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REVIEW

Smart stethoscopes, smart inhalers, and ChatGPT: latest developments of digital health in childhood asthma

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ABSTRACT

Asthma is the most common chronic disease in children, yet outcomes remain suboptimal, with high rates of exacerbations, emergency visits, and preventable deaths. Despite well-established treatment guidelines, care delivery continues to be limited by three major structural barriers: incomplete or unreliable symptom assessment, infrequent and reactive follow-up, and insufficient day-to-day support for families. Digital health technologies offer new opportunities to address these challenges by enabling objective data collection, continuous monitoring, and accessible guidance outside clinical settings. This mini-review explores three key innovations that are transforming paediatric asthma care: smart stethoscopes, smart inhalers, and large language models (LLMs). Smart stethoscopes use artificial intelligence to detect wheezing and other abnormal breath sounds at home with high sensitivity. Although evidence in routine clinical practice is still limited, they offer promise in improving symptom recognition, especially in preschool-aged children. Smart inhalers and spacers provide objective data on medication use and inhaler technique, helping clinicians distinguish poor asthma control from non-adherence. Real-time monitoring systems have also been shown to improve asthma control scores, although they may increase healthcare utilisation due to heightened clinical vigilance. Predictive modelling based on inhaler sensor data has demonstrated good accuracy in forecasting exacerbations several days in advance, offering a shift from reactive to preventative care. LLMs such as ChatGPT, Claude, and Gemini provide immediate, comprehensible responses to asthma-related questions from families, filling a critical gap in support between clinic visits. Recent studies show that their responses are generally accurate, clear, and appropriate for parents, particularly when using paid versions. They may also assist healthcare professionals by generating educational materials and synthesising clinical guidance, though concerns around hallucinations, data privacy, and safety in acute settings currently limit their clinical use. Together, these digital tools offer promising avenues to personalise and modernise asthma care for children. However, further validation, integration into care pathways, and attention to safety and equity will be essential to translate this potential into improved outcomes.

IMPACT STATEMENT

Digital health tools can provide objective monitoring, timely interventions, and accessible support, offering new opportunities to improve outcomes in childhood asthma.

KEY WORDS
Digital inhalers; adherence; inhaler technique; digital health; remote monitoring; eHealth; electronic monitoring.

INTRODUCTION

Asthma is the most common chronic disease in children, yet outcomes remain unacceptably poor, with persistently high rates of exacerbations, emergency visits, and preventable deaths (1-3). Despite advances in treatment and management guidelines, three key structural limitations continue to impede the delivery of optimal asthma care for children.

First, clinical assessment is often undermined by incomplete or unreliable data. One of the primary challenges for clinicians is determining whether the respiratory symptoms reported by families genuinely reflect asthma manifestations. Studies have shown that parents frequently describe a range of respiratory noises as “wheezing”, even when these sounds are more consistent with snoring or stridor (4). This misreporting can complicate diagnostic clarity and lead to inappropriate management decisions. A second key limitation is the difficulty in obtaining reliable information about short-acting β_2-agonist (SABA) use at home. SABA use is a critical indicator of asthma control, and excessive reliance on reliever medication has been linked to an increased risk of severe, and even fatal, asthma attacks (3, 5, 6). Equally, clinicians have no reliable way of assessing adherence to maintenance therapy or the correctness of inhaler technique in the home setting - yet these are fundamental considerations when evaluating poor asthma control (7). Without objective insight into these elements, treatment escalation decisions may be made without addressing the true underlying cause, such as poor adherence or incorrect inhaler use. Finally, environmental factors known to influence asthma - such as air pollution, weather conditions, and allergen exposure - are rarely documented in a systematic or meaningful manner (8, 9). The lack of tools to capture these parameters continuously and objectively means they are often overlooked or reduced to simplistic screening questions, despite their recognised clinical relevance.

Second, follow-up remains episodic and reactive, rather than aligned with the continuous and dynamic nature of asthma. While children live with the condition 24 hours a day, clinical assessments are typically limited to brief, scheduled visits occurring every 3 to 12 months (10). In the meantime, day-to-day changes in symptoms, medication use, or environmental exposures may go undetected. This gap in monitoring can delay necessary treatment adjustments and increase the risk of sudden, potentially preventable exacerbations.

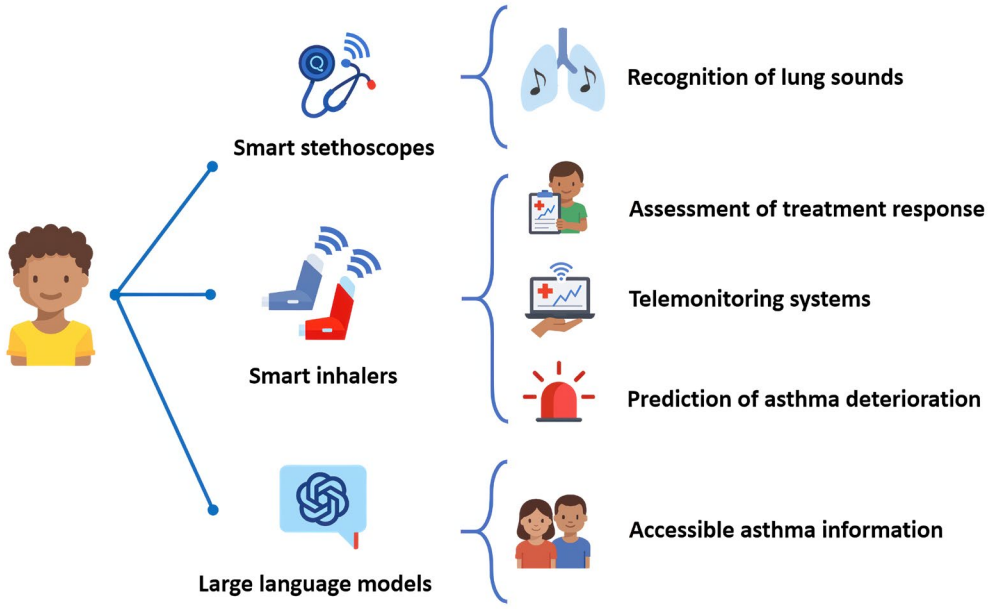

Figure 1. *Overview of emerging digital health tools in paediatric asthma. Smart stethoscopes enable recognition of lung sounds at home. Smart inhalers provide objective data for assessment of treatment response, allow integration into telemonitoring systems, and can contribute to predictive modelling of asthma deterioration. Large language models such as ChatGPT support families with accessible asthma information and education.*

Third, families often lack the day-to-day support needed to manage asthma effectively. Questions, concerns, and uncertainties frequently arise between clinic visits - precisely when professional advice is not readily available. Without timely access to guidance, families may feel isolated in managing the condition, which can lead to anxiety, suboptimal decisions, and inconsistent adherence (11). Addressing this unmet need is essential to empower families, support confident self-management, and ultimately improve outcomes.

Digital health technologies and artificial intelligence (AI) are increasingly being investigated as potential solutions to these structural limitations (12-16). By enabling objective data collection, continuous monitoring, and accessible support outside of clinical settings, these tools may help bridge longstanding gaps in paediatric asthma care. The aim of this mini-review is to explore how emerging innovations - such as smart stethoscopes, digital inhalers, and conversational AI - could contribute to improving asthma care in children (**Figure 1**).

SMART STETHOSCOPES

The aim of smart stethoscopes is to enable reliable assessment of lung sounds in children outside of clinical settings, particularly at home. These devices are designed to detect abnormal respiratory sounds - most notably wheezing - with greater objectivity and consistency than traditional parental reporting (17). These portable devices typically connect via Bluetooth to a smartphone and, once placed on the child's chest, record and analyse breath sounds using artificial intelligence (AI) algorithms.

Validation studies have demonstrated that AI-driven acoustic analysis, particularly neural network–based models, can identify wheezes, rhonchi, and crackles with higher sensitivity and comparable specificity to experienced clinicians (18). Smart stethoscopes may be especially useful in preschool-aged children, where differentiating asthma exacerbations from viral upper respiratory infections remains a common clinical challenge.

To date, no studies have evaluated the role of smart stethoscopes in routine clinical practice for the diagnosis of asthma. The only trial conducted - the WheezeScan study - focused instead on their use for home monitoring (19). This multicentre trial, conducted in Berlin, London, and Istanbul, enrolled 167 children aged 4 months to 7 years with recurrent wheeze. Families in the intervention group used the device at home for 120 days, while those in the control group received usual care. The primary outcome, asthma control assessed by the TRACK questionnaire at day 90, did not differ significantly between groups. However, a major limitation of the study was that families were not given systematic instructions on how to respond when wheeze was detected, likely limiting the clinical impact of the intervention. Secondary outcomes, including parental quality of life and self-efficacy, also showed no significant differences, although improvements were seen in both groups over time. Most parents in the intervention arm found the device easy to use and perceived it as beneficial for their child, despite challenges such as background noise interference and difficulty keeping younger children calm during recordings.

In summary, smart stethoscopes offer a promising opportunity to generate objective data and support the recognition of wheeze in the home environment. However, their effective integration into paediatric asthma management will require structured guidance for families on how to interpret and act upon device outputs.

SMART INHALERS

The latest generation of smart inhalers and smart spacers are equipped with sensors that capture objective data on both inhaler use and technique. These data can be leveraged in various ways: retrospectively, to inform treatment decisions; prospectively, for real-time telemonitoring; and increasingly, as inputs for predictive modelling and personalised care strategies.

Objective and reliable data on adherence and inhalation technique

Poor adherence and incorrect inhaler technique remain two of the most significant barriers to achieving asthma control in children. First-generation smart inhalers, which recorded only the timing of actuations, already provided valuable retrospective insights. A paediatric study demonstrated that electronic monitoring of inhaled corticosteroid (ICS) use was key to distinguishing true severe asthma from uncontrolled disease due to non-adherence (20). Among children with persistently poor control after a three-month monitoring period, two-thirds were found to have suboptimal adherence, while only one-third required treatment escalation, including biologics.

In adults, the INCA Sun trial extended this principle by incorporating a smart inhaler capable of assessing both ICS adherence and inhalation technique, alongside digital peak flow monitoring (21). In this six-month study involving 213 adults with difficult-to-control asthma, participants in the intervention arm were significantly less likely to require escalation to biologics or high-dose ICS, and more likely to have treatment stepped down. Importantly, this was achieved without any deterioration in asthma control, lung function, quality of life, or exacerbation rates. The findings demonstrated that objective digital monitoring can safely reduce unnecessary treatment intensification and associated healthcare costs, while maintaining clinical stability.

Beyond adherence to maintenance therapy, smart inhalers also enable detailed tracking of reliever use – particularly SABA - in everyday life, offering a level of granularity that is unattainable through routine clinical assessment. These devices provide clinicians with accurate data to replace or complement self-reporting by families. In a recent prospective study, smart inhalers used to monitor home salbutamol use revealed frequent deviations from prescribed action plans (22). Such insights enable more individualised action plan reviews, helping to align actual SABA use with intended strategies - particularly important given the well-established association between SABA overuse and severe, or even fatal, asthma exacerbations.

Collecting data in real time for telemonitoring systems

While retrospective analysis of smart inhaler data provides valuable insights during clinical consultations, real-time telemonitoring systems take this approach further by enabling timely responses to concerning usage patterns as they emerge. This proactive model of care allows healthcare teams to intervene before asthma control deteriorates significantly, potentially preventing exacerbations.

The largest paediatric randomised controlled trial to date in this area is the iTRACC study, which enrolled 252 children aged 4-17 years across the United States (23). Participants in the intervention group used sensor-enabled inhalers linked to a digital platform, which triggered automated alerts to a nurse when predefined thresholds were exceeded (*e.g.*, more than four SABA doses in a day or more than four days without ICS use). Over the 12-month follow-up period, children in the intervention group experienced significantly greater improvements in asthma control, with a mean ACT score increase of +2.7 compared to +0.5 in the control group ($p < 0.01$). However, the study also reported a paradoxical increase in emergency visits and hospitalisations in the intervention group. This was attributed to enhanced clinical vigilance and more frequent referrals in response to real-time alerts.

These findings suggest that while smart inhalers with telemonitoring capabilities can improve symptom control and patient-reported outcomes, they may also lead to increased healthcare utilisation due to more proactive identification and management of risk patterns.

Prediction of asthma deterioration

The most advanced application of smart inhaler technology lies in predictive modelling - using sensor data to anticipate asthma exacerbations before they occur. This approach enables a shift from reactive management to a more proactive, preventative model of care.

Lugogo and colleagues developed the first machine learning model based on data from digital reliever inhalers to forecast impending asthma deterioration (24). In their 12-week study involving 360 adults with poorly controlled asthma, participants used the *ProAir® Digihaler®*, which recorded inhaler usage along with inhalation parameters such as peak inspiratory flow, inhalation volume, and duration. A gradient-boosting algorithm was trained on this dataset, combined with baseline patient characteristics, to predict the risk of an exacerbation occurring within five days. The model achieved a strong predictive performance, with an area under the receiver operating characteristic curve (AUC) of 0.83.

The most powerful predictive variable was the mean number of daily inhalations in the four days preceding the prediction window. Patients who experienced an exacerbation averaged 7.3 inhalations in the 24 hours prior to the event. In addition, both peak inspiratory flow and inhalation volume were found to decline in the days leading up to deterioration, offering further early-warning signals.

These findings illustrate the potential of smart inhalers not only to monitor asthma control but also to provide real-time risk stratification, opening the door to earlier and more targeted interventions. However, for such predictive tools to be clinically useful, implementation must carefully

balance sensitivity and specificity to minimise false positives while ensuring timely responses to true deterioration.

CHATGPT AND OTHER COMMERCIAL LARGE LANGUAGE MODELS

The third major innovation transforming childhood asthma care stems from large language models (LLMs) such as ChatGPT, Claude, Gemini, Copilot, Deepseek or Mistral. These conversational agents are capable of delivering immediate, comprehensible responses to natural language queries, thereby offering timely support when families have questions outside the context of scheduled consultations.

