# CLINICAL PRACTICE GUIDELINES MANAGEMENT OF CHILDHOOD ASTHMA

2024 Consensus Statement Fourth Edition





Malaysian Thoracic Society

Lung Foundation of Malaysia

# Table of Contents

Foreword									
Members of the Expert Panel									
1	The need for an asthma consensus								
2	Definition								
3	Diag	nosis		10					
	3.1	Present	tation	10					
	3.2	Investig	gations	12					
4	Goal	s of ther	ару	15					
5	Mana	ngement	of asthma	16					
	5.1	Educat	ion for parents and children	16					
	5.2	Preven	tion	18					
		5.2.1	Avoidance of smoke and air pollutants	18					
		5.2.2	Environmental allergen exposure reduction	18					
		5.2.3	Food allergy	19					
		5.2.4	Respiratory tract infections	19					
		5.2.5	Exercise	20					
		5.2.6	Obesity	20					
		5.2.7	Breastfeeding	20					
	5.3	Drug tł	nerapy	21					
		5.3.1	Reliever therapy	21					
		5.3.2	Controller therapy	21					
		5.3.3	Side effects of asthma medications	23					
6	Long	-term as	thma control and follow up	24					
	6.1	Assess	ment of asthma control	24					
	6.2 Achieving and maintaining asthma control								

# Table of Contents

7	Special categories of asthma						
	7.1	Difficult-to-treat asthma	30				
	7.2	Severe asthma	31				
	7.3	Exercise-induced bronchoconstriction (EIB)	33				
8	Inhale	er devices	35				
9	Asthma in preschool children (5 years and younger)						
	9.1	Wheeze classification	36				
	9.2	Diagnosis of asthma	37				
	9.3	Investigations and differential diagnoses of asthma	38				
	9.4	Management of asthma in children aged 5 years and younger	40				
	9.5	Treatment for asthma in children aged 5 years and younger	41				
10	Mana	gement of acute asthma exacerbations in clinical setting	44				
	10.1	Definition of asthma exacerbation / asthma attack	44				
	10.2	Goals of treatment of acute asthma exacerbations	44				
	10.3	General principles in the treatment of acute asthma	44				
	10.4	First-line treatment or standard therapy	45				
		10.4.1 Short-acting B <sub>2</sub> -agonists (SABA)	45				
		10.4.2 Inhaled short-acting muscarinic antagonists (SAMA)	45				
		10.4.3 Controlled/titrated oxygen therapy	46				
		10.4.4 Corticosteroids (systemic, parenteral, oral, or nebulised)	46				
	10.5	Second-line / adjunct therapies	47				
		10.5.1 Intravenous magnesium sulphate (IV MgSO_4)	47				
		10.5.2 Systemic β <sub>2</sub> -agonists (parenteral or subcutaneous)	47				
		10.5.3 Ventilatory support	47				
	10.6	Paediatric asthma score and asthma clinical pathway	49				

# Table of Contents

	10.7	Therapies not recommended for acute exacerbation	51				
	10.8	Role of chest X-ray in acute exacerbation	51				
	10.9	Blood gases	51				
	10.10	Management of acute asthma exacerbations	52				
	10.11	Respiratory support and transfer of severe/life-threatening exacerbation of bronchial asthma	52				
	10.12	Discharge planning and follow-up	56				
11	Asthma	a action plan (AAP)	57				
	11.1	What should the AAP entail?	57				
	11.2	What to do with the AAP?	59				
Refe	References						
Acknowledgement							

# Foreword

The first edition of the local guidelines for the management of childhood asthma was published in 1997, followed by revisions in 2004 and 2014. The main objective of the earlier guidelines was to offer a clear framework for use by healthcare providers at all levels. This third revision builds upon the 2014 standards, reflecting the latest advancements in asthma management. Notable improvements include the introduction of biologic therapies, a deeper understanding of the role of nebulised corticosteroids in acute asthma, adoption of the paediatric asthma score and asthma clinical pathway in asthma management.

