The Evolving Role of Lung Function Interpretation: Clinical Implications of the new ERS/ATS Standards in Asthma Care

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ABSTRACT

Asthma remains a significant public health challenge, requiring precise diagnostic and management strategies. Pulmonary function tests (PFTs) are essential in assessing disease severity, guiding treatment decisions, and monitoring disease progression. The 2022 ERS/ATS technical standards introduced critical updates to enhance the accuracy and standardization of pulmonary function interpretation. These modifications include the adoption of Global Lung Initiative (GLI) reference values, the transition from race-based to race-neutral equations, the replacement of percent-predicted values with z-scores, and a redefinition of bronchodilator responsiveness criteria. Additionally, new spirometric patterns such as dysanaptic impairment and preserved ratio impaired spirometry (PRISm) have been recognized, improving the detection and characterization of airflow limitation. These updates significantly impact asthma management by refining disease phenotyping, improving diagnostic precision, and guiding more personalized treatment strategies. Furthermore, advancements in artificial intelligence are expected to enhance predictive analytics and early intervention strategies in pulmonary function assessment. However, challenges remain in the clinical adoption of these modifications, particularly regarding the classification of disease severity and the impact of race-neutral equations on diagnostic thresholds. Future research is necessary to validate the long-term implications of these changes on asthma outcomes. Clinicians must familiarize themselves with the evolving standards to optimize patient care and reduce health disparities. The 2022 ERS/ATS guidelines represent a substantial advancement in pulmonary function assessment, with the potential to improve both clinical decision-making and patient prognosis in asthma management.

Key words: Asthma; Lung Function; Spirometry; Reference Equations; Guidelines.

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RESUMEN

Las pruebas de función pulmonar son fundamentales para evaluar la gravedad del asma, guiar las decisiones terapéuticas y monitorizar su progresión. Las recomendaciones técnicas de la ERS/ATS de 2022 introdujeron actualizaciones clave para mejorar la precisión y estandarización en la interpretación de la función pulmonar. Estas modificaciones incluyen la adopción de los valores de referencia de la *Global Lung Initiative* (GLI), la transición hacia ecuaciones neutras, la sustitución de los valores porcentuales del predicho por los z-scores y la redefinición de los criterios de respuesta broncodilatadora. Además, se han reconocido nuevos patrones espirométricos, como la alteración disanápica y la espirometría con cociente preservado y alteración de la función pulmonar (PRISm), lo que mejora la detección y caracterización de la limitación del flujo aéreo. Estas actualizaciones refinan la caracterización fenotípica del asma, mejoran la precisión diagnóstica y facilitan estrategias terapéuticas más personalizadas. No obstante, persisten desafíos en la adopción clínica de estas modificaciones, en particular en la clasificación de la gravedad de la enfermedad y en el impacto de las ecuaciones neutras sobre los umbrales diagnósticos. Aunque se necesita conocer las implicaciones a largo plazo de estos cambios en los pacientes con asma, resulta conveniente la familiarización con estos estándares para optimizar la atención del paciente y reducir las disparidades en salud. Las guías ERS/ATS de 2022 representan un avance significativo en la evaluación de la función pulmonar, con potencialidad para mejorar la toma de decisiones clínicas y el pronóstico de los pacientes con asma.

Palabras clave: Asma; Función pulmonar; Espirometría; Ecuaciones de referencia; Guías clínicas.

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INTRODUCTION

Asthma remains a major public health concern, affecting millions of individuals worldwide and contributing significantly to morbidity, healthcare utilization, and economic burden [1, 2]. Given its chronic nature and the inherent variability in disease expression, effective monitoring tools are essential for optimizing disease control and guiding therapeutic interventions. Among these, pulmonary function assessment is a cornerstone in the evaluation and management of asthma, providing critical insights into asthma pathophysiology [3]. Spirometry remains the primary tool for detecting bronchial obstruction, assessing both baseline lung function and responsiveness to bronchodilators, while additional assessments, including lung volume measurements and diffusing capacity of carbon monoxide (DLCO), offer further insights into disease profile and severity [4].

Recognizing the need for standardization and accuracy in pulmonary function interpretation, leading scientific societies such as the European Respiratory Society (ERS) and the American Thoracic Society (ATS) have continuously refined guidelines to improve the reliability and clinical applicability of PFTs [5, 6]. These efforts have culminated in the 2022 ERS/ATS technical standards [7], which introduce critical updates aimed at addressing persistent challenges in the interpretation of lung function parameters, including the refinement of reference equations and diagnostic thresholds (Table 1). Given the pivotal role of lung function assessment in asthma care, these modifications may have significant implications for disease diagnosis, phenotyping, and treatment strategies.

This review aims to critically examine the recent updates in ERS/ATS pulmonary function interpretation standards, assessing their impact on the clinical approach to asthma management. By analyzing the rationale behind these changes and their potential influence on diagnostic and therapeutic decision-making, we seek to provide clinicians with a comprehensive perspective on how these evolving guidelines shape the landscape of asthma care.