Supporting families with asthma information

Parents of children with asthma frequently turn to the internet - most commonly via general search engines such as Google - when seeking information about their child's condition (25). LLMs now offer an alternative, allowing parents to pose asthma-related questions and receive rapid, personalised responses. A critical issue, however, is the reliability, clarity, and appropriateness of the information provided.

Recent evaluations of LLM performance in this context have shown encouraging results. Girault *et al.* assessed ten LLMs using the ten most common questions posed by parents of children with asthma attending a tertiary care centre (26). Responses were independently rated by both paediatric pulmonologists and parents. Medical accuracy, as evaluated by paediatric pulmonologists, was rated highly (median 4/5), with 91% of responses scoring ≥4. Paid versions of LLMs consistently outperformed their free counterparts. Comprehensibility was also rated favourably by parents, with 93% of responses scoring ≥4/5. The way information was phrased - specifically its clarity, tone, and suitability for a lay audience - was considered appropriate in 72% of cases by physicians and 90% by parents.

Other potential applications of LLMs include helping families better understand complex medical information discussed during consultations, and providing real-time translation of instructions into their native language.

Applications for healthcare professionals

For clinicians, large language models may support a range of tasks, including the rapid summarisation of clinical guidelines, synthesis of relevant literature, and the development of patient education materials tailored to different developmental stages.

Early evidence also suggests potential value in medical education. A randomised trial conducted in China found that brief training in the use of ChatGPT improved doctors' knowledge and management of paediatric asthma (27). This effect was particularly notable in resource-limited settings, where access to specialist training and up-to-date guidelines may be constrained.

Limitations and safety concerns

Despite these promising applications, several limitations restrict the current clinical use of LLMs. Most notably, they can produce plausible - sounding but factually inaccurate responses - a phenomenon known as "hallucination" (28). In addition, commercial LLM platforms do not meet the data protection standards required for use in healthcare settings, raising concerns around confidentiality and regulatory compliance.

To date, no study has assessed the safety or reliability of LLMs in acute clinical situations such as asthma exacerbations, and these tools are not validated for use as clinical decision support systems. As such, while they may offer valuable educational and supportive functions, they should not be relied upon for urgent or high-stakes medical decision-making.

CONCLUSIONS

Digital health technologies offer promising solutions to longstanding challenges in childhood asthma care. Smart stethoscopes, smart inhalers, and LLMs provide new ways to collect objective data, monitor disease in real time, and support families between clinic visits. Together, these tools have the potential to improve symptom recognition, optimise treatment, and promote proactive, personalised care. However, their clinical integration remains limited. Most tools require further validation, particularly in real-world settings, and key concerns persist around data privacy, safety, and appropriate use. Ensuring equitable access and embedding these innovations into care pathways will be essential. If these challenges can be addressed, digital tools will play a key role in transforming paediatric asthma management in the years ahead.

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During the preparation of this work, DD used ChatGPT to proofread and improve grammar and sentence flow.

After using this tool, DD reviewed and edited the content as needed and take full responsibility for the content of the publication.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interest

David Drummond is the secretary of the group 1.04 mHealth/eHealth at the European Respiratory Society. He is the principal investigator of several ongoing studies involving electronic monitoring devices (NCT04810169) and social robots (NCT04942639), the latter being funded by the company Ludocare.

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Authors' contributions

DD is the sole author of the article.

Ethical approval

Human studies and subjects

N/A.

Animal studies

N/A.

Data sharing and data accessibility

The data that support the findings of this study are available from the corresponding author upon reasonable request. Due to the nature of the survey and the anonymized dataset, no individual identifiable information is included. Data sharing will be considered for academic and research purposes in compliance with applicable data protection regulations.

Publication ethics

The author declare that this manuscript is original, has not been previously published, and is not under consideration for publication elsewhere.

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PEDIATR RESPIR J

REVIEW

Long-term ventilation in children: state of the art and future perspectives

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ABSTRACT

Home mechanical ventilation (HMV) has transformed the care of children with chronic respiratory failure, improving survival, reducing hospital dependence, and enabling better quality of life. The choice between invasive and noninvasive modalities must be individualized, but successful outcomes universally depend on structured initiation, careful parameter adjustment, and systematic follow-up. Local practices, health system organization, reimbursement policy, and home care provider availability have significant influence on HMV successes. Future advances will rely on technology, multidisciplinary expertise, and broader access to specialized home-care services.

IMPACT STATEMENT

This review provides a comprehensive and up-to-date overview of long-term home mechanical ventilation in children, integrating current evidence with practical clinical considerations. It aims to support clinicians in decision-making, optimize patient selection and ventilatory strategies, and guide future development of pediatric home ventilation programs.

KEY WORDS
NIV; IMV; HMV in children; chronic respiratory failure; home care.

INTRODUCTION

Chronic respiratory failure (CRF) is a major cause of morbidity and mortality in both adult and pediatric populations. Advances in diagnostic and therapeutic care have enabled survival in many patients with conditions once deemed untreatable or incompatible with long-term life (1, 2). Consequently, the number of children living with CRF and requiring long-term assisted ventilation has steadily increased. The introduction of home mechanical ventilation (HMV) has opened new possibilities for comprehensive care, while simultaneously reducing the burden on healthcare systems and facilitating social integration for some of the most vulnerable children. Although HMV has been available for decades, continuous technological innovation in ventilator design and functionality, along with the advent of disease-modifying therapies, has made this field highly dynamic and constantly evolving (1, 2).

HMV is typically delivered through two modalities: invasive mechanical ventilation (IMV) via tracheostomy and non-invasive ventilation (NIV) using an appropriate interface such as a nasal or oronasal mask. The choice between these approaches largely depends on the underlying disease, the degree of respiratory dysfunction, and the individual patient's characteristics (1, 2).

DIAGNOSIS OF SLEEP-DISORDERED BREATHING (SDB)

Diagnostic procedures for early detection of sleep-disordered breathing (SDB) are recommended in all children with chronic, stable medical conditions that increase the risk of SDB, regardless of the presence of symptoms (3-5). In otherwise healthy children, diagnostic evaluation is warranted when clinical signs suggest SDB (3-5). The gold standard for early detection is video-polysomnography (PSG) combined with continuous non-invasive transcutaneous capnometry during sleep. In resource-limited settings, respiratory polygraphy may serve as an acceptable alternative (6).

When advanced diagnostics are unavailable, morning arterial blood gas analysis (ABG) and overnight oximetry trends can provide useful additional information (7, 8). However, elevated $PaCO_2$ (>50 mmHg) in morning samples usually indicates a late manifestation of chronic respiratory failure. A difference in $PaCO_2$ >10 mmol/L favoring the morning sample strongly suggests alveolar hypoventilation. Elevated serum bicarbonate (HCO_3^- >28 mmol/L) reflects metabolic compensation but is not specific for respiratory acidosis; hence, these findings must always be interpreted in clinical context (7, 8).

Children at increased risk—including those with neuromuscular disorders, chronic primary lung diseases, severe obesity, craniofacial malformations, or impaired respiratory control—should undergo systematic evaluation as part of a standardized diagnostic protocol (2, 5, 6).

Long-term noninvasive ventilation (NIV) in children generally encompasses modes that provide ventilatory assistance, most notably bilevel positive airway pressure (BiPAP). Continuous positive airway pressure (CPAP), although frequently classified under the broader NIV umbrella due to its noninvasive interface, is not strictly considered a *ventilatory* modality, as it delivers a constant distending pressure without augmenting tidal volume or providing true ventilatory support. Accordingly, both BiPAP and CPAP may be indicated in children with chronic, stable conditions characterized by severe SDB and impaired gas exchange (**Table 1**), although their mechanisms of action and therapeutic objectives differ (5).

In pediatrics, severe SDB is typically defined by an apnea–hypopnea index (AHI) greater than 10 events per hour (6). Reference values differ significantly between adults and children, with pediatric thresholds being much stricter (**Table 2**).

Table 1. *Key differences between CPAP and BiPAP in pediatric home ventilation.*

Feature	CPAP	BiPAP
Pressure pattern	Constant, fixed pressure throughout the entire respiratory cycle	Variable pressures: higher inspiratory pressure (IPAP) and lower expiratory pressure (EPAP)
Indications	Primarily obstructive disorders (*e.g.*, OSAS)	Central, restrictive, and obstructive disorders
Mode of breathing	Spontaneous breathing only	Can support spontaneous breathing and provide backup ventilation if needed
Flexibility	Limited – single continuous pressure	Flexible – can adapt to more complex ventilatory needs
Transition	May be escalated to BiPAP if CPAP is insufficient	Typically used when CPAP fails or in more severe disorders

Table 2. *AHI thresholds for sleep-disordered breathing (SDB) in pediatric and adult populations.*

Severity of SDB	Pediatric population (AHI, events/hour)	Adult population (AHI, events/hour)
Normal finding	<1.5/h	<5/h
Mild SDB	1.5–5/h	5–15/h
Moderate SDB	5–10/h	15–30/h
Severe SDB	>10/h	>30/h

Criteria for nocturnal alveolar hypoventilation in children vary slightly depending on the source (5, 6). The European Respiratory Society (ERS) defines hypoventilation when gas exchange impairment is documented by any of the following:

- morning arterial $PaCO_2$ ≥50 mmHg on ABG, or
- transcutaneous CO_2 ($TcCO_2$) >50 mmHg for ≥2% of total sleep time, or
- oxygen saturation (SpO_2) <90% for >2% of total sleep time (5).

However, the American Academy of Sleep Medicine (AASM) applies a different threshold for scoring hypoventilation during sleep in children (6). According to pediatric AASM criteria, hypoventilation is scored when **>25% of total sleep time is spent with PCO_2 >50 mmHg**, measured either by arterial sampling or a validated surrogate. This definition is therefore more stringent in terms of required duration of hypercapnia compared with the ERS threshold of ≥2% TST with CO_2 >50 mmHg. In adults, AASM criteria differ further and define hypoventilation when either:

- PCO_2 exceeds 55 mmHg for ≥10 minutes, or
- PCO_2 increases by ≥10 mmHg from the awake supine value to a level >50 mmHg for ≥10 minutes.

These differing reference standards are clinically relevant, as certain patient populations—such as children with neuromuscular disorders—may require adapted $TcCO_2$ thresholds or additional indicators of respiratory compromise. A recent international expert panel (RIND study) proposed criteria for nocturnal hypoventilation in these patients, including $TcCO_2$ >45 mmHg for >25% of total sleep time, or $TcCO_2$ >50 mmHg for >2% of total sleep time or at least 5 continuous minutes (9). Importantly, initiation of nocturnal ventilation is not based solely on $TcCO_2$, but also considers functional parameters such as reduced forced vital capacity (FVC <50% predicted), weakened maximum inspiratory pressure (<60 cm H_2O), or daytime SpO_2 <95% (9). In Duchenne Muscular Dystrophy (DMD), these adapted criteria are particularly critical due to progressive weakness of the diaphragm and accessory respiratory muscles, which often leads to alveolar hypoventilation first occurring during sleep. Routine screening for nocturnal hypoventilation is recommended when FVC falls below 50% predicted and mandatory at ≤40%, with NIV initiated when these functional and $TcCO_2$ criteria are met or when clinical symptoms such as morning headaches or daytime fatigue appear (5, 9).

Although the proportion of children requiring invasive mechanical ventilation (IMV) has declined markedly in recent decades, it remains the therapy of choice for a subset of patients with the most severe phenotypes (7, 10). Typical candidates include children with global chronic respiratory insufficiency requiring ≥16 hours of assisted ventilation, as well as those with bulbar dysfunction in whom noninvasive modalities are insufficient or not feasible (7, 10).

Importantly, the decision between noninvasive and invasive home mechanical ventilation does not need to be final or immutable over time. For example, certain conditions—such as congenital central hypoventilation syndrome (CCHS) or severe forms of bronchopulmonary dysplasia (BPD)—may necessitate IMV during infancy or early childhood, yet decannulation and transition to NIV can be achieved later in selected patients (11, 12). Conversely, in progressive disorders where NIV initially provides satisfactory support, the clinical course may eventually require tracheostomy and initiation of IMV. The best way to make these complex decisions is within a multidisciplinary framework, always in close consultation with the family and caregivers.

INPATIENT INITIATION OF LONG-TERM HMV

Research indicates that the initiation of home mechanical ventilation (HMV) in children can be effectively managed in either inpatient or outpatient settings (13, 14). Traditionally, initiation of long-term NIV was undertaken in the hospital setting, where the process requires close collaboration between healthcare professionals, social services, parents, and the child. Traditionally, several days of inpatient training for both the patient and caregivers have been recommended. Although some healthcare systems with well-developed home-care infrastructure have reported successful home-based initiation, safety and efficacy in children remain insufficiently validated (13, 14). For this reason, inpatient initiation continues to represent the standard of care, particularly in resource-limited settings or in children with complex medical needs (15, 16).

In contrast, IMV is almost invariably initiated in the hospital, as it is most often required in children with complex underlying conditions (17). Hospitalization is typi-

cally longer than for NIV, reflecting both the severity of the primary disorder and the necessity of establishing a stable tracheostomy, which is essential for IMV. Preparation for discharge is also more demanding, as it involves not only caregiver training but also securing a wide range of supportive equipment, such as oxygen concentrators, suction devices, and other home-care aids. Collectively, these factors make the initiation of IMV considerably more resource-intensive compared with NIV (17, 18).

PATIENT SELECTION AND CLINICAL APPROACH TO LONG-TERM HMV

In children with obstructive sleep apnea syndrome type 1 (OSAS type 1), long-term nocturnal CPAP is indicated when symptoms and abnormal polygraphic findings persist after adenotonsillectomy. If residual symptoms remain following surgery, repeat polygraphy after 4–6 weeks is recommended, and CPAP should be initiated when the apnea–hypopnea index (AHI) exceeds 10 events per hour (19). The prevalence of obesity-related obstructive SDB (OSAS type 2) is steadily rising. In some of these children, dietary interventions and innovative pharmacological approaches may reduce body weight and lead to symptom resolution. In cases of severe SDB without alveolar hypoventilation, long-term CPAP therapy is indicated, accompanied by active nutritional management (19). The rarest yet most therapeutically challenging group includes patients with genetically determined craniofacial anomalies and upper airway malformations (OSAS type 3). These involve abnormalities of the maxilla and mandible, palate, tongue, or pharyngeal and laryngeal structures. In such cases, CPAP is indicated when a fixed level of positive pressure is sufficient to normalize breathing patterns and restore gas exchange (20-22).
Long-term BiPAP therapy at home is indicated during sleep and, when necessary, during the daytime in children with disorders characterized by alveolar hypoventilation (5). BiPAP with a backup rate is the first-line therapeutic option for alveolar hypoventilation due to:

- neuromuscular disorders,
- pediatric obesity hypoventilation syndrome (OHS),
- disorders of respiratory rhythm control in selected cases,
- advanced primary pulmonary diseases (*e.g.*, cystic fibrosis, interstitial lung disease, bronchopulmonary dysplasia).

