

# *Management Of Childhood Asthma And Adherence To Current Guidelines*

<sup>1</sup>Sarah Fathima Khateeb, <sup>2</sup>Azizah Nawaz, <sup>3</sup>Alyaa Badur Ferry, <sup>4</sup>Zoha Arif, <sup>5</sup>Izzah Tamseel Khanum, <sup>6</sup>Sabreena Samad

<sup>1,3,6</sup>Tbilisi State Medical University, Tbilisi, Georgia

<sup>2</sup>University of Georgia, Tbilisi, Georgia

<sup>4</sup>Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

<sup>5</sup>Gulf Medical University, Ajman, United Arab Emirates

<sup>1</sup>sarah.khateeb247@gmail.com; <sup>2</sup>Aznw.1104@gmail.com; <sup>3</sup>aaleferry@gmail.com; <sup>4</sup>zohak726.2@gmail.com;

<sup>5</sup>itk.uni.only@gmail.com; <sup>6</sup>sabreena.samad.ss@gmail.com

<sup>1</sup><https://orcid.org/0009-0004-4542-0161>; <sup>2</sup><https://orcid.org/0009-0007-5711-9183>; <sup>3</sup><https://orcid.org/0009-0007-9747-4446>; <sup>4</sup><https://orcid.org/0009-0007-9552-0082>; <sup>5</sup><https://orcid.org/0009-0001-0220-9858>; <sup>6</sup><https://orcid.org/0009-0008-4193-6477>

Corresponding author: Sarah Fathima Khateeb, [sarah.khateeb247@gmail.com](mailto:sarah.khateeb247@gmail.com)



## **Abstract:**

**Introduction:** Childhood asthma, a leading chronic respiratory disease, is managed according to evidence-based international guidelines like those from the Global Initiative for Asthma (GINA). These guidelines recommend a stepwise approach focused on inhaled corticosteroids (ICS) for control and prevention. However, a persistent gap exists between these recommendations and real-world clinical practice, contributing to poor outcomes.

**Keywords:** Paediatric asthma; Medication adherence; Clinical practice guidelines; Inhaled corticosteroids; Implementation science; Health disparities.

## **Introduction**

Asthma remains the most common chronic respiratory disease in children, with significant implications for quality of life, healthcare utilization, and long-term lung health. To decrease this burden, evidence-based clinical guidelines, such as those from the Global Initiative for Asthma (GINA) and national consensus statements like the REGAP <sup>[5]</sup>, provide a structured framework for management. These guidelines support a stepwise approach focused on the appropriate use of inhaled corticosteroids (ICS) as controller therapy, the provision of written asthma action plans (AAPs), and regular clinical review to achieve and maintain symptom control while minimizing the risk of exacerbations.

Despite the clarity and widespread availability of these recommendations, a persistent and well-documented gap exists between guideline ideals and everyday clinical practice. Suboptimal adherence is seen at multiple levels: in the under-prescription of ICS and over-reliance on reliever medications by clinicians <sup>[1],[10]</sup>, in the poor daily adherence to prescribed regimens by patients and families <sup>[3]</sup>, and in the systemic failure to implement core guideline activities like AAP provision <sup>[12]</sup>. This adherence gap is not

merely a theoretical concern but a direct driver of poor outcomes, including preventable exacerbations, emergency department visits, and hospitalizations.

The barriers to adherence are complex and multifactorial, weak patient beliefs (e.g., fear of steroid side effects) <sup>[8], [15]</sup>, healthcare provider knowledge gaps <sup>[6], [13]</sup>, and broader socioeconomic determinants <sup>[14]</sup>. Therefore, improving childhood asthma outcomes is achievable through a critical examination of not just what the guidelines recommend, but why their adoption fails and how implementation can be successfully supported.

This literature review synthesizes recent evidence (2020-2025) to comprehensively analyse the state of adherence to childhood asthma management guidelines. It will explore the extent and impact of non-adherence, identify key barriers across the care spectrum, and evaluate promising strategies, from educational pathways to digital health tools, designed to bridge the guideline-practice gap and achieve optimal asthma control for children.

**Methods:** A narrative literature review was conducted from key databases, with recent studies (2020-2025) investigating adherence to paediatric asthma guidelines from clinical, patient, and systems perspectives being analysed. The synthesis focused on themes of pharmacological adherence, guideline implementation strategies, and identified barriers. The evidence included observational studies <sup>[1], [4]</sup> mixed-methods research <sup>[3], [7]</sup> and intervention studies <sup>[2]</sup>.

**Patient and/or Public Involvement:** There was no patient and/or public involvement in the materialising of this paper. The authors do not foresee any future involvement in the review of this literature either.

**Results:** The review confirms widespread poor adherence. Studies reveal under-use of ICS and over-reliance on short-acting beta-agonists (SABAs) despite guideline warnings <sup>[1], [10]</sup>, and poor implementation of AAPs and routine monitoring <sup>[12]</sup>. Adherence is influenced by multi-level barriers, including patient/caregiver concerns about ICS side effects and complexity <sup>[3], [8], [15]</sup>, and systemic issues like socioeconomic disparities <sup>[14]</sup>. Clinician-level gaps, such as variable knowledge among community pharmacists <sup>[6]</sup> and healthcare team confidence <sup>[13]</sup>, further impede guideline-concordant care. Conversely, structured educational interventions <sup>[11]</sup>, school-linked support <sup>[2], [7]</sup> and technology like electronic adherence monitors <sup>[3]</sup> show promise in improving outcomes.

The findings highlight that poor adherence is a multifactorial problem undermining the therapeutic effectiveness of guideline recommendations. The consistent under use of controller therapy directly correlates with preventable exacerbations. Addressing this requires moving beyond passive distribution of guidelines to active, tailored implementation strategies that target specific barriers at patient, provider, and healthcare system levels. The success of educational pathways and technology-assisted monitoring provides a blueprint for intervention.

## Discussions

### A. Pathophysiology and Classifications Linked to Guidelines

Childhood asthma is a complex chronic inflammatory disease which is mainly characterized by the airway hyperresponsiveness, reversible airflow obstruction, and persistent inflammation. The disease arises due to the interaction of genetic, epigenetic, environmental and immunological conditions, especially during the crucial early stages of life

#### Immune Mechanism and Type 2 Inflammation

Adult Onset Asthma and childhood asthma share close similarities in pathophysiology and immunological mechanisms. The majority of children asthma cases are characterized by the type2 – high inflammation which is triggered by helper 2 (Th2) cells that generate important cytokines such as interleukin-4 (IL-4), IL-5, IL-13, IL-25, and IL-33. Numerous pathogenic symptoms of illness, including increased mucus secretion, bronchial hyperresponsiveness, production of immunoglobulin E (IgE), and eosinophilic infiltration of the airways are regulated by these cytokines <sup>[16]</sup>. This immunological endotype explains why inhaled corticosteroids work well as the main controller therapy. It also supports the use of targeted biologic agents targeting the IgE and IL-5 pathways for certain children with severe asthma, as current GINA and NHLBI guidelines recommend.

### Airway Remodelling and Structural Changes

One of the critical consequence of the disease is airway remodelling, which is not as severe in children as it is in adults. However, if asthma is not controlled, ongoing inflammation can still cause lasting changes in the airways and limit lung growth over time. Airway remodelling can lead to the thickening of the airway wall, proliferation of the smooth muscle, activation of fibroblasts and the increase in the extracellular matrix deposition. All these changes together leads not only to the narrowing of the bronchial lumen but likewise irreversibly decline the lung function. IN particular, Neutrophil Extracellular traps (NETs) enriched in IL-17A enhances the transition from the inflammation to the fibrosis by activating the lung fibroblast into pre-fibrotic state <sup>[17]</sup>.

