

To the Editor:

Using a very large number of predominantly Chinese nonsmoking females aged 30–79 years, SMITH *et al.* [1] studied the relationship between airflow obstruction, household air pollution, household income, educational level and prior tuberculosis. They defined airflow obstruction as a ratio of forced expiratory volume in 1 s (FEV₁) to forced vital capacity (FVC) of <0.7 or <5th percentile, and graded the severity of respiratory impairment using FEV₁ 80% of predicted as a cut-off point, according to Global Lung Function Initiative 2012 prediction equations [2]. There are two fundamental problems with these criteria that affect the interpretation of their findings.

First, the fixed ratio of 0.7 does not represent the lower limit of normal for FEV₁/FVC, because this ratio declines with age in healthy nonsmokers (table 1). Inevitably, the fixed ratio does not delimit mild airways obstruction and its use introduces an important age and sex bias [2–4]. As the normal FEV₁/FVC ratio in most East Asians is somewhat higher and the scatter smaller than in Caucasians [2], use of a fixed ratio of 0.7 as a cut-off will result in more under-diagnosis in younger adults and less over-diagnosis in the elderly than in white people (table 1).

Secondly, the use of per cent predicted for FEV₁ is flawed: in adults the predicted FEV₁ declines with age, but the scatter in absolute terms declines proportionally much less (table 1). Therefore, the lower limit of normal expressed as a percentage of the FEV₁ declines with age. Consequently, the proportion of healthy nonsmoking East Asian females with an FEV₁ below any fixed percentage increases progressively with age (fig. 1). The use of per cent predicted was introduced 50–60 years ago [5, 6] and adopted despite prompt and fundamental criticism [7, 8]. Despite lack of clinical evidence of its validity, its use has been canonised in countless international and national guidelines and has therefore become engrained in respiratory medicine, explaining its widespread and uncritical use. The use of per cent predicted discriminates against people over the age of 45 years (fig. 1). Misclassification due to the age bias will become a progressively larger problem as an increasing proportion of people remain healthy and fit to a ripe old age. Per cent predicted of a spirometric index does not represent a percentile. However, it is treated as such, leading to biases in research and clinical medicine. The bias arising from the use of 80% predicted as a cut-off leads to over-estimation of the severity of respiratory impairment and its prevalence rate; it has undoubtedly also affected the otherwise excellent study of SMITH *et al.* [1].

One can bring a horse to water, but one cannot make it drink. By analogy, does this explain the persistence of the use of the fixed ratio and per cent predicted in respiratory medicine? It is time for a new dawn, and a quotation from a Nobel laureate might provide clinicians and researchers with an incentive to reconsider the use of these flawed rules of thumb: “It is a good morning exercise for a research scientist to discard a pet hypothesis every day before breakfast. It keeps him young” [9].



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Use of fixed ratio FEV₁/FVC and % pred FEV₁ cut-off points causes misclassification due to age bias <http://ow.ly/Cr9xx>

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TABLE 1 Predicted FEV₁ and the lower limit of normal for FEV₁ and FEV₁/FVC in healthy nonsmoking East Asian females

	Age years									
	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79
Predicted FEV₁ L										
Mean	2.79	2.71	2.60	2.48	2.30	2.17	2.03	1.89	1.73	1.61
SD	0.35	0.34	0.33	0.33	0.32	0.32	0.32	0.31	0.30	0.29
Lower limit of normal										
FEV ₁ % pred	79.4	79.3	78.9	78.0	76.8	75.5	74.1	72.8	71.4	70.1
FEV ₁ /FVC	0.77	0.75	0.74	0.73	0.72	0.72	0.71	0.69	0.68	0.67

Data from the Global Lung Function Initiative 2012 study [2]; n = 7898. FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity. The predicted FEV₁ declines by 42% but the SD by only 17%, leading to a decline in the lower limit of normal for FEV₁ expressed as % predicted with age. Conversely, the 5th percentile (z-score –1.64) is age independent.

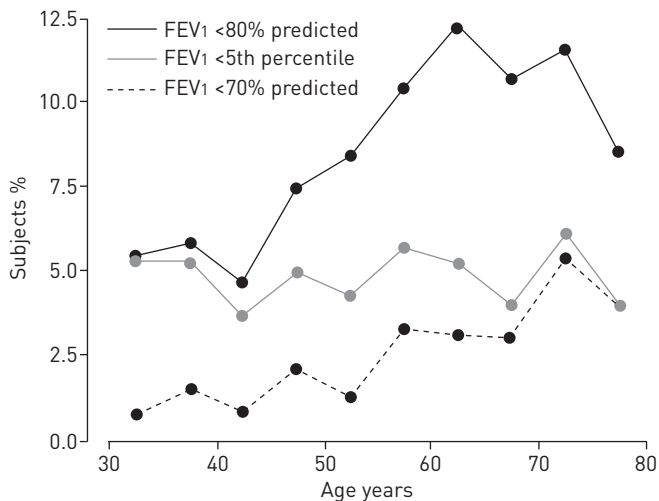


FIGURE 1 Percentage of healthy nonsmoking East Asian females aged 30–79 years in whom the forced expiratory volume in 1 s (FEV₁) was below the 5th percentile (mean 4.85%), or <80% or <70% of predicted according to the Global Lung Function Initiative (GLI) 2012 prediction equations [2]. Data from the GLI 2012 study [2]; n=7898. Note the age-related trend when using per cent predicted as the lower limit of normal, whereas the 5th percentile (z-score –1.64) is not associated with an age bias.

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