



## Editorial

New Spirometric Reference Values<sup>☆</sup>

## Nuevos valores espirométricos de referencia

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Spirometry is an essential technique in the study of patients with respiratory symptoms, both in the hospital setting and in primary care, where its use has become widespread in recent years.

The parameters for lung function tests have large interindividual variability and, unlike other biological variables, depend on the patients' anthropometric characteristics (sex, age, height, weight, and race). Spirometry interpretation is usually based on comparing the values produced by the patient with those that would theoretically correspond to a healthy individual with the same anthropometric characteristics, the theoretical values. This theoretical or reference value is obtained from prediction equations, in which a fixed value of 80% of the predicted value has been used as the limit of normal. Although this figure is close to the 5th percentile in subjects of average age and stature, if subjects fall outside the normal range for age or height, this fixed value may classify them incorrectly.

Alternatively, the results can be expressed in relation to the expected range, using the lower limit of normal (LLN) equivalent to the 5th percentile as the cut-off point. If they are not included in the prediction equations provided by the spirometers, the percentiles can be calculated using the estimated standard error (SE) of the equation. The LLN is equal to the predicted value minus the result of  $1.645 \times SE$ .

Recently, authors like Quanjer et al.,<sup>1</sup> who initially formed the *Global Lung Function Initiative* (GLI 2012) before subsequently becoming the *Task Force* (ERS), published reference values that are intended to derive prediction equations and LLN which are applicable at world level and for population groups between 3 and 95 years old. More than 160 000 data points from 72 centres in 33 countries were evaluated. Finally, 97 759 records from healthy non-smokers (55.3% females) aged between 2.5 and 95 years, who met standardised measurement conditions with well-documented data on the equipment and software used, were analysed.

After discarding 23 572 records, mostly because they could not be included in defined ethnic or geographic groups, reference equations were obtained for healthy individuals aged between 3 and 95 years for Caucasians (n=57 395), African-Americans (n=3545), and North and South East Asians (n=4992 and n=8255, respectively). Of the total number of subjects originally included in the study, 47.7% were in the age range <20 years and 0.8% in the age range >80 years.

The study by Quanjer et al. is an attempt to standardise subjects into single reference ranges that can be used regardless of ethnicity or age. The current difficulties in standardising evaluation criteria and classification of patients according to the spirometric values obtained are well known, as they can vary substantially according to the theoretical values used or evaluation criteria employed, by predicted value or LLN. There are a few studies<sup>2–4</sup> that have evaluated populations other than Caucasian, and have correctly determined the LLN in these populations.

This study has helped to determine the differences between the different ethnic groups with respect to their spirometric values. The authors found that the forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) values differ in their lower limit values in ethnic groups other than Caucasian, in similar proportions for both parameters, so that the FEV1/FVC is independent of the ethnic group, which is important when determining normal levels, as other authors have learned.<sup>5,6</sup>

The use of predicted values implies significant restrictions in patients outside the normal range with limitations when assessing the bias involved in growth changes in relation to age changes, which can cause errors especially in the young population.

It has been observed that for the same height and sex, a one year difference in age can alter the predicted value by 8.5% in subjects aged under 20 years. Stature is a determining factor in the determination of lung function, with a major influence in the preschool age group, where very large coefficients of variation that decline in adolescence are observed, with a subsequent decrease in this variation in the third decade until stabilisation towards old age. This implies a pattern in which the FEV1/FVC, instead of decreasing steadily from childhood to adolescence, increases.

It has been observed that the non-Caucasian population have lower values, which means that falls over time are 15% smaller in the African-American population than in Caucasian males of the same age and height.

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With respect to non-Caucasian ethnic groups, the Latin American population should be mentioned. The authors assume that this is a population with difficulties associated with factors such as height, body morphology and the fact that this group tends to be a mix of people of Spanish descent and the indigenous population, which leads to a diversity of populations that limits the usefulness of these reference values in the Latin American population of non-European descent.

With respect to the presentation of results, the authors agree on the need to express the results using the LLN. They make reference to the general use of 80% of the predicted value as the LLN, which implies a potential error, as this ratio varies considerably with age and leads to misclassification.<sup>7–9</sup> A value outside the normal range, defined as the mean  $\pm$  SE (1.96) is compatible with disease. Both the *American Thoracic Society* (ATS) and the *European Respiratory Society* (ERS) accept the use of the 5th percentile to define this LLN, which unlike the percentage of the predicted, is free from bias due to age, height, sex or ethnic group. However, the authors observed that a substantial percentage of subjects ( $\pm$ 10.4%) have values lower than the 5th percentile. The authors suggest the possibility of using the 2.5th percentile in epidemiological studies and using the 5th percentile where there is evidence or suspicion of disease in a clinical context.

The authors confirm international society (ATS/ERS) criteria with respect to limiting the use of a parameter such as the FEF 25%–75% as a diagnostic value, as it has intra-individual variations, both its own and others attributable to variations in the FVC, the parameter on which it depends.

In summary, it can be concluded that the *Global Lung Function Initiative* (GLI2012) is a real approximation to achieving uniformity when evaluating spirometry results that aims to be useful in all geographical areas and likewise attempts to standardise the expression of results. As the authors agree, this initiative needs

further study in ethnic groups that are not clearly represented, and in those age ranges with a small population, where the application of theoretical reference values presents major difficulties.<sup>10</sup> The publication of this article will probably lead both medical professionals and manufacturers to enter these theoretical values in their equipment in the coming years. It is likely that in the near future, these values will be considered for common use for the performance and interpretation of spirometry tests carried out in any setting.

## References

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