In addition, BiPAP is recommended in two specific contexts: (i) in children with obstructive SDB who fail CPAP or cannot tolerate the high pressures required to maintain airway patency, and (ii) in those with OSAS type 2 (obesity-related) or OSAS type 3 (craniofacial anomaly-related) when alveolar hypoventilation is documented (5, 9, 19, 22).
By contrast, IMV is reserved for children in whom noninvasive modalities cannot ensure adequate ventilation or are not feasible. Certain conditions require IMV from the outset—most notably disorders of respiratory rhythm control, whether primary (*e.g.*, CCHS) or secondary (*e.g.*, sequelae of severe perinatal asphyxia, severe metabolic diseases) (11, 23, 24). Children with restrictive or mixed obstructive–restrictive ventilatory patterns, as seen in neuromuscular disorders, may also ultimately require IMV during acute decompensation of previously stable respiratory insufficiency, particularly when endotracheal intubation is necessary and extubation fails (25). In addition, neonates with generalized muscle weakness who cannot be weaned from the ventilator represent another group requiring early IMV (26).

VENTILATOR SETUP: DEVICE, CIRCUIT, AND INTERFACE

Devices for mechanical ventilation can generally be divided into two categories: intensive care unit (ICU) ventilators and those specifically designed for home mechanical ventilation (HMV). Home ventilators are typically smaller, more portable, and optimized for ease of use in a non-hospital environment (27).
The choice of ventilator type is guided primarily by the underlying indication. While many different models from various manufacturers are currently available, most share a core set of technical features and clinical functionalities. These common elements provide a framework for classifying pediatric HMV devices, as outlined in **Table 3** (28, 29).
The ventilator circuit is a critical, though sometimes underappreciated, component of the setup. Two main types are commonly employed: single-limb and dual-limb circuits (**Figure 1**) (30, 31).
In a **single-limb circuit**, a single tube serves both inspiratory and expiratory flow. Depending on how exhaled gas is eliminated to prevent rebreathing, two main configurations exist:

Table 3. Ventilators for pediatric home mechanical ventilation: technical features and clinical use.

Device type	Key features	Limitations	Typical use
Level 1 – Standard CPAP devices	Easy to handle, integrated humidifier	No battery or alarm; limited flow detection (13–30 kg); auto-CPAP usable >30 kg	OSAS without hypoventilation
Level 2 – Intermediate devices (BiPAP)	Support <16 h/day; integrated humidifier; medium size; basic alarms; battery (2–6 h); flow detection >2.5–5 kg	Limited backup capacity, not robust for continuous support	Children with SDB and hypoventilation, neuromuscular diseases, obesity-hypoventilation
Level 3 – Life-support ventilators	Full support (24 h/day); integrated alarms; longer battery (~8 h); precise flow detection (>2.5–5 kg)	More expensive; larger; external humidifier required	Children needing continuous ventilation, invasive ventilation via tracheostomy, medically fragile patients

- **Vented circuits**, in which the mask itself incorporates exhalation ports (intentional leak openings). In this design, a minimum PEEP of approximately 4 cm H_2O is required to ensure effective clearance of exhaled CO_2 and avoid rebreathing.
- Circuits with an active expiratory valve, in which the valve is positioned close to the patient. The valve opens during exhalation, actively directing expired gas out of the circuit and thereby preventing rebreathing.

Single-limb circuits are most often used for NIV, as they are simple, portable, and cost-effective. Nevertheless, they present limitations, including reduced accuracy in monitoring exhaled volumes, reliance on intentional leaks, and greater susceptibility to unintentional air leaks. By contrast, a **dual-limb circuit** employs separate inspiratory and expiratory tubes connected via a Y-piece. This arrangement allows more precise regulation of tidal volume and gas exchange, reduces the risk of rebreath-

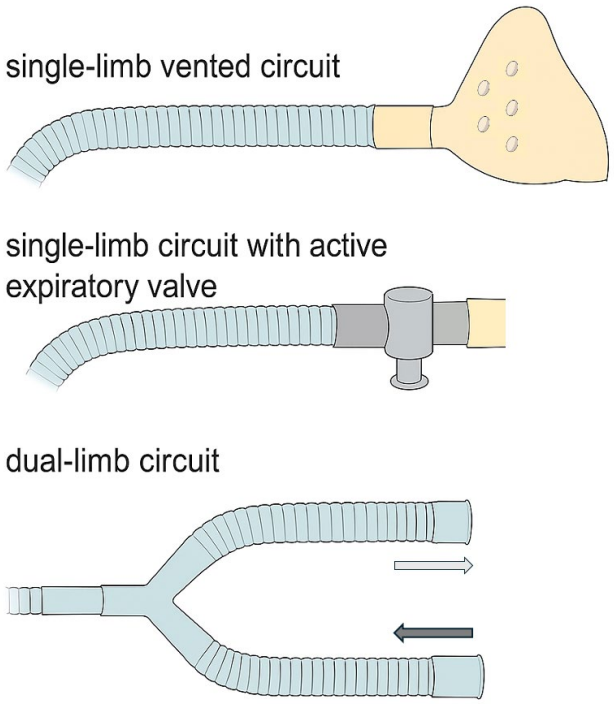

Figure 1. Types of ventilator circuits used in pediatric home mechanical ventilation.

ing, and facilitates accurate monitoring of exhaled volumes. Dual-limb systems are the standard for IMV via tracheostomy, but they may also be applied in NIV when precise volume monitoring is required. Their disadvantages include greater technical complexity, larger size, and reduced portability compared with single-limb systems (30, 31).

The choice of mask that best matches the child's long-term ventilatory requirements and facial anatomy at different ages is a critical determinant of successful NIV (31, 32). Current evidence does not demonstrate the superiority of any specific mask type with respect to ventilation efficacy. Nevertheless, the **nasal mask** is generally the preferred interface in children, given its wide availability in different sizes, the possibility of oral feeding and speech, and its relative ease of application. However, it may be associated with complications such as nasal bridge skin breakdown, xerophthalmia, or midface flattening, and its effectiveness can be reduced by mouth air leaks. In some cases, chin straps may help mitigate this problem (31, 32).

Alternative interfaces include **oronasal and full-face masks**, although these may be difficult to use in younger children because of claustrophobic sensations and the limited availability of appropriately sized models. Furthermore, they can increase the risk of aspiration in children with gastroesophageal reflux (31, 32). **Mouthpiece ventilation** can be useful in selected patients with stable chronic respiratory insufficiency, particularly during daytime use, and is often combined with another interface at night (**Table 4**) (33).

ADJUSTMENT OF LONG-TERM NIV PARAMETERS

For **CPAP**, treatment should be initiated at 4 cm H_2O and titrated upward until both adequate oxygenation and relief of obstruction are achieved, while maintaining patient tolerance (34, 35). PSG-guided titration remains the gold standard; however, in settings without PSG availability, oximetry trends and subsequent ventilator software analysis provide reliable alternatives (36). In most cases, effective pressures are achieved at approximately 8 ± 3 cm H_2O. Auto-CPAP may be considered in children exceeding the manufacturer's minimum weight threshold (typically >10 kg), although current evidence does not demonstrate clear superiority over fixed-pressure CPAP in pediatrics (5, 34).

For **BiPAP**, initial settings generally start with IPAP at 8 cm H_2O and EPAP at 4 cm H_2O, with subsequent adjustments guided by age, underlying disease, and clinical response (5, 37). The primary goal is to achieve a tidal volume of 6–10 mL/kg of ideal body weight. Final EPAP values typically range from 4 to 8 cm H_2O, though higher pressures may be required in the presence of structural airway anomalies predisposing to collapse (*e.g.*, pharyngomalacia, laryngomalacia, tracheomalacia). Final IPAP values are usually 10–14 cm H_2O, although higher levels (>20 cm H_2O) have been used safely (2, 5, 37).

The **backup respiratory rate** should be set slightly below the child's spontaneous rate during N3 sleep or physiologic age-based norms (38). Breath cycling—that is, the initiation of inspiration and the transition to expiration—must be carefully tailored to the underlying pathology (38, 39). The sensitivity of the **inspiratory trigger** depends on both respiratory muscle strength and the adequacy of central respiratory control. Conversely, the **expiratory trigger** should reflect the ventilatory pattern: in restrictive disorders, prolongation of the inspiratory phase is desirable, and the trigger is commonly set at 20–25% of peak inspiratory flow, whereas in obstructive disorders such as severe tracheomalacia, earlier cycling is advantageous, with settings adjusted to 50–75% of inspiratory flow (30, 40, 41).

At present, no validated reference values exist for other ventilatory parameters; most recommendations rely on expert consensus and retrospective studies (**Table 5**).

Table 4. *Advantages and limitations of different patient interfaces for pediatric home mechanical ventilation.*

Interface type	Advantages	Limitations
Nasal mask	- Wide range of sizes - Allows speech - Possibility of oral feeding	- Air leakage through the mouth - Risk of midface hypoplasia
Oronasal mask	- Prevents mouth leak - Lower risk of midface hypoplasia	- Not suitable for very young children - Interference with feeding, speaking, and secretion clearance - Risk of aspiration/asphyxia

DISCHARGE AND FOLLOW-UP

Regular clinical follow-up after discharge is essential. The first visit is recommended one month after discharge, followed by evaluations every three to six months depending on the underlying disease, type of SDB, and treatment adherence (5, 9). Each visit should include a detailed medical history, physical examination with particular attention to mask-related complications, and analysis of ventilator software. Device data provide important insights into adherence, duration of use, patient–ventilator synchrony, and air leaks (36). Importantly, careful fine-tuning of ventilator parameters based on these data can significantly improve both patient comfort and the overall effectiveness of ventilation. Some devices generate automated estimates of AHI, but these should be interpreted with caution, as most algorithms have been validated only in adults (36, 42).

Where available, transcutaneous capnometry every six months is advisable. Follow-up PSG, or respiratory polygraphy, should be performed whenever ventilator settings are modified or when interventions—such as orthodontic or orthopedic treatments—have the potential to alter airway function (43, 44).

Follow-up practices differ substantially across healthcare systems (7, 16, 45-47). In highly developed countries, most follow-up, including continuous non-invasive transcutaneous capnometry, is provided by specialized home-care services (48-50). In middle-income settings, this monitoring is more commonly hospital-based, which may limit frequency and accessibility (7, 16, 45-47).

Recent technological progress has enabled telemonitoring, whereby ventilator software data are transmitted to secure remote servers and analyzed by clinicians without the need for in-person visits. This approach has proven particularly valuable for monitoring adherence and detecting technical or clinical issues at an early stage (51, 52).

WEANING AND DISCONTINUATION OF LONG-TERM HMV

Weaning from long-term IMV via tracheostomy is a complex, stepwise process that requires careful clinical judgment and multidisciplinary collaboration (53, 54). The ultimate goal is decannulation and transition to NIV, whenever feasible, in order to minimize long-term complications and improve quality of life (53, 54).

The key steps in the weaning process include:

1. Overall assessment – evaluation of disease stability, improvement or resolution of the original indication for IMV, adequate spontaneous respiratory drive, and sufficient bulbar function to protect the airway.
2. Gradual reduction of ventilatory support – progressive shortening of IMV duration, initially maintaining nocturnal ventilation, followed by stepwise daytime trials off the ventilator.
3. Capping and tolerance trials – daytime tracheostomy capping to evaluate the child's ability to maintain adequate gas exchange without ventilatory support, with continuous monitoring of SpO_2 and $TcCO_2$.
4. Transition to NIV – initiation of mask ventilation once spontaneous breathing with capping is tolerated, typically starting during sleep and extending as feasible.

***Table 5**. Recommended BiPAP settings for long-term HMV in children.*

Parameter	Settings
IPAP	Start at 8 cm H_2O; Target tidal volume: 6–10 mL/kg/ideal body weight per breath
EPAP	Minimum: 4 cm H_2O; Typical final range: 6–10 cm H_2O
Respiratory Rate	*Controlled ventilation*: 2–3 breaths below physiologic rate for age; *Spontaneous breathing*: based on rate during N3 sleep
Inspiratory Time (Ti)	*Controlled ventilation*: Ti = 1/3 of total cycle time; *Spontaneous breathing*: Ti-min and Ti-max defined by device
Inspiratory Trigger	High sensitivity for neuromuscular disorders; Low sensitivity for central hypoventilation syndromes
Expiratory Trigger	Restrictive patterns: 20–25% of flow; Obstructive patterns: 50–75% of flow

5. Decannulation – performed once NIV is established and airway patency is confirmed (endoscopic assessment recommended), ensuring the child can maintain adequate ventilation and secretion clearance.
6. Post-decannulation monitoring – close observation in a controlled hospital setting to promptly detect respiratory compromise, followed by structured outpatient follow-up.

Children with neuromuscular disorders or residual central hypoventilation may continue to require nocturnal NIV even after successful decannulation (55). The timing of decannulation must balance the risks of prolonged tracheostomy (*e.g.*, infection, tracheal injury, psychosocial burden) against the safety of airway protection and effective ventilation (56). A multidisciplinary team—pulmonologist, intensivist, ENT surgeon, respiratory therapist, and speech/swallow therapist—should oversee the process in close cooperation with the family.

Discontinuation of home NIV may be considered in selected patients if normalization of SDB and gas exchange occurs spontaneously or following a therapeutic intervention (5). This is more commonly achievable in children treated with CPAP and less frequent in those requiring BiPAP. Before discontinuation, PSG or respiratory polygraphy with transcutaneous capnometry must be repeated. Criteria include resolution of SDB symptoms, AHI <10/h, $TcCO_2$ >50 mmHg for less than 2% of total sleep time, and SpO_2 <90% for less than 2% of total sleep time (5). Because recurrence of symptoms is possible, structured follow-up remains essential even after discontinuation.

