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BRIEF REPORT

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COMPARISON OF BRONCHODILATOR TEST THRESHOLDS: ATS/ERS 2005 VS. ERS/ATS 2022

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ABSTRACT

The ATS/ERS 2005 standard defines a significant bronchodilator response (BDR) in terms of FEV_1 as an increase of ≥12% and ≥200 mL, while ERS/ATS 2022 proposes a ≥10% increase in percent predicted FEV_1. Data from 482 children aged 4-17 years, all diagnosed with asthma, were analyzed to evaluate the concordance between these two thresholds. Results showed substantial agreement (Cohen's kappa = 0.83) between the two criteria, with 93.1% concordance across the pediatric asthma cohort. While the ERS/ATS 2022 threshold classified slightly more children as bronchodilator responders, particularly among those with preserved lung function, this did not significantly alter overall clinical interpretation. However, among children with baseline airway obstruction, ERS/ATS 2022 identified significantly more positive cases than ATS/ERS 2005, suggesting greater sensitivity in this subgroup. These findings support the applicability of ERS/ATS 2022 in pediatric practice but highlight the need for further research in specific clinical contexts. These results contribute to the ongoing discussion on optimal bronchodilator response thresholds and may help streamline asthma management in children by offering reliable and consistent diagnostic criteria.

KEY WORDS

ATS/ERS 2005 criteria; GLI-2022 criteria; Bronchodilator response (BDR); FEV_1; Race-neutral Approach.

INTRODUCTION

The different criteria so far used for bronchodilator response evaluation have introduced inconsistencies in clinical practice, particularly regarding the appropriate threshold for interpreting forced expiratory volume in one second (FEV1) improvements, as highlighted by Guezguez and Ben Saad (2020) [1]. The ATS/ERS 2005 guidelines defined a significant bronchodilator response as an absolute increase in FEV_1 of at least 12% and 200 mL compared to the pre-bronchodilator test [2, 3]. In contrast, the ERS/ATS 2022 standard defines a positive response as an increase greater than 10% in the percent predicted FEV_1 value, rather than the absolute volume increase, compared to the pre-bronchodilator test [3].

While earlier expectations suggested that this shift might reduce BDR+ prevalence—particularly among children with milder impairments—more recent pediatric studies, including Beydon & Rosenfeld (2024) [6], have shown either no reduction or a slight increase in BDR+ classification using the ERS/ATS 2022 criteria. This may reflect the generally better-preserved lung function in children, which can result in relatively larger post-bronchodilator percent predicted improvements, thereby increasing sensitivity to positive responses.

Potential implications of the new recommendation for clinical decision-making might lead to a decrease in the evidence of positive response to the bronchodilators, particularly in pediatric populations [1, 4].

Bronchodilator reversibility testing remains fundamental in diagnosing pediatric asthma [5]. Recent ATS-ERS updates reflect a shift toward using predicted values in assessing bronchodilator response, a methodological change that has been associated with differences in the frequency of positive test results [6, 7], without asserting the superiority of one criterion over the other. For instance, McCarthy et al. (2023) [7] observed that the adoption of predicted values may lead to fewer positive responses, particularly in individuals with severe airway obstruction.

Our aim was to compare the diagnostic implications of the ATS/ERS 2005 and ERS/ATS 2022 criteria, focusing on whether the adoption of the newer thresholds significantly alters or not clinical decision-making, especially in managing pediatric asthma.

METHODS

Spirometry was conducted according to the European Respiratory Society (ERS) – American Thoracic Society (ATS) guidelines, using standardized equipment. Spirometry measurements of (FEV_1) were performed before and 15 minutes after inhalation of 400 µg salbutamol bronchodilator administration [8]. To account for normal diurnal variations, all testing was performed at a consistent time of day.

For assessing bronchodilator response, the following criterion was applied:

- **ATS/ERS 2005 Criteria**: A positive response was defined as both a ≥12% increase and a ≥200 mL absolute increase in FEV_1 from the baseline (pre-bronchodilator value).

$$[(FEV_1\ post\ \text{bronchodilator}\ /\ FEV_1\ pre\ \text{bronchodilator}) - 1] * 100$$

All the data were stored on a PC in the CNR Institute.

Subsequently, the new criterion was released:

- **ERS/ATS 2022 Criteria**: A positive response was defined as a >10% increase in percent predictedFEV_1, with reference to the patient's predicted FEV_1 based on age, sex, height, and ethnicity.

$$\frac{(FEV_1\ post\ \text{bronchodilator}\ -FEV_1\ pre\ \text{bronchodilator}\ )}{FEV_1\ predicted} * 100$$

To compare bronchodilator response (BDR) between the ATS/ERS 2005 and ERS/ATS 2022 criteria, the original data of the CHASER study were retrieved: on them, also the ERS/ATS 2022 criterion was applied.