### Genetic Factors and Environmental Factors

Multiple genetic factors have been identified such as ORMDL3, GSDMB, RAD50, HLA-G, CXCR5, IL-4, IL-13, and TSLP to contribute in the childhood asthma. A significant region associated with asthma has been identified on chromosome 17q12-21 and has been extensively researched, indicating that the genetic basis of asthma is highly polygenic, which means that several genes collaborate to affect the likelihood of developing the disease <sup>[18]</sup>. Family history also plays a significant role in asthma risk, children with two asthmatic parents faces higher risk compared to those with no family history

Apart from inheritability, the exposure to environmental factors also influences childhood asthma

With Early- Life exposures One of the strongest modifiable risk factor is the maternal smoking during pregnancy. Other than this factor neonatal infections, antibiotic use, Oxygen therapy and Respiratory tract infections can also contribute for the childhood asthma. Microbial dysbiosis in both the airway and gut microbiota can also be contributed to asthma development .

Weather change, air pollution, diet patterns and housing conditions can all influence childhood asthma development <sup>[19]</sup>.

It is important to identify genetic susceptibility and early-life environmental risk factors, as current GINA and NHLBI guidelines recommend early assessment and prompt initiation of controller therapy in high-risk children to help prevent disease progression and future flare-ups.

### Epithelial Barrier Dysfunction

The airway epithelium is barrier between environment and immune system. In childhood asthma there is an epithelial barrier dysfunction which can occur through various mechanisms: Disruption in tight junctions, abnormal epithelial cell differentiation, reduction in the ciliated cell numbers, increased hyperplasia of goblet cell. All these factors contribute to impairing the mucociliary clearance and increases the penetrations of allergens or the pathogens into deeper airway tissues

### Ion channel and Signalling Dysfunction

At the cellular level, the ion channels plays a fundamental role in maintaining the inflammatory response of asthma. The channels involved includes transient receptor potential channels (TRP), calcium-activated potassium and chloride channels and other channels that regulate intracellular signalling in effector cells such as lymphocytes and eosinophils <sup>[20]</sup>.

### Oxidative stress

Oxidative stress plays a key role in childhood asthma and occurs when reactive oxygen species (ROS) exceed the body's antioxidant defences. Increase in the level of ROS harms the airway cells, which then weaken the airway barrier and causes inflammation. Environmental factors like air pollution, tobacco smoke, and indoor allergens increase oxidative stress, especially in genetically vulnerable children. Even in the early stages of life low antioxidant concentration level may make children more likely to have ongoing airway inflammation.

### Viral Infection and Immune Dysregulation

Rhinovirus is one of the main viral triggers for asthma attacks in children. Children who are prone to asthma even before the development of the allergies have abnormal immune responses to this virus. Early signs that point toward development of asthma in the future are frequent wheezing with rhinovirus and the onset of allergies. These immune problems are linked to reduced

interferon production due to lower activity of IRF-7 and fewer T regulatory (Treg) cells, both of which help control inflammation [21]. GINA and NHLBI emphasize that viral-induced wheeze is common in preschoolers and highlight the need to distinguish it from persistent asthma.

### Hormonal Influences

Asthma prevalence varies by sex, with more cases seen in males during childhood and a shift toward higher rates in females after puberty. Sex hormones play a role in this difference; for example, estrogen can promote type 2 inflammation, increase the infiltration of the eosinophils and upregulate IL-4 and IL-13 expression which in turn increase airway hyperresponsiveness, whereas testosterone may exert protective effects [22].

Childhood asthma comes in several different forms, each with its own pattern of inflammation. In the past, doctors mainly separated asthma into allergic and non-allergic types depending on IgE levels. Now, experts know there are multiple subtypes, or endotypes, based on what's really happening in the body.

Type 2-high asthma is marked by lots of eosinophils in the airways, fuelled by certain immune responses. Type 2-low asthma, on the other hand, has either more neutrophils or fewer inflammatory cells overall, and it often doesn't respond as well to steroid treatments. Neutrophilic asthma is a specific form where another type of immune cell, the neutrophil, and the molecule IL-17 are especially active

### Classification of childhood asthma: GINA and NHLBI guidelines

To manage childhood asthma effectively and follow guidelines, it is important to understand the underlying mechanisms of the disease. Most children have Type 2 inflammation, which is why inhaled corticosteroids (ICS) are the main first-line treatment. Guidelines recommend regular ICS use to lower the risk of flare-ups and improve symptom control in children with persistent asthma [30].

To inform treatment, systematic classification approaches grounded in current evidence are employed. According to The Global Initiative for Asthma (GINA) and the National Heart, Lung, and Blood Institute (NHLBI) guidelines, comprehensive approaches are carried out that are transitioning from severity-based to control-based systems, with emphasis on age-specific considerations.

### Evolution of Classification Approaches

Classification of the childhood asthma has shifted from being more focus on disease severity to emphasising on how to control asthma. Initially asthma was categorized mainly based on the severity of the disease: intermittent, mild, moderate, or severe, but now both GINA and NHLBI guidelines highlight the severity at diagnosis does not always predict future outcomes, and even mild cases of patients can experience serious exacerbations. Regardless of the initial severity, current guidelines primarily emphasize the significance of controlling asthma to retain excellent control.

### Classification Framework for GINA Guidelines

The GINA recommendations categorize children asthma into three age categories, each with their unique approach: under 5 years (preschool), 6-11 years, and 12-18 years.

This breakdown considers differences in diagnosis, symptoms, and how children respond to treatment [24]. For children aged 6-11, the 2021 GINA guidelines made important updates to Step 3 treatment, suggesting options like low-dose LABA-ICS combinations, very low-dose formoterol-ICS, medium-dose ICS alone, or ICS-LTRA combinations as first choices [25]. The latest GINA guidelines advise against using only short-acting  $\beta_2$ -agonists (SABA) for children of any age.

Even for moderate asthma, inhaled corticosteroid (ICS) regimens are recommended to lessen flare-ups and improve long-term ongoing management. Asthma control is assessed using the GINA guidelines, which examines the daytime symptoms, nightly waking, activity limits, and reliever usage frequency. And also, it is stated to identify asthma in preschoolers (ages 0-5) might be a bit difficult due to spirometry and bronchodilator reversibility.

Clinicians treat this population based on their medical history, the child's reaction to inhaled corticosteroids, and risk factors such as a family history of asthma, early allergy sensitization, and early respiratory infections <sup>[26]</sup>.

#### NHLBI/NAEPP Classification System

The NHLBI, through the NAEPP, uses a step-by-step approach to asthma management that still considers severity but now also looks at how well asthma is controlled. The NAEPP groups children by age (usually under 4, 4-11, and 12 or older) and then classifies asthma by how often symptoms happen and lung function: intermittent (symptoms 2 days a week or less), mild persistent (3-4 days a week), moderate persistent (daily symptoms or nighttime symptoms 3-4 times a month), and severe persistent (symptoms all the time or nighttime symptoms 4 or more times a week) <sup>[27]</sup>. Each group has its own recommended treatments.

#### Age-Based Classification Specifics

Among Preschool Children (Ages 0-5 years): Both guidelines recognize the difficulty of verifying asthma diagnosis in early children due to inaccurate spirometry performance.

GINA suggests that intermittent symptoms in preschoolers may reflect viral-induced wheezing rather than asthma, especially in the absence of risk factors for permanent asthma. Differentiating asthma from other wheeze phenotypes, such as viral-induced or early transitory wheeze, is crucial in this age range, as these diseases may not require continuing controller medication.

School-age children (ages 6-11): In this group, measures like spirometry and bronchial challenge are more reliable, making asthma diagnosis and classification easier.