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CLINICAL IMPLICATIONS OF KEY UPDATES IN ERS/ATS STANDARDS

Adoption of Global Lung Initiative (GLI) Reference Values

A major update in the new ERS/ATS standards is the recommendation to use GLI reference values for spirometry and other pulmonary function parameters. The GLI project provides age-, sex-, and height-specific reference equations derived from a large, multiethnic population. Currently, reference equations are available for spirometry [8], lung volumes [9], DLCO [10], and multiple-breath washout [11], with additional equations in various stages of development.

The universal adoption of GLI reference equations offers several advantages, including improved standardization of PFT reporting and interpretation, consistency across different PFTs—preventing discordant results [12]—and applicability across all ages, thereby eliminating the need for transitional equations. While some controversy remains regarding the impact of transitioning from traditional pediatric reference equations (e.g., Zapletal), available evidence confirms that this change has minimal effect [13] or, at most, results in a slight overestimation of pulmonary function impairment [14]. Additionally, the availability of algorithms and open-source software for applying GLI equations in calculating functional parameters provides further advantages (https://www.lungfunction.org/; https://gli-calculator.ersnet.org).

The main implications of GLI reference adoption in asthma patients can be summarized as follows: 1) The GLI reference values enhance accuracy in identifying airflow limitation across different demographic groups; 2) By incorporating data from diverse populations, GLI reference equations reduce bias in lung function assessment, particularly for underrepresented ethnic groups; 3) Clinicians must transition from previously used reference values to the GLI system, ensuring appropriate classification of lung function abnormalities; 4) The use of GLI reference values may require updated training for healthcare professionals to facilitate accurate interpretation and application in diverse clinical settings; and 5) Comparative studies between older reference equations and the GLI system suggest improved detection of subclinical airflow limitation in pediatric and elderly populations, necessitating adjustments in early asthma diagnosis and intervention strategies.

Beyond the 2022 ERS/ATS recommendations [7], an additional significant development occurred the following year with the introduction of race-neutral reference equations

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[15]. The GLI-2023 Global equations were derived from the same dataset as conventional GLI equations but incorporated inverse probability weighting to ensure equal contribution from all racial and ethnic groups. According to the ERS, the new GLI-2023 Global equations, designed to encompass the full spectrum of lung function across all populations, should be applied with careful consideration of symptoms and medical history, particularly in clinical, occupational, and insurance contexts [16]. In alignment with this, various academic societies have endorsed these new equations for PFT interpretation. In April 2023, the ATS issued an official statement [17] recommending the use of race-neutral equations in PFT interpretation to improve diagnostic accuracy and mitigate potential harms, such as delayed diagnoses or inappropriate clinical decisions. The statement also underscores the need for further research and education to understand the impact of this shift, emphasizing that race should not be used to infer biological characteristics [17].

However, transitioning to race-neutral reference equations requires careful consideration, particularly in children, to avoid unintended consequences. An analysis of 8,719 North American children aged 5–12 years showed that race-neutral equations overestimate FEV_1 and FEV_1/FVC reference values in Black and Hispanic children, leading to a nearly 14% increase in asthma diagnoses. This shift was also associated with higher emergency visit rates and hospitalizations [18]. Another study of 24,630 children and adolescents confirmed that race-neutral equations generate lower predicted percentages and z-scores in Black children, while causing minimal differences in White children [19]. Consequently, adjusted models indicate that Black children are nearly three times more likely to present abnormal spirometry findings when transitioning from race-based to race-neutral equations [19].

Current evidence suggests similar findings in children and adolescents with asthma, where race-neutral equations yield lower predicted percentages and z-scores for FEV_1 in Black children, resulting in a higher percentage of abnormal spirometry findings in both controlled and uncontrolled asthma cases [20].

The clinical implications of employing race-neutral reference equations in asthma care include: 1) Eliminating race-based adjustments in PFT interpretation promotes equity in respiratory medicine; 2) Transitioning to race-neutral equations ensures that lung function impairments are not underestimated in certain racial groups, leading to

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earlier and more accurate diagnoses; 3) Clinicians must be aware of this change and educate patients and colleagues on its significance in reducing healthcare disparities; 4) Adopting race-neutral equations may improve health outcomes in minority populations previously at risk of underdiagnosis or undertreatment; 5) The removal of race-specific reference values aligns with broader global initiatives aimed at eliminating implicit biases in medical practice, reinforcing ethical principles of equitable healthcare delivery; and 6) Studies examining the clinical impact of this shift suggest that race-neutral equations may lead to increased diagnoses of restrictive lung disease in previously overlooked populations, prompting more aggressive early interventions.

Replacement of Percent Predicted with Lower Limit of Normal or z-score

The 2022 ERS/ATS recommendations for pulmonary function interpretation propose replacing the traditional percent predicted value (%Pred) with the lower limit of normal (LLN) and the z-score [7]. While this shift has been discussed for some time, the current guidelines reinforce its adoption to enhance diagnostic precision and reduce misclassification of ventilatory disorders, allowing for a more individualized assessment that aligns with the statistical distribution of spirometric values in the general population.