Although FVC reversibility is acknowledged in ATS-ERS guidelines, our study focused solely on FEV_1 changes, considering that FEV_1 has a primary role in assessing airway obstruction and a greater applicability in pediatric populations, where consistent FVC measurements may be harder to obtain.
Baseline bronchial obstruction was assessed using the FEV_1/FVC ratio. The Lower Limit of Normal (LLN) was defined based on the 5th percentile of the predicted FEV_1/FVC ratio, calculated according to the ERS/ATS 2022 reference equations, which account for age, sex, height, and ethnicity. An FEV_1/FVC ratio below LLN was interpreted as indicative of baseline airway obstruction.
The primary outcome was the proportion of patients classified as having a significant BDR according to each criterion. Subgroup analyses were conducted by age group (4-7, 8-11, 12-17 years) and sex in order to evaluate whether differences existed in bronchodilator response.
The primary outcome was the proportion of patients classified as having a significant BDR by each criterion. Subgroup analyses were conducted by age group (4–7, 8–11, 12–17 years) and sex to evaluate any demographic differences in bronchodilator response. A p-value of <0.05 was considered statistically significant for all analyses. In subgroups with baseline obstruction (defined as FEV_1/FVC ≤ LLN), McNemar's test was applied to assess whether the differences in classification between ATS/ERS 2005 and ERS/ATS 2022 criteria were statistically significant.
To assess the agreement degree between the two criteria, Cohen's kappa coefficient was employed. This statistical measure adjusts for the agreement that might occur by chance, offering a more accurate evaluation of inter-rater reliability than simple percentage agreement [9].
The value of K ranges from −1 to 1: a value of 1 indicates perfect agreement, while a value of 0 suggests no agreement beyond what would be expected by chance. Negative values imply agreement less than by chance, indicating systematic disagreement. According to the guidelines proposed by Landis and Koch (1977) [10], values can be interpreted as follows: values less than 0.2 indicate slight agreement, 0.21 to 0.4 fair agreement, 0.41 to 0.6 moderate agreement, 0.61 to 0.8 substantial agreement, and values above 0.81 reflect almost perfect agreement.

RESULTS

The study population included 482 pediatric asthma patients, of whom 65% were male, with an age range from 4 to 17 years (mean age: 9.24 ± 2.71 years), between October 31,

2011, and March 1, 2016. Children were recruited from the Clinical and Environmental Epidemiology Institute of Pulmonary and Allergic Pediatric Diseases (CEEPAPD), an outpatient clinic of the CNR Institute of Biomedicine and Molecular Immunology (IBIM), Palermo, Italy [11]. We used data from the CHildhood ASthma and Environment Research (CHASER) study (ClinicalTrials.gov ID: NCT02433275). The study was approved by the local Ethics Committee (N° 8/2014), and informed consent was obtained from parents or legal guardians. Asthma diagnoses were confirmed according to the Global Initiative for Asthma (GINA), based on clinical history, symptoms, and standardized lung function tests. Each participant underwent spirometry testing before and after administration of a short-acting bronchodilator.

The analysis on the overall population revealed a substantial level of agreement between the two bronchodilator response (BDR) thresholds. The weighted Kappa coefficient was 0.83 (95% CI: 0.77 to 0.89), indicating an "almost perfect" agreement between classifications.

As shown in **Table 1** below, approximately 93.1% of subjects were identically classified under both criteria. Specifically, 331 children were negative and 118 were positive according to both standards. In 6.9% of cases (n = 33), classifications differed: 26 cases were positive by ERS/ATS 2022 but negative by ATS/ERS 2005, while 7 showed the opposite pattern. This discrepancy likely reflects variations in sensitivity between the two thresholds.

Table 1. Contingency Table of the global agreement between ERS/ATS 2022 and ATS/ERS 2005 Criteria.