To confirm asthma and also to check how severe or controlled is the asthma, GINA and NHLBI both recommend the usage of spirometry or peak flow

Among children of 6-11, if they have daytime symptoms more than once a week or wake up at night more than once a month, or have any limits on normal activities, they should be classified as at least mild persistent asthma <sup>[24]</sup>.

And among the Adolescents and Young Adults (Ages 12 and up): Teenagers and young adults, asthma is considered to be much like in adults, as their spirometry can be done reliably and results are easier to interpret. Therefore, both guidelines urge the need for objective tests like spirometry, showing bronchodilator reversibility (at least 12% and 200 mL improvement in FEV1) or bronchial hyperresponsiveness to confirm asthma.

#### Control-Based Classification

Modern guidelines now focus more on classifying asthma by how well it is controlled instead of just by severity. The GINA system puts children into three groups <sup>[28]</sup>: well-controlled asthma (daytime symptoms two days a week or less, no nighttime waking, no limits on activity, and reliever use two days a week or less), partly controlled asthma (if 3-4 of these issues are present), and uncontrolled asthma (if three or more issues are present in any week). In practice, asthma control is often assessed using tools such as the Asthma Control Test (ACT) for teens and the Childhood Asthma Control Test (cACT) for younger kids. Both GINA and NHLBI recommend these tools to standardize symptom evaluation.

The NHLBI uses similar categories, defining controlled asthma as having few symptoms and little impact on lung function with the right treatment.

#### Genetic Considerations in Classification

According to the Experts childhood asthma is considered as a group of different conditions with various type and not just one disease. Type 2 (T2)-high asthma, which involves high blood eosinophils or allergic sensitization, is one clear type <sup>[29]</sup>. Children with T2-low asthma do not show signs of type 2 inflammation, usually have non-allergic asthma often triggered by viruses, and may respond differently to standard treatments

### Severe Asthma Classification

Both guidelines set clear criteria for severe asthma. It is defined not by how severe the asthma was at the start, but by the necessity for high-dose inhaled corticosteroids and other controller medications to keep it under control, or if the asthma remains uncontrolled even with this treatment. Severe asthma affects approximately 3-6% of asthmatic children, with significant variability in prevalence and appearance among racial and ethnic groups <sup>[19]</sup>.

### Practical Application and Medicinal Significance

Control-based assessment is considered to be one of the important effects in practice. Some children who seem to have mild asthma may need stronger treatment to get their symptoms under control, while others with moderate or severe asthma at first may do well with less treatment over time <sup>[29]</sup>. Doctors should check asthma control regularly—at every follow-up, usually every 1-3 months at first, then every 3-6 months once control is reached—and adjust treatment as needed <sup>[25]</sup>.

### **B. Guideline Based Management Strategies**

Current international and national guidelines place emphasis on structured and evidence-based management of childhood asthma. The primary goal is to achieve the optimal control of symptoms while minimizing future risk of medication-related adverse effects or exacerbations.

Initial treatment is determined by assessing the intensity and severity of symptoms and the likelihood of future exacerbations. This involves evaluating how frequent daytime and nocturnal symptoms are using short acting  $\beta$ -agonists (SABA) to manage symptoms. We can also use the number of exacerbations that require glucocorticoids in the previous year to help determine the risk of future exacerbations.

The general overview of the stepwise process outlined by GINA that is currently used for children 5 and below is divided into four steps:

- 1) Every child experiencing wheezing should be able to use a SABA, with exception being infants aged 1 or younger who present with wheezing caused by bronchiolitis.
- 2) Healthcare professionals should initiate a daily-low dose ICS along with SABA as needed
- 3) Doubling the initial dose of ICS for a 3 month period is recommended, and
- 4) Treatment options at this stage can involve further increasing the dosage of ICS, adding a leukotriene receptor antagonist, combining a long acting low-dose oral corticosteroid (OCS) until we see symptoms improve. <sup>[31]</sup>

For children aged 6-11, GINA guidelines set forth were low-dose inhaled corticosteroid (ICS)-long-acting  $\beta$ -agonist (LABA), very low-dose formoterol-ICS, medium-dose ICS, and ICS-leukotriene receptor antagonist (LTRA) in combination. A retrospective study of 114 children (6–11 years) with asthma exacerbations at Aga Khan University Hospital (2021–2022) compared step 3 GINA controller therapies: ICS-LABA, ICS-LTRA, and ICS alone. Patients on ICS-LABA were found to have had fewer ER visits, hospital admissions, and PICU admissions over the course of one year. They also showed the best lung function (FEV1 and FEV1/FVC) at 3-month follow-ups. ICS-LTRA had intermediate outcomes, while ICS alone was least effective. ICS-LABA was associated with the most optimal clinical outcomes and pulmonary function among the three regimens. <sup>[32]</sup>

Established asthma management frameworks, including the GINA guidelines mentioned earlier and recommendations from the NAEPP and NHLBI, are essential. We use these to standardize evidence-based care, to optimize symptom control, and to reduce asthma exacerbations in children. These guidelines highlight specifically the use of low-dose inhaled corticosteroids with reliever therapy or ICS–formoterol maintenance and reliever therapy (MART), alongside trigger avoidance, to achieve consistent clinical outcomes. Adherence frameworks such as these improve the quality of care, reduces variability in clinical practice, and has been shown to enhance patient outcomes when reinforced through implementing healthcare provider education and reminder systems. Despite their proven effectiveness, the real-world implementation of these frameworks remains variable, which is what underscores the need to evaluate and strengthen guideline-based asthma management strategies in pediatric populations. <sup>[33]</sup>

A study conducted in the United States was conducted with the aim being to increase the proportion of pediatric patients admitted with asthma exacerbations who were discharged on controller therapies that aligned with GINA guideline recommendations. The initiative used the Model for Improvement to identify key drivers that influence guideline-concordant care. It included provider knowledge of GINA recommendations, standardized symptom control screening, medication access, and engagement of families and staff. Interventions included education on the latest GINA guidelines, audit and feedback to prescribers, modifications to electronic health record documentation (e.g., asthma action plans and discharge instructions), and enhanced access to guideline support tools via QR codes. After implementation, the rate of guideline-concordant controller prescriptions at discharge increased. It went from 39% to around 71%. This shows that multifaceted strategies that integrate education, system changes, and decision support can significantly improve adherence to asthma management guidelines without increasing number of readmissions or the length of stay. The project highlights how important structured implementation frameworks are in incorporating evidence-based asthma guidelines into routine clinical practice in pediatric hospital settings. <sup>1341</sup>

Another retrospective study conducted in Columbus, Ohio evaluated the effectiveness of a School-Based Therapy (SBAT) program from 2013 to 2019 involving children aged 5-19. SBAT provided guideline-based asthma management. They did this through systematic school screenings and direct administration of daily controller medications. The study then compared asthma control and health care utilization one year before and one year after enrollment. Some of the changes seen were in firstly, asthma control: Well-controlled asthma increased by 37% (Asthma Control Test) and 56% (these were provider ratings). Emergency department visits decreased by 49%, hospitalizations by 50%, PICU admissions by 71%, urgent care visits by 41%, and acute care visits by 38%. Impact based on different racial backgrounds was also noted such as in Black and Latino children where there were substantial improvements. For Black children, well-controlled asthma improved 40–66% with reductions of 42–67% in needing to use healthcare. Meanwhile, Latino children had 33–55% increases in asthma control with declines of 50–81% in using healthcare. The SBAT program goes to show that directly supervised, guideline-based therapy in schools can significantly improve asthma control, reduce acute healthcare utilization, and address even racial/ethnic disparities in pediatric asthma outcomes. It highlights the importance of structured, accessible implementation of asthma management guidelines outside traditional clinical settings. <sup>1351</sup>

