Significant heterogeneity in the definitions and nomenclature used for low lung function characterized by proportionate reductions in FEV₁ and FVC exists. The most widely used term, “restrictive spirometry,” is typically defined by a nonobstructive FEV₁:FVC ratio and reduced FVC. Concurrent with the introduction of the Global Initiative for Chronic Obstructive Lung Diseases (GOLD) guidelines, which defined obstruction as an FEV₁:FVC ratio of less than 0.7, a category known as “unclassified” (GOLD-U) was introduced to capture individuals with an FEV₁:FVC ratio of 0.7 or more with FEV₁ of <80% predicted on spirometry. The term, “Preserved Ratio Impaired Spirometry” (PRISm) was subsequently proposed (1) as an alternative to GOLD-U as a more informative name that would distinguish the pattern from “restriction” and “nonspecific abnormality,” both of which require assessment of total TLC. Although controversy regarding whether fixed or lower limit of normal thresholds should be used in each of these definitions, the body of literature regarding the epidemiology, risk factors, and clinical outcomes associated with symmetrically reduced FEV₁ and FVC has increased substantially over the past decade.

The prevalence of PRISm in population-based studies ranges from 7.1% to 20.3% (2–11); although PRISm is enriched for current and former smokers relative to normal spirometry, prevalence estimates in smoking cohorts (12.3%) (1, 12) are similar to those from population-based cohorts. The mean age and cumulative smoking exposure of PRISm as a group tends to be greater than those for normal spirometry and slightly less than that for obstructed spirometry (4–6, 11), and although a prominent and consistent summary statistic associated with PRISm is an increased mean body mass index relative to other spirometry groups (4–6, 11), it is notable that both high and low body mass index are associated with an increased risk for PRISm (13). Given the older age and increased prevalence of obesity and obesity-related comorbidities, including diabetes and hypertension, in PRISm, an increase in crude all-cause mortality associated with PRISm relative to normal spirometry is not unexpected (7); however, the persistence of PRISm as a risk factor for mortality despite adjustment for comorbid conditions and smoking exposure supports that impaired lung function contributes independent information relevant to survival (2–4, 11, 13, 14).

A distinctive feature of PRISm that has recently gained attention is the increased rates of transitions to both normal and obstructed spirometry over time (14). This increased frequency in transitions to other lung function categories has been validated in multiple independent cohorts (3, 9, 11) and emerging data supports that subsets of PRISm with distinct trajectories (e.g., “persistent PRISm” and “PRISm-to-normal”) may be differentially associated with mortality (9). Concerns regarding whether the increase in transitions in PRISm represent artifacts owing to measurement variability or imprecision (e.g., noise) exist; however, recent work focusing on transitions associated with substantial changes in lung function (15), which may be more likely to reflect pathological changes, continues to support an enrichment of “significant transitions” among individuals with PRISm.

Despite an increasing body of literature on PRISm, significant knowledge gaps remain. First, the majority of studies examining prospective outcomes, such as mortality and hospitalizations, have been conducted in cohorts primarily comprised of individuals of European descent; data on outcomes associated with PRISm in other races, ethnicities, and societies is modest. Second, the number of studies with longitudinal spirometry data remains limited. Among studies with such data available, the number of spirometry assessments typically ranges between two and three, often with extended periods between assessments. Third, data on anatomical, functional, or genomic variation that may contribute to the development, progression, and clinical outcomes associated with PRISm is also severely limited.

In this issue of the Journal, the study by Washio and colleagues (pp. 563–572), which examines both the cross-sectional features and longitudinal behavior of PRISm within a Japanese population-based...
cohort, addresses several of the existing knowledge gaps (10). In addition to confirming associations between PRISm and all-cause and cardiovascular mortality reported in studies based in Western societies (9, 11, 13), the authors identify a potential interaction between current smoking and PRISm with respect to increased all-cause mortality. In the authors’ analyses of their longitudinal data, which was unique in both the number of (median, 4) and interval between assessments (annual), the rates of recurrent PRISm (59.4%) were lower than the rates of recurrent normal spirometry (79.9%) and recurrent airflow limitation (76.8%) (10); these findings extend observations reported in previous studies (11, 12, 14) by confirming that increased transitions in PRISm are observable over relatively short periods. Finally, the risk of incident airflow limitation was increased among PRISm relative to normal spirometry, supporting early hypotheses that PRISm may be a precursor of chronic obstructive pulmonary disease in some individuals (10). Strengths of the study include 1) a deeply phenotyped cohort with objective data on multiple comorbid conditions (e.g., serum cholesterol, creatinine, etc.); 2) consistent results in numerous subgroup and sensitivity analyses regardless of whether fixed thresholds or lower limit of normal criteria were used to define lung function categories; and 3) an inclusive approach to the analysis of longitudinal data from multiple time points. Relative weaknesses include the lack of post-bronchodilator spirometry and modest sample sizes with a short duration of follow-up for prospective outcomes (median, 5.3 yr), which may have limited power for cause-specific mortality and other subgroup analyses.

Although work by Washio and colleagues (10) and others in the field has helped to increase awareness of the existence and significance of PRISm, it has also highlighted the lack of diagnostic and management guidelines for PRISm, especially when standard clinical evaluations fail to identify a specific underlying cause. PRISm is associated with significant morbidity, including increased respiratory symptoms (1, 4), reduced exercise tolerance (1), and increased rates of respiratory-related hospitalizations and deaths (9, 13) relative to normal spirometry. Individuals with PRISm have increased rates of receiving clinical diagnoses of asthma as well as chronic obstructive pulmonary disease (1, 4, 11) and have increased rates of inhaled medication use despite the lack of evidence for their efficacy in nonobstructive respiratory disease. Continued coordinated efforts by researchers and clinicians to improve our collective understanding of the pathophysiologic disturbances which contribute to the development, progression, and potential resolution of PRISm will be necessary to build on the progress made thus far.

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