COPD (confusion over proper diagnosis) in the zone of maximum uncertainty

To the Editor:

In an excellent statement on chronic obstructive lung disease (COPD) that focuses on questions that are relevant for the patient's well-being and quality of life [1, 2], one issue should have received more critical attention. For research into COPD, it is vital that the diagnosis of airway obstruction, which traditionally hinges on a forced expiratory volume in 1 s (FEV₁)/forced vital capacity (FVC) ratio below a threshold, can be accurately established. *CELLI et al.* [1, 2] state that this threshold is uncertain, leaving the recommendations open ended to some extent. They refer to the discussion whether in ascertaining a diagnosis of COPD the threshold for the FEV₁/FVC ratio should be the lower limit of normal (LLN), defined in respiratory medicine as the 5th centile in a representative sample of healthy nonsmokers, or the post-bronchodilator FEV₁/FVC of 0.7 first proposed in 2001 by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) group [3]. The latter threshold has not been clinically validated; it was intended to simplify recognition and increase awareness of COPD, particularly in less developed countries where the LLN might not be presented with the test results. The use of the fixed ratio has been extensively criticised. Cross-sectional data show that it leads to underestimating the prevalence of airflow limitation in younger people and to large overestimates in those older than 45 years. In 80-year-old healthy subjects, this leads to a 75–80% false positive rate [4]. The Burden of Obstructive Lung Disease (BOLD) group also routinely uses the LLN cut-off for reporting the prevalence of abnormal ventilatory function [5]. Follow-up studies have shed light on the question of whether observations in the zone between the fixed ratio and LLN represent respiratory disease. In asymptomatic subjects and very elderly subjects, an FEV₁/FVC above the LLN but below 0.7 was not associated with premature death [6–10], an abnormal decline in FEV₁ [11–13], respiratory care use [11], hospitalisation [10] or quality of life [11]. Conversely, an FEV₁/FVC ratio below the LLN is associated with increased risk of hospitalisation [10] and mortality [8–10, 12, 13]. Three reports [9, 16, 17] suggested that use of the LLN cut-off would miss individuals at risk, but these findings have been contested [18–21].

In a discussion of a diagnostic test that establishes disease, it is important to note that clinical decisions often require a three-zone interpretation of “present”, “absent” or “uncertain”, rather than yes *versus* no [21]. Uncertainty may persist in a proportion of patients who have results that lie just above or below diagnostic thresholds, the zone of maximum uncertainty, thus requiring clinical judgment. The LLN approach facilitates clinical judgment by better distinguishing aging related changes in lung function from COPD related airflow obstruction, whereas GOLD criteria impede clinical judgment by applying a fixed ratio threshold across all ages [23].

There is overwhelming evidence that, unlike the LLN, the fixed ratio as a cut-off value is an inappropriate criterion for including or excluding subjects in COPD research projects, and will bias the findings. The American Thoracic Society (ATS) and European Respiratory Society (ERS) have previously agreed that the LLN is the proper diagnostic criterion for airflow limitation [24]. The present document [1, 2] re-introduces confusion on diagnostic criteria and therefore does not indicate a clear route for research into COPD using the best target group. The confusion first arose 14 years ago from an effort to simplify the diagnosis of airflow limitation when people might not have an appropriate LLN at their disposal. Now even small hand-held spirometers provide that information, so there is no justification for a rule of thumb which leads to so much misclassification in people below middle-age and old people, particularly in a world where more people are living longer [25]. Therefore, we ask the ATS, ERS, British Thoracic Society, National Institute for Care Excellence and other international and national respiratory organisations to carefully review all the evidence, and end the present confusion by issuing an unequivocal guideline. It's one of the great strengths of science that it can fix its own mistakes: let us do it now.

@ERSpublications

A A fixed cut-off in FEV₁/FVC ratio is not an appropriate measure for diagnosing COPD

<http://ow.ly/RZyLe>

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