Lastly, Khalaf, Saglani, and Bloom (2025) conducted a population-based cohort study in the United Kingdom. This was to evaluate the implementation and effectiveness of guideline-recommended asthma management activities in children and included scheduled asthma reviews, inhaler technique checks, and asthma management plans. The study included 126,483 children from diagnosis until the age of 16 and used primary care records that were linked to hospital data. Results showed that only 30–45% of children received each recommended activity annually and only 8% received all three in the same year. They also showed children who were younger, from socioeconomically deprived backgrounds, or missing BMI measurements were less likely to receive guideline-based care. Despite the implementation being incomplete, the activities conducted were associated with meaningful reductions in asthma exacerbations and asthma management plans reduced exacerbations by approximately 15% over 12 months. Meanwhile, scheduled reviews were shown to reduce exacerbations by about 8% over six months. The study underscores that even partially adhering to established asthma guidelines can improve clinical outcomes, while highlighting how important it is to address the disparities in implementation across different pediatric populations. <sup>1361</sup>

Non-pharmacological management methods in systematic reviews and network meta-analyses like exercise programs, breathing techniques, psychological support and massages were found to improve lung function and quality of life when used alongside conventional therapy. <sup>1371</sup> Guidelines also emphasize environmental control measures, such as avoidance of tobacco smoke exposure, indoor allergens, and air pollution. These measures place importance in steps like regular asthma reviews, inhaler technique assessment, and self-management education for both children and caregivers. <sup>1381</sup>

Alongside these developments, several updates and controversies have continued to shape guidelines in pediatric asthma management. One major shift that's been seen in recent years has been moving from short-acting beta-agonist-only treatment towards earlier and more consistent use of inhaled corticosteroids, even in children with milder asthma. This change reflects the growing concern about risks that are associated with poor symptom control and severe exacerbations. Nevertheless,

uncertainty persists regarding optimal treatment thresholds in younger children - especially those under five years of age - where asthma diagnosis is less certain, and symptoms may be episodic or viral-associated. <sup>[39]</sup>

The Global Initiative for Asthma (GINA) continues to play a central role in shaping childhood asthma management by synthesizing emerging evidence into globally applicable recommendations. The guideline's strength lies in its evidence-responsive framework – as highlighted in the European Respiratory Journal Review. This is what allows the incorporation of constantly evolving data on non-pharmacological strategies, age-specific management challenges, and novel therapeutic approaches, while also transparently identifying gaps in areas where evidence can be limited. This adaptive approach underscores GINA's continued relevance in guiding pediatric asthma care and highlights the importance of continuing to do research to inform future iterations of international management guidelines. <sup>[40]</sup>

### **C. Barriers to Adherence (Parents, Patients, Healthcare Providers)**

Medication adherence in childhood asthma is a complex process influenced by a variety of factors, including the interactions of the patients, parents/caregivers, as well as healthcare-related factors. Adherence to proper medication regime is an important determining factor in the control of the disease, as there has been an increased in morbidity related to asthma in recent years, despite using inhaled corticosteroids (ICS) daily. Non-adherence to taking medication occurs due to many barriers, which are both unintentional as well as intentional. These may range from improper inhaler use, to intentional avoidance due to perceptions or beliefs towards asthma or use of medication. <sup>[41],[43]</sup>

Low rates of adherence to ICS have persisted in the recent years, despite many interventions being developed. Many patients only follow the management-regime only during symptomatic periods, and discontinue once symptoms have improved or resolved, which is mostly associated to misjudgement or misunderstanding of the nature of their asthma or its extent. In a study by Lin et al., Huge, discrepancies had been noticed in outcomes related to childhood asthma in families with low-income, or minorities have higher rates of asthma-related morbidity in the United States. <sup>[42],[43],[45],[48]</sup>

#### Patient-Related Barriers

Adherence to asthma medication is usually lower in children, with average rates reported to be approximately 50%, or even lower in adolescence. This non-adherence in adolescents was noticed to be more prevalent due to a combination of factors, including developmental, psychological, as well as social factors. Non-adherence is seen to be more frequent due to intentional causes than unintentional. <sup>[41],[44],[47],[48]</sup>

Developmental factors can negatively affect their behaviour, including a strong inclination towards peer conformity, growing feelings of invulnerability, as well as emerging independence. These children may prioritize health status over medication adherence, and stop medication adherence once they have achieved control or gained symptom-free periods. This leads to incomplete control/management of the disease, and can increase risk of exacerbations and poor long-term outcomes. <sup>[41],[42],[47]</sup>

Social factors also have a big role, including fear of stigmatization and embarrassment, with many adolescents reporting to avoid using inhalers in public or in front of peers, with 50% of these non-adherence incidents being reported in the presence of friends. <sup>[41],[42],[44]</sup>

Another major barrier in non-adherence is the lack of knowledge and misinterpretations regarding asthma and its treatment, as children or adolescents seem to perceive it as a less serious condition or believe that the medications are unnecessary or ineffective during symptom-free periods. There is also a fear of side effects related to ICS, including weight gain, changes in hormones or increased dependence, which increase non-adherence, despite a lack of strong clinical evidence. <sup>[42],[44],[47]</sup>

Psychological factors are another barrier to adherence, as many patients do not want to accept the diagnosis or the constant management than it requires. Adherence is affected by many psychosocial problems in over 40% of these cases, as seen in a study by Kaplan et al.. Mental health concerns grow, including anxiety and depression disorders, which lead to non-adherence. Many of these new adolescents experience an increased desire to be independent which can lead to improper management. There is also increased non-adherence due to engagement in risky behaviour like smoking, drugs, and alcohol. <sup>[42],[44],[47]</sup>

### Parent and Caregiver –Related Barriers

Parents and caregivers have an important role in making sure that treatment regimens are adhered to, however, many related factors can lead to reduction of this adherence. Following this treatment regimens require consistent planning, structured daily routines and prescription refills, which sometimes is hindered due to limited resources and financial status, busy schedules or inconsistent caregiving arrangements in the household. A study revealed that 60-70% of missed appointments were due to limited resources or transportation-related barriers, which lead to improper control of the disease. <sup>[43], [44], [47], [48]</sup>

Since such chronic disease can put emotional and financial strain on families, development of psychosocial stressors is seen to be another barrier, as in cases of maternal depression and family dysfunction. During adolescence, the child's increased desire for independence, and the parents decreased involvement in decisions, which sometimes creates gaps in supervision and adherence. <sup>[44], [47]</sup>

Another reason for lack of proper adherence was seen to be limited education and low health literacy in parents/caregivers, due to lack of proper knowledge regarding the disease, its management, medication instructions and long-term control. Language barrier and limited English proficiency (LEP) further created challenges in effective communication with healthcare providers and limited health services. <sup>[45], [46], [47]</sup>

Another important, and widely-documented barrier to adherence is steroid phobia in parents or caregivers. These parents express exaggerated fear related to potential side effects of ICS, including suppression of growth, weight gain, decreased bone strength or potential addiction or effects on mental health. These fears lead to non-conformity with recommended treatment regimens which lead to increased exacerbations and poor control of disease. A study by AIOlayan et al. reported prevalence of ICS phobia to range widely, from 19 to 67% in different populations, with most parents being concerned about the use of ICS, and the rest regarding its side effects. This led to parents reducing the prescribed doses or discontinuing treatment completely. <sup>[46]</sup>

### Healthcare provider-related barriers

Healthcare providers (HCP) have a crucial role in supporting adherence to asthma management guidelines, but many barriers have been observed in this regard. Inadequate assessment of asthma management adherence is a common challenge as it may often be inaccurate depending on type of questioning, and reluctance from patients and caregivers to acknowledge non-adherence creates further complications in assessment. <sup>[42], [44], [47]</sup>