MANAGEMENT OF LONG-TERM NIV FAILURE AND ALTERNATIVE OPTIONS

The most common cause of NIV failure in the home setting is poor adherence by the child or caregivers (57). Among adherent patients, failure may occur due to suboptimal patient–ventilator synchrony, excessive air leaks, progression of the underlying disease, or associated comorbidities (57). Alternative therapeutic options remain limited, but in selected cases, high-flow nasal cannula therapy or hypoglossal nerve stimulation may be considered as substitutes for CPAP (58, 59). Surgical or orthodontic interventions may be appropriate in children with Pierre–Robin sequence (60, 61). In the most severe cases, tracheostomy with invasive long-term ventilation remains the ultimate therapeutic option.

PREOPERATIVE USE OF LONG-TERM HOME NIV

Children with severe skeletal deformities, particularly kyphoscoliosis, should undergo preoperative evaluation for potential NIV initiation (62). While long-term NIV is clearly indicated in patients with alveolar hypoventilation and severe SDB, normal polygraphic and capnometric findings do not necessarily exclude the need for NIV (62, 63). Preoperative initiation has been shown to reduce the risk of prolonged postoperative ventilation, underscoring the importance of thorough evaluation and timely initiation of therapy (62, 63).

Risk assessment should include clinical features, non-invasive pulmonary function tests, the underlying condition (idiopathic scoliosis *versus* neuromuscular-associated scoliosis), and polygraphic/capnometric studies (62). Although reductions in FVC and FEV1 are inversely correlated with the need for postoperative ventilation, no universally accepted preoperative thresholds exist. Consequently, a low threshold for initiating NIV is advisable, particularly in patients with severe restrictive ventilatory patterns, pronounced spinal deformity, FEV1 <40% predicted, concomitant neuromuscular disease, or those scheduled for thoracotomy (5, 62).

CONCLUSION

Home mechanical ventilation has transformed the care of children with chronic respiratory failure, improving survival, reducing hospital dependence, and enabling better quality of life. The choice between invasive and non-invasive modalities must be individualized, but successful outcomes universally depend on structured initiation, careful parameter adjustment, and systematic follow-up. Future advances will rely on technology, multidisciplinary expertise, and broader access to specialized home-care services.

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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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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POSITION PAPER

Position Paper on management of mild asthma in childhood. A statement proposed by the SIMRI Asthma Committee and approved by the SIMRI Advocacy Council and Executive Committee

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ABSTRACT

Mild asthma in children and adolescents has traditionally been considered a less impactful condition characterized by infrequent symptoms. However, emerging evidence recognizes it as a chronic inflammatory disease with potential for severe, life-threatening exacerbations. Recent evidence and guidelines highlight the need for a paradigm shift in the management of mild asthma, moving away from exclusive reliance on short-acting beta2-agonists (SABA), towards proactive, inflammation-targeted asthma management across pediatric age groups. Non-pharmacological interventions—such as avoiding exposure to tobacco smoke, promoting healthy lifestyles, addressing psychosocial factors, and controlling environmental triggers—are equally critical to improving outcomes. A holistic, personalized approach that incorporates both medical and lifestyle interventions is pivotal for effective control of mild asthma, reduction of exacerbation risks, and improvement of long-term outcomes and quality of life in pediatric patients.

This statement summarizes current evidence and presents the official recommendations of the Italian Pediatric Respiratory Society (IPRS, Società Italiana per le Malattie Respiratorie Infantili/Ente Terzo Settore– SIMRI/ETS) to guide best practices in the management of mild asthma in childhood.

IMPACT STATEMENT

Mild asthma in children has long been viewed as a minor condition with occasional symptoms. However, new evidence identifies it as a chronic inflammatory disease capable of triggering severe, potentially life-threatening exacerbations. Current research and updated guidelines call for a shift in management—moving beyond exclusive reliance on short-acting beta2-agonists toward a proactive, inflammation-focused approach. This statement presents the latest evidence and outlines the official recommendations of the Italian Pediatric Respiratory Society (IPRS, Società Italiana per le Malattie Respiratorie Infantili/Ente Terzo Settore – SIMRI/ETS) to support best practices in managing mild asthma in childhood. The statement aims to play a key role in advancing national standards for care.

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KEY WORDS
Children; inflammation; inhaled corticosteroids; management; mild asthma.

INTRODUCTION

Asthma is one of the most common chronic diseases in all age groups. It is estimated that its prevalence is increasing worldwide, that can be explained by increased diagnosis of mild asthma (1, 2), which frequency ranges between 50% and 75% among asthmatic patients (3). The definition of mild asthma differs across studies and between guidelines. Its clinical variability adds to the challenge: symptoms can be occasional, or triggered only by specific risk factors. This sporadic nature makes it difficult to determine the precise amount of medication needed to maintain effective control (4). Therefore, an important research need is to determine a definition of the disease that accurately reflects the heterogeneity and risks noted in these patients (5). According to Global Initiative for Asthma (GINA) mild asthma is asthma that is suitable to receive Step 1-2 of treatment (1). Remarkably, the diagnosis of "mild" asthma does not prevent patients from an underappreciated exacerbation burden (6, 7); severe or even fatal exacerbations account for 30% to 40% of exacerbations requiring emergency care with an estimated frequency between 0.12 and 0.77 episodes per patient-year (3). Growing evidence propose several mechanisms underlying the increased adverse events in mild asthmatic patients, particularly those that regularly use Short Acting beta2 Agonists (SABAs) (8). First, the acute symptoms relief obtained with SABA may mask patients' perception of asthma worsening. Moreover, they can have a desensitization and downregulation of the β2-receptors resulting in failure of rescue SABA treatment during an exacerbation; this mechanism can be compensated using corticosteroids that mediates transcription of the β2-receptors-gene (9). Finally, β2-agonists have been suggested to exert pro-inflammatory effects through a shift in the human type-1/type-2 cytokine balance toward a type-2 response (10) (**Figure 1**). Notably, inflammation of the bronchial mucosa with eosinophilic infiltrates (11) and airway remodeling have already been demonstrated even in children with mild asthma (12).

Thus, patients with mild asthma should be considered patients with a chronic inflammatory condition with mild and infrequent symptoms, but still at risk of severe to fatal exacerbations, who can benefit of anti-inflammatory relievers.

In November 2024, the British Thoracic Society (BTS), the National Institute for Health and Care Excellence (NICE), and the Scottish Intercollegiate Guidelines Network (SIGN) released an updated guideline, revising recommendations on the diagnosis, treatment, and

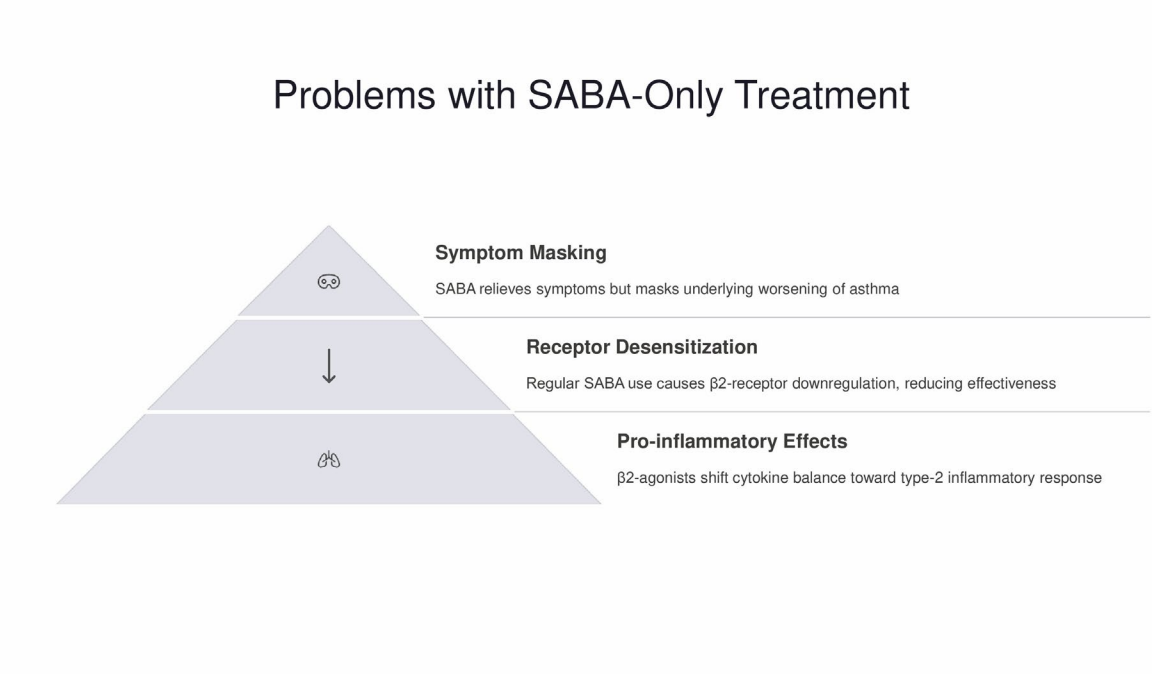

Figure 1. *Problems with SABA-Only Treatment.*

monitoring of asthma (13). In addition, the update of the GINA Report has been published very recently (1) and even recently has been discussed on Lancet Respiratory Medicine (14).

Starting from these key documents, the present statement outlines the current evidence and provides the official recommendations of the Italian Pediatric Respiratory Society (IPRS, Società Italiana per le Malattie Respiratorie Infantili – SIMRI/ETS) to support best practices in the management of mild asthma in children and adolescents.

REDEFINING THE TREATMENT OF MILD ASTHMA IN CHILDREN AND ADOLESCENTS

Recent updates to asthma guidelines issued by BTS, NICE, and SIGN have introduced significant changes to treatment strategies in patients with asthma. In detail, for individuals aged 12 years and older with newly diagnosed asthma, the guidelines recommend offering a low-dose ICS/formoterol combination inhaler as needed (anti-inflammatory reliever -AIR- therapy). This recommendation is based on evidence comparing three approaches:1) SABA as needed; 2) Regular low-dose ICS plus SABA as needed; 3) As-needed ICS/formoterol (AIR).

ICS-based strategies (AIR or regular ICS) consistently outperform the SABA-only approach in reducing asthma exacerbations and improving asthma control (15, 16). The AIR strategy significantly reduces severe exacerbations compared to both SABA-only and regular ICS/SABA regimens (17, 18). Moreover, when compared to as-needed SABA alone, the use of as-needed low dose ICS/formoterol avoids the need for daily ICS, where adherence is often poor, and simplifies asthma management by using a single medication for both relief and maintenance therapy. The use of ICS-formoterol may also have a role in management of exercise-induced bronchoconstriction (EIB), as there is evidence that it improves symptoms control as well as regular ICS treatment with a substantially lower total steroid dose and is superior to SABA monotherapy (19). Health economic analyses demonstrated that as-needed AIR therapy is more cost-effective than regular ICS plus SABA (20). Taking into account the available evidence, the guidelines support adoption of as-needed AIR therapy as a first-line strategy in adolescents with newly diagnosed asthma and suggests that patients currently managed on SABA-only regimens should be switched to as-needed AIR therapy. Moderate-dose MART (maintenance and reliever therapy) to people aged 12 and over with asthma that is not controlled on low-dose MART is offered as medicine combination and sequencing in people aged 12 and over.

For currently people with confirmed asthma that is not controlled on using regular low-dose ICS plus SABA as needed or regular low-dose ICS/LABA (long-acting beta2 agonist) combination inhaler plus SABA as needed or regular low-dose ICS and supplementary therapy (leukotriene-receptor antagonists, LTRA) plus SABA as needed or regular low-dose ICS/LABA combination inhaler and supplementary therapy (LTRA) plus SABA as needed, change treatment to a low-dose ICS/formoterol combination inhaler used as needed (as-needed AIR therapy) is recommended.

For children aged 5–11 years with newly diagnosed asthma, the recommended initial treatment is a regular use twice-daily of low-dose ICS with as-needed SABA. A recent systematic review and network meta-analysis showed that regular ICS use may be the most effective treatment for preventing exacerbation and increasing lung function in children with mild asthma, while no supporting evidence for the use of as-needed ICS/formoterol is available (21).

With regard to MART therapy for children whom asthma is not controlled on low-dose ICS plus SABA as needed, BTS/NICE/SIGN 2024 recommend the increasing to moderate-dose MART therapy or considering moderate-dose ICS/LABA maintenance treatment (with or without an LTRA, depending on previous response) based on the use of a dry powder inhaler. When a child has uncontrolled asthma and is assessed as unable to manage the MART regimen, BTS/NICE/SIGN 2024 recommend to add a LTRA (for a trial period of 8 to 12 weeks, unless there are side effects, then stop it if it is ineffective) or offer twice daily low-dose ICS/LABA combination inhaler plus SABA as needed.

Overall, the guideline revisions advocate a shift from traditional SABA-dominated regimens towards more consistent use of anti-inflammatory therapies, particularly ICS/formoterol. These recommendations are supported by both clinical and economic evidence. Importantly, the guidelines underscore the need for individualized therapy, considering inhaler technique, adherence, and patient preference.

The latest GINA report introduces a nuanced, evidence-based framework for managing asthma in adolescents and children. Central to the update is the stratification of treatment into two tracks for adolescents (**Figure 2**).

Track 1 (preferred): as-needed low-dose ICS/formoterol.

Track 2 (alternative): step 1, SABA as needed, with concurrent administration of low-dose ICS (either via a combination ICS-SABA inhaler or by taking ICS immediately after SABA use); step 2, daily low-dose ICS maintenance therapy, with SABA as needed for symptom relief.