Historically, %Pred has been the most widely used criterion for pulmonary function assessment. However, this method has significant limitations [21]. Notably, it does not account for the natural variability of values within a healthy population, potentially leading to misclassification of individuals with expected variability as abnormal, or failing to detect impairments in individuals whose values fall within the reference range but at the lower end of the distribution. Moreover, %Pred lacks uniform applicability across age groups, as lung function values change with age; thus, %Pred tends to overestimate impairment in older adults and underestimate it in children and adolescents. Additionally, %Pred relies on arbitrary cutoff points (typically 80% of the predicted value), which do not reflect the true population distribution and may result in inaccurate classifications.

In contrast, the 2022 ERS/ATS recommendations emphasize the use of LLN and z-score, two statistical approaches that allow for a more precise interpretation of pulmonary

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function [7]. The lower limit of normal (LLN) is defined as the value below which approximately 5% of the healthy population falls, adjusted for age, sex, height, and ethnicity. This approach more accurately differentiates pathological values from those that simply reflect individual variability within normal limits, preventing misclassification of individuals with low but physiologically normal lung function.

The z-score expresses the deviation of a measured value from the population mean in terms of standard deviations. A z-score ≤ -1.64 indicates that the functional parameter falls at or below the 5th percentile (Figure 1), suggesting clinically relevant impairment. Unlike %Pred, the z-score enables standardized comparisons across individuals of different ages and physiological backgrounds [21], improving diagnostic sensitivity and specificity while reducing both overdiagnosis and underdiagnosis [22].

Implementing LLN and z-score instead of %Pred has significant clinical implications, particularly for vulnerable populations such as children, older adults, and individuals with anthropometric characteristics outside the standard reference range [7, 23]. More accurate classification of obstructive or restrictive ventilatory patterns facilitates better therapeutic decision-making, preventing unnecessary medication use in individuals with low but normal pulmonary function and enabling earlier intervention in patients with incipient decline who still fall within the traditional %Pred reference range.

However, despite the advantages of LLN and z-score, it is important to acknowledge that much of the available evidence on asthma prognosis and treatment is based on patient stratification using %Pred. This includes defining study populations in clinical trials as well as establishing diagnostic and prognostic scales [24, 25]. Therefore, further scientific research is needed to validate these new functional assessment parameters in clinical practice.

Recognition of New Spirometric Patterns

An important novelty in the 2022 ERS/ATS pulmonary function interpretation guidelines [7] is the identification of new spirometric impairment patterns, including the dysanaptic and nonspecific patterns (Figure 2).

Obstructive impairment is once again defined based on the LLN of the FEV_1/FVC ratio rather than using a fixed threshold of 0.70. While this spirometric criterion for

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obstructive ventilatory impairment aligns with the 1991-ATS [26] and 2005-ATS/ERS [5] guidelines, it differs from definitions provided by major obstructive disease management guidelines. Notably, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [27] and the ATS/ERS COPD guidelines [28] continue to use a fixed FEV_1/FVC threshold of 0.70 to identify obstruction, whereas asthma guidelines such as GEMA [29] and GINA [1] acknowledge the possibility of defining airflow limitation based on the LLN. Increasing evidence supports the definitive dismissal of the fixed 0.70 threshold for airflow limitation diagnosis [30]. This is primarily because the FEV_1/FVC ratio declines with age, leading to an underestimation of obstructive impairment prevalence in younger individuals and an overestimation in the elderly [30]. In fact, the FEV_1/FVC ratio decreases with age and height even in nonsmokers, where the LLN drops below the fixed 0.70 threshold beyond age 45 [16]. Consequently, using the 0.70 threshold results in misclassification rates of up to 50% in older adults [16]. Furthermore, the fixed ratio fails to accurately distinguish mild obstruction and introduces significant age- and sex-related biases [30].

A newly recognized spirometric pattern is the dysanaptic impairment. Under maximal effort conditions, a low FEV_1/FVC ratio with a normal FEV_1 in an otherwise healthy individual may result from disproportionate growth between the airways and lung parenchyma [7]. Dysanapsis involves an unequal growth pattern, where lung parenchyma and airway length expand more than airway caliber [7]. While this profile may represent a normal variant in healthy individuals, it can also indicate a predisposition to obstructive disease [31-34]. This functional profile should be considered a potential normal variant, particularly in healthy, asymptomatic young, tall males, especially if FVC is increased and distal flows remain normal [31]. In children, dysanaptic growth is associated with obesity or rapid weight gain in early childhood and predicts expiratory flow limitation, serving as an indicator of obstruction susceptibility [32-34]. Determining whether dysanaptic growth signifies obstruction or a normal variant requires clinical context assessment and additional tests, such as bronchodilator response testing, DLCO measurements, respiratory muscle strength evaluation, and cardiopulmonary exercise testing [7]. Furthermore, proper execution of forced expiratory maneuvers must be verified, as submaximal effort can overestimate FEV_1 and consequently lead to misinterpretation [31].

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Another recognized pattern is preserved ratio impaired spirometry (PRISm). In the absence of plethysmography to confirm total lung capacity (TLC) reduction, a decreased FVC or FEV_1 with a normal FEV_1/FVC ratio corresponds to PRISm [35, 36]. This impairment can be observed in restrictive lung disease, small airway disease, or result from suboptimal effort, where incomplete inspiration or expiration leads to overestimated FEV_1 and FVC values [7]. In such cases, the flow-volume curve may display a downward concavity at the end of expiration [7]. Under optimal effort conditions and in the absence of TLC determination, bronchodilator testing may be useful [7, 37]. A significant response to bronchodilation could indicate a degree of bronchial reactivity [7, 37]. Additionally, evaluating slow vital capacity (SVC) can help. If FVC is at least 200 mL lower than SVC, this may suggest small airway collapse with air trapping during forced expiration [12, 16, 38].