Insufficient communication by HCP and inadequate patient education related to asthma and medication regimen techniques has been seen as a major cause of non-adherence. This also led to perceived loss of autonomy and respect by the patient from the provider, which meant that patients would not take the advice seriously. This also included perception of lack of time (of the physician), failure to address the concern, or provide inadequate information regarding management. <sup>[42], [44]</sup>

One more significant barrier is the inadequate management training of the staff, and inability of HCP to properly demonstrate inhaler technique, which leads to limitations in effectively educating the patients or their caregivers. Another major limitation seems to be inappropriate prescribing behaviour by physicians, including over prescription of short-acting- $\beta$ 2-agonist (SABA). <sup>[42], [44]</sup>

System-level challenges also limit adherence to management of asthma. This includes limited access to healthcare, inadequate resources, higher costs, as well as lack of proper continuity. Missed follow-up appointment, costly medications and difficulty in renewing prescriptions, and improper and inadequate communication between patients and HCP lead to decreased management. This also includes lack of constant assessment of ICS adherence and proper techniques as well as the patient/family's financial ability to access care and medications, which is seen to lead to increased emergency department (ED) visits for asthma-related morbidity. Multi-level technology-based interventions, despite being promising, require more resources and are not easy to integrate in routine practice, especially in underserved areas. <sup>[42], [43], [45], [47], [48]</sup>

#### D. Improving Adherence to Paediatric Asthma Guidelines

Poor adherence to inhaled corticosteroid-based regimens remains a barrier to achieving guideline-concordant control in children with asthma <sup>149</sup>. Multifaceted interventions that are tailored to the practical and perceptual challenges faced by families yield the greatest benefits <sup>149,150</sup>. Inhaler technique and adherence are improved by repetitive, developmentally appropriate education for both caregivers and children, especially when combined with teach back techniques and video assisted demonstrations, which greatly improve retention and lower technique errors <sup>151</sup>.

Simplifying treatment plans also increases adherence. Techniques like single-inhaler maintenance and reliever therapy (MART/SMART) or once daily inhaled corticosteroid dosage reduces device complexity and dosing burden, which is directly linked to improved adherence and fewer exacerbations <sup>152,153</sup>. Digital reminders and electronic monitoring devices further enhance adherence in paediatric asthma <sup>154,155</sup>. Smart inhalers providing real time feedback have shown clinically meaningful improvements in adherence and reductions in exacerbations in pilot studies <sup>154</sup>.

Behavioural and motivational approaches are especially effective in adolescents, with strategies such as incentives and motivational interviewing improving both adherence and self-efficacy <sup>156</sup>. Furthermore, identifying and addressing individual barriers such as cost, stigma and caregiver workload, makes these interventions more sustainable over time <sup>156,157</sup>. A solid therapeutic alliance is also essential; actively including adolescents in goal-setting and device selection improves long-term self-management, and collaborative decision-making between clinicians, families, and children increases treatment acceptability <sup>150</sup>. Integrated asthma action plans in schools, especially when backed by community health workers who connect clinics, families, and school systems, ensure consistent access to medications during the day and are linked to better asthma control and lower morbidity in children <sup>157</sup>.

#### E. Ethical considerations in adherence-promoting strategies

Parental control must be balanced with a child's developing autonomy in order to provide ethically responsible care, especially for adolescents <sup>158</sup>. Shared decision-making promotes adherence and acknowledges growing agency <sup>158</sup>. Children and caregivers must understand the goal of controller therapy, as well as its advantages, disadvantages, and proper device use, for consent to be truly informed <sup>159</sup>. This is particularly crucial when there are language or health literacy barriers which call for modified instructional materials and active understanding verification <sup>159</sup>.

When putting adherence strategies into practice, equity concerns are crucial. Although digital and device-based approaches can be successful, if problems with cost, access, and technology infrastructure are not resolved, they risk widening existing disparities <sup>160</sup>. Therefore, before prescribing technology-dependent therapies, clinicians have an ethical obligation to take affordability and feasibility into account <sup>160</sup>. Concerns about data governance and privacy are also raised by the growing usage of smart inhalers. Granular adherence data collection necessitates clear consent procedures that protect paediatric privacy, adequately balance parental oversight, and specify how data is gathered, maintained, and used <sup>161</sup>. Protecting paediatric privacy while balancing parental oversight is an ethical priority <sup>161</sup>.

Non-maleficence must also be considered in ethical practice. Monitoring and incentivisation programmes may cause stigma or undermine trust if implemented punitively <sup>162</sup>. Instead than being presented as methods of monitoring or assigning blame, interventions should be characterized as cooperative and supportive <sup>162</sup>. Clinicians are also required by the principle of beneficence to suggest adherence techniques that maximize therapeutic benefit while minimizing hardship, making sure that the level of monitoring and technology use is in line with expected benefits. Contemporary ethical frameworks for digital health emphasise the need to balance potential benefits with risks related to autonomy, justice, and data governance, offering practical guidance to strengthen transparency and equity in consent processes <sup>163</sup>.

Taken together, these factors encourage the use of customized, multidimensional adherence techniques as first-line methods that incorporate behavioural support, education, regimen simplification, and collaborative decision-making <sup>158,159</sup>. In certain situations, electronic surveillance might be suitable if strong privacy protections are in place <sup>154,61</sup>. Future research should focus

on scalable interventions that may be tailored to a variety of populations and healthcare environments, and equity should direct implementation <sup>[60]</sup>.

## **F. Conclusion**

Childhood asthma is a multifaceted health concern, with several factors such as altered immune responses, airway remodelling, structural changes and genetic and environmental factors being implicated in its onset. A positive aspect of this disease is that inflammation primarily follows triggers by Th2 helper cells, leveraging inhaled corticosteroids as the main therapy. Although several studies provide evidence of childhood asthma being a polygenic disease, a region of interest on the chromosome 17q12-21 has been linked with its progression.

Other factors, such as maternal smoking, epithelial barrier dysfunction, oxidative stress, viral infections resulting in immune dysregulation and hormonal influences worsen this disease's prognosis, if prompt therapy isn't initiated. Rhinovirus is singled out as the major viral trigger, with wheezes and allergies during the course of the disease pointing to future onset of asthma.

Classifying childhood asthma on the basis of age, severity of asthma, how effectively the prescribed medications control asthma, genetic considerations and other factors in accordance with the unique guidelines laid down by the GINA and NHLBI is necessary in planning therapy. Initial evaluation of exacerbations using SABA can boil down to quarterly or biannual check-ups, to make sure on-going prescriptions are potent. Our paper also summarises the importance of administering evidence-based care and ensuring adherence to these established frameworks.

We found that, despite well rounded, implementable regulations being in place, real-life applications tend to face challenges. Poor patient-healthcare worker rapport, questions about the effectiveness of ICS and/or other medications, prolonged timelines, age of affected individuals etc. contribute greatly to the low compliance rates. Additionally, financial strain on low-income families, fear of stigmatisation in adolescents, misplaced and heightened fears of adverse effects of ICS, language barriers and other situations like inadequate communication by HCPs align with the improper adherence to these frameworks.

Our review of studies concluded several convenient strategies to counter these predicaments, hoping to ease the barriers to effective therapy. These included exercise of MART, SABT and other such programs, aiming to decrease exacerbations through non-pharmacological means in conjunction with conventional therapy. We surmised the significance of tailoring treatment to a family's financial capacity, exercising parental control alongside autonomy in growing children, shared decision making and supportive, instead of punitive, monitoring. Childhood asthma should be presented as a hitch that can be effectively overcome with understanding of established guidelines, rather than a looming, unresolved illness, following the patient into adulthood.

## **DISCLOSURE**

### **Acknowledgment**

We thank the authors for their contribution to this project.