Track 1 is favored due to its superior efficacy in reducing severe exacerbations compared with Track 2, while providing comparable symptom control. Clinical trials demonstrate reductions in emergency department visits or hospitalizations compared to SABA-only therapy, and to regular low-dose ICS plus SABA as needed (22-24). The use of ICS plus formoterol is supported by formoterol's rapid bronchodilatory action—faster than that of other LABAs like salmeterol—and by the concept that increasing ICS dosing during symptom flare-ups may help prevent exacerbations (25). The combination of budesonide-formoterol is the suggested formulation, as other combinations, such as beclomethasone/formoterol, have not been studied for as-needed use. The usual dose of as-needed budesonide-formoterol for mild asthma is a single inhalation of 200/6 mcg (delivered dose 160/4.5 mcg) taken whenever symptoms relief is needed. The maximum total daily dose of formoterol for both reliever and controller use is 72 mcg (equivalent to a delivered dose of 54 mcg). Treatment can be administered using either a Dry Powder Inhaler (DPI) or a pressurized Metered Dose Inhaler (pMDI). This approach is preferably recommended for: 1) step-down treatment for patient whose asthma is well controlled on low-dose MART with ICS-formoterol or on regular low-dose ICS with as-needed SABA; 2) initial asthma treatment for patients previously using SABA alone. Moreover, it is recommended for patients with low adherence, since reliance on SABA-only poses increased risks. Notably, ICS-formoterol should not be used as a reliever in patients already on a maintenance ICS-LABA regimen containing a LABA other than formoterol.

Indications for Track 2 include both patients with asthma symptoms occurring less (Step 1) and more than twice a week (Step 2). Indeed, the Track 2 should be considered when Track 1 is not possible or not preferred by patients who have no exacerbations with the current treatment. In patients aged 6–17 years with mild asthma, the as-needed combination of ICS/SABA showed a

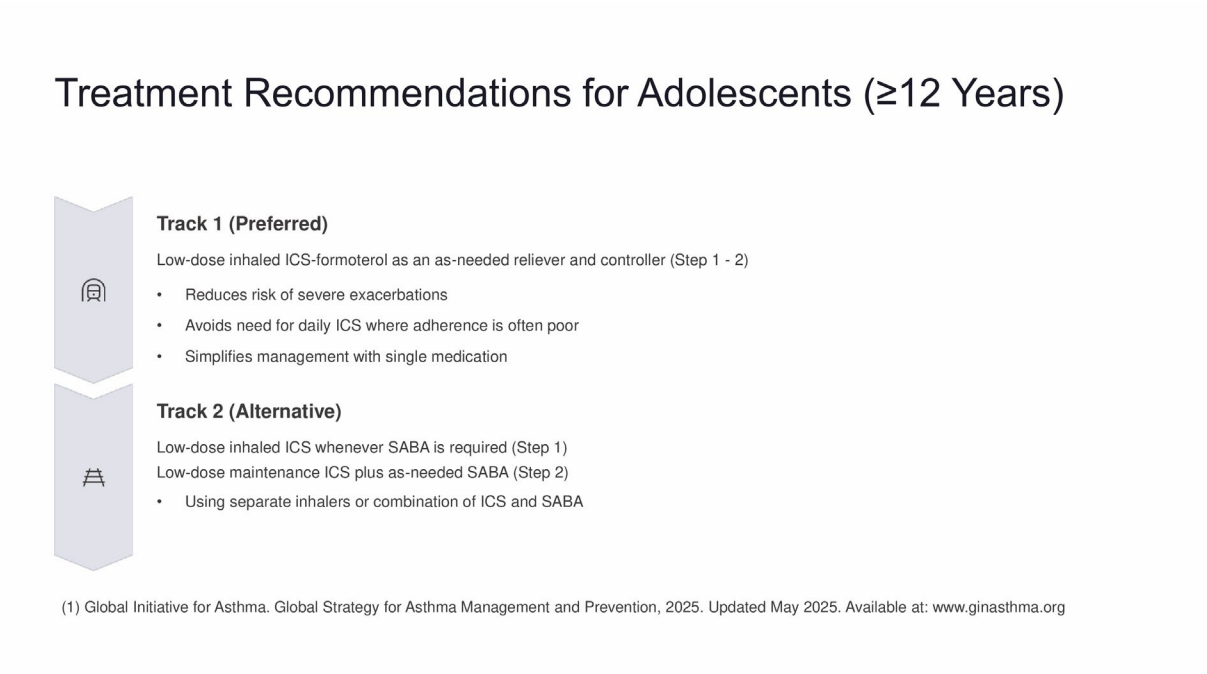

Figure 2. *Treatment Recommendations for Adolescents (≥12 Years) (1). Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2025. Updated May 2025. Available at: www.ginasthma.org.*

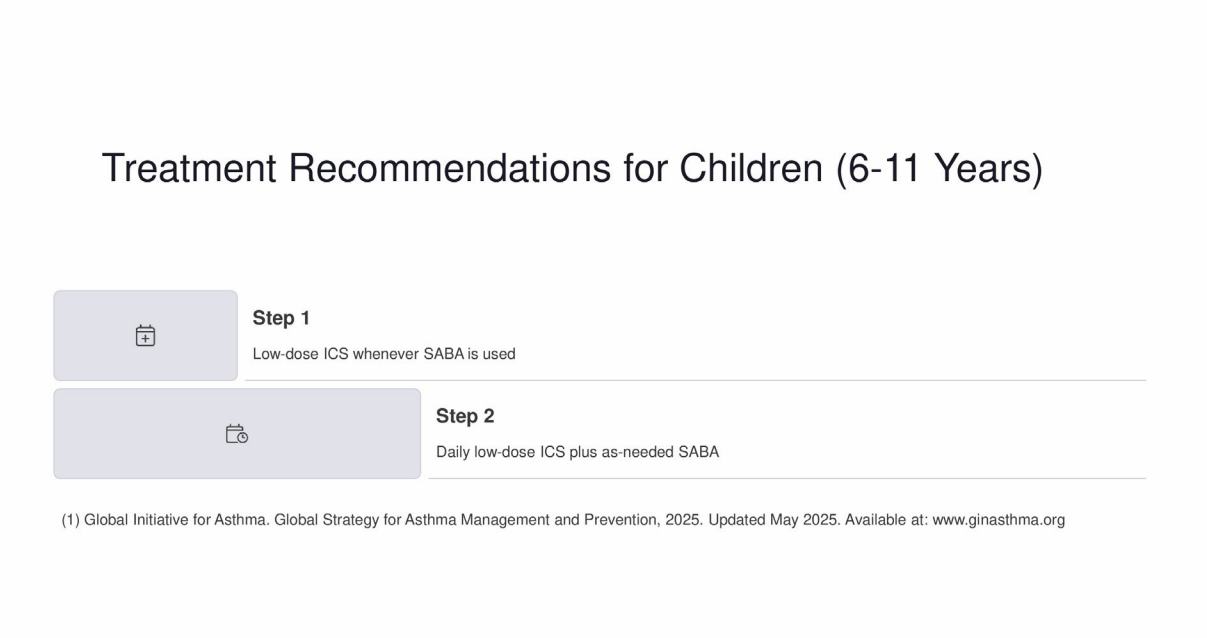

Figure 3. *Treatment Recommendations for Children (6-11 Years) (1). Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2025. Updated May 2025. Available at: www.ginasthma.org.*

similar effect compared to regular ICS use in terms of asthma control and exacerbation frequency, with lower cumulative ICS exposure over the year (26). There is also strong evidence that this strategy reduces the risks of severe exacerbations, than as-needed use of SABA alone (27). At last, evidence supports the superiority of daily ICS—even at low doses—over SABA-only treatment in terms of reducing exacerbations, improving lung function, and alleviating symptoms (21).

When choosing between the two recommended tracks, GINA emphasizes the need to consider: the presence of one or more non-modifiable risk factors for exacerbations or progressive loss of lung function; the patient's attitude toward self-management and ability to accurately perceive symptoms; and previous treatment experiences, including any potential side effects.

With respects to adolescents, a more conservative approach is outlined in younger children (age 6-11 years), due to limited evidence for ICS/formoterol use in this population (**Figure 3**). Accordingly, treatment for patients in this age group using SABA for symptoms relief less than twice per week should be as-needed SABA, combined with administration of low-dose ICS at each instance of symptom occurrence (Step 1), as poor treatment adherence is highly likely in this group of patients; Step 2 involves regular daily low-dose ICS therapy, supplemented with as-needed SABA.

OPTIMIZING ASTHMA TREATMENT

Asthma control can be usually achieved through tailored pharmacological treatment. However, nonpharmacological strategies should also be considered and implemented. Data from twenty-eight thousand five hundred eighty-four asthma patients (≥18 y) from nationwide Swedish asthma cohort study reported that over 50% of patients treated for mild/moderate asthma had an uncontrolled disease and non-pulmonary treatable traits (TTs), such as smoking, may affect asthma control negatively (28). As a matter of fact, it has been shown that both non-healthy lifestyles and environmental triggers determine detrimental effects on the airways which might cause worsening of symptoms and lower response to treatments. Therefore, to optimize asthma management patients and caregivers should be continuously educated on the risks deriving from avoidable risk factors. Firstly, it is well known that exposure to environmental tobacco smoke worsens asthma control and symptoms: many studies have shown that both active and passive smoking (including second and third

hand exposure) have negative effects on the bronchial mucosa mainly by promoting inflammation, by causing direct tissue damage and by favoring the development of allergy and airway hyperreactivity (29). As a consequence, every form of tobacco smoke exposure must be avoided, especially in children, who are particularly vulnerable. Notably, in active smokers, the risk of worse symptom control and reduced lung function is higher and associated with marked reduced response to ICS, so that such habit should be routinely screened among adolescents. Recently, evidence showed that also exposure to active and passive vape from both e-cigarette and heated tobacco products increases the risk of respiratory symptoms and asthma exacerbations and is not harmless as commonly thought and must be avoided as well (30-33).

As for pollution, exposure to air pollutants should be reduced as much as possible, due to their well-known detrimental effects on the airways. Traffic and industry-related gaseous pollutants, including nitrogen dioxide, sulfur dioxide, ozone, together with particulate matter cause disruption of epithelial integrity, exert a pro-inflammatory effect and induce oxidative stress, thus worsening asthma inflammation and airway hyperreactivity (34-36). Children are particularly at risk due to their inclination to play outside, usually on the ground, and to put their hands on their mouths, not mentioning their higher respiratory rates and immaturity of the respiratory and immune systems (37). Notably, in asthmatic patients outside physical activity should be promoted, but considering the quality of air. Regarding indoor pollution, in addition to tobacco smoke the most common source of pollution are heating devices and cooking behaviors, together with building materials, furnishings and products used for household cleaning and maintenance (38). Caregivers must be educated accordingly to improve the quality of their household air (39). Frequent windows opening can be useful, avoiding days in which outdoor air quality is poor. Indoor mold must be detected and removed due to its pro-inflammatory and irritant effects on the airways. Airborne allergens exposure, such as to house dust mite, should be avoided or at least reduced, even if there is limited evidence on the efficacy of such strategy on asthma control.

Secondly, healthy lifestyles must be encouraged. In particular, patients with asthma should be doing regular physical activity, which has been shown to be able to improve cardiopulmonary fitness, asthma control and quality of life (40, 41). In patients with exercise-induced asthma symptoms, maintenance treatment must be carefully reviewed and stepping up could be useful to better control their condition. However, premedication with SABA or ICS-formoterol before exercising could be considered on a case-by-case basis. Moreover, a healthy diet (meaning rich in fruits and vegetables) should be followed, not only to maintain adequate weight, but also for its benefits on general health (42). As for asthma control, fruits and vegetables might improve symptoms control through their anti-inflammatory properties as well as modulation effects on the immune system and microbial composition in both the gut and lungs (43, 44).

Last but not least, mental health and emotional stress must be evaluated and managed when appropriate, especially in adolescents, in which signs or symptoms of anxiety and depression must be detected early. Psychiatric comorbidities reduce asthma control and quality of life and are usually associated with overall lower medication adherence (45).

MANAGEMENT OF MILD ASTHMA IN CHILDHOOD: WHAT DOES SIMRI SUGGEST?

The adoption of AIR strategies in mild asthma aims to decrease underlying inflammation and potentially reduce the risk of exacerbations (46), while reducing cumulative steroid exposure (22, 24, 26), and providing a way for patients with inconsistent maintenance use to receive ICS whenever reliever medication is used (47). SIMRI advocates for improved management of mild asthma in children and adolescents, supporting AIR strategies while highlighting some critical points that need to be addressed.

First of all, clinical evidence supporting ICS-SABA therapy in children remains limited. Questions persist regarding the optimal ICS dosage for intermittent use in this population and more research is needed to evaluate safety, efficacy, and the potential for long-term effects. Misunderstanding the “as-needed” concept may lead to overuse, mirroring past challenges observed with SABA-only treatment. Nonetheless, the convenience of ICS-SABA single inhaler therapy can improve patient adherence. Having one device for both control and symp-

Table 1. *Main benefits and barriers of AIR strategies in childhood asthma.*

Benefits	Barriers
Reducing airways inflammation	Limited evidence in children
Reducing risk of future exacerbations	Regulatory discrepancies among countries
Improving treatment adherence	Poor clinicians' awareness
Reducing cumulative steroid exposure	Inconsistent prescribing habits among specialists and primary care providers

tom relief simplifies the regimen, reduces confusion, and improves inhaler technique, especially in younger patients. Inhaler design can play a significant role in patient acceptance and adherence, which are critical for effective asthma management. Adolescents in particular may benefit from DPIs, which are more discreet and easier to use than pMDIs with spacers (48). Anyway, we believe that tailoring therapy to each patient remains essential. While both ICS-SABA combination inhalers and separate ICS plus SABA regimens are viable options, the best approach depends on individual needs, preferences, and treatment goals (49).

With regard to ICS-formoterol, evidence for this combination in children is poor. Key trials like SYGMA included only small numbers of adolescents, and they were criticized for being overly controlled and lacking external validity, as patients demonstrated unusually high inhaler adherence rates that do not reflect real-world practice. Moreover, real-world data in younger children are lacking (48). Consequently, while current asthma guidelines, including GINA's dual-track framework, provide flexibility in treatment options for adolescents, where both ICS–SABA and ICS–formoterol are considered appropriate options, a gap of knowledge regarding treatment in children still exists. Nonetheless, the combination of budesonide-formoterol is the only suggested formulation, as other combinations have not been studied for as-needed use. In this context, fluticasone propionate has substantially advantageous peculiarities for asthma therapy, including a stronger topical anti-inflammatory activity than budesonide and beclomethasone (50-52), and quick achievement of protective effect (53). Moreover, its systemic availability occurs solely via absorption from lungs, whereas for the other ICS oral bioavailability also needs to be considered (54).

