The lower limit of normal *versus* a fixed ratio to assess airflow limitation: will the debate ever end?

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Identifying airflow limitation using an FEV1/FVC less than 0.70 in a general population of young adults can no longer be justified http://ow.ly/MRzo30iWja5

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A normal test result is typically differentiated from an abnormal result by identifying those values that fall within (normal) and outside (abnormal) the 95% confidence interval for that test, after the test is evaluated in healthy individuals from the intended population. This approach acknowledges that 5% of a normal population will have an abnormal test result and some individuals with a normal test result will have the disease the test is designed to identify. Such trade-offs are common in the practice of medicine.

For the major components of spirometry (forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and FEV_1/FVC), the lower limit of normal (LLN), representing the lower 5% of test results from a normal population, differentiates a normal from an abnormal value. Age, sex, height and race/ethnicity corrected values have been used for years to identify airflow limitation. Yet, international guidelines for FEV_1/FVC continue to support [1] and clinical trials continue to use [2] a static cut-off point to identify airflow limitation. This approach remains from when spirometry was performed with equipment that did not have computing capabilities, such as built-in sets of normal values from several populations. The FEV_1/FVC ratio of 0.70 was chosen to separate normal from abnormal since it identified a population in which airflow limitation was associated with disease and reasonably approximated the LLN in that population of mostly middle-age and older adults [3]. However, for years it has been recognised that using a value of 0.70 may underestimate airflow limitation in younger individuals [4], a population in which preventive measures could be employed, and may overestimate airflow limitation in older individuals [5], in whom unnecessary treatment results in increased healthcare costs and may cause adverse health effects.

Most previous studies on the differences between the LLN and a fixed ratio have focused on the older adult, potentially over-diagnosed population [2, 6]. However, more than 10 years ago, Cerveri *et al.* [4] reported on the differences between the two measures in approximately 6200 young adults, aged 20–44 years in the European Community Respiratory Health Survey. They found that using a fixed FEV_1/FVC of 0.70 or less misidentified 318 individuals (5.1%) of this population as normal when they had airflow limitation using the LLN. Further, the misidentified individuals had an increased risk of developing chronic obstructive pulmonary disease (COPD), chronic cough or phlegm, and increased use of health resources for breathing problems during the subsequent 9 years.

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In this issue of the *European Respiratory Journal*, Çolak *et al.* [7] add to the previous literature by studying more than 95 000 adults aged 20–100 years in the Copenhagen General Population Study [8]. They focused on the young and middle age adults in this population, following them for a median of 6 years. The authors tested the hypothesis that young and middle-age European adults taken from the general population and who were not diagnosed with airflow limitation based on an FEV1/FVC ⩾0.70, but who had airflow limitation based on their FEV1/FVC being less than the LLN, had a poorer prognosis than those who did not have airflow limitation by either measure. The participants were divided into four groups: no airflow limitation, FEV1/FVC ⩾0.70 and ⩾LLN (83% of participants); potential under-diagnosis of airflow limitation, FEV1/FVC ⩾0.70 and ⩽LLN (1% of participants); potential over-diagnosis of airflow limitation, FEV1/FVC ⩽0.70 and ⩾LLN (3% of participants); and definite airflow limitation, FEV1/FVC ⩽0.70 and ⩽LLN (13% of participants). The outcomes evaluated were COPD exacerbations, pneumonia, ischaemic heart disease, heart failure and all-cause mortality. Compared to those without airflow limitation, the 1056 participants with potentially undiagnosed airflow limitation had an increased risk of pneumonia, heart failure and all-cause mortality. The younger members of this group, defined as those between 20 and 50 years of age at the time of entry into the study and representing 3% of this age group (*versus* 0.5% among older participants), had an increased risk of severe COPD exacerbations, heart disease and all-cause mortality.

This study is important in several ways. First, it defined the prevalence of potential under-diagnosed airflow limitation and its age distribution in a very large, well-characterised population-based sample. In this population more than 1000 individuals met the criteria for under-diagnosed airflow limitation. Although they represented only a small proportion (1%) of those evaluated, 76% of them were between the ages of 20 and 50 years. Second, the study confirmed a linkage between the under-diagnosed population and several clinically important outcomes including severe COPD exacerbations and all-cause mortality. Third, the study substantiated in the large population of those without airflow limitation, defined by an FEV1/FVC greater than 0.70, an association between worsening lung function and an increase in adverse health outcomes [9, 10].

Like all population-based epidemiology studies, there are limitations. A major one, discussed by the authors, is the lack of post-bronchodilator spirometry. This is a common limitation in general population-based studies. Yet, it does not reduce the importance of the findings as post-bronchodilator spirometry assesses reversibility, not the presence of airflow limitation. Additional clinical information is often needed to identify the cause of the airflow limitation. The collection of relevant symptoms, asthma and smoking history, and additional respiratory health information minimises the impact of not having post-bronchodilator data. Another potential limitation is the absence of chest computed tomography measurements of the airways and lung parenchyma. These measurements are providing new insights into lung diseases in general and airflow limitation in particular [11].

In summary, although the LLN as currently used to define airflow limitation (the lower 5% of the FEV1/FVC in a healthy, nonsmoking population) may be imperfect [12], the comprehensive, longitudinal, population-based data presented by Çolak *et al.* [7], along with data from others, provide strong support for not continuing to use a fixed FEV1/FVC of 0.70 to identify patients with airflow limitation, especially those younger than 50 years of age, who are most likely to benefit from early intervention.

Conflict of interest: None declared.

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