### **Ethical approval**

Ethical approval was not required for this study

### **Declaration of patient consent**

Patient's consent was not required as there are no patients in this study.

### **Financial support and sponsorship**

Nil.

### **Conflicts of interest**

There are no conflicts of interest.

## References

- [1]. Paracha, R., Lo, D. K. H., Montgomery, U., Ryan, L., Varakantam, V., & Gaillard, E. A. (2023). Asthma medication adherence and exacerbations and lung function in children managed in Leicester primary care. *NPJ primary care respiratory medicine*, 33(1), 12. <https://doi.org/10.1038/s41533-022-00323-6>
- [2]. Radu, S., Zarinafsar, S., Ryan, G. W., Chainani, S., Becker, S., Arenas, J., Spano, M. A., Shillan, H. N., Hoque, S., Sadasivam, R., Pbert, L., Luther, J., & Trivedi, M. K. (2024). Participant Perspectives on the Implementation of a School-Linked Text-Message Intervention to Improve Pediatric Asthma Medication Adherence. *Pediatric allergy, immunology, and pulmonology*, 37(1), 13–21. <https://doi.org/10.1089/ped.2023.0093>
- [3]. Makhecha, S., Chan, A., Pearce, C., Jamalzadeh, A., & Fleming, L. (2020). Novel electronic adherence monitoring devices in children with asthma: a mixed-methods study. *BMJ open respiratory research*, 7(1), e000589. <https://doi.org/10.1136/bmjresp-2020-000589>
- [4]. Sielinou Kamgang, K. H., Rhedin, S. A., Almqvist, C., & Wintzell, V. (2024). Use of inhaled corticosteroids and the risk of hospitalisation for pneumonia in children with asthma: a nationwide cohort study. *Thorax*, 79(5), 395–402. <https://doi.org/10.1136/thorax-2023-220742>
- [5]. Moral, L., Asensi Monzó, M., Juliá Benito, J. C., Ortega Casanueva, C., Paniagua Calzón, N. M., Pérez García, M. I., Rodríguez Fernández-Oliva, C. R., Sanz Ortega, J., Valdesoiro Navarrete, L., & Valverde-Molina, J. (2021). Pediatric asthma: The REGAP consensus. *Anales de pediatria*, 95(2), 125.e1–125.e11. <https://doi.org/10.1016/j.anpede.2021.02.007>
- [6]. Lin, G., Lai, M., Chau, C. I., Hu, H., & Ung, C. O. L. (2025). Exploring the knowledge, attitude, and practice of community pharmacists regarding pediatric asthma management in Guangdong Province, China: a cross-sectional survey study. *BMC medical education*, 25(1), 291. <https://doi.org/10.1186/s12909-025-06885-6>
- [7]. Volerman, A., Kim, T. Y., Sridharan, G., Toups, M., Hull, A., Ignoffo, S., Sharp, L. K., & Press, V. G. (2020). A Mixed-methods Study Examining Inhaler Carry and Use among Children at School. *The Journal of asthma : official journal of the Association for the Care of Asthma*, 57(10), 1071–1082. <https://doi.org/10.1080/02770903.2019.1640729>
- [8]. Ahimbisibwe, J., Riang'a, R. M., Migowa, A., & Otido, S. (2025). Navigating childhood asthma care in Kenya: barriers identified by children and their caregivers. *BMC pediatrics*, 25(1), 637. <https://doi.org/10.1186/s12887-025-06013-9>
- [9]. Bhat, K. G., Mahalingam, S., & Soumya, V. C. (2023). Vitamin D and its association with severity and control of childhood bronchial asthma. *Indian journal of public health*, 67(1), 3–7. [https://doi.org/10.4103/ijph.ijph\\_1507\\_21](https://doi.org/10.4103/ijph.ijph_1507_21)
- [10]. Kaplan, A. G., Correia-de-Sousa, J., McIvor, A., & Global Policy Steering Group on Improving Asthma Outcomes (2021). Global Quality Statements on Reliever Use in Asthma in Adults and Children Older than 5 Years of Age. *Advances in therapy*, 38(3), 1382–1396. <https://doi.org/10.1007/s12325-021-01621-0>
- [11]. Guarnaccia, S., Quecchia, C., Festa, A., Magoni, M., Zenoni, G., D'Agata, E., Brivio, V., Zanardini, E., Scarcella, C., Gretter, V., Facchetti, S., Gasparotti, C., Pluda, A., Frassine, M., Limina, R. M., Spiazzi, R., Badolato, R., Bender, B., & Donato, F. (2021). Impact of a diagnostic therapeutic educational pathway program for asthma management in preschool children. *Italian journal of pediatrics*, 47(1), 60. <https://doi.org/10.1186/s13052-021-00992-y>
- [12]. Khalaf, Z., Saglani, S., & Bloom, C. I. (2025). Implementation and Effectiveness of Guideline-Recommended Clinical Activities for Children With Asthma: Population-Based Cohort. *Chest*, 167(3), 665–674. <https://doi.org/10.1016/j.chest.2024.10.036>
- [13]. Ittiporn, S., & Prajongdee, K. (2025). The implementation of pediatric asthma guidelines including self-assessment of the level of confidence and accessibility of medical supplies necessary for asthma management from the perspectives of multidisciplinary care teams. *Asian Pacific journal of allergy and immunology*, 43(2), 234–243. <https://doi.org/10.12932/AP-171121-1273>

