based on pre-bronchodilator spirometry.

9. *Answer the Clinical Question for Which the Test was Ordered*

The laboratory director or the physician must examine the spirometry report with clinical data and other investigations for a meaningful interpretation. It is important to consider the pre-test probability of disease or the pre-test diagnosis. This is especially necessary to avoid wrong labelling in borderline measurements. Given the high standard error of estimate, and therefore, the wide range of normal values as well as an inherent false positive rate of 5%, values just below the LLN in an asymptomatic subject with no other abnormality on other investigations must be interpreted carefully taking into account the likelihood or otherwise of disease. Parameters in patients with mild disease can overlap with values in healthy persons.[70] Wrongly labelling a normal subject as diseased and missing an early diagnosis by labeling a borderline subject as normal are obviously undesirable and interpretation of data in such situations is best left to clinical judgment, expertise and experience of the physician.

A normal spirometry does not rule out a significant disease process. In diseases such as IPF, gas exchange abnormalities, especially on exertion, may be the first physiological manifestation of disease with spirometry being affected only later.

10. *Compare with Any Previous Spirometry Report*

Comparison with self provides useful clinical information especially for monitoring the therapeutic response and following the natural history and progression the of disease. Most softwares provide trend reports for this purpose. It is also sometimes useful in early detection the of disease. Given the large range of normal values for a subject, there may be a substantial decrease in values over time with these still above the LLN. This decline may suggest disease. As spirometry is not a test routinely carried out in healthy individuals, usually values at a time during health are not available.

11. *Advise Further Lung Function Testing (if necessary)*

Spirometry only provides information about the mechanical properties of the thorax including the airways. Diseases that affect gas exchange, pulmonary haemodynamics and cardiovascular function may cause symptoms, such as dyspnoea without affecting spirometry measurements, especially in early stages. Many diseases, such as COPD, affect not only the mechanical properties of the airways and the parenchyma but also adversely affect the gas exchange. Moreover, the interpretation algorithm shown in figure 8 may require additional tests to supplement the information obtained on spirometry, especially in patterns suggestive of a restrictive or a mixed disease process. Body plethysmography to measure airway resistance and thoracic gas volume, static lung volumes estimation with gas dilution techniques, diffusion capacity measurements and exercise tests may be required to obtain a comprehensive assessment of the cardio-pulmonary functional status.

Conclusions

Spirometry is a valuable and informative tool in the management of a diverse variety of chest diseases and disorders. Properly calibrated and validated equipment, and a trained technician who can deliver quality assured spirometry according to standardised methodology are mandatory. The laboratory director and the physician should not only be familiar with the standardisation of methodology and the pathophysiology of lung diseases but also with the statistical issues related to prediction equations and the definition of abnormality in interpretation. Selection of appropriate prediction equations is a vital step in the interpretation of spirometry. The definition of abnormality should be based on a statistically valid LLN and use of fixed cut-offs is discouraged. To obtain maximum and meaningful information, the flow-volume curve and the measured data should be viewed in conjunction with clinical information, including results of other investigations. Further testing may be necessary as spirometry has limitations in detecting early disease and in patients with borderline values, and also because it provides information only about the mechanical properties of the airways, the lung and the chest wall.

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