In preparing these guidelines, we reviewed the latest research, analysed emerging data, and consulted with experienced practitioners to ensure our recommendations are aligned with current evidence-based practices. This document is designed to assist healthcare professionals in providing optimal care for children with asthma, from basic diagnosis and management to advanced treatment for severe cases.

By updating the guidelines, we aim to enhance asthma control, reduce morbidity, and improve the overall quality of life for children affected by asthma. We hope this update serves as a crucial resource for clinicians, enabling them to offer effective and tailored care for young asthma patients.

A downloadable PDF version is available, and we encourage users to consult these guidelines alongside reputable international publications for a comprehensive understanding.

We also extend our sincere thanks to the committee members for their invaluable contributions. Their expertise and dedication have been essential in crafting a guideline that is both practical and reflective of the most recent scientific insights.

Dr. Norzila Mohamed Zainudin Prof. Emeritus Dato' Dr. Azizi Haji Omar

# Members of The Expert Panel

#### **Co-chairpersons**

Dr. Norzila Mohamed Zainudin Sunway Medical Centre, Selangor

**Prof. Emeritus Dato' Dr. Azizi Haji Omar** Damansara Specialist Hospital, Selangor

Committee members Assoc. Prof. Dato' Dr. Ahmad Fadzil Abdullah International Islamic University Malaysia, Pahang

Dr. Anis Siham Zainal Abidin Sunway Medical Centre, Selangor

Prof. Dr. Anna Marie Nathan Universiti Malaya Medical Centre

Dr. Asiah Kassim Hospital Tunku Azizah, Kuala Lumpur

Dr. Dayang Zuraini Sahadan Hospital Sultan Idris Shah Serdang, Selangor

Assoc. Prof. Dr. Eg Kah Peng Universiti Malaya Medical Centre

Dr. Hafizah Zainuddin Universiti Sultan Zainal Abidin, Terengganu

Assoc. Prof. Dr. Hasniah Abdul Latif Hospital Pakar Kanak-Kanak, Universiti Kebangsaan Malaysia, Kuala Lumpur

Assoc. Prof. Dr. Jessie de Bruyne Universiti Malaya Medical Centre

Dr. Mariana Daud Hospital Raja Perempuan Zainab II, Kelantan

Dr. N. Fafwati Faridatul Akmar Mohammad Hospital Tunku Azizah, Kuala Lumpur

Dr. Noor Ain binti Noor Affendi Hospital Sultanah Nur Zahirah, Terengganu Dr. Noor Hafiza Binti Noordin Hospital Cyberjaya, Selangor

Dr. Patrick Chan Wai Kiong Gleneagles Hospital Kuala Lumpur

Dato' Dr. Rus Anida Awang Hospital Pulau Pinang

Dr. Su Siew Choo Pantai Hospital Kuala Lumpur

Dr. Yap Hsiao Ling Hospital Tunku Azizah, Kuala Lumpur

# 1 The Need for An Asthma Consensus

The National Health Mortality and Morbidity Survey 2023 reported that almost half a million children aged 6 to 17 years old in Malaysia have asthma. Prevalence of probable asthma was 7.1% and prevalence of doctor-diagnosed asthma was 5.3%. It was found that 70% of them have 1-3 exacerbations in the past year and 30% have 4 or more attacks in the past year.<sup>1</sup> There is evidence to show that the prevalence of childhood asthma is higher among the urban and inner-city communities, from 6.4% in Muar to 24% in Selangor.<sup>2-5</sup> Asthma still gives rise to considerable morbidity as well as mortality.<sup>6</sup>

Alongside asthma, there has also been a rise in other atopic conditions such as allergic rhinitis and eczema.<sup>2,7,8</sup> Recognising and treating allergic rhinitis has been shown to improve asthma control.<sup>7</sup>