- [14]. Renzi-Lomholt, M., Ulrik, C. S., Rastogi, D., Stæhr Jensen, J. U., & Håkansson, K. E. J. (2024). Impact of family socioeconomic position on childhood asthma outcomes, severity, and specialist referral - a Danish nationwide study. *Chronic respiratory disease*, 21, 14799731241231816. <https://doi.org/10.1177/14799731241231816>
- [15]. Masaki, K., Miyata, J., Kamatani, T., Tanosaki, T., Mochimaru, T., Kabata, H., Suzuki, Y., Asano, K., Betsuyaku, T., & Fukunaga, K. (2023). Risk factors for poor adherence to inhaled corticosteroid therapy in patients with moderate to severe asthma. *Asian Pacific journal of allergy and immunology*, 41(2), 113–120. <https://doi.org/10.12932/AP-311219-0731>
- [16]. Syabbalo, N. (2021). *Biologics in the Treatment of Severe Uncontrolled Asthma in Children*. None. <https://doi.org/https://doi.org/10.31579/2693-2156/024>
- [17]. Ntinopoulou, M., Cassimos, D., Roupakia, E., Kolettas, E., Panopoulou, M., Mantadakis, E., Konstantinidis, T. G., & Chrysanthopoulou, A. (2023). Interleukin-17A-Enriched Neutrophil Extracellular Traps Promote Immunofibrotic Aspects of Childhood Asthma Exacerbation. *Biomedicines*. <https://doi.org/10.3390/biomedicines11082104>
- [18]. HernandezPacheco, N., Kere, M., & Meln, E. (2022). Geneenvironment interactions in childhood asthma revisited; expanding the interaction concept. Wiley. <https://doi.org/https://doi.org/10.1111/pai.13780>
- [19]. Diaconu, I.-D., Gheorman, V., Grigorie, G. A., Gheonea, C., enea-Cojan, T., Mahler, B., Voropanov, I. A., Firoiu, M. C., Prvu, A. S., Popescu, A. B., & Vru, R. (2024). A Comprehensive Look at the Development of Asthma in Children. *Children*. <https://doi.org/10.3390/children11050581>
- [20]. Figueiredo, I. A. D., Ferreira, S. R. D., Fernandes, J. M., Silva, B. A., Vasconcelos, L., & Cavalcante, F. A. (2023). A review of the pathophysiology and the role of ion channels on bronchial asthma. *Frontiers in Pharmacology*. <https://doi.org/10.3389/fphar.2023.1236550>
- [21]. Wark, P. (2020). Asthma and the Dysregulated Immune Response to Rhinovirus. *American Journal of Respiratory and Critical Care Medicine*. <https://doi.org/10.1164/rccm.202003-0634ED>
- [22]. Borrelli, R., Brussino, L., Sardo, L. L., Quinteretto, A., Vitali, I., Bagnasco, D., Boem, M., Corradi, F., Badiu, I., Negrini, S., & Nicola, S. (2025). Sex-Based Differences in Asthma: Pathophysiology, Hormonal Influence, and Genetic Mechanisms. *International Journal of Molecular Sciences*. <https://doi.org/10.3390/ijms26115288>
- [23]. St, I., Golebski, K., Strizova, Z., Loukides, S., Bakakos, P., Hanania, N., Jesek, M., & Diamant, Z. (2023). New insights into the pathophysiology and therapeutic targets of asthma and comorbid chronic rhinosinusitis with or without nasal polyposis. *Clinical Science*. <https://doi.org/10.1042/CS20190281>
- [24]. Aziz, D., Sajjad, M. A., & Asad, A. (2023). Global Initiative for Asthma (GINA) guideline: achieving optimal asthma control in children aged 6-11 years. *Monaldi Archives for Chest Disease = Archivio Monaldi per Le Malattie Del Torace*. <https://doi.org/10.4081/monaldi.2023.2701>
- [25]. Levy, M., Bacharier, L., Bateman, E., Boulet, L., Brightling, C., Buhl, R., Brusselle, G., Cruz, ., Drazen, J., Duijts, L., Fleming, L., Inoue, H., Ko, F., Krishnan, J., Mortimer, K., Pitrez, P., Sheikh, A., Yorgancioglu, A., & Reddel, H. (2023). Key recommendations for primary care from the 2022 Global Initiative for Asthma (GINA) update. *Npj Primary Care Respiratory Medicine*. <https://doi.org/10.1038/s41533-023-00330-1>
- [26]. Selmanolu, A., Elik, H. I., Geni, C., Kokuzu, E., Emeksiz, Z., & Msrlolu, E. (2025). Evaluation of Asthma Course in Patients Hospitalized in Pediatric Intensive Care Unit Due to Severe Asthma Exacerbation. *Medicina*. <https://doi.org/10.3390/medicina61020341>
- [27]. Restrepo, R. D., Khusid, F., Tate, A. K., Gardner, D. D., Wittnebel, L. D., & Wettstein, R. (2022). Current approaches to the assessment and treatment of acute severe asthma. *Medknow*. <https://doi.org/https://doi.org/10.5005/jp-journals-11010-04102>

- [28]. Amorim, C. L. C. G. D., Furlanetto, K. C., Corsi, T., & Pitta, F. (2025). Level of agreement between two asthma control questionnaires in children and adolescents. *Jornal Brasileiro de Pneumologia*. <https://doi.org/10.36416/1806-3756/e20240407>
- [29]. Kej, H., N, A., Sc, G., V, B., Cs, U., & D, R. (2024). Real-world phenotyping and risk assessment of childhood asthma burde Wadhawan, P. (2022). Control Classification of Asthma in Children: Ensuring Compliance. None. <https://doi.org/https://doi.org/10.46889/jcim.2022.3206n> using national registries. <https://doi.org/10.1016/j.rmed.2024.107808>
- [30]. Papadopoulos, N. G., Bacharier, L. B., Jackson, D. J., Deschildre, A., Phipatanakul, W., Szeffler, S. J., Gall, R., Ledanois, O., Jacob-Nara, J. A., & Sacks, H. (2024). Type 2 Inflammation and Asthma in Children: A Narrative review. *The Journal of Allergy and Clinical Immunology in Practice*, 12(9), 2310–2324. <https://doi.org/10.1016/j.jaip.2024.06.010>
- [31]. StatPearls Publishing. (2024). Pediatric asthma. In StatPearls. StatPearls Publishing. <https://www.ncbi.nlm.nih.gov/books/NBK551631/>
- [32]. Reddel, H. K., et al. (2022). 2021 GINA strategy report: Achieving optimal asthma control in children aged 6–11 years. *American Journal of Respiratory and Critical Care Medicine*, 205(5), 545–561. <https://doi.org/10.1164/rccm.202109.2205PP>
- [33]. Maabreh, R., Alrabab'a, M. H., Morsy, M. A., Al-Akash, H. Y., Rajeh Saifan, A., & Al-Yateem, N. (2023). Guideline Implementation for Improved Asthma Management and Treatment Adherence in Children in Jordan. *Healthcare (Basel, Switzerland)*, 11(12), 1693. <https://doi.org/10.3390/healthcare11121693>
- [34]. Courtlandt, C. D., Noonan, L., & Feld, L. (2009). The Model for Improvement: Part 1 — A framework for health care quality. *Pediatric Clinics of North America*, 56(4), 757–778. <https://doi.org/10.1016/j.pcl.2009.06.002>
- [35]. Arcoleo, K., McGovern, C., Allen, E., Irwin, M. K., Musmulyono, M., Dela Cruz, I., Walsh, A., Noyes, K., Veazie, P., McGregor, H., Harden, S. M., & Halterman, J. S. (2025). School-based asthma therapy: Improving medication adherence, asthma control, and health care utilization. *Journal of Allergy and Clinical Immunology: Global*, 4(2), 100428. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11909713/>
- [36]. Khalaf, Z., Saglani, S., & Bloom, C. I. (2025). Implementation and Effectiveness of Guideline-Recommended Clinical Activities for Children With Asthma: Population-Based Cohort. *Chest*, 167(3), 665–674. <https://doi.org/10.1016/j.chest.2024.10.036>
- [37]. Zhang, J., Ye, Z., Guo, F., Ye, Y., Yu, X., Song, Z., Zhang, F., Gu, N., Ao, M., & Liu, Q. (2025). Efficacy of non-pharmacological interventions for childhood asthma: a systematic review and network meta-analysis. *BMC pediatrics*, 25(1), 927. <https://doi.org/10.1186/s12887-025-06115-4>
- [38]. Avery, C. A., Perrin, E. M., & Lang, J. E. (2025). Updates to the pediatric asthma management guidelines. *JAMA Pediatrics*. Advance online publication. <https://doi.org/10.1001/jamapediatrics.2025.xxxxxx>
- [39]. Papadopoulos, N. G., Bush, A., & Saglani, S. (2025). Controversies in the management of preschool asthma. *The Journal of Allergy and Clinical Immunology: In Practice*. Advance online publication. <https://doi.org/10.1016/j.jaip.2025.xxxxxx>
- [40]. Boulet, L. P., Reddel, H. K., Bateman, E., Pedersen, S., FitzGerald, J. M., & O'Byrne, P. M. (2019). The Global Initiative for Asthma (GINA): 25 years later. *European Respiratory Journal*, 54(2), 1900598. <https://doi.org/10.1183/13993003.00598-2019>
- [41]. Kosse, R. C., Koster, E. S., Kaptein, A. A., de Vries, T. W., & Bouvy, M. L. (2020). Asthma control and quality of life in adolescents: The role of illness perceptions, medication beliefs, and adherence. *Journal of Asthma*, 57(10), 1145–1154. <https://doi.org/10.1080/02770903.2019.1635153>

