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Is there an appropriate FEV1/FVC threshold for predicting lung function decline in COPD? http://ow.ly/pPIlU

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From the authors:

We thank F.A.A. Mohamed Hoesein and P. Zanen for their interest in our work [1]. In our study, we performed secondary analyses on data from the Lung Health Study (LHS) [2]. We subdivided the LHS study population into four categories based on the presence or absence of airflow obstruction as defined the fixed forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) <0.70 cut-off point and by the lower fifth percentile using the LMS (lambda, mu, sigma) method definitions. The LMS method accounts for sex- and age-specific predicted values (mu), and adjusts for nonuniform dispersion (sigma) and skewness of the lung function values distribution (lambda). The original LHS study population consisted of 5887 smokers aged 35–60 years. We excluded 1842 subjects because 1276 subjects were in different categories based on the fixed and LMS definitions for airflow obstruction during their baseline and first annual visits, and 566 subjects had missing spirometry results during either their baseline visit or their first annual follow-up visit. This means that for these 566 subjects we did not have the two measurements required to either confirm or refute their consistent classification in a particular category, which was the only reason to exclude them. We agree with F.A.A. Mohamed Hoesein and P. Zanen that missing data (if completely at random) in mixed-models analysis do not influence the validity of the outcome and that subjects with missing data can be included in the analysis. But as explained above, the reason to exclude the 566 subjects from our analysis was not missing data, but uncertainty about their classification.

Because the goal of our study was to compare clearly defined and consistent groups of subjects based on the fixed and LMS definitions for airflow obstruction, we only included those subjects who did not shift between categories during their baseline and first annual follow-up visit (table 1). As a consequence, 1276 (24%) subjects were excluded from the analysis. This finding shows that a one-off spirometry test does not seem to be sufficient to determine airflow obstruction in a substantial proportion of subjects and suggests that a chronic obstructive pulmonary disease (COPD) diagnosis should not be based on a single spirometry test. However, excluding these subjects clearly comes at the cost of generalisability. Therefore, as stated in the Discussion section of the paper [1], our analysis should be seen as a "proof of concept" and illustrating that, when diagnosing COPD, it seems more appropriate to use sex- and age-specific cut-off points for the FEV1/FVC ratio than it is to use a "one size fits all" fixed (0.70) cut-off point.

The mean decline in both groups is indeed steeper than one would expect in healthy subjects, but this study included only heavy smokers (with a mean $\pm$ SD cumulative cigarette smoke exposure of 40.1 ± 18.3 pack-years and 31.1 ± 12.6 cigarettes smoked per day). We see this as an explanation for the relatively strong annual FEV1 decline of 43.8 $mL \cdot year^{-1}$. A systematic review by LEE and FRY [3] showed an annual decline of 42.8 $mL \cdot year^{-1}$ for continuing smokers, which is comparable with the decline we observed in our population. LEE and FRY [3] also showed that continuing smokers have a decline over 10 $mL \cdot year^{-1}$ greater than never-smokers, ex-smokers or quitters. Despite the relatively steep overall decline, we still found a

TABLE 1 Distribution based on screening measurement compared with first measurement

Screening	Visit 1				
	LMS$^-$/fixed$^-$	LMS$^+$/fixed$^-$	LMS$^-$/fixed$^+$	LMS$^+$/fixed$^+$	Total
LMS$^-$/fixed$^-$	583	124	43	201	951
LMS$^+$/fixed$^-$	127	173	0	158	458
LMS$^-$/fixed$^+$	57	0	59	69	185
LMS$^+$/fixed$^+$	256	182	59	3230	3727
Total	1023	479	161	3658	5321

LMS$^-$/fixed$^-$: absence of airflow obstruction according to both definitions (''nonobstructed'' subjects); LMS$^+$/fixed$^-$: presence of airflow obstruction according to the LMS definition but absence of airflow obstruction according to the fixed definition (''discordant young'' subjects); LMS$^-$/fixed$^+$: absence of airflow obstruction according to the LMS definition but presence of airflow obstruction according to the fixed definition (''discordant old'' subjects); LMS$^+$/fixed$^+$: presence of airflow obstruction according to both definitions (''obstructed'' subjects).

comparable difference of 10 mL·year^{-1} between the LMS$^-$/fixed$^+$ category (FEV_1/FVC <0.70 but above the fifth percentile) and the LMS$^+$/fixed$^+$ category (FEV_1/FVC <0.70 and below the fifth percentile).

In this study, it was not our intention to detect "rapid decliners", but we used post-bronchodilator lung function decline as an important marker of COPD prognosis to prospectively compare two different methods (LMS and the fixed FEV_1/FVC <0.70 cut-off point definitions), which are used to define and categorise airway obstruction. To detect rapidly declining subjects, a prolonged period of repeated spirometry testing has to be organised to obtain accurate individual estimates for FEV_1 decline [4], which is far from practicable in routine patient care and, at least in Dutch primary health care, has previously been shown not to be a feasible option. Therefore, the general practice guideline on COPD from the Dutch College of General Practitioners no longer recommends serial spirometry testing to measure a patient's annual FEV_1 decline, but instead recommends annual spirometry to re-assess the severity grade of airflow obstruction after the diagnosis of COPD has been established [5].

@ERSpublications
COPD prognosis in relation to diagnostic criteria for airflow obstruction in smokers
http://ow.ly/qh8Pk

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