Additionally, concerns about overuse of as-needed ICS-formoterol persist. Although no serious safety signals have been reported, inappropriate or excessive use could lead to overtreatment or, conversely, inadequate control of inflammation. Ultimately, while the ICS-formoterol AIR approach shows promise, more pediatric-specific research is needed. Until robust data are available, clinicians should apply this strategy cautiously, guided by ongoing monitoring and individual patient response (48).

It should also be acknowledged that, in spite of potential benefits, the adoption of AIR strategies remains limited in real-world practice due to several barriers (**Table 1**). These include regulatory restrictions, clinical uncertainty, and inconsistent prescribing habits (47). Notably, the use of ICS–formoterol as a reliever without maintenance therapy remains off-label in many countries, underscoring significant regulatory discrepancies (55). It should be also emphasized that good asthma control depends not only on appropriate prescribing but also on patient self-management. This includes recognizing symptom worsening and adjusting therapy accordingly. On the other hand, clinicians should base decisions on thorough assessments of asthma severity, lung function, symptom patterns, adherence, and inhaler technique. Regular follow-up and therapy adjustment based on the patient's response and monitoring for side effects, should be part of routine care and shared decision-making with families. In summary, whether as-needed ICS-formoterol is truly superior and suitable to replace maintenance ICS in all patients with mild asthma remains a subject of debate. The choice should be tailored to the individual, taking into account patient preferences and their risk of asthma-related complications. In line with the European Respiratory Society, we suggest adolescents in GINA treatment steps 1 or 2 use either strategy (56), being regular ICS therapy considered for those with low lung function, and in particular if lung function is worsening. Finally, education of caregivers and patients is recommended as a core component of pediatric asthma management (57). Providing clear, age-appropriate informa-

tion about the disease, the role of each medication, and the importance of symptom monitoring can significantly improve adherence and empower families to take an active role in care. This education should also include practical training on correct inhaler technique, recognition of early warning signs of exacerbations, and appropriate use of action plans.

CONCLUSIONS

In accordance with current guidelines, SIMRI endorses the adoption of AIR strategies as a foundational treatment for mild asthma (**Table 2**). Nonetheless, we highlight the urgent need for additional randomized controlled trials involving large pediatric populations and testing different ICS/formoterol combinations for as-needed use other than budesonide/formoterol. However, pharmacological treatment alone is not sufficient; non-pharmacological interventions are equally critical. Multidisciplinary collaboration among healthcare providers, caregivers, and patients is essential to achieving long-term, meaningful outcomes. Therefore, a proactive and holistic approach should be embraced as the new standard for managing mild asthma in children and adolescents.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interest

The authors declare that they have no conflicts of interest relevant to the content of this article.

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Authors' contributions

Conceptualization, GF and SLG; writing - original draft preparation, GF, MEDC, GFen, RN, and FP; writing - review and editing, GF and SLG; supervision, SLG. All authors have read and agreed to the submitted version of the manuscript.

Ethical approval

Human studies and subjects

N/A.

Animal studies

N/A.

Table 2. *SIMRI recommendations on management of mild asthma in children and adolescents.*

1	Mild asthma must be considered as a chronic inflammatory condition capable of sudden, severe, and potentially life-threatening exacerbations.
2	Treatment strategies must target the underlying pathophysiology of asthma.
3	Treatment for adolescents aged 12 years and older should be as-needed ICS-formoterol (a single inhalation as needed is recommended, with a maximum daily dose of 72 mcg of formoterol) or as-needed SABA combined with administration of low-dose ICS at each instance of symptom occurrence; regular daily low-dose ICS therapy supplemented with as-needed SABA is suggested for adolescents with low lung function, and in particular if lung function is worsening.
4	Treatment for children aged 6 to 11 years using SABA for symptoms relief less than twice per week should be as-needed SABA, combined with administration of low-dose ICS at each instance of symptom occurrence; regular daily low-dose ICS therapy supplemented with as-needed SABA is suggested when symptoms occur more than twice per week.
5	Tailoring therapy to each patient remains essential: the best approach depends on individual needs, preferences, and treatment goals.
6	Avoidance of environmental tobacco smoke and exposure to vapors from e-cigarettes or heated tobacco products is recommended to mitigate asthma symptoms and inflammation, as well as reducing exposure to air pollutants and aeroallergens.
7	Encouraging a healthy lifestyle, including regular physical activity and a diet rich in fruits and vegetables, is recommended to improve asthma outcomes.
8	Screening for mental health issues like anxiety and depression is recommended, as these conditions are known to negatively impact asthma control and treatment adherence, especially during adolescence.
9	Education of caregivers and young patients is recommended to ensure adherence and foster long-term management success.
10	Assessing and managing mild asthma should be conducted in a holistic manner based on multidisciplinary collaboration among healthcare providers, caregivers, and patients in order to achieve sustained outcomes.

Data sharing and data accessibility

The data that support the findings of this study are available from the corresponding author upon reasonable request. Due to the nature of the survey and the anonymized dataset, no individual identifiable information is included. Data sharing will be considered for academic and research purposes in compliance with applicable data protection regulations.

Publication ethics

The authors declare that this manuscript is original, has not been previously published, and is not under consideration for publication elsewhere. All authors have approved the final version of the manuscript and agree with its submission to this journal. The authors affirm that the work complies with the highest standards of research integrity. No data have been fabricated, manipulated, or falsified. The manuscript is free from plagiarism, and all sources and contributions have been appropriately acknowledged. The authors confirm adherence to ethical principles regarding authorship, data transparency, and responsible communication of scientific results.

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POSITION PAPER

Digital Tools in Pediatric Chronic Respiratory Disease Management: Technical, Ethical, and Social Challenges – A Position Paper by the Italian Pediatric Respiratory Society (SIMRI/IPRS)

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ABSTRACT

Digital technologies are increasingly integrated into the management of pediatric chronic respiratory diseases, offering new opportunities for monitoring, diagnosis, treatment adherence, and patient engagement. However, their implementation raises important technical, ethical, and social challenges, including issues of interoperability, data protection, equitable access, and clinical validation. This position paper, endorsed by the Italian Pediatric Respiratory Society (SIMRI/IPRS), synthesizes current evidence and expert consensus to provide a structured overview of these challenges. It highlights areas of unmet need, such as the development of standardized guidelines, the promotion of responsible data sharing, and the creation of inclusive digital health policies. By addressing these aspects, the paper aims to inform clinicians, researchers, policymakers, and technology developers, fostering the safe, effective, and equitable integration of digital innovations into pediatric respiratory care.

IMPACT STATEMENT

This position paper synthesizes current evidence to guide the safe, equitable, and effective integration of digital health tools in pediatric respiratory care.

HIGHLIGHTS BOX

What is already known about this topic? Digital tools are increasingly used in pediatric respiratory care, but their adoption is inconsistent and challenged by issues of interoperability, data protection, clinical validation, and health equity. **What does this article add to our knowledge?** This multidisciplinary position paper from the Italian Pediatric Respiratory Society defines technical, ethical, social, and regulatory priorities for the safe, equitable, and sustainable integration of digital technologies into pediatric respiratory medicine. **How does this study impact current management guidelines?** It provides expert-based recommendations supporting the development of standardized guidelines and policies that ensure responsible, child-centered use of digital tools in pediatric chronic respiratory disease management.

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KEY WORDS

Digital health; pediatric respiratory diseases; chronic disease management; telemedicine; digital therapeutics; data sharing; health equity; ethical implications.

INTRODUCTION

Pediatric chronic respiratory diseases, such as asthma, cystic fibrosis (CF), bronchopulmonary dysplasia (BPD), bronchiectasis, and primary ciliary dyskinesia, represent a significant burden for patients, families, and healthcare systems worldwide. These conditions are associated with long-term morbidity, recurrent exacerbations, reduced quality of life, and considerable healthcare costs (1). Early diagnosis, close monitoring, and individualized management are crucial to improving clinical outcomes and preventing disease progression.

Over the past two decades, digital health technologies have progressively reshaped the management of chronic respiratory conditions. These include mobile health (mHealth) applications, wearable sensors, telemonitoring platforms, and artificial intelligence (AI)–driven analytics. These tools offer new ways to track symptoms, promote adherence and enable timely clinical decisions, complementing traditional in-person care (2).

The COVID-19 pandemic acted as a catalyst for the adoption of digital tools (DTs) in pediatric respiratory medicine. Physical distancing measures, combined with the need to maintain continuity of care, accelerated the implementation of telemedicine and remote monitoring systems, demonstrating their potential to complement traditional in-person care. At the same time, this rapid integration has exposed critical gaps. These include limited interoperability, concerns regarding data security, inequalities in access, and insufficient evidence on long-term clinical impact (2).

Despite growing enthusiasm, the use of DTs in pediatrics presents unique challenges. Children and adolescents differ from adults not only in physiology but also in their developmental, cognitive, and psychosocial needs. Digital solutions must therefore be tailored to children's specific needs to ensure usability, safety, and engagement, while preserving their autonomy and well-being.

This position paper, endorsed by the Italian Pediatric Respiratory Society (SIMRI/IPRS), presents a structured analysis of the technical, ethical, and social challenges in adopting DTs for the management of pediatric chronic respiratory diseases. It reviews current evidence, identifies areas of unmet need, and highlights key factors for ensuring their safe, effective, and equitable integration into pediatric respiratory care.

TECHNOLOGICAL OVERVIEW

The term DTs refers to a wide range of technologies designed to perform specific tasks, enhance functions, or facilitate processes through digital means. DTs may be either physical (*e.g.*, electronic devices) or virtual (*e.g.*, software, mobile applications, artificial intelligence (AI) solutions, web-based platforms). These tools can be integrated into electronic devices, allowing for complex functionalities.

In the field of respiratory medicine, DTs are typically categorized by their location and level of portability: home devices, hand-held devices, and portable or wearable devices (2). When properly supported, these devices can collect biometric data and transmit it to mobile applications installed on patients' devices or to web-based platforms accessible to clinicians. Mobile applications may synchronize with third-party devices and offer functionalities such as symptom diaries, educational resources, serious games (3), reminders, and secure communication channels with healthcare professionals.

This integration of DTs facilitates remote patient monitoring or telemonitoring, becoming a vital part of telemedicine workflows. When equipped with AI capabilities, these tools can analyze complex datasets to support disease recognition, risk stratification, exacerbation prediction, and early detection of clinical deterioration (4, 5) (**Table 1**).

Home devices

Home digital devices are advanced medical tools designed for use by patients in their own homes. Examples of these devices include smart home-care ventilators, home respiratory polygraphy systems, long-term oxygen therapy devices, sphygmomanometers, contactless (or "invisible") monitors, and environmental sensors. Smart ventilators, respiratory polygraphy systems, and oxygen therapy devices can continuously measure multiple respiratory parameters. This can be done either directly or indirectly through sensors mounted on the patient, and these measurements are supported by embedded software (6-9). Environmental monitors can detect and report local air pollution levels, alerting patients in cases of hazardous exposure (10). Emerging non-contact systems ("invisible") use fixed-position infrared or standard cameras, microphones, and environmental sensors placed in the patient's home. These systems

Table 1. *Key Elements of the Technological Overview.*

Definition of digital tools (DTs) – Encompass physical and virtual technologies designed to perform specific tasks, enhance functions, or facilitate processes in healthcare, including devices, software, applications, artificial intelligence solutions, and web-based platforms.
Classification by portability – DTs in pediatric respiratory medicine can be categorized as home devices, hand-held devices, and portable/wearable devices, each with distinct functions and integration potential.
Home devices – Include smart home-care ventilators, home respiratory polygraphy, long-term oxygen therapy devices, environmental monitors, and emerging contactless ("invisible") monitoring systems for continuous data collection in domestic settings.
Hand-held devices – Such as digital peak flow meters, portable spirometers, and forced oscillation technique devices, often equipped with Bluetooth connectivity for real-time data transfer and remote monitoring.
Portable and wearable devices – Including smartphones, tablets, smartwatches, activity trackers, and sensor-based wearables capable of tracking respiratory and non-respiratory parameters during daily life.
Clinical integration – DTs support remote monitoring, telemedicine, and AI-assisted decision-making, with current applications primarily in asthma, cystic fibrosis, sleep-disordered breathing, and rare pediatric lung diseases.
Evidence base – Randomized controlled trials (mainly in asthma) suggest benefits for adherence and disease control, although larger, long-term studies are needed to confirm sustained impact.

monitor physiological and environmental parameters without requiring physical interaction (11-13).

Hand-held devices

Hand-held digital devices are small, portable tools designed for manual operation. In pediatric respiratory medicine, these devices include digital peak flow meters, hand-held spirometers, and devices that utilize the forced oscillation technique (FOT). These devices aim to reduce measurement variability and usually come equipped with Bluetooth connectivity, allowing them to integrate with mobile applications (14). FOT devices require minimal patient cooperation and can assess lung mechanical properties without supervision (15). Additionally, inhaler-integrated sensors can record actuation events, which provide indirect measures of adherence and disease control, particularly in asthma management (16).

Portable and wearable devices

Portable and wearable devices are designed for mobility and continuous use. Portable devices, such as smartphones, tablets, and compact hand-held instruments, are lightweight and easy to carry. Wearable devices include smartwatches, activity trackers, chest straps, sensor patches, pulse oximeters, and smart textiles. These devices are worn on the body and often incorporate multiple biosensors (17). These devices can measure both respiratory and non-respiratory parameters, with data typically transmitted to applications held by patients or platforms monitored by clinicians. Additional features may include electronic symptom diaries and automated alerts (18).