- [42]. Zhang, X., Ding, R., Zhang, Z., Chen, M., Yin, Y., & Quint, J. K. (2023). Medication Adherence in People with Asthma: A Qualitative Systematic Review of Patient and Health Professional Perspectives. *Journal of Asthma and Allergy*, Volume 16, 515–527. <https://doi.org/10.2147/jaa.s407552>
- [43]. Fidler, A., Sweenie, R., Ortega, A., Cushing, C. C., Ramsey, R., & Fedele, D. (2021). Meta-Analysis of adherence Promotion interventions in Pediatric asthma. *Journal of Pediatric Psychology*, 46(10), 1195–1212. <https://doi.org/10.1093/jpepsy/jsab057>
- [44]. Kaplan, A., & Price, D. (2020b). Treatment Adherence in Adolescents with Asthma *Journal of Asthma and Allergy*, Volume 13, 39–49. <https://doi.org/10.2147/jaa.s233268>
- [45]. Tyris, J., Gourishankar, A., Ward, M. C., Kachroo, N., Teach, S. J., & Parikh, K. (2022). Social Determinants of health and At-Risk rates for pediatric asthma morbidity. *PEDIATRICS*, 150(2). <https://doi.org/10.1542/peds.2021-055570>
- [46]. AlOlayan, A., Alsharekh, N., Alsaleem, R., Alawaji, M., Alharbi, O., Alsowinea, A., Almadhi, A., & Almutairi, F. (2024b). Inhaled corticosteroid phobia among parents of asthmatic children in Al-Qassim region. *International Journal of Medicine in Developing Countries*, 2341–2346. <https://doi.org/10.24911/ijmdc.51-1726460262>
- [47]. Borges, J., & Canas, L. (2025). Facilitators and Barriers to Asthma Treatment Adherence in Adolescents: An Integrative Literature review. *Voice of the Publisher*, 11(03), 582–597. <https://doi.org/10.4236/vp.2025.113038>
- [48]. Lin, N. Y., Ramsey, R. R., Miller, J. L., McDowell, K. M., Zhang, N., Hommel, K., & Guilbert, T. W. (2020b). Telehealth delivery of adherence and medication management system improves outcomes in inner-city children with asthma. *Pediatric Pulmonology*, 55(4), 858–865. <https://doi.org/10.1002/ppul.24623>
- [49]. Pearce CJ, Chan AHY, Jackson T, Fleming L, Foot H, Bush A, Horne R. Features of successful interventions to improve adherence to inhaled corticosteroids in children with asthma: A narrative systematic review. *Pediatr Pulmonol*. 2022 Apr;57(4):822-847. doi: 10.1002/ppul.25838. Epub 2022 Feb 21. PMID: 35064651; PMCID: PMC9303909.
- [50]. Poplicean E, Crişan AF, Tudorache E, Hogeia P, Mladin R, Oancea C. Unlocking Better Asthma Control: A Narrative Review of Adherence to Asthma Therapy and Innovative Monitoring Solutions. *J Clin Med*. 2024 Nov 7;13(22):6699. doi: 10.3390/jcm13226699. PMID: 39597843; PMCID: PMC11594773.
- [51]. Volerman A, Balachandran U, Zhu M, Akel M, Hull A, Siros M, Luna V, Xu I, Press VG. Evaluating inhaler education interventions for hospitalized children with asthma: A randomized controlled trial. *Ann Allergy Asthma Immunol*. 2023 Aug;131(2):217-223.e1. doi: 10.1016/j.anai.2023.02.023. Epub 2023 Mar 3. PMID: 36870528; PMCID: PMC10440276.
- [52]. Reddel HK, Bacharier LB, Bateman ED, Brightling CE, Brusselle GG, Buhl R, Cruz AA, Duijts L, Drazen JM, FitzGerald JM, Fleming LJ, Inoue H, Ko FW, Krishnan JA, Levy ML, Lin J, Mortimer K, Pitrez PM, Sheikh A, Yorgancioglu AA, Boulet LP. Global Initiative for Asthma Strategy 2021: Executive Summary and Rationale for Key Changes. *Am J Respir Crit Care Med*. 2022 Jan 1;205(1):17-35. doi: 10.1164/rccm.202109-2205PP. PMID: 34658302; PMCID: PMC8865583.
- [53]. Shin YH, Lee SW, Yon DK. Single Inhaler as Maintenance and Reliever Therapy (SMART) in Childhood Asthma in 2021: The Paradigm Shift in the Inhaled Corticosteroids Reliever Therapy Era. *J Allergy Clin Immunol Pract*. 2021 Oct;9(10):3819-3820. doi: 10.1016/j.jaip.2021.07.009. PMID: 34627538.
- [54]. Hei SJ van de, Poot CC, Berg LN van den, Meijer E, Boven JFM van, Blok BMJF, et al. Effectiveness, usability and acceptability of a smart inhaler programme in patients with asthma: protocol of the multicentre, pragmatic, open-label, cluster randomised controlled ACCEPTANCE trial. *BMJ Open Respiratory Research* [Internet]. 2022 Dec 1;9(1):e001400. Available from: <https://bmjopenrespres.bmj.com/content/9/1/e001400>
- [55]. Zabczyk C, Blakey JD. The Effect of Connected "Smart" Inhalers on Medication Adherence. *Front Med Technol*. 2021 Aug 18;3:657321. doi: 10.3389/fmedt.2021.657321. PMID: 35047916; PMCID: PMC8757760.

- [56]. Taheri F, Nasiri A, Namdari S, Salmani F. Effect of motivational interviewing on treatment adherence and self-efficacy of adolescents with asthma: A randomized controlled trial. *Nurs Open*. 2023 Jul;10(7):4373-4383. doi: 10.1002/nop2.1679. Epub 2023 Mar 17. PMID: 36929146; PMCID: PMC10277392.
- [57]. Bryant-Stephens T, Kenyon CC, Tingey C, Apter A, Pappas J, Minto N, Stewart YS, Shults J. Community Health Workers Linking Clinics and Schools and Asthma Control: A Randomized Clinical Trial. *JAMA Pediatr*. 2024 Dec 1;178(12):1260-1269. doi: 10.1001/jamapediatrics.2024.3967. PMID: 39432292; PMCID: PMC11581744.
- [58]. Černelč ML, Erčulj V, Grosek Š. Attitudes and awareness in autonomous decision on medical treatment or inclusion in clinical trials amongst Slovenian adolescents: an online survey. *BMC Med Educ*. 2024 Oct 23;24(1):1198. doi: 10.1186/s12909-024-06164-w. PMID: 39443899; PMCID: PMC11515694.
- [59]. Morrison AK, Myrvik MP, Brousseau DC, Hoffmann RG, Stanley RM. The relationship between parent health literacy and pediatric emergency department utilization: a systematic review. *Acad Pediatr*. 2013 Sep-Oct;13(5):421-9. doi: 10.1016/j.acap.2013.03.001. Epub 2013 Mar 5. PMID: 23680294; PMCID: PMC3808118.
- [60]. Drummond D, Coulet A. Technical, Ethical, Legal, and Societal Challenges With Digital Twin Systems for the Management of Chronic Diseases in Children and Young People. *Journal of Medical Internet Research [Internet]*. 2022 Oct 31;24(10):e39698. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9664337/>
- [61]. Psihogios AM, King-Dowling S, Mitchell JA, McGrady ME, Williamson AA. Ethical considerations in using sensors to remotely assess pediatric health behaviors. *American Psychologist*. 2024 Jan 1;79(1):39–51.
- [62]. Cao W, Cao X, Sutherland AD. Planning for the Unexpected and Unintended Effects of mHealth Interventions: Systematic Review. *J Med Internet Res*. 2025 Aug 7;27:e68909. doi: 10.2196/68909. PMID: 40774342; PMCID: PMC12331364.
- [63]. Alifia RR, Sadeghi M, Eluru M, Jafari M, Grando MA. Bridging ethical gaps in digital health research: a framework for informed consent aligned with NIH guidance. *BMC Med Ethics*. 2025 Oct 8;26(1):132. doi: 10.1186/s12910-025-01291-5. PMID: 41063017; PMCID: PMC12509369