PRISm is a relatively common entity, with a prevalence ranging from 1.4% to 10% in the general population [35, 36, 39]. In Norwegian males, identified risk factors for PRISm include obesity, smoking history, and respiratory symptoms such as cough, sputum production, wheezing, asthma, or bronchitis [39]. Furthermore, in this population, PRISm is associated with an increased risk of respiratory mortality (hazard ratio 4.00 [95% CI: 1.22–13.16]) [39]. Another study in individuals aged 35–65 years from primary care centers confirms that asthma history and smoking are risk factors for PRISm, which, in turn, represents an independent risk factor for airflow limitation over the following five years [40]. Thus, PRISm could reflect a pre-obstructive impairment. It has also been linked to an increased risk of small airway dysfunction, as defined by oscillometry and imaging techniques [41].

When TLC measurement is available, spirometric impairment can be better characterized. The presence of normal TLC, a normal FEV_1/FVC ratio, and a reduced FVC or FEV_1 characterizes nonspecific ventilatory impairment [37, 42]. The significance of this pattern remains unclear. It may be a precursor to either a restrictive or obstructive process [42]. Long-term follow-up of patients with nonspecific impairment revealed that two-thirds remained stable, while one-third progressed to either restriction or obstruction [42]. In obstructive processes, small airway collapse may lead to FVC reduction and residual volume increase before a decline in FEV_1/FVC is observed.

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Finally, the presence of a low FEV_1/FVC ratio with reduced TLC allows for the diagnosis of mixed ventilatory impairment, which, while less frequent, can be present in some asthma patients. This pattern represents the combination of airflow limitation and parenchymal or extraparenchymal lung pathology. Although less common than obstruction, it can be observed in asthmatic patients with comorbid congestive heart failure or obesity.

In summary, the incorporation of these new spirometric patterns enables a more precise assessment of functional impairments in asthma, leading to improved diagnostic accuracy and tailored therapeutic strategies. While PRISm is more commonly associated with restrictive diseases, in asthma patients, it may indicate significant airflow obstruction with air trapping, warranting static lung volume measurements for comprehensive evaluation. In the context of asthma, identifying a nonspecific pattern may suggest obstruction with concurrent vital capacity reduction, potentially due to hyperinflation or air trapping. Lastly, evidence of a mixed impairment in asthma patients may reflect substantial obstruction accompanied by restrictive changes, possibly secondary to bronchial remodeling or comorbid conditions.

Interpretation of Lung Volumes and Pulmonary Diffusion Capacity

Recent international recommendations have been published regarding the measurement of static lung volumes [43], encompassing plethysmography, dilution techniques, and multiple-breath inert gas washout procedures, while also introducing, for the first time, a classification of quality levels for these measurements.

The two most relevant contributions of lung volume assessment in asthma are the identification of restriction or hyperinflation/air trapping. Restriction is defined by a reduced total lung capacity (TLC) (below the lower limit of normal) and is typically due to decreased muscle strength, increased elastic recoil pressure, or reduced chest wall compliance.

The new interpretation consensus differentiates between simple and complex restriction. Simple restriction involves a proportional decrease in forced vital capacity (FVC) and TLC and is characteristic of diffuse interstitial lung diseases. In contrast, complex restriction is characterized by a disproportionate decline in FVC relative to

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TLC, leading to an increased residual volume (RV) and RV/TLC ratio, suggesting air trapping without an associated decrease in the FEV_1/FVC ratio [44]. Air trapping may reflect hidden obstruction or mechanical inability to reduce thoracic cavity volume, as seen in neuromuscular diseases or obesity.

Another novelty in the updated interpretation strategy is the unification of the terms air trapping and hyperinflation into a single abnormality, characterized by an increased RV/TLC ratio or functional residual capacity (FRC)/TLC above the upper limit of normal [7]. Both air trapping and pulmonary hyperinflation are conditions that can be present in asthma patients. Therefore, static lung volume measurements have significant clinical implications in asthma, aiding in differentiating between reversible obstruction characteristic of asthma and permanent structural changes, as well as guiding the use of specific therapies to reduce hyperinflation and improve respiratory mechanics.

Regarding the diffusion capacity of carbon monoxide (DLCO), four possible abnormalities are recognized: low DLCO with low alveolar volume (VA) and reduced DLCO/VA (KCO); low DLCO and VA with normal KCO; low DLCO and VA with normal KCO; low DLCO with normal VA; and elevated DLCO [7]. The latter may result from increased pulmonary blood flow (as occasionally seen in asthma patients, as well as in obese individuals or those with left-to-right shunts), erythrocytosis, or alveolar hemorrhage. The interpretation of the three scenarios with reduced DLCO is based on evaluating alveolar volume (VA) and, in cases with reduced VA, the DLCO/VA ratio (KCO) [7]. However, Pristi and Johnson [45] identified important issues in the proposed algorithm for interpreting DLCO. Although the algorithm acknowledges that KCO increases with lower VA, it does not account for the predictable relationship between KCO, DLCO, and VA [45, 46]. Additionally, the algorithm overlooks the fact that patients with interstitial lung disease may have low, normal, or high KCO, and that patients with reduced VA due to incomplete lung expansion may exhibit normal DLCO when adjusted for VA [45].