Diagnosing asthma in children under the age of six is challenging.<sup>9</sup> It is not feasible to perform objective measurements in younger children to aid in the clinical decision. In addition, the pathology of asthma in younger children may vary from that of older children, suggesting that the treatment approach needed may differ as well.<sup>10,11</sup> Emerging evidence has affirmed the difference between childhood and adult asthma, notably in the phenotype, remission, and factors associated with severity and mortality.<sup>12</sup>

Despite available guidelines, the management of asthma remains sub-optimal. Many patients are under-treated and take only rescue therapy during attacks rather than daily controller therapy, including patients with severe asthma.<sup>1,13,14</sup> There remains an over-reliance on symptomatic treatment and oral therapy, and under-utilisation of anti-inflammatory therapy, leading to inadequate control.<sup>13,15</sup>

New groups of medications namely biologics, such as interleukin antagonists and anti-immunoglobulin E (IgE), have been introduced to treat certain types of asthma. Moreover, with new evidence on the efficacy of nebulised steroid<sup>16</sup> and the proposition to use intermittent inhaled corticosteroid (ICS) in asthmatic children (especially mild asthma)<sup>17</sup>, there are merits to review and update the 2014 consensus.

Therefore, this document is an update on the Malaysian Guidelines for the Management of Childhood Asthma 2014<sup>18</sup>, developed as a quick guide for local practitioners' reference.

## 1 | The Need for An Asthma Consensus

New additions to this consensus include:

- Recognition of likelihood of asthma and recurrent wheeze.
- Management of asthma for patients five years old and below, and adolescents.
- Maintenance and reliever therapy (MART) and anti-inflammatory reliever (AIR) therapy.
- Evidence of nebulised corticosteroids in acute asthma.
- Role of biologics in severe asthma.
- Adoption of paediatric asthma score and asthma clinical pathway in the management of acute asthma.
- Respiratory support and transfer of severe/life-threatening asthma patients.

# 2 Definition

Asthma is a heterogeneous condition characterised by paroxysmal or persistent symptoms such as cough, dyspnoea, wheezing and chest tightness, coupled with chronic persistent inflammation and/or structural changes associated with variable airflow limitation and airway hyperresponsiveness.<sup>19,20</sup>

# 3 Diagnosis

#### 3.1 Presentation

Children with asthma present with recurrent episodes of one or more of the following symptoms, triggered by factors such as viral infections, allergen exposure or exercise:<sup>11</sup>

- Cough, especially nocturnal and early morning
- Shortness of breath
- Wheezing
- Chest tightness

These respiratory symptoms vary over time and in intensity, together with variable expiratory airflow limitation.

The presence of atopic conditions like eczema, allergic rhinitis, and conjunctivitis in either the child or their family provides supportive evidence for diagnosing asthma.<sup>11,21</sup> However, the absence of these conditions does not rule out the possibility of an asthma diagnosis.

Children who present with chronic cough alone (daily cough for more than four weeks) and have never wheezed are less likely to have asthma.<sup>22,23</sup> These children require further evaluation for other illnesses that may cause the chronic cough.

In children with chronic respiratory symptoms, especially those exhibiting signs such as chronic wet cough, clubbing, cyanosis, failure to thrive, or persistent wheezing not responding to conventional treatment, other differential diagnosis needs to be considered (Table 1).

## 3 | Diagnosis

 Table 1. Differential diagnosis and relevant investigations for chronic cough and/or recurrent wheeze in infants and children.

.....

