Beyond airflow obstruction: acknowledging the diversity of abnormal spirometry patterns

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To the Editor:

The primary purpose of spirometry is to identify the obstructive ventilatory defect, indicated by diminished forced expiratory volume in 1 s to forced vital capacity ratio (FEV_1/FVC). However, it also has several screening and prognostic applications by detecting nonobstructive abnormal spirometry (NOAS), a condition where either FEV_1 or FVC or both are reduced while the ratio remains normal. Both FVC and FEV_1 are known to be related to all-cause mortality and morbidity even in the general population [1]. Studies indicate that NOAS is prevalent in up to 30% of the general population [2] and an even greater proportion of those experiencing symptoms. However, there is substantial variation in how NOAS is interpreted. Additionally, it is worth noting that NOAS differs from the nonspecific pattern (NSP) described by Hyatt *et al.* [3], around 15 years ago. NSP is characterised by an abnormally low FEV_1 with normal FEV_1/FVC ratio and normal total lung capacity.

Pulmonary function interpretation guidelines [4], including the recently published European Respiratory Society (ERS)/American Thoracic Society (ATS) 2022 guidelines [5], only focus on a reduced FVC with a normal FEV_1/FVC ratio as a possible restrictive ventilatory impairment (restrictive spirometry) within their interpretation algorithms, while overlooking the importance of reduced FEV_1. Additionally, over the past decade, more than 50 publications have studied reduced FEV_1 with normal FEV_1/FVC ratio, referring to it as preserved ratio impaired spirometry (PRISm) [6], yet we neglect the significance of decreased FVC. Regrettably, current guidelines and research studies often treat restrictive spirometry and PRISm as similar entities, despite their potential for exclusivity. No studies have been published that directly compare these two physiological groups.

While FEV_1 and FVC are strongly correlated [7], both restrictive spirometry and PRISm approaches have limitations. Diminished FVC is a poor predictor of true restriction [8, 9] and FEV_1 is heavily reliant on FVC and is thought to rarely decrease independently when the FEV_1/FVC ratio and FVC are normal. Given these limitations, we suggest the identification of three patterns by considering both abnormal FEV_1 and FVC in interpretation, as follows: 1) NOAS due to isolated reduced flow (FEV_1), which may indicate early airflow obstruction [10] or suboptimal effort; 2) NOAS due to isolated reduced volume (FVC), which may represent early restriction or suboptimal effort; and 3) NOAS due to both reduced flow and volume (FEV_1 and FVC), likely due to restriction or airflow obstruction with air trapping or suboptimal effort. These three potential functional phenotypes might also have different outcomes.

In our Burden of lung disease (BOLD)-Trinidad and Tobago study, we examined these NOAS patterns through a national community-based cross-sectional investigation. The study received approval from the ethics committees of the Faculty of Medical Sciences at the University of the West Indies and the Ministry of Health, Trinidad and Tobago. Noninstitutionalised adults aged 40 years and older were chosen using two-stage stratified cluster sampling across the country. After giving consent, participants completed several questionnaires and underwent spirometry testing. Spirometry was conducted following the 1994 ATS criteria [11], using the Easy-One portable spirometer (ndd Medizintechnik; Zurich, Switzerland). Spirometry quality control was performed by the BOLD central pulmonary function reading centre in London, UK. A more detailed description of our study's methodology has been previously published [12]. In this study, we employed the Global lung Function Initiative (GLI) race-neutral lower limit of normal

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Restrictive spirometry patterns and PRISm may not be the same, potentially leading to missed detection of a considerable number of individuals with abnormal spirometry. It is essential to consider all spirometry indices carefully during interpretation. https://bit.ly/43pXzep

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values for interpretation, considering the Caribbean population, which predominantly includes Afro-Caribbean and Indo-Caribbean ethnic groups, is likely distinct from their ancestors and not represented in the GLI database. Furthermore, the GLI recognises the need for ethnicity-free reference equations to accurately understand disparities in lung health and avoid underestimating the impact of social determinants on lung health [13]. The 2022 ERS/ATS guidelines recommended a z-score-based classification and was used to estimate the severity of FEV_1 and FVC reductions [2]. Chi-square tests were applied to assess differences in categorical variables and the t-test was used to examine differences in continuous variables.

Out of 1104 participants, 382 reported experiencing respiratory symptoms (cough, phlegm or shortness of breath). Among the individuals who reported symptoms, 65% of were female, 68% were between the ages of