Beyond these considerations, the updated guidelines emphasize the need to interpret DLCO in conjunction with other parameters, such as VA and the DLCO/VA ratio, to differentiate between various phenotypes and comorbid conditions. This approach has multiple clinical implications in asthma management, including 1) differentiation from other respiratory pathologies, as a reduced DLCO suggests the presence of

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concomitant diseases such as asthma-COPD overlap or early interstitial lung damage, which influence therapeutic strategies; 2) monitoring pulmonary vascular involvement, since in severe asthma or patients with secondary pulmonary hypertension, DLCO assessment allows for early detection of vascular impairment, facilitating timely interventions; 3) evaluation of treatment response, assuming that DLCO normalization following inflammation control may indicate functional improvement in patients with difficult-to-control asthma, guiding adjustments in anti-inflammatory or biologic therapy; and 4) optimization of asthma phenotypic stratification, given that an elevated DLCO may be associated with specific phenotypes, such as eosinophilic asthma.

Ultimately, the 2022 ERS/ATS guideline updates reinforce the role of DLCO as a key complementary tool in the comprehensive assessment of asthma patients, enabling more precise diagnosis and treatment optimization based on underlying pathophysiology.

Classification of Functional Impairment Severity

Another significant innovation introduced in the 2022 ERS/ATS document on pulmonary function interpretation is the establishment of a unified severity classification for all assessments based on the z-score. According to this system, any impairment is considered mild when the z-score of the corresponding parameter is between -2.5 and -1.64, moderate when the z-score ranges from -4.0 to -2.5, and severe when the z-score is below -4.0 [7].

It is important to note that this classification is based solely on mortality risk as a reference point and may not necessarily reflect the severity of symptoms, the risk of exacerbations, or social consequences. Neder [12] asserts that such a classification should primarily reflect the current functional impairment rather than future risk, as the latter is a complex construct that extends beyond pulmonary function in individual patients. Nevertheless, some uncertainties persist regarding the suitability of the ERS/ATS-recommended classification system for stratifying the severity of obstructive ventilatory impairment [47].

Assessing the severity of ventilatory impairment is often challenging and uncertain [48]. Traditionally, this evaluation has relied on arbitrary thresholds to categorize

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results into three to five levels, which correlate only loosely with disease symptoms and mortality rates [49]. It remains unclear whether the three-tier severity scale derived from the ERS/ATS z-score classification will prove more effective than previous scales based on percent predicted values [48]. In fact, studies in COPD patients have demonstrated that mortality discrimination is better achieved using percent predicted-based classifications rather than z-score-based systems, particularly in individuals over 65 years of age [50].

Additionally, other classification models based on absolute FEV_1 values in relation to the square or cubic power of height [51] or on the FEV_1/FVC ratio [52, 53] have also demonstrated high prognostic value in both healthy individuals and patients with obstructive ventilatory impairments.

Given these uncertainties and considering that the new classification has yet to be adopted by major national and international guidelines for the management of asthma and other obstructive diseases, its real impact on clinical practice and decision-making remains to be determined. This is particularly relevant considering that nearly all available evidence derives from severity stratification schemes based on percent predicted FEV_1 values.

Bronchodilator Test

The 2022 ERS/ATS consensus document introduces significant modifications in the interpretation of the bronchodilator test. The assessment remains based on changes in both FEV_1 and FVC. FEV_1 primarily reflects the degree of airflow limitation and is considered the most sensitive marker of reversible airway obstruction, as it quantifies the maximal expiratory flow in the first second of a forced maneuver. An increase in FEV_1 after bronchodilator administration is indicative of bronchodilation and improved airway patency. At the same time, FVC provides additional information, particularly in patients with obstructive lung diseases characterized by air trapping. An increase in FVC post-bronchodilator suggests a reduction in dynamic hyperinflation and improved lung emptying, which may not be captured solely by FEV_1. This response is particularly relevant in conditions where air trapping contributes significantly to respiratory symptoms. The differential behavior of FEV_1 and FVC highlights the importance of a

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comprehensive assessment of bronchodilator response, not only in terms of airflow improvement but also in evaluating changes in lung volume and ventilatory mechanics.

Instead of considering the absolute change associated with the percentage change relative to the baseline value [5], it now defines a positive test as an increase in FEV_1 or FVC >10% compared to the predicted value [7]. This new interpretation criterion aims to mitigate the impact of baseline pulmonary function on the response expressed as a percentage of the baseline value or in absolute terms, recognizing that patients with high baseline FEV_1 values are penalized when assessing percentage changes, while those with very low baseline FEV_1 values face notable limitations in achieving an increase greater than 200 mL [7]. Evaluating the bronchodilator test based on the predicted value also minimizes the effects of sex and height. Additionally, evidence suggests improved survival rates in patients with obstructive ventilatory impairment who exhibit a reversibility of more than 8% of the predicted FEV_1 [54].

