

Pre-COPD and PRISM: Wrong definitions with significant clinical impact

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ABSTRACT

'Pre-COPD' is defined as a high-risk state in individuals with symptoms like cough with sputum production and dyspnea, physiological abnormalities like low FEV1, faster decline of FEV1, low DLCO etc and radiological abnormalities like airway abnormalities and emphysema, with a normal FeV1/ FVC ratio in the spirometry. The term 'PRISM—Preserved Ratio Impaired Spirometry' was also introduced as a subset of Pre-COPD with FEV1 < 80%, but with preserved or normal FEV1/ FVC ratio. If a person is symptomatic with lung function test, radiology and even histology suggestive of COPD, how can we call them 'Pre-COPD' just because the spirometric FEV1/FVC ratio did not fall less than 70% or below the 5th percentile. There are various reasons why we might fail to demonstrate an airway obstruction just by FeV1/ FVC ratio alone. Overdependence on spirometry to define clinical terminologies in COPD can have adverse effects on the disease management. In this article, we discuss the pit falls in the definitions of 'Pre-COPD' and 'PRISM' and also the need of better clinical definitions in detail.

Keywords: Pre-COPD, PRISM, Spirometry, Oscillometry, COPD

INTRODUCTION

GOLD 2025 defines Chronic Obstructive Pulmonary Disease (COPD) as a heterogeneous lung disease characterized by chronic symptoms like cough, dyspnea and sputum production with exacerbations, due to airway or alveolar abnormalities like bronchitis, emphysema etc, resulting in persistent and often progressive airflow obstruction.¹ About 4% of the world population is affected by COPD.² It is the third leading cause of death worldwide, claiming the life of around 3.2 million people every year.³

The estimated global prevalence of COPD is about 12.16%.⁴ Distribution of COPD is irregular around the world and the data from different parts of the world, especially with low health care facilities are scarce.⁵

The prevalence of COPD in these regions with no proper investigation and documentation are expected to be higher than the global prevalence. Hence identifying COPD cases at the earliest and managing them appropriately to prevent complications is always a challenge.

In 2021, Han et al proposed a new terminology 'Pre-COPD' which was defined as a high risk state in individuals with symptoms like cough with sputum production and dyspnea, physiological abnormalities like low FEV1, faster decline of FEV1, low DLCO etc and radiological abnormalities like airway abnormalities and emphysema.⁶ The term 'PRISM—Preserved Ratio Impaired Spirometry' was also introduced as a subset of Pre-COPD with FEV1 < 80%, but with preserved or normal FEV1/FVC ratio.⁷ 'Pre COPD' was projected as a pre disease status similar to pre eclampsia, pre hypertension, pre diabetes and pre cancer. Identifying a pre disease condition and taking adequate precautions to prevent the incidence of the disease and cautiously following them up to avoid complications in the future is a much needed strategy

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DOI: 10.12746/swjm.v14i60.1676

for any disease. But is using an exclusive spirometry based definition for Pre COPD, an appropriate strategy?

Various studies referred to come to the conclusion of introducing the new terminology shows that those cohorts were

- **Symptomatic**

They had symptoms like dyspnea on exertion, cough, expectoration and wheeze^{8,9}

- **Abnormal spirometry**

Spirometry findings like low FEV1, faster decline of FEV1 and low DLCO were evident in them, except for a normal FEV1/ FVC ratio^{10,11}

- **Radiological abnormalities**

The so called 'Pre COPD' patients were shown to be having various radiological abnormalities suggestive of air way obstruction and other COPD related findings including emphysema and lower smaller airway diameter.^{12,13}

Even histopathological analysis of the tissue samples from these regions have showed significant airway obstruction.¹⁴

If a person is symptomatic with lung function test, radiology and even histology suggestive of COPD, how can we call them 'Pre-COPD' just because the spirometric FEV1/FVC ratio did not fall less than 70% or below the 5th percentile. There are various reasons why we might fail to demonstrate an airway obstruction just by FeV1/ FVC ratio alone. Even though, spirometry is widely used detect and demonstrate bronchial obstruction, spirometry is grossly a patient effort-dependent test where the patient has to forcefully inhale and exhale. The values depend on various factors like the effort by the spirometry technician, the understanding of the patient and the co-existing lung diseases and the co-morbidities. According to Landman et al, only less than 2/3rd of the spirometry tests in dedicated respiratory laboratories fulfil the ERS/ATS criteria.¹⁵ Spirometry tests done in other centres are even lower than this. Extremes of age also adds on to the difficulty.¹⁶ International population-based BOLD study demonstrated a restrictive

pattern in spirometry in those with systemic hypertension, diabetes mellitus, and cardiovascular diseases.¹⁷