	Diagnostic possibilities	Investigations
Upper airway disease	<ul><li>Allergic rhinitis/rhinosinusitis</li><li>Sinusitis</li><li>Vocal cord dysfunction</li></ul>	<ul><li>Paranasal sinuses X-ray</li><li>Flow-volume loop (spirometry)</li><li>Laryngoscopy</li></ul>
Obstruction of large airways	<ul> <li>Foreign body inhalation</li> <li>Vascular ring</li> <li>Laryngeal web</li> <li>Laryngotracheomalacia, tracheal stenosis</li> <li>Enlarged lymph nodes</li> </ul>	<ul><li>Chest X-ray</li><li>Rigid/flexible bronchoscopy</li><li>Contrast-enhanced CT thorax</li></ul>
Obstruction of small airways	<ul> <li>Viral bronchiolitis</li> <li>Bronchiolitis obliterans</li> <li>Bronchiectasis</li> <li>Heart disease/heart failure</li> <li>Bronchopulmonary dysplasia</li> <li>Cystic fibrosis</li> </ul>	<ul> <li>Chest X-ray</li> <li>High-resolution CT thorax</li> <li>Electrocardiogram/ echocardiogram</li> <li>Sweat test</li> </ul>
Other causes	<ul> <li>Gastroesophageal reflux disease</li> <li>Aspiration due to dysfunctional swallowing</li> <li>Immunodeficiency</li> <li>Tuberculosis</li> </ul>	<ul> <li>24-hour pH study</li> <li>Upper gastrointestinal study</li> <li>HIV screening</li> <li>Primary immunodeficiency screening</li> <li>Mantoux test/ IGRA test</li> <li>Gastric lavage/sputum for AFB smear and mycobacterium tuberculosis culture and sensitivity</li> </ul>

AFB: acid-fast bacilli; CT: computed tomography; HIV: human immunodeficiency virus; IGRA: interferon gamma release assay Adapted from National Heart, Lung, and Blood Institute. Guidelines for the Diagnosis and Management of Asthma. 2007.<sup>24</sup>

#### 3.2 Investigations

Asthma is diagnosed based on patient history, physical examination and variable expiratory airflow limitation.<sup>11</sup> Response to bronchodilator therapy (10-15 minutes after inhaling bronchodilator) by symptomatic improvement (for patients below 6 years old), or improvement in forced expiratory volume in one second (FEV<sub>1</sub>) by  $\geq$  12%, or peak expiratory flow rate (PEFR) by  $\geq$  15%, is supportive of the diagnosis of asthma; however, this may not be the case for mild asthmatics (Boxes 1 and 2).<sup>9,25,26</sup> Other objective measurements that suggest asthma include  $\geq$  12% improvement in FEV<sub>1</sub> after four weeks of ICS, 12% reduction in FEV<sub>1</sub> in exercise challenge test or a positive ( $\geq$  15% reduction in FEV<sub>1</sub>) bronchial hyperresponsive challenge test, or PEFR showing significant diurnal variability ( $\geq$  15%).<sup>9,25</sup> Raised fractional exhaled nitric oxide and positive skin prick tests to aeroallergens are also supportive of asthma.<sup>27-29</sup>

In atypical cases, investigations will be necessary to exclude other conditions.

## 3 | Diagnosis

	E	Boys	Girls		
Height (cm)	FEV <sub>1</sub> (L) <sup>a</sup>	PEF (L/min) <sup>c</sup>	FEV₁ (L) <sup>ь</sup>	PEF(L/min) <sup>d</sup>	
110	0.94	180	0.78	165	
112	0.98	187	0.83	172	
114	1.03	194	0.87	179	
116	1.08	201	0.92	186	
118	1.13	209	0.97	194	
120	1.18	216	1.02	201	
122	1.23	224	1.07	209	
124	1.28	232	1.13	217	
126	1.33	240	1.18	225	
128	1.39	249	1.24	234	
130	1.44	257	1.30	242	
132	1.50	266	1.36	251	
134	1.56	274	1.43	259	
136	1.62	283	1.49	268	
138	1.68	292	1.56	277	
140	1.75	301	1.63	287	
142	1.81	311	1.70	296	
144	1.88	320	1.78	306	
146	1.95	330	1.86	316	
148	2.02	340	1.93	326	
150	2.09	350	2.01	336	
152	2.16	360	2.10	346	
154	2.24	370	2.18	357	
156	2.31	380	2.27	367	
158	2.39	391	2.36	378	
160	2.47	402	2.45	389	

Box 1. Mean FEV, and PEF of normal Malaysian children.