The different scenarios considered in the interpretation of the bronchodilator test, as well as the subsequent steps in clinical and functional assessment, are summarised in Table 2.

However, applying the new criteria may not always confirm a bronchodilator response compared to classical criteria [45, 55], although the test result is not definitive for selecting asthma treatment [24]. Various studies in asthma patients indicate that the frequency of a positive bronchodilator test is slightly lower when applying the 2022 ERS/ATS criteria compared to the 1991 ERS/ATS recommendation [55-58]. Nevertheless, at the individual level, there is strong concordance between test results under both recommendations, with Cohen's kappa indices ranging from 0.78 to 0.89, regardless of whether GLI reference equations or other reference groups are applied [57, 58].

In any case, these potential discrepancies have little impact on the overall value of the bronchodilator test. In fact, although a bronchodilator response may indicate changes in a patient's clinical status, its utility in differentiating between various airway diseases remains imprecise [7, 59]. Therefore, some experts have suggested using non-binary reversibility criteria [60], particularly in the pediatric population [16].

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In summary, the revised bronchodilator test interpretation system has several clinical implications: 1) it improves the standardization of assessment based on predicted values, minimizing variability due to patient-specific factors such as height, sex, and baseline pulmonary function; 2) a slightly more restrictive bronchodilation criterion enhances the identification of a true bronchodilator response; and 3) shifting to a predicted value-based evaluation reduces the misclassification of asthma severity in patients with mild airflow limitation.

Longitudinal Assessment of Pulmonary Function

Longitudinal assessment of pulmonary function tests (PFTs) allows for the identification of excessive pulmonary function decline due to exposure to harmful agents, underlying disease, or disease progression [61]. Ideally, an individual's pulmonary function before disease onset would serve as the reference point [61]. However, since this information is often unavailable, comparisons are made with the physiological decline observed in the healthy population [7], accounting for biological variability and measurement errors [7, 16]. Given that variability between tests (e.g., up to 150 mL for FEV_1) far exceeds even an accelerated annual decline rate, multiple measurements over an extended period are required to establish a valid decline rate for an individual [5, 62].

Longitudinal pulmonary function assessment requires parameters that enable precise analysis of changes over time. Traditionally, % predicted has been widely used. However, it has a key limitation: it is calculated in relation to a predicted value that changes with age and other factors, complicating its interpretation in long-term follow-ups. To address this limitation, the z-score provides a more robust alternative, reflecting the standard deviation of the observed value relative to the expected value at any given time, allowing for more precise comparisons.

However, the 2022 ERS/ATS pulmonary function interpretation guidelines recommend using FEV_1Q in adults and change score in children [7]. In adults, FEV_1Q is an interesting method for evaluating pulmonary function decline [63]. It expresses FEV_1 in relation to a lower limit that represents the “survival threshold,” below which the risk of mortality increases significantly [63]. Consequently, FEV_1Q is calculated as the ratio of FEV_1 (in liters) divided by 0.5 in men or 0.4 in women [63], values corresponding to the 1st

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percentile. Under normal conditions, FEV_1Q decreases by one unit every 18 years in healthy individuals and by one unit every 10 years in smokers and older adults [63]. Therefore, FEV_1Q should remain stable for up to a year, while a rapid decline indicates a significant change in pulmonary function [7]. However, specific thresholds defining stability or rapid decline in FEV_1Q do not yet exist [64], and in practice, detecting excessive changes reliably can be challenging. Additionally, Neder [12] highlights the complexities of FEV_1Q, noting that the 1st percentile can vary significantly depending on age, body size, and underlying diseases.

Several considerations must be taken into account for pediatric populations [7]. A child or adolescent is not simply a miniature version of an adult [65, 66], and thus, longitudinal assessment of pulmonary function during a period of rapid growth and development cannot be extrapolated from adult studies [16]. Consequently, interpreting decline in children and adolescents must account for the complexity of pulmonary function during this stage of life [23]. In 2020, a change score was developed to evaluate pulmonary function decline in children and adolescents [23]. This index considers longitudinal changes in the z-score of FEV_1 using a specific formula. While this is a promising tool for assessing pulmonary function decline in pediatric populations, further studies are needed to validate its relevance.

IMPACT ON ASTHMA CARE

The recent modifications in pulmonary function interpretation introduced by the ERS and the ATS have far-reaching implications for asthma care. These changes refine diagnostic precision, optimize disease monitoring, personalize treatment approaches, and contribute to health equity. Below, we explore the most relevant aspects of these updates and their impact on asthma management.

Improved Diagnostic Accuracy

Accurate lung function assessment is essential for diagnosing asthma, particularly in patients with borderline or mild disease. The adoption of Global Lung Function Initiative (GLI) reference values enhances diagnostic precision by providing more representative and standardized baseline values across different populations. This update minimizes misclassification errors that could lead to unnecessary treatments or

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missed diagnoses. The improved accuracy is particularly relevant for distinguishing between asthma and other obstructive or restrictive pulmonary diseases, thereby optimizing patient management.

