



Published in final edited form as:

*Respir Med.* 2015 July ; 109(7): 928. doi:10.1016/j.rmed.2013.09.024.

## Fixed ratio or lower limit of normal (LLN) as cut-off value for FEV<sub>1</sub>/VC

Carlos A. Vaz Fragoso<sup>1</sup>, Jeffrey J. Pretto<sup>2</sup>, and Philip H. Quanjer<sup>3</sup>

<sup>1</sup>Yale University School of Medicine, Department of Internal Medicine, New Haven, CT, and Veterans Affairs Clinical Epidemiology Research Center, West Haven, CT, USA <sup>2</sup>Department of Respiratory and Sleep Medicine, John Hunter Hospital, and School of Medicine and Public Health, University of Newcastle, Newcastle, New South Wales, Australia <sup>3</sup>Department of Pulmonary Diseases and Department of Paediatrics, Erasmus Medical Centre, Erasmus University, Rotterdam, the Netherlands

In a recent article,<sup>1</sup> Wollmer and Engström concluded that “FEV<sub>1</sub>/VC<0.70, LLN” increased the risk of death and likely indicated airways disease. We respectfully disagree, as follows:

- Their 95% confidence interval (0.94–1.9) for the hazard ratio (HR) of death included unity, and is therefore not statistically significant.
- Their analysis did not account for restrictive impairment (VC<LLN), a known risk factor for cardiovascular death.<sup>2,3</sup>
- Their interpretation of prior work requires clarification.<sup>4</sup> In a population study, we showed that the risk of death in older persons who had FEV<sub>1</sub>/VC<0.70 was increased in the 21.5% who also had a decreased FEV<sub>1</sub> (<5<sup>th</sup> SR-tile [LLN]), adjusted HR: 2.01 (1.60–2.54), but not in the 78.5% who had a normal FEV<sub>1</sub> (≥5<sup>th</sup> SR-tile [LLN]), adjusted HR: 1.06 (0.89–1.25).<sup>4</sup> Thus, the majority of older persons who have FEV<sub>1</sub>/VC<0.70 will have a normal FEV<sub>1</sub> and no increased mortality.<sup>4</sup>
- FEV<sub>1</sub>/VC<0.70 often occurs in asymptomatic never-smokers aged >50.<sup>5–7</sup>

Misidentification of chronic disease adversely affects patient care. The use of FEV<sub>1</sub>/FVC<0.70 as proposed by Wollmer and Engström increases the risk of poor outcomes in aging populations — clinical findings are incorrectly attributed to a respiratory impairment (potentially delaying the consideration of other diagnoses),<sup>5,8,9</sup> and respiratory therapies are inappropriately prescribed.<sup>10–13</sup>

## References

1. Wollmer P, Engström G. Fixed ratio or lower limit of normal as cut-off value for FEV<sub>1</sub>/VC: an outcome study. *Respiratory Medicine*. 2013; 107:1460–1462. [PubMed: 23845882]

2. Friedman GD, Klatsky AL, Siegelaub AB. Lung function and risk of myocardial infarction and sudden cardiac death. *NEJM*. 1976; 294:1071–5. [PubMed: 1256523]
3. Lee HM, Le H, Lee BT, et al. Forced vital capacity paired with Framingham risk score for prediction of all-cause mortality. *Eur Respir J*. 2010; 36:1002–6. [PubMed: 20562119]
4. Vaz Fragoso CA, Concato J, McAvay G, et al. Chronic obstructive pulmonary disease in older persons: a comparison of two spirometric definitions. *Respir Med*. 2010; 104:1189–96. [PubMed: 20199857]
5. Stanojevic S, Wade A, Stocks J, et al. Reference ranges for spirometry across all ages. *Am J Respir Crit Care Med*. 2008; 177:253–60. [PubMed: 18006882]
6. Quanjer PH, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3–95 year age range: the global lung function 2012 equations. *Eur Respir J*. 2012; 40:1324–43. [PubMed: 22743675]
7. Celli BR, Halbert RJ, Nordyke RJ, Schau B. Airway obstruction in never smokers: results from the third national health and nutrition examination survey. *Am J Med*. 2005; 118:1364–72. [PubMed: 16378780]
8. Vaz Fragoso CA, Concato J, McAvay G, et al. Respiratory impairment and COPD hospitalization: a competing risk analysis. *Eur Respir J*. 2012; 40:37–44. [PubMed: 22267770]
9. Vaz Fragoso CA, Gill TM, McAvay G, et al. Respiratory impairment in older persons: when less means more. *Am J Med*. 2013; 126:49–57. [PubMed: 23177541]
10. Singh S, Loke YK, Furberg CD. Inhaled anticholinergics and risk of major adverse cardiovascular events in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *JAMA*. 2008; 300:1439–50. [PubMed: 18812535]
11. Stephenson A, Seitz D, Bell CM, et al. Inhaled anticholinergic drug therapy and the risk of acute urinary retention in chronic obstructive pulmonary disease. *Arch Intern Med*. 2011; 171:914–20. [PubMed: 21606096]
12. Taylor DR. The  $\beta$ -agonist saga and its clinical relevance: on and on it goes. *Am J Respir Crit Care Med*. 2009; 179:976–8. [PubMed: 19286624]
13. Drummond MB, Dasenbrook EC, Pitz MW, et al. Inhaled corticosteroids in patients with stable chronic obstructive pulmonary disease: a systematic review and meta-analysis. *JAMA*. 2008; 300:2407–16. [PubMed: 19033591]