#### Formulae

 $\begin{array}{lll} \mbox{a} & : 5.0753 \mbox{ x } 10^{-6} \mbox{ } H^{2.5802} & \mbox{c} & : 7.33 \mbox{ x } 10^{-3} \mbox{ } H^{2.15} \\ \mbox{b} & : 4.5497 \mbox{ x } 10^{-7} \mbox{ } H^{3.0542} & \mbox{d} & : 3.49 \mbox{ x } 10^{-3} \mbox{ } H^{2.29} \\ \end{array}$ 

Adapted from Ministry of Health Malaysia. Respiratory medication therapy adherence clinic protocol: asthma/COPD (adult & paediatric).<sup>20</sup>

## 3 | Diagnosis

Box 2. Calculations of peak expiratory flow rate and percentage of bronchodilator response.

.....

#### Peak expiratory flow rate (PEFR) measurement

- 1. Based on patient's height and gender, identify the predicted PEFR value, i.e. x (Refer to Box 1)
- 2. Take the patient's best PEFR, i.e. y
- 3. Calculate PEFR percentage:

 $(y/x) \times 100\% = z\%$ 

4. Classification of severity.

#### Bronchodilator response<sup>31</sup>

- 1. Measure the best pre-bronchodilator PEFR, i.e. a
- 2. Measure the best post-bronchodilator PEFR, i.e. b
- 3. Calculate percentage of bronchodilator response:

 $(\frac{b-a}{a}) \times 100\% = c\%$ 

# 4 Goals of therapy

The goals for asthma treatment are as follows:<sup>9</sup>

- To achieve good control of symptoms and maintain normal activity levels.
- To minimise future risk of asthma-related morbidity and mortality.
- To minimise asthma exacerbation.
- To minimise persistent airflow limitation.
- No/minimal side effects from treatment.
- To achieve patients' own goals regarding their asthma and treatment.

# 5 Management of asthma

A thorough asthma management plan incorporates patient education, avoidance of triggers, and optimisation of pharmacotherapy strategies.<sup>9</sup>

The management plan should be personalised, as patients have different trigger factors, asthma phenotypes and responses to medications.<sup>9</sup>

This management plan should include:<sup>9</sup>

- 1. Patient and/or parental education
- 2. Prevention and risk reduction of asthma flare-ups
- 3. Pharmacotherapy

A child with problematic severe asthma (PSA) must be referred to a paediatrician or respiratory paediatrician (if available) for further assessment to confirm asthma diagnosis, plan appropriate management and monitoring.

## 5.1 Education for parents and children

A crucial part of an asthma education programme is a high level of agreement between the patient/family and doctor regarding the goals of treatment. The checklist for an asthma education package is summarised in Table 2.

## 5 | Management of asthma

Table 2. Childhood asthma education checklist.

Торіс	Notes	Check (x)
1. Nature of asthma disease	<ul> <li>Chronic inflammation</li> <li>Abnormally sensitive airways</li> <li>Long-term condition</li> <li>Aim to enjoy a normal active life</li> </ul>	
2. Signs and symptoms	Cough, wheezing, shortness of breath	
3. Trigger factors	<ul><li>Colds, exposure to tobacco smoke, allergens, etc.</li><li>Which trigger factors should be avoided?</li></ul>	
4. Reliever	<ul> <li>Mechanism of action: Short-acting</li> <li>Use as needed when the child has symptoms</li> <li>Not for regular use</li> <li>Exercise/sports activity</li> </ul>	
5. Controller	<ul><li>Mechanism of action: Anti-inflammatory</li><li>Use regularly</li></ul>	
<ol> <li>Medication dosages and technique of using delivery devices</li> </ol>	Refer to Table 4 and Table 13	
7. Potential side effects of medication*	• E.g. oral thrush, hoarseness of voice, tinea versicolor	
8. Written asthma action plan	Refer to Chapter 11 for more details	
9. Safety issues	Emergency action plan	

\*Refer to Table 5.