Enhanced Disease Monitoring

Asthma is a chronic condition that requires continuous monitoring to assess disease progression and treatment efficacy. The updated bronchodilator response (BDR) criteria and standardized interpretation strategies ensure that changes in lung function are detected with greater reliability over time. These modifications allow clinicians to identify subtle declines in pulmonary function, prompting timely adjustments in therapy. The standardization of spirometric interpretation also facilitates longitudinal comparisons, improving the ability to track disease evolution and response to treatment across different clinical settings.

Personalized Treatment Adjustments

The redefinition of the bronchodilator response has direct implications for therapeutic decision-making, particularly regarding the initiation or intensification of bronchodilator therapy. Patients who were previously in a diagnostic 'grey zone' can now be classified more precisely (57), potentially facilitating the implementation of personalized therapeutic interventions. This refinement may be particularly relevant when considering the optimal timing for the introduction of inhaled corticosteroids or combination therapies, as it could help ensure that patients receive treatment that is both evidence-based and appropriately tailored to their needs. Additionally, the updated guidelines encourage a more nuanced approach to bronchodilator testing, potentially reducing the overuse of medications in cases where reversibility criteria are less clear.

Addressing Health Disparities

Historically, pulmonary function reference values have incorporated race-based adjustments, a practice increasingly recognized as problematic due to its potential to reinforce health disparities. The transition to race-neutral GLI reference equations represents a significant step toward equitable asthma care. This change ensures that

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spirometric assessments are not influenced by race-based biases, which previously could have led to underdiagnosis or undertreatment in certain populations. Clinicians must be aware of these updates and advocate for their implementation to promote equitable care across diverse patient groups.

Implications for Pediatric Asthma Management

The use of GLI reference values holds particular significance in pediatric asthma care, where lung function trajectories change dynamically with growth and development. More accurate and age-appropriate reference equations improve early detection of abnormal pulmonary function patterns, enabling earlier and more effective interventions. This refinement supports clinicians in differentiating between transient wheezing, persistent asthma, and other obstructive conditions in children. Additionally, standardized lung function interpretation can guide treatment adjustments during key developmental stages, optimizing long-term respiratory health outcomes.

Integration with Emerging Technologies

The growing incorporation of artificial intelligence (AI) and machine learning in pulmonary medicine presents new opportunities for enhancing asthma management. The updated ERS/ATS standards provide a robust framework for integrating predictive analytics into clinical practice. AI-driven algorithms, leveraging refined reference values and bronchodilator response criteria, can enhance the detection of subtle lung function changes, facilitate personalized treatment recommendations, and improve risk stratification. These advancements hold promise for early intervention strategies, potentially reducing exacerbations and improving long-term disease control.

CONCLUSION

The revised ERS/ATS standards in pulmonary function interpretation mark a significant advancement in asthma diagnosis and management. By improving diagnostic accuracy, enhancing disease monitoring, supporting personalized treatment approaches, addressing health disparities, refining pediatric asthma care, and integrating with emerging technologies, these updates have the potential to transform asthma care.

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Widespread adoption and implementation of these standards will be critical in ensuring optimal outcomes for patients across different clinical settings and demographic groups.

Conflicts of interest

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Table 1. Summary of the main modifications introduced in the 2022 ERS/ATS recommendations for pulmonary function interpretation*

Parameter/Test	Recommendations
Reference equations	To use GLI reference equations Clarify that biological sex, not gender be used To assess race-neutral equations
Defining normal range	General use of LLN (5^{th} percentile) and ULN (95^{th} percentile) Use of fixed ratio $FEV_1/FVC < 0.7$ or 80% predicted not recommended
Classification of physiological impairments	Spirometry: airflow obstruction; use lung volumes to detect hyperinflation/air trapping; dysanapsis; non-specific pattern; PRISm
	Lung volumes: restrictive disorder (simple *versus* complex); hyperinflation/air trapping; mixed disorder
	Gas transfer: using VA and KCO to classify low DLCO
Severity of lung function impairment	For all measures use z-score: Mild: -1.65 to -2.5 Moderate: -2.51 to -4.0 Severe: <-4.1
Bronchodilator response	>10% of predicted value in FEV_1 or FVC
Interpretation of change over time	FEV_1Q in adults Conditional change score in children

*Abbreviations: GLI, Global Lung Initiative; LLN, lower limit of normal; ULN, upper limit of normal; FEV_1, forced expiratory volume at 1 second; FVC, forced vital capacity; PRISm, preserved ratio impaired spirometry; VA, alveolar volume; DLCO, diffusing capacity of the lungs for carbon monoxide; KCO, DLCO/VA ratio; FEV_1Q, quotient FEV_1.