Current state of adoption in pediatric pulmonology

The COVID-19 pandemic further accelerated the adoption of DTs in pediatric pulmonology, highlighting the value of remote monitoring and virtual care (19, 20). Most randomized controlled trials (RCTs) in pediatric respiratory medicine have focused on asthma, the most common chronic respiratory disease in children (21, 22). These interventions have included health education for patients and caregivers, behavioral strategies such as serious games and educational apps, electronic adherence monitoring devices linked to mobile applications, and the integration of mobile health into routine care. Evidence indicates that these tools can enhance adherence and improve asthma control; however, there is a need for larger, longer-term RCTs with follow-up after interventions to confirm the sustainability of these benefits (3). For sleep-disordered breathing, no RCT has directly compared telemedicine follow-ups with standard in-hospital care. Nonetheless, existing reports show promising feasibility and acceptance (23-26). In the case of CF, telehealth and remote monitoring have demonstrated good feasibility and reliability, facilitating interactions with patients and their families (27-29). Similar advantages have been observed in other rare pedi-

atric respiratory diseases, including primary ciliary dyskinesia, BPD, and interstitial lung disease (2).

Telemonitoring is becoming increasingly common for children receiving long-term continuous positive airway pressure (CPAP) or non-invasive ventilation (NIV), with data primarily used to assess adherence, leaks, and respiratory parameters (30, 31).

TECHNICAL CHALLENGES

Despite their rapid development, implementing digital technologies in pediatric respiratory medicine still presents several technical challenges. These challenges include system interoperability, data accuracy and reliability, and cybersecurity and data protection. In pediatrics, age-specific physical and psychological challenges underline the importance of user-centered design (**Table 2**).

System Interoperability

System interoperability is defined as "the ability of different information systems, devices and applications to access, exchange, integrate, and cooperatively use data in a coordinated manner, within and across organizational, regional, and national boundaries, to provide timely and seamless portability of information and optimize the health of individuals and populations globally" (32). Effective interoperability allows secure data sharing across platforms while maintaining data integrity and reducing the need for human intervention. In contrast, a lack of interoperability can compromise the safety, effectiveness, patient-centeredness, timeliness, efficiency, and equity of DTs (33). Clear and shared standards for terminology, data structure and security are essential to achieve seamless interoperability between home-monitoring systems and clinical platforms. Strengthening integration reduces fragmentation and supports more efficient and timely care (2).

Data accuracy and reliability

A key challenge is ensuring the accuracy, reliability, and integrity of data collected by DTs. Inaccurate or incomplete data can result in misdiagnosis, flawed prognostic assessments, and inappropriate clinical decisions. In pediatrics, the variations in age, size, and physiology often require datasets to be divided into smaller cohorts, which negatively impact the performance of digital models. However, advanced data-science techniques, such as model fine-tuning, may help address these limitations in the future (34).

Cybersecurity and data protection

Cybersecurity is a critical concern in safeguarding pediatric patients from privacy breaches, cyberbullying, and exposure to inappropriate content. The European regulatory framework aims to balance technological innovation with the protection of children's rights and sensitive health information (35).

Among the key instruments, the General Data Protection Regulation (GDPR) strengthens transparency, security, and accountability in the collection and processing of personal and health data, introducing specific safe-

***Table 2**. Key Technical Challenges in the Use of Digital Tools for Pediatric Chronic Respiratory Disease Management.*

System interoperability – Need for standardized terminology, content, and security protocols to enable seamless integration between home-monitoring tools and healthcare systems, ensuring timely and coordinated patient care.
Data accuracy and reliability – Ensuring completeness and validity of collected data, avoiding errors that could lead to inappropriate clinical decisions, and addressing pediatric heterogeneity that may impact model performance.
Cybersecurity and data protection – Safeguarding sensitive health and biometric data from breaches, ensuring compliance with European and national regulations, and applying specific protections for minors.
Child-specific physical challenges – Designing devices adapted to children's size and growth, preventing discomfort, pressure injuries, or interference with treatment adherence, and exploring customizable solutions such as 3D-printed interfaces.
Child-specific psychological challenges – Adapting tools to the cognitive and emotional needs of children and adolescents, promoting engagement without fostering screen dependency, and tailoring educational strategies to developmental stages.
User-centered design – Involving children and caregivers in co-development, ensuring devices are safe, affordable, easy to use, and socially compatible, while minimizing physical and environmental risks.

guards for minors, such as the requirement for parental consent when processing the personal information of individuals under 16 years of age, and the obligation to provide age-appropriate explanations regarding the implications of data use (36). The Medical Device Regulation (MDR) establishes minimum safety and security standards for all medical devices, including digital ones (37). Additional legislative initiatives, such as the Data Act, Data Governance Act, Cybersecurity Act, and Artificial Intelligence Act, further regulate fairness, cybersecurity, and innovation in information and communication technologies and AI-driven products (38).

In the healthcare domain, the European Health Data Space (EHDS) represents a pivotal initiative to create a unified framework for cross-border access, sharing, and reuse of electronic health data, enforcing interoperability, privacy, and cybersecurity standards (39). A dedicated extension, the Pediatric Health Data Space (PHDS), is under development to facilitate secure data exchange among pediatric hospitals, ensure compliance with data protection laws, and support AI-driven research and collaborative pediatric care (40). For high-risk data processing involving children's biometric or health information, additional safeguards—such as Data Protection Impact Assessments—are recommended to ensure the highest standards of privacy and security (35, 36).

Child-specific technical challenges

There are specific technical challenges related to children, which can be either physical or psychological in nature. Children often need miniaturized devices or equipment that can adapt as they grow (2). In the context of chronic respiratory care, examples include appropriately sized oxygen saturation (SpO_2) sensors for BPD and well-fitting interfaces for long-term NIV. Bulky or uncomfortable interfaces can lead to reduced data accuracy, increased air leaks, and impaired patient-ventilator synchrony. Additionally, interfaces that are too narrow may cause pressure injuries on the forehead, nasal bridge, cheeks, or chin, which can decrease patient adherence. Customized 3D-printed interfaces have the potential to improve comfort, minimize side effects, and enhance outcomes for home NIV (41).

DTs should be tailored to meet the changing cognitive and emotional needs of children, supporting disease self-management while promoting independence. This is especially important during adolescence, as greater engagement can enhance adherence to treatment (34). DTs must also consider age-related physiological changes and should utilize interactive and engaging strategies, which tend to be more effective than passive education (2). Additionally, it is crucial for digital tools to avoid increasing daily screen time or encouraging digital dependency, such as smartwatch addiction (42). Ideally, device connectivity should be restricted to healthcare-related functions only (34).

User-centered design

A user-centered approach is crucial in pediatrics. Children's needs and caregivers' insights should be actively incorporated into the design and customization of digital technologies to ensure safety, usability, and accessibility. Devices must be affordable, intuitive, and suitable for children of different ages, featuring interfaces that children can use independently, without interfering with their social activities. Instructions should be simple and tailored to developmental stages, using oral guidance for younger children and text-based prompts for adolescents (34). Additionally, devices should be designed to protect children from the devices and vice versa (34). This includes minimizing risks of ingestion or inhalation of small parts, preventing mechanical breakage, and avoiding exposure to harmful materials.

Clinical risks and practical barriers in the use of digital tools

DTs may generate false alarms or low-quality signals, which can contribute to alert fatigue and increase workload for clinicians and caregivers (2). Continuous data streams may also lead to information overload when systems are not well integrated or when algorithms lack pediatric validation (33, 34). These challenges can elevate clinicians' workload and create anxiety for families, particularly when exposed to frequent alerts or continuous surveillance (34). Addressing these barriers requires streamlined workflows, reliable alert management, and appropriate training for both healthcare professionals and families.

ETHICAL CHALLENGES

The integration of DTs into pediatric respiratory care brings important ethical considerations that must be addressed to ensure responsible and equitable use. These chal-

Table 3. Key Ethical Challenges in the Use of Digital Tools for Pediatric Chronic Respiratory Disease Management.

Privacy and informed consent – Protecting children's rights in the collection, storage, and use of health data, with age-appropriate communication to ensure understanding and meaningful participation.
Data security – Safeguarding sensitive pediatric information from breaches, misuse, or unauthorized access while complying with relevant regulations.
Equity of access – Avoiding disparities in availability and use of digital tools caused by socioeconomic status, infrastructure gaps, or low digital literacy, and promoting inclusion through targeted support programs.
Patient and family autonomy – Encouraging shared decision-making and self-management skills while preventing over-reliance on technology or excessive surveillance that may undermine independence.
Child-centered design – Developing digital tools that reflect children's cognitive, emotional, and developmental needs, ensuring usability, safety, and engagement without compromising well-being.

lenges can be grouped into three main domains: privacy and informed consent, equity of access, and impact on patient and family autonomy. Each domain reflects the need to balance technological innovation with the protection of children's rights, well-being, and developmental needs (**Table 3**).

Privacy and informed consent in pediatric patients

Digital technologies have transformed healthcare by enabling personalized treatments, continuous monitoring, and remote care. In pediatrics, however, these advancements raise specific ethical concerns related to privacy, data security, and informed consent. In the digital era, personal and medical data circulate widely. This requires a careful balance between protecting children's rights and ensuring access to appropriate care. Because children may not fully understand the implications of data processing, enhanced safeguards and age-appropriate explanations are essential.

The concept of acting in the "*best interests of the child*", as framed by Beauchamp and Childress (43) through the four principles of biomedical ethics, autonomy, beneficence, non-maleficence, and justice, provides a foundation for ethical decision-making in this context. Parental supervision through DTs may contribute to a surveillance culture in which children's privacy is overlooked in favor of perceived safety. Moreover, children's consent is rarely sought in medical decision-making (44), and insufficient or misleading information may generate anxiety or mistrust toward digital health. To address these concerns, children should receive clear, age-appropriate explanations about how DTs work and their intended purpose (2). Education for both families and healthcare providers on transparent, developmentally appropriate communication can improve acceptance and adherence to digital interventions in pediatric care.

Inequalities in access to digital tools

Digital health offers benefits that extend beyond individual care to population-level health improvements (45). Nevertheless, pediatric DTs remain underrepresented compared with adult-targeted technologies, partly due to lower financial investment (46). Recent regulatory efforts in Europe and the United States have sought to address this gap by encouraging industry to address children's specific health needs (47).

The ethical principle of justice demands equitable access to healthcare. However, DTs may unintentionally widen disparities, particularly among economically disadvantaged families, due to high device costs, inadequate infrastructure, and low digital literacy (34). In addition, self-exclusion from digital health initiatives is more common in lower-income groups, exacerbating the divide between wealthier and poorer families (48). Strategies to mitigate these inequalities include reimbursement programs for eligible households, community-based digital literacy initiatives, and targeted policies ensuring that all children, regardless of socioeconomic background, can benefit from technological innovation in healthcare.

Impact on patient and family autonomy

Autonomy is defined as self-governance in thought and action (49). In pediatric care, children rely on adults for decision-making (34), but a child-centered approach—actively involving young patients in their own care—can foster informed choice, responsibility, and self-management skills (2). Digital technologies may enhance

Table 4. Key Social Challenges in the Use of Digital Tools for Pediatric Chronic Respiratory Disease Management.

Acceptance and usability – Variability in patient, family, and clinician acceptance; potential reduction in in-person interactions; limitations in assessing qualitative and psychological aspects; risk of weakened trust when digital outputs differ from clinical judgment.
Cultural and socioeconomic barriers – Financial constraints, low digital literacy, self-exclusion due to mistrust or unfamiliarity, language barriers, and culturally rooted resistance; influence of parental attitudes and automation bias.
Education and training – Need for tailored programs for children, caregivers, and healthcare providers to ensure correct use, integration into care, and awareness of benefits and limitations.
Community engagement – Importance of collaboration with schools, local organizations, and cultural leaders; provision of multilingual and culturally adapted resources to promote inclusion and trust.

autonomy by enabling self-monitoring and shared decision-making.

However, potential drawbacks exist. Automated digital algorithms can contribute to depersonalization, with children perceived primarily as sources of data (2). Discrepancies between device-generated information and the child's own symptom reports may undermine the child's credibility (50), and caregivers may place greater trust in device outputs than in the patient's experience. Excessive parental monitoring via DTs may also reduce opportunities for independent self-management, increasing anxiety and dependence (2, 34).

Ethically sound practice requires a balance between leveraging digital tools for improved health outcomes and preserving children's mental and emotional well-being. Clinical teams should promote informed participation, respect for autonomy, and guidelines to prevent over-surveillance, ensuring that technology supports rather than diminishes the child's role in their own care.

SOCIAL CHALLENGES

The integration of DTs into pediatric respiratory care also raises important social challenges that can influence their acceptance, accessibility, and effectiveness. These challenges relate primarily to acceptance and usability, cultural and socioeconomic barriers, and education and training for users, each of which has implications for equitable and sustainable adoption (**Table 4**).

Acceptance and usability by patients, families, and healthcare providers

The use of DTs in pediatric care can reshape the physician–child–parent relationship, particularly by reducing the frequency of in-person consultations. Evidence from pediatric asthma research shows that attitudes toward DTs have evolved over time. Before the SARS-CoV-2 pandemic, only 19% of parents preferred DT-based consultations over traditional visits (48); during the pandemic, this figure rose to 43%, with 53% of children expressing a preference for digital health solutions (51).

Despite growing acceptance, DTs may not fully capture the relational and qualitative dimensions of care that emerge during in-person encounters. Emerging digital twin systems (DTS) create a virtual representation of the patient and may weaken the empathic bond between patients, families, and healthcare providers (34). Discrepancies between DTS-generated recommendations and physician advice may also undermine mutual trust (53).

Socioeconomic and cultural barriers

The implementation of DTs in pediatric healthcare can be hindered by financial barriers, as lower-income families may struggle to afford these technologies, exacerbating existing healthcare disparities (53). Limited digital literacy further compounds these inequalities, making effective use of DTs more challenging (34).

Self-exclusion is another concern. Individuals with lower educational attainment or socioeconomic status may be reluctant to engage with digital health initiatives due to mistrust or unfamiliarity. Language barriers and cultural attitudes toward healthcare technology can also contribute to resistance, especially in communities where traditional models of care are deeply rooted (34, 48).

Parental attitudes strongly influence the acceptance of DTs. Some families may be hesitant to grant children greater autonomy in managing their conditions, while automation bias, a tendency to trust digital out-

puts over human judgment, can create conflicts when device-generated results contradict patient-reported symptoms (54). Addressing these cultural and attitudinal factors is essential for equitable and effective DT adoption.