Adapted from Child Health BC Provincial. Asthma Guideline Pediatric Asthma Education Checklist.<sup>32</sup>

Patients should be regularly assessed for their asthma control, competency in using inhalers and adherence to their medications. Parental asthma knowledge is essential as parents play an integral role in the management of asthmatic children.<sup>33</sup>

Useful information on asthma for parents and clinicians is available on the following websites:

- www.lfm.org.my
- www.mts.org.my

#### 5.2 Prevention

Interactions between genetic susceptibility and environmental influences play a significant role in determining the heterogeneity of asthma.<sup>34</sup> While pharmacologic treatments target host factors, addressing environmental factors is also essential for optimal management and prevention of allergic diseases.<sup>34</sup>

#### 5.2.1 Avoidance of smoke and air pollutants

Exposure to tobacco smoke (ETS) is associated with increased prevalence and severity of asthma and wheezing.<sup>35-39</sup> In a systematic review, pre- or postnatal ETS was associated with a 21-85% increased risk for asthma.<sup>37</sup> Exposure to secondhand smoke moderately increased the overall risk of atopic sensitisation, with the most pronounced effect seen in children < 7 years of age.<sup>38</sup> In addition, newborn infants whose mothers smoked during pregnancy showed increased airway responsiveness (a characteristic of asthma), compared with those whose mothers did not smoke.<sup>40</sup> A significantly increased risk of childhood asthma occurs if both parents or the mother smoke.<sup>41</sup> Clinicians should routinely inquire about parental smoking in children with asthma. Parents of asthmatics should be advised that their child should always be in a smoke-free environment.

Despite the unclear mechanisms by which air pollution causes lung injury, a study estimated that up to 14% of annual childhood asthma cases were directly attributable to traffic-related air pollution.<sup>42</sup>

Indoor pollutants, such as mosquito coil smoke and volatile organic compounds (VOCs), were found to be independently associated with an increased risk of asthma and persistent wheezing.<sup>43,44</sup>

#### 5.2.2 Environmental allergen exposure reduction

Early allergen exposure and sensitisation has been associated with an increased risk of persistent asthma, bronchial hyperresponsiveness and reduced lung function.<sup>45</sup> Common indoor allergens include house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), cat/dog dander, cockroach, mould, secondhand tobacco smoke, home items (e.g. cleaning chemicals, fragrance, insecticide, mosquito coils, incense sticks, etc.), and cooking fuel (e.g. wood, charcoal), whereas common outdoor allergens include pollen, emissions from carbon powered vehicles and factories.<sup>45-47</sup>

For children whose asthma is difficult to control, it is reasonable to reduce exposure to the offending allergen. A comprehensive environmental intervention to decrease exposure to indoor allergens has been proven to reduce asthma-associated morbidity in children with atopic asthma.<sup>46</sup> Table 3 shows the recommended avoidance strategies for common allergens.<sup>48</sup>

## 5 | Management of asthma

Table 3. Allergen control recommendations in sensitised individuals.

Allergens	Control Measures
House dust mites	<ul> <li>Allergen-permeable mattress and pillow covers</li> <li>Wash bedding in hot water ~ 60°C (as often as possible)</li> <li>Reduce indoor dampness and humidity</li> <li>Avoid exposure to carpets and upholstered furniture</li> <li>Only use washable toys/soft furnishing (e.g. curtains) that do not retain dust</li> </ul>
Pets	<ul> <li>Removal of pets only if sensitisation is proven</li> <li>If removal impossible, logical steps include exclusion of pets from bedroom, HEPA filtration, HEPA vacuuming</li> </ul>
Cock- roaches	<ul> <li>Clean home</li> <li>Use professional pest control, allergen-impermeable mattress covers</li> </ul>
Molds	<ul> <li>Wash mouldy surfaces with weak bleach solution, fix leaks, remove carpets, use HEPA filtration or dehumidifying equipments</li> </ul>

\*HEPA- High Efficiency Particle Arrestor. Adapted from O'Connor. J Allergy Clin Immunol. 2005.<sup>48</sup>