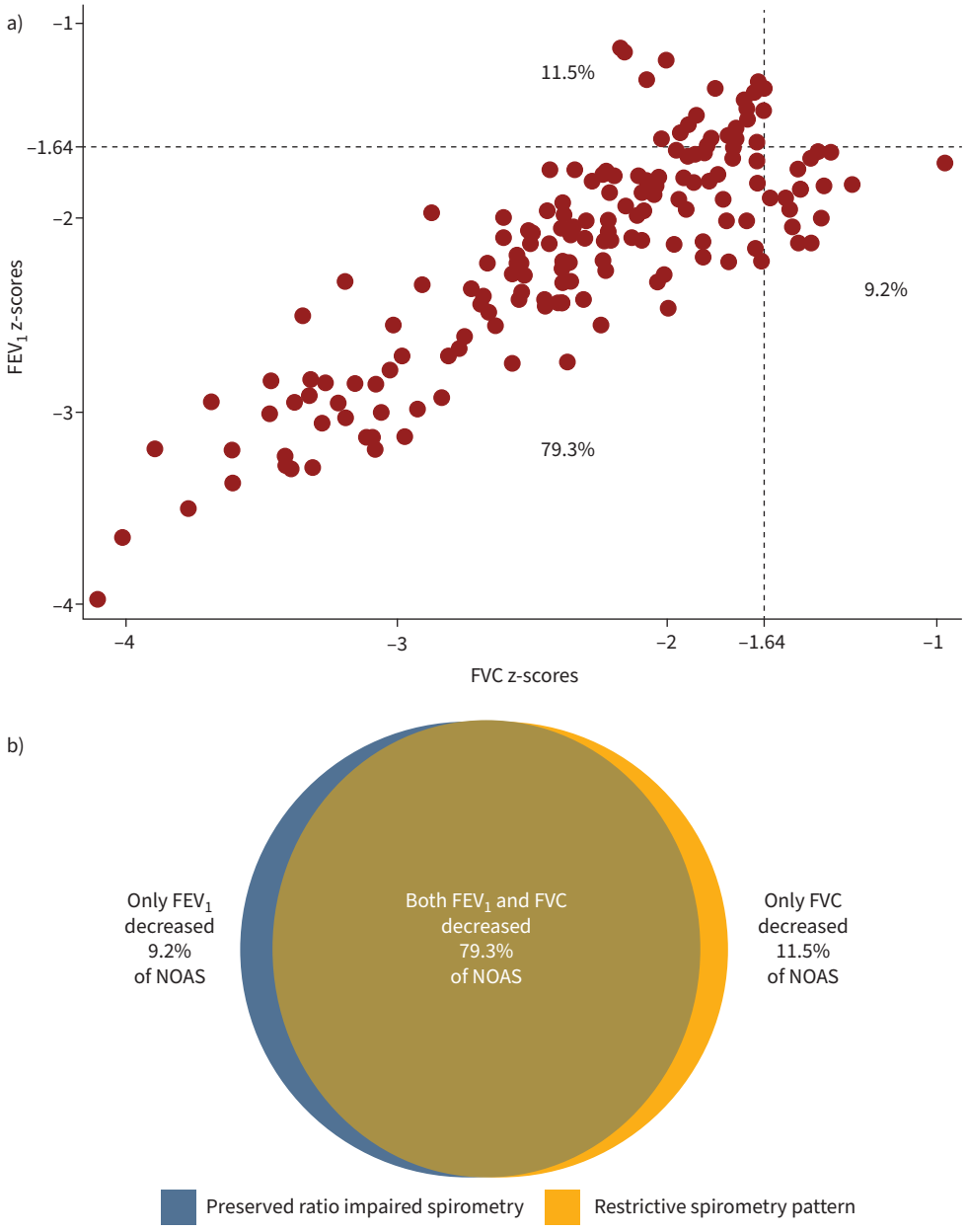

FIGURE 1 a) Scatterplot graph and b) Venn diagram distribution of nonobstructive abnormal spirometry (NOAS) based on forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) changes in the participants of the Burden of lung disease (BOLD)-Trinidad and Tobago study with respiratory symptoms.

40–60, 43% were of Indo-Caribbean ethnicity and 34% were of Afro-Caribbean ethnicity. Additionally, 45% of the symptomatic individuals were obese, 69% were nonsmokers and 27% were exposed to dust or fumes.

Among the symptomatic individuals, 45.5% were found to have NOAS, while 10.2% displayed airflow obstruction. Within the NOAS group, 79.3% exhibited reductions in both FEV_1 and FVC, while a smaller but significant percentage showed reduced FEV_1 or FVC alone (9.2 and 11.5%, respectively) (figure 1). In their respective isolated abnormal groups, FEV_1 and FVC displayed only mild decreases (z-scores −1.65–−2.5). Meanwhile, in nearly all cases within the combined abnormal group (99%), FEV_1 and FVC exhibited mild to moderate reductions (z-scores −1.65–−4.0). No statistically significant differences were observed among the three NOAS groups regarding gender, age, ethnicity, body mass index, smoking status, occupational dust or fumes exposure and comorbidities.

Limitations of the current study include its cross-sectional design and the reliance on self-reported data. These results warrant validation through additional large-scale studies. Furthermore, more research is needed to evaluate these functional groups with static lung volumes and assess their functional progression, mortality and morbidity outcomes.

Our study demonstrates that the current NOAS patterns, restrictive spirometry and PRISm may not be the same entities. They might overlook a significant portion of individuals with abnormal spirometry, who may deserve further work-up. Given that spirometry is a well-established screening and diagnostic tool for pulmonary dysfunction, morbidity and mortality, it is essential not to neglect any of its indices and miss the opportunity to investigate further. Consequently, we recommend that pulmonary function guidelines and research groups consider incorporating both abnormal FEV_1 and FVC values in interpretation when the FEV_1/FVC ratio is normal.

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