Education and training for use

Targeted education and training programs are key to overcoming these barriers and ensuring that DTs are accessible, user-friendly, and culturally appropriate (55). For parents and caregivers, digital literacy initiatives should explain how DTs function, their benefits, and their limitations. Practical workshops and online resources can bridge knowledge gaps and build confidence in using these tools (55). For children, educational materials should be engaging, interactive, and age-appropriate, with gamified tools, mobile apps, and instructional videos that teach correct device use and symptom reporting, fostering active participation in care.

Healthcare providers also require dedicated training to integrate DTs into practice effectively. Pediatricians should be able to interpret DT-generated data, combine digital insights with clinical judgment, and address family concerns (56). Training should also cover ethical aspects, including data privacy, patient autonomy, and potential biases in digital assessments.

Finally, community engagement is essential to build trust in DTs. Collaboration with schools, local organizations, and cultural leaders can help dispel misconceptions, while multilingual and culturally adapted resources can ensure that diverse populations are informed, included, and empowered to use DTs effectively.

REGULATORY ASPECTS AND CHILDREN'S RIGHTS

DTs used in pediatric respiratory care are regulated within a broad and evolving framework that aims to balance innovation with safety, privacy, and children's rights. Depending on their intended purpose and associated risk, digital tools may qualify as medical devices and must comply with the Medical Device Regulation (MDR) and, when applicable, the In Vitro Diagnostic Regulation (IVDR) (37). Additional guidance from regulatory bodies, such as Medical Device Coordination Group (MDCG) documents and international harmonization initiatives, supports consistent interpretation and implementation of these requirements (57).

Networked or software-based devices must also meet cybersecurity and data-governance obligations, as defined by the GDPR (36) and complemented by recent European initiatives on data governance and interoperability (58, 59). In parallel, emerging frameworks such as the European Health Data Space (EHDS) (39) and the Artificial Intelligence Act (60) establish further standards for data protection, transparency, and the responsible use of AI-enhanced systems in healthcare.

Children require particular protection in the digital environment because they may not fully understand how their personal and health data are collected, shared, and reused. International and European policy instruments - including the Council of Europe Recommenda-

***Table 5**. Key Regulatory Aspects and Children's Rights in Pediatric Digital Tools.*

Regulatory frameworks – DTs must comply with MDR/IVDR and follow MDCG guidance and harmonization initiatives. Networked or software-based devices require GDPR compliance and alignment with emerging EU governance frameworks, including the EHDS and the AI Act.
Device-specific requirements – Regulatory obligations vary by device type, with additional safeguards for connected and AI-driven systems, particularly regarding data governance and transparency.
Children's rights – European and international instruments - Council of Europe Recommendation, UN CRC General Comment No. 25, and relevant Digital Services Act provisions - highlight the best interests of the child, age-appropriate design, and protections for vulnerable groups.
Safety and usability – Devices must minimize physical risks (including PFAS exposure), limit screen time, and support developmental appropriateness while avoiding excessive surveillance or stress for families.
Regulatory incentives – The absence of structured pediatric-specific pathways limits innovation. Strengthened oversight, dedicated routes, and targeted incentives are needed to promote validated and equitable child-centered DTs.

AI Act – Artificial Intelligence Act; EHDS – European Health Data Space; GDPR – General Data Protection Regulation; IVDR – In Vitro Diagnostic Regulation; MDCG – Medical Device Coordination Group; MDR – Medical Device Regulation; PFAS – Per- and Polyfluoroalkyl Substances; UN CRC – United Nations Convention on the Rights of the Child

tion on children's rights in the digital environment (61), the UN Committee on the Rights of the Child General Comment No. 25 (62), and binding provisions of the Digital Services Act - emphasize the best interests of the child, age-appropriate communication, enhanced safeguards for sensitive data processing, and attention to children living in vulnerable circumstances or with disabilities.

Safety, design, and usability requirements are especially relevant for pediatric DTs. Beyond regulatory compliance, devices should minimize physical risks, such as choking, ingestion, or exposure to harmful substances including per- and polyfluoroalkyl substances (PFAS)-containing components (63), and limit unnecessary screen time (42). Interfaces must match children's developmental and cognitive abilities, supporting autonomy without creating excessive surveillance or stress for families (34, 64). Child-centered design and human-factors engineering play a key role in ensuring usability, comfort, and psychological well-being.

Compared with pharmaceuticals, where pediatric investigation plans are mandatory, the medical device sector lacks systematic pediatric-specific evaluation. This gap is particularly relevant for DTs that influence clinical decision-making or daily disease management. Dedicated regulatory pathways, stronger involvement of pediatric expert committees, and targeted incentives could promote child-centered innovation. European initiatives in this field (65) underscore the importance of developing, validating, and equitably implementing digital technologies adapted to children's needs (**Table 5**).

SUSTAINABILITY ASPECTS

DTs offer substantial clinical advantages in pediatric respiratory care but also raise sustainability considerations that must be addressed to ensure responsible long-term implementation (**Table 6**). While telemedicine and remote monitoring can reduce emissions associated with travel and in-person appointments, thereby lowering the overall carbon footprint of healthcare delivery (66, 67), the production, operation, and disposal of digital devices contribute to energy consumption, resource depletion, and electronic waste. Globally, the healthcare sector already represents a significant environmental burden (66), and the growing use of digital tools may further increase this impact if not accompanied by appropriate mitigation strategies.

Electronic waste remains a critical challenge. Medical and consumer-device components, including batteries, sensors, plastics, and circuit boards, generate pollutants that pose risks to ecosystems and human health if not properly managed (68). Energy-intensive infrastructures such as data centers, required to store and process large-scale health data, also contribute to greenhouse gas emissions (69). A sustainability-oriented approach therefore requires assessing the full lifecycle of DTs, from manufacturing to end-of-life disposal, and promoting design principles that extend device lifespan, support repairability, and facilitate recycling.

Several strategies can help minimize environmental impact. These include using energy-efficient cloud services, optimizing software and data-processing sys-

***Table 6**. Key Sustainability Aspects of Digital Tools in Pediatric Chronic Respiratory Disease Management.*

Environmental impact – DTs reduce travel-related emissions and paper use but contribute to e-waste, energy consumption, and environmental degradation from device manufacturing and mineral extraction.
Data center footprint – Large-scale storage of electronic health data consumes significant electricity, often from non-renewable sources, increasing the carbon footprint.
Resource use in manufacturing – Production of smartphones, wearables, and sensors relies on critical minerals and generates waste during the device lifecycle.
E-waste management – Improper disposal of medical electronics and plastics can cause pollution; recycling and safe disposal programs are essential.
Sustainable strategies – Adopt renewable-powered, energy-efficient data centers; use optimized software and AI for energy management; apply lifecycle assessment before implementation.
Circular economy principles – Extend product lifespans through modular upgrades, refurbishing, reusing, and recycling; promote biodegradable materials and eco-friendly packaging.
Policy and awareness – Mandate environmental criteria in procurement, incentivize sustainable design, integrate green principles into healthcare training, and raise awareness among patients and providers.

tems, applying data-minimization principles, and promoting renewable-energy solutions for digital infrastructures (69). Lifecycle assessments and responsible procurement processes can guide healthcare institutions in selecting devices and platforms with lower ecological footprints. In addition, recycling and take-back programs for digital health devices, such as inhalers, sensors, or remote-monitoring equipment, should be encouraged to reduce e-waste generation (68). Educational initiatives for families and clinicians can improve awareness of proper disposal practices and support a more sustainable culture of device use.

Embedding sustainability criteria into digital health strategies, including eco-design, reduced energy consumption and circular-economy approaches, can minimize the environmental footprint of DTs and support long-term responsible adoption (70, 71).

CLINICAL AND RESEARCH PERSPECTIVES

DTs have the potential to become integral components of therapeutic pathways for pediatric chronic respiratory diseases. Effective integration requires a hybrid model that combines in-person clinical care with remote monitoring and virtual consultations. Such models can enable early detection of exacerbations, personalized treatment adjustments, and enhanced patient engagement. The integration process should follow structured protocols, ensuring interoperability between DTs and electronic health records, and establishing clear criteria for clinical action based on device-generated data.

Collaboration between pediatric respiratory specialists, general practitioners, allied health professionals, and technical experts is essential to ensure smooth incorporation into existing care workflows. Additionally, integration should be accompanied by training programs for healthcare providers, as well as educational support for patients and caregivers, to maximize usability and adherence.

Despite significant progress, several unmet needs must be addressed to optimize the use of DTs in pediatric respiratory care. First, there is a lack of evidence-based guidelines specifically focused on the responsible implementation of DTs in children. These guidelines should cover safety, efficacy, ethical considerations, and long-term follow-up. Second, policies are needed to promote equity, ensuring that DT adoption does not exacerbate existing socioeconomic or geographic disparities. This includes supporting infrastructure development in underserved areas, reimbursement schemes, and digital literacy initiatives. Third, sustainability considerations must be embedded in policy and procurement processes, incentivizing eco-friendly design, energy efficiency, and responsible e-waste management. Finally, fostering collaborative approaches among clinicians, researchers, industry stakeholders, patient advocacy groups, and policymakers will be critical to drive innovation, validation, and widespread adoption of high-quality, child-centered digital health solutions.

OPERATIONAL FRAMEWORK AND KEY RECOMMENDATIONS FOR THE INTEGRATION OF DIGITAL TOOLS IN PEDIATRIC RESPIRATORY CARE

The implementation of DTs in pediatric respiratory care benefits from a structured and pragmatic framework that supports clinicians, families, and policymakers in daily practice. Based on current evidence and expert consensus, we propose the following operational recommendations:

- Clinical Assessment and Prioritization: DTs should be selected according to the child's clinical profile, disease severity, and specific monitoring needs. Before implementation, clinicians should assess the potential benefits, risks, and feasibility of integrating each tool into existing care pathways.
- Data Governance, Privacy, and Transparency: Healthcare teams must ensure compliance with data protection regulations and provide families with clear, age-appropriate information about data use, storage, and access. Transparent communication fosters trust and encourages engagement.
- Integration into Clinical Workflows: Digital tools should complement, not replace, clinical evaluation. Clear action thresholds, alert hierarchies, and response workflows are needed to prevent data overload, false alarms, or misinterpretation. Institutions should ensure interoperability with electronic health records and avoid parallel, non-integrated platforms.
- Training and Digital Literacy: Clinicians, patients, and caregivers require tailored training to use digital tools effectively. Educational resources should cover device

functionality, correct data interpretation, and troubleshooting, while promoting realistic expectations and shared decision-making.

- Family Engagement and Psychosocial Support: Digital solutions should empower, but not overburden, families. Monitoring intensity should match the clinical scenario to avoid unintended stress or anxiety. Supportive communication and regular feedback loops help maintain adherence and prevent technology-related fatigue.
- Continuous Evaluation and Quality Improvement: Implementation should include mechanisms for ongoing assessment of usability, clinical impact, safety, and equity. Feedback from children, families, and clinicians should guide iterative refinement of digital systems and institutional policies.
- Equity and Accessibility: To prevent widening health disparities, programs should incorporate strategies to support families with socioeconomic vulnerabilities, limited digital literacy, or technological barriers. Reimbursement policies and institutional lending programs may improve access to essential devices.

CONCLUSIONS

DTs can enhance the management of pediatric chronic respiratory diseases by supporting early detection, treatment adherence and patient engagement. Their integration, however, requires careful attention to safety, equity, interoperability and sustainability.

The successful integration of DTs into pediatric respiratory care requires a careful balance between innovation and responsibility, aligning technological capabilities with the developmental needs, rights, and well-being of children. Clinicians must be supported by clear protocols, robust evidence, and interoperable systems; policymakers must enact regulations and incentives that promote both equity and sustainability; and industry must commit to child-centered design and high safety standards.

Looking ahead, the vision for the future is a digitally empowered, patient-centered healthcare ecosystem in which DTs complement, rather than replace, the human elements of care. Such a model would leverage real-time data, artificial intelligence, and telehealth to provide personalized, proactive, and participatory care, while maintaining empathy, trust, and respect for children's rights. Achieving this vision will require ongoing research, multidisciplinary collaboration, and a shared commitment to ensuring that digital innovation serves the best interests of every child.

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COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interest

The authors declare that they have no conflicts of interest relevant to the content of this article.

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Authors' contributions

AL and GF conceived the position paper, coordinated the working group, and drafted the initial version of the manuscript. BA, AG, VM, MN, GR, and LV contributed to the literature review, methodology definition, and manuscript writing. DD and SLG critically revised the manuscript for important intellectual content and supervised the overall work. All authors contributed to the study design, reviewed the manuscript critically, and approved the final version. They all agree to be accountable for the integrity and accuracy of the work.

AL and GF contributed equally as co-first authors. DD and SLG contributed equally as co-last authors.

Ethical approval

Not applicable.

Data sharing and data accessibility

The data that support the findings of this review are available from the corresponding author upon reasonable request.

Publication ethics

The authors declare that this manuscript is original, has not been previously published, and is not under consideration for publication elsewhere. All authors have

approved the final version of the manuscript and agree with its submission to this journal.

The authors affirm that the work complies with the highest standards of research integrity. No data have been fabricated, manipulated, or falsified. The manuscript is free from plagiarism, and all sources and contributions have been appropriately acknowledged.

The authors confirm adherence to ethical principles regarding authorship, data transparency, and responsible communication of scientific results.

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BRIEF REPORT

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).

$$\left(\frac{FEV_1\ post\ bronchodilator}{FEV_1\ pre\ bronchodilator} - 1\right) \cdot 100$$

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 predicted FEV_1, with reference to the patient's predicted FEV_1 based on age, sex, height, and ethnicity.

$$\frac{FEV_1\ post\ bronchodilator - FEV_1\ pre\ bronchodilator}{FEV_1\ predicted} \cdot 100$$

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.

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,

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%)

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**.

***Table 2**. Proportion of children with significant reversibility (using the two definitions) according to baseline obstruction using Lower Limit Normal FEV1/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%)

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 ≤ 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.

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 (χ^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 ≤ 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.

CONCLUSIONS

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

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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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