GLOBAL			
	ERS/ATS 2022 Criteria ≤ 10	ERS/ATS 2022 Criteria > 10	Total
ATS/ERS 2005 Criteria < 12	331 (68.67%)	26 (5.39%)	357 (74.07%)
ATS/ERS 2005 Criteria ≥ 12	7 (1.45%)	118 (24.48%)	125 (25.93%)
Total	338 (70.12%)	144 (29.88%)	482 (100%)
FEMALES			
	ERS/ATS 2022 Criteria ≤ 10	ERS/ATS 2022 Criteria > 10	Total
ATS/ERS 2005 Criteria < 12	120 (71.43%)	9 (5.36%)	129 (76.79%)
ATS/ERS 2005 Criteria ≥ 12	3 (1.79%)	36 (21.43%)	39 (23.21%)
Total	123 (73.21%)	45 (26.79%)	168 (100%)
MALES			
	ERS/ATS 2022 Criteria ≤ 10	ERS/ATS 2022 Criteria > 10	Total
ATS/ERS 2005 Criteria < 12	211 (67.2%)	17 (5.41%)	228 (72.61%)
ATS/ERS 2005 Criteria ≥ 12	4 (1.27%)	82 (26.12%)	86 (27.39%)
Total	215 (68.47%)	99 (31.53%)	314 (100%)

Sex-based analysis indicated minimal differences: 7.1% of females and 6.7% of males had discordant classifications. Although only slightly higher in females, this minor variation warrants further exploration.

To further evaluate the relationship between baseline airway obstruction and bronchodilator responsiveness, we analyzed the proportion of children classified as having significant reversibility according to both the ATS/ERS 2005 and ERS/ATS 2022 criteria, stratified by whether their FEV_1/FVC ratio was above or below the Lower Limit of Normal (LLN). These findings are summarized in **Table 2**.

Among children with FEV_1/FVC below the lower limit of normal (LLN), 25.8% met the ATS/ERS 2005 criterion for a significant BDR (≥12% change), whereas only 9.4% of those with FEV_1/FVC above LLN met this threshold. Conversely, 74.2% of children with normal baseline function did not meet the BDR criterion, compared to 90.6% among those without obstruction.

When stratifying by the ≥12% threshold of the ATS/ERS 2005 criteria, a higher proportion of children with obstruction met the BDR criterion (25.8%) than those who did not (9.4%). Among those without obstruction, the majority fell below the 12% threshold (74.2%), while 90.6% did not meet the criterion.

Sex-stratified analysis revealed consistent patterns across both groups. Among males with $FEV_1/FVC \leq LLN$, 27.9% met the ATS/ERS 2005 BDR threshold, compared to 20.7% of females. In both sexes, the proportion of responders was slightly higher among those with preserved lung function when the ≥12% threshold was applied.
Applying the ERS/ATS 2022 criteria led to a modest reclassification of bronchodilator responsiveness. Among those with baseline obstruction, 27.0% were classified as BDR-positive, while 5.4% did not meet the criterion. In contrast, 73.0% of those without obstruction met the BDR threshold, and 94.6% did not. As with the ATS/ERS 2005 definition, males showed a slightly higher rate of bronchodilator responsiveness than females.

Table 2. Proportion of children with significant reversibility (using the two definitions) according to baseline obstruction using Lower Limit Normal FEV_1/FVC.

FEV_1/FVC < LLN			
ATS/ERS 2005 Criteria			
GLOBAL			
	< 12	≥ 12	Total
≤ LLN	36 (9.40%)	25 (25.77%)	61 (12.71%)
> LLN	347 (90.6%)	72 (74.23%)	419 (87.29%)
Total	383 (100%)	97 (100%)	480 (100%)
FEMALES			
	< 12	≥ 12	Total
≤ LLN	12 (8.69%)	6 (20.68%)	18 (10.78%)
> LLN	126 (91.31%)	23 (79.32%)	149 (89.22%)
Total	138 (100%)	29 (100%)	167 (100%)
MALES			
	< 12	≥ 12	Total
≤ LLN	24 (9.79%)	19 (27.94%)	43 (13.74%)
> LLN	221 (90.21%)	49 (72.05%)	270 (86.26%)
Total	245 (100%)	68 (100%)	313 (100%)

ERS/ATS 2022 Criteria			
GLOBAL			
	≤ 10	> 10	Total
≤ LLN	17 (5.36%)	44 (26.99%)	61 (12.71%)
> LLN	300 (94.64%)	119 (73.01%)	419 (87.29%)
Total	317 (100%)	163 (100%)	480 (100%)
FEMALES			
	≤ 10	> 10	Total
≤ LLN	6 (5.30%)	12 (22.22%)	18 (10.78%)
> LLN	107 (94.46%)	42 (77.78%)	149 (89.22%)
Total	113 (100%)	54 (100%)	167 (100%)
MALES			
	≤ 10	> 10	Total
≤ LLN	11 (5.39%)	32 (29.35%)	43 (13.73%)
> LLN	193 (94.60%)	77 (70.65%)	270 (68.26%)
Total	204 (100%)	109 (100%)	313 (100%)

