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FEV1Q: what (even) is normal lung function?

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People come in different shapes and sizes and so do their lungs. This seemingly trivial observation raises significant problems when it comes to defining the presence and severity of lung function impairment using spirometry – a fundamental test in respiratory physiology. A common approach is to make a lung function measurement such as Forced Expiratory Volume in 1 second (FEV_1), and to compare that measurement to a so-called healthy normal population by making adjustments for age, sex at birth, height and – controversially – race. Many populations – often those systemically disadvantaged for diverse reasons and those in the Global South where chronic lung disease is highly prevalent– do not have relevant reference populations for comparison, and it is not clear how what is said to be 'normal' should take account, or not, of systemic disadvantages. In part to address this, the American Thoracic Society has made a clear recommendation to replace race-specific spirometry reference equations with race-neutral approaches [1], based on race being a social construct without biological basis and inclusion of race perpetuating structural racism [2].

An alternative approach to expressing lung function as impaired below an expected 'normal' reference, is to express it as multiples above a first percentile value that represents a value below which survival is unlikely. This approach is called the FEV1 Quotient (FEV1Q, see Figure), the value of which is 400mL in women and 500mL in men, independent of age over 50 years [3]. FEV1Q was derived from a UK population of almost 12000 people attending for lung function testing, rather than a random population sample, and so includes a greater proportion of people likely to have lung disease. Although these lung function data were collected in Birmingham in the UK, serving an ethnically diverse population, there is little information reported on the characteristics of this original derivation population for FEV1Q. FEV1Q has already been shown to perform well, and better than other approaches using spirometry in predicting COPD exacerbations and death [4]. It has also been reported that FEV1Q cut-points of 2.8, 4.1 and 5.2 were better than the standard GOLD classification using FEV_1 (% predicted) in predicting clinical outcomes [5]. However, less is known about FEV1Q in other populations, in other diseases, and how FEV1Q relates to clinically important outcome measures other than COPD exacerbations and death.

An important paper in this issue of the Journal progresses the field [6]. Balasubramanian and colleagues report on the utility of FEV1Q in predicting survival, and on the relationship between race and FEV1Q. The datasets used are both from the United States (US): the well-known population-based NHANES cohort, and a separate lung transplant referral database called the United Network for Organ Sharing (UNOS). There were sufficient participants to allow comparison between (US) black and white individuals. FEV1Q did not vary between US black and white people. A lower FEV1Q was associated with increasing risk of death (NHANES

Hazard Ratio (HR) 1·33, 95% CI 1·28-1·39; UNOS HR 1·18, 95% CI 1·12-1·23) and this association was not confounded or modified by race. FEV1Q had greater discriminative power for death compared to alternative FEV_1 approaches such as absolute FEV_1 and FEV_1 expressed as % predicted in both black and white individuals.

These new data support the concept that FEV1Q provides a race-neutral assessment of lung function that predicts survival. We agree. However, there is much more to learn. We know little about FEV1Q in other settings – particularly those from the Global South – or how this metric performs in people other than those reported here. Whilst predicting survival, survival is not the commonest application of spirometry in clinical practice, where results are generally used to classify people as having obstructive and/or restrictive diseases, and for describing the severity of that impairment in relation to clinical features of disease. We are not provided with data to know if FEV1Q performs better than assessments of vital capacity in predicting survival. Mechanistic relationships between FEV1Q with other structural and functional consequences of lung disease that lead to the observed reduction in survival remain unclear. And, crucially, we need studies reporting longitudinal data: longitudinal monitoring of FEV1Q may indeed be where the test has most utility, necessitating an understanding of the minimum clinically important difference in FEV1Q over time.

How to move forwards? The world will not have healthier lungs until we better address the many factors, acting across the life course and which are associated with systemic disadvantage, that contribute to poor lung health. Until then, we need reliable measurements that help us make a diagnosis, prognosis and treatment plan in those with lung disease. Spirometry remains central to that. There is no 'gold standard' method of interpreting spirometry results, and so it is inherent on the respiratory community to understand the strengths and weaknesses of diverse approaches to expressing lung function including FEV1Q. The concept of 'normal' in health is complex and can be based on very different definitions of health [7]. Whichever method of interpretation we choose, we should not be adding to disadvantage by applying 'corrections' for race which in reality reflect many other factors. FEV1Q is one approach to that – but we need more information from different populations, and a deeper understanding of how it relates to disease phenotypes, progression over time and other outcome measures before it is ready for prime time. What (even) is normal lung function? Not at all a straight-forward question.

Figure Legend

FIGURE: FIGURE: *Contrasting approaches to the assessment of lung function: FEV1Q expresses FEV_1 as multiples of a theoretical minimum required for survival derived from the first percentile of FEV1 in a population attending lung function assessments, whilst FEV_1 % predicted expresses FEV_1 as the percentage below an 'expected' normal derived from a specified reference population.*

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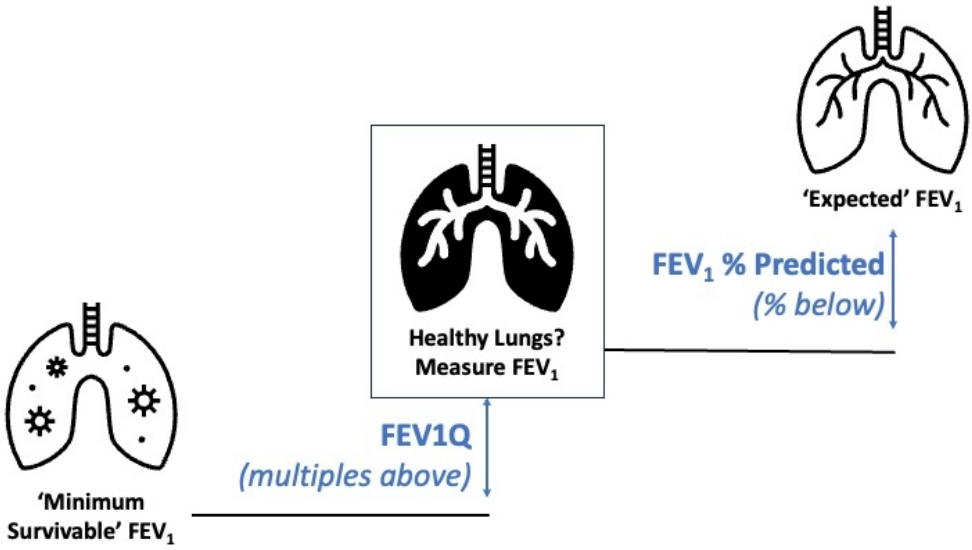

FIGURE: Contrasting approaches to the assessment of lung function: FEV1Q expresses FEV1 as multiples of a theoretical minimum required for survival derived from the first percentile of FEV1 in a population attending lung function assessments (0.4L for women and 0.5L for men), whilst FEV1 % predicted expresses FEV1 as the percentage below an 'expected' normal derived from a specified reference population.

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