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Table 2. Interpretation of bronchodilator response and subsequent clinical steps according to ERS/ATS 2022 criteria*

Post-BD Spirometry Pattern	**Interpretation**	**ERS/ATS 2022 Positive Response Criteria**	**Next Steps**
Increase in FEV_1 and FVC (FEV_1/FVC ≥ LLN)	**Reversible airflow limitation** (Asthma, ACO without fixed obstruction)	FEV_1 and/or FVC increase ≥10% of predicted value	Assess FeNO, blood eosinophils, or allergy markers to confirm asthma or ACO
Increase in FEV_1 and FVC (FEV_1/FVC < LLN)	**Reversible airflow limitation with persistent obstruction** (Asthma, ACO with fixed component)	FEV_1 and/or FVC increase ≥10% of predicted value	Evaluate for fixed obstruction using HRCT or DLCO testing
Stable FEV_1, increased FVC (FEV_1/FVC ≥ LLN)	**Bronchodilator-reversible air trapping** (Early COPD, small airway dysfunction, hyperinflation improvement)	FEV_1 remains stable, FVC increases ≥10% of predicted value	Assess RV, IC/TLC ratio for hyperinflation; consider impulse oscillometry (IOS), DLCO, or HRCT
Stable FEV_1, increased FVC (FEV_1/FVC < LLN)	**Bronchodilator-reversible air trapping with persistent airway obstruction**	FEV_1 remains stable, FVC increases ≥10% of predicted value	Evaluate for fixed obstruction in addition to hyperinflation studies

*Abbreviations: FEV_1, forced expiratory volume at 1 second; FVC, forced vital capacity; LLN, lower limit of normal; FeNO, fractional exhaled nitric oxide; ACO, asthma COPD overlap; HRCT, high-resolution computed tomography; DLCO, diffusing capacity of the lungs for carbon monoxide; RV, residual volume; IC, inspiratory capacity; TLC, total lung capacity.

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Figure 1. Schematic representation of the normal distribution curve of a respiratory function parameter and the correspondence of different percentiles with z-score values. In the lower panel, the blue arrows represent the z-score values of a patient with an obstructive impairment.

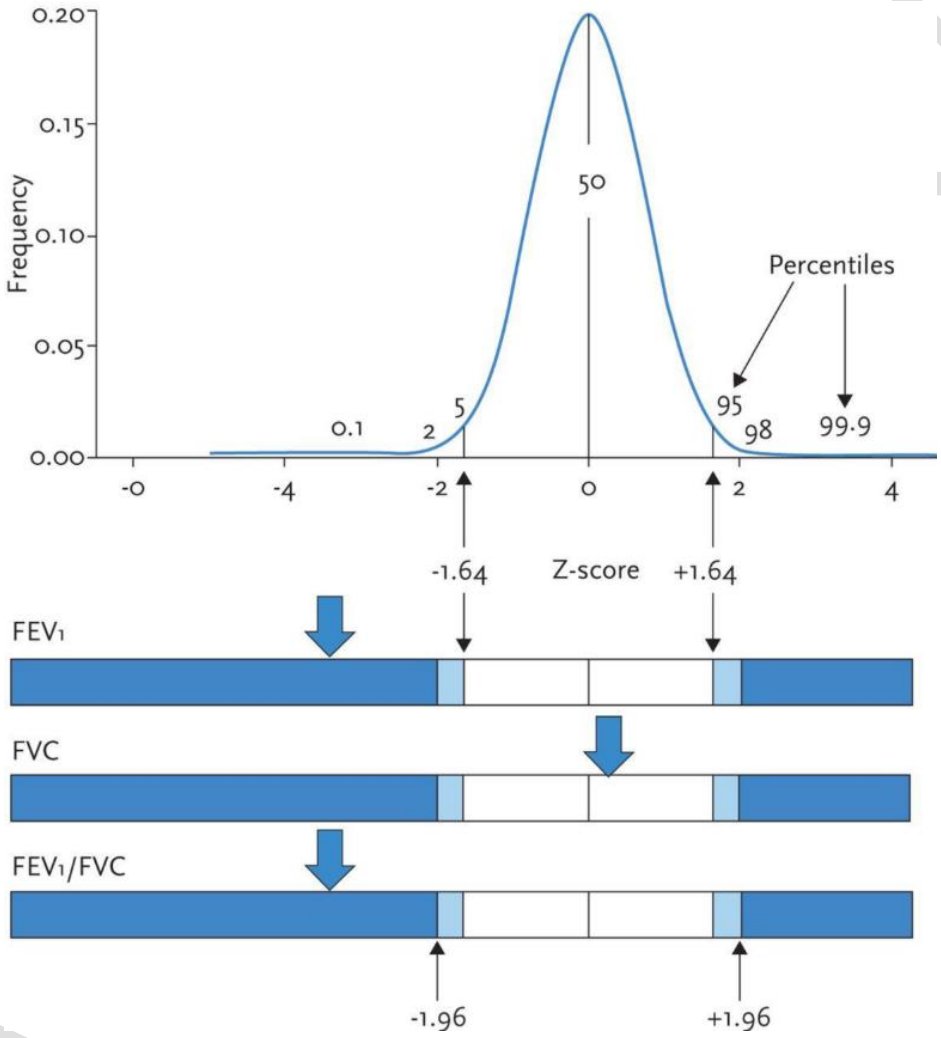

Figure 2. Algorithm for the interpretation of spirometry proposed by the 2022 ERS/ATS recommendations for pulmonary function interpretation. It includes the assessment of static lung volumes for the definitive characterization of certain patterns. Abbreviations: ↓, reduced value (< lower limit of normality); ↑, increased value (> upper limit of normality); N, normal value (between both limits of normality).