In children with baseline obstruction, agreement between criteria was moderate (Kappa = 0.42, 95% CI: 0.25–0.60), while among children without obstruction, agreement was stronger (Kappa = 0.69, 95% CI: 0.61–0.77). A significant McNemar's test ($\chi^2 = 17.05$, $p < 0.001$) in the obstructed subgroup suggested systematic differences in classification.
Sex-stratified analysis showed nearly perfect agreement in both females (Kappa = 0.81) and males (Kappa = 0.84). Discrepancies were minimal and balanced in direction.
Age-group analysis also confirmed robust agreement across all strata: children <11 years (Kappa = 0.82), those aged 11–13 (Kappa = 0.80), and >13 years (Kappa = 0.87). These results support the reliability of both criteria across demographic subgroups.
Overall, while both thresholds identify similar proportions of responders, the ERS/ATS 2022 criterion appears slightly more inclusive, especially among children with mild obstruction.

DISCUSSION

The absence of significant differences between the ATS/ERS 2005 and ERS/ATS 2022 thresholds in the overall study population suggests that both may be used interchangeably in clinical practice. Across the full cohort, agreement between the two criteria was almost perfect (Cohen's Kappa = 0.83), and 93.1% of the children were classified consistently. This consistency was further supported by subgroup analyses by sex and age group, which showed similarly high levels of agreement.
Although our original hypothesis considered the possibility that the shift to percent predicted values in ERS/ATS 2022 might reduce the number of BDR+ cases, especially in pediatric cohorts, our findings did not support this. On the contrary, we observed a slightly higher number of children classified as BDR+ under the ERS/ATS 2022 criteria. This aligns

with prior pediatric studies and is likely due to physiological factors such as better preserved baseline lung function in children, which may result in greater proportional improvements and higher sensitivity under percent predicted thresholds.
However, since among the discordant cases there was a trend for ERS/ATS 2022 to classify more cases as positive, further research is necessary to evaluate the relative sensitivity and specificity of these criteria to ensure the most accurate diagnostic performance.
However, the subgroup of children with baseline airway obstruction (defined as $FEV_1/FVC \leq LLN$) revealed a more complex picture. In this subgroup, agreement between the two definitions was only fair to moderate (Cohen's Kappa = 0.42), and a statistically significant difference in BDR classification was observed (McNemar's test, $p < .0001$). Specifically, the ERS/ATS 2022 criterion identified more children with baseline obstruction as having a significant bronchodilator response than the ATS/ERS 2005 criterion. These disagreements may indicate differences in threshold sensitivity or underlying physiological variations that each criterion captures differently.
This discrepancy highlights that while the two thresholds yield largely comparable results in the general pediatric asthma population, their clinical implications may diverge in children with obstructive baseline spirometry. Since the functional definition of asthma includes the presence of reversible airway obstruction, the higher sensitivity of the ERS/ATS 2022 criterion in this context could influence diagnostic decisions and subsequent management.

CONCLUSION

Our study found a high degree of concordance between the ATS/ERS 2005 (>12% and 200 mL) and ERS/ATS 2022 (>10% predicted) thresholds for bronchodilator reversibility testing in children, with nearly identical diagnostic outcomes in the overall cohort. These findings support the clinical utility of the ERS/ATS 2022 criteria for routine pediatric assessment.
Importantly, the slight increase in BDR+ detection under ERS/ATS 2022, particularly among children with better preserved lung function, suggests that the newer criteria may offer enhanced sensitivity in pediatric populations without compromising agreement. This observation aligns with previous pediatric studies and may reflect physiological differences that influence response thresholds.
However, in the subgroup of children with baseline airway obstruction, ERS/ATS 2022 classified a significantly higher number of cases as BDR-positive compared to ATS/ERS 2005. This may suggests that adopting the ERS/ATS 2022 criteria could affect asthma diagnosis in specific clinical scenarios and underscores the need for awareness of criterion sensitivity in obstructed populations.
Exploring the broader implications of transitioning to the ERS/ATS 2022 standard, particularly its impact on specific subgroups warrants further investigation to ensure optimal and equitable clinical decision-making, including adults, will help determine whether any nuanced advantages exist in using one criterion over the other.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interests

The Authors declare that they have no financial or personal conflicts of interest that might have influenced the work reported in this article.

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Author contributions

All the Authors confirmed the contribution to the manuscript's conception and approved its final version.

Ethical approval

Human studies and subjects

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the local Institutional Ethics Committee (n. 08/2014).

Animal studies

N/A.

Publication ethics

Plagiarism

Authors declare no potentially overlapping publications with the content of this manuscript and all original studies are cited as appropriate.

Data falsification and fabrication

The data is based on real-world observations.

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