Spirometry was our only tool to detect airway obstruction in the past. But in the current era, giving a superior value to a weaker tool like spirometry over the patient's symptoms, other extended lung function test parameters and even radiology to define a 'pre-disease' status should be prevented. A 'Pre disease' condition should be a state detected as a subtle change in one of the very sensitive parameter in a screening test in the absence of symptoms or any other signs in contributing investigations. For example 'Pre-Eclampsia' is a serious clinical condition during pregnancy characterized with elevated systemic blood pressure and proteinuria after 20 weeks of gestation or any other organ damage.¹⁸ If this condition left undetected or uncontrolled, it can lead to a detrimental condition called eclampsia where the pregnant woman can have severe convulsions leading to even death.¹⁹ 'Pre-eclampsia' is a clinical condition which can progress to eclampsia, a serious clinical complication with high mortality. Thus, a disease and its pre-disease state need to be defined clinically rather than the presence or absence of a single questionable finding in a test.

Defining 'Pre-COPD' on the basis of a normal FeV1/FVC ratio even in the presence of symptoms, abnormal lung function test and radiology is like defining a lung cancer in a patient with cough, loss of weight and appetite and contrast enhanced CT thorax showing a lung mass causing superior venacaval compression syndrome with adrenal metastasis as 'Pre Cancer' just because the chest x ray failed to identify the lung lesion. A clinically, pathologically and radiologically established disease should never be tagged as a pre-disease condition based on a single finding in a particular test.

Introduction of the terms 'Pre COPD' and 'PRISM' have led to various clinical trials and studies trying to find the role of already established medications for COPD in these new entities. These will lead to unwanted expenditure of money, time and efforts and unnecessary duplication of studies which had been already conducted in COPD and the results of which were already established. Calling a pathologically

established COPD in a patient with all the related complications as 'Pre-COPD' just because the spirometry failed to demonstrate a significantly reduced FeV1/FVC ratio, will lead to suboptimal medical management by the clinician.

Forced Oscillometry Technique has proven to be a more sensitive and effective tool than spirometry in detecting an airway obstruction.²⁰ Various studies where oscillometry was performed in 'Pre COPD' patients, had detect significant airway obstruction.²¹ These studies and the existing definitions of 'Pre-COPD' and 'PRISM' are not pointing towards a pre-disease state, but to the weakness of the spirometry test and the disadvantage of overdependence on the FeV1/FVC ratio. Clinical findings along with lung function test parameters and radiological findings should be incorporated appropriately in making a diagnosis of COPD.

'Pre-COPD' should be ideally defined by positivity in a particular test or parameter in people who are asymptomatic and no other investigation suggestive of an active COPD. This screening tool need to be applied to the population who are at risk of developing COPD including genetic risk (alpha 1 antitrypsin deficiency and other genetic variants), abnormal lung development (pre mature birth, low birth weight), environmental risk (cigarette smoking, biomass fuel exposure), infections (tuberculosis, HIV, childhood infections) and bronchial asthma, to identify them before acquiring the active disease. Those who are found to be having 'Pre COPD' need to be followed up to see how many of them actually develops COPD in the future. Confirmation of the disease should be based on the clinical, lung function test and radiological evidence, and just not spirometry.

Interventions need to be applied to the 'Pre COPD' group and analysis need to be done to find out the effectiveness of the interventions in preventing the development of active COPD. 'Isolated rise of R5–R20' the increase in R5–R20 in oscillometry without an increase in R5, proposed by Paul et al²² can be considered as an early sign of small airway obstruction, a screening tool in this aspect.

All the experts and global professional organizations in this field should take a strong stand to erase

the current definition of 'Pre COPD' and replace it with a better logical and reasonable one and also to step down 'PRISM' from being a risk factor for COPD, for the better utilization of resources in a meaningful manner.

Article citation: Paul A. Pre-COPD and PRISM: Wrong definitions with significant clinical impact. *The Southwest Journal of Medicine*. 2026;14(60):4–7
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Conflicts of interest: none

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