#### 5.2.3 Food allergy

Food allergy is common in early life, affecting up to 8% of children.<sup>49</sup> The usual foods implicated are cows' milk, egg, soy and wheat.<sup>49</sup> Some food allergies have a high rate of resolution, whereas allergy to peanuts, tree nuts, fish and shellfish generally persists.<sup>49</sup> There is limited data on the effect of food avoidance or supplementation on asthma.<sup>49</sup> Food additives (e.g. monosodium glutamate, sulphites and dyes) have been implicated in inducing lower airway symptoms.<sup>50</sup>

#### 5.2.4 Respiratory tract infections

Respiratory tract infections are the most common triggering factors for asthma exacerbations, particularly viral infections (i.e. rhinovirus, respiratory syncytial virus [RSV], influenza, coronavirus, human metapneumovirus, parainfluenza, adenovirus and bocavirus).<sup>51</sup> Respiratory tract infections may be avoided by vaccinations and good hand hygiene.

#### 5.2.5 Exercise

Exercise is important for the growth and development of children. Children should be encouraged to participate in all forms of exercise and sports activities, including swimming. Physically fit children are better able to cope with their asthma.<sup>52</sup> Exercise intolerance may suggest inadequate asthma control, which needs further evaluation and optimisation of treatment.<sup>52</sup>

#### 5.2.6 Obesity

An increased prevalence of asthma is reported among obese children, in which body mass index is correlated with asthma risk.<sup>53</sup> Children with obesity have an increased lung volume relative to airway calibre ("dysanapsis"), which is reflected by a lower-than-normal ratio of FEV<sub>1</sub>/forced vital capacity (FVC), despite normal values of FEV<sub>1</sub> and FVC.<sup>54</sup> Dysanapsis contributes to airflow limitation in obesity, and is associated with increased asthma exacerbations and use of systemic glucocorticoids in children.<sup>54</sup>

#### 5.2.7 Breastfeeding

There is evidence of protective effect of breastfeeding against transient childhood wheeze, but not in the development of childhood asthma and other allergic diseases.<sup>55,56</sup> In a systematic review and meta-analysis observing the effect of duration of breastfeeding on asthma development in children, a longer duration of breastfeeding was associated with a decreased risk of asthma in children 5-18 years of age.<sup>57</sup> Breastfeeding should be encouraged in view of its other beneficial effects as well.

#### 5.3 Drug therapy

The pharmacological treatment of asthma consists of two components:9

- Reliever therapy
- Controller therapy

#### 5.3.1 Reliever therapy

All patients should be given reliever therapy to alleviate respiratory symptoms associated with an acute asthma event. An intermittent short-acting  $\beta_2$ -agonist (SABA) is the drug of choice for this purpose, which may be used alone or in combination with an inhaled corticosteroid (ICS), such as as-needed ICS formoterol or as-needed ICS-SABA.<sup>9,58</sup> Routine use of oral bronchodilators is discouraged because of their narrow therapeutic index and inconsistent gastrointestinal absorption, which result in variable and unreliable efficacy.

#### **5.3.2 Controller therapy**

Anti-inflammatory therapy is the mainstay treatment for the prevention of asthma symptoms. The child's age, asthma phenotype and severity of symptoms determine the choice of controller therapy and duration of treatment.<sup>9</sup> To a certain degree, parental acceptance of medication may also influence the choice of controller therapy in view of ensuring compliance.<sup>60</sup>

ICS-containing medications remain the anti-inflammatory treatment of choice for asthma; ICS reduces asthma symptoms and prevents asthma-associated hospitalisation and deaths.<sup>9,59</sup> ICS equivalent doses for children aged 6 years old and above are shown in Table 4.

## 5 | Management of asthma

Table 4.	ICS doses	(alone o	r with L	ABA) for	children	aged 6-1	1 years and	$\geq$ 12 years old.
----------	-----------	----------	----------	----------	----------	----------	-------------	----------------------

-

Children aged 6-11 years old						
ICS (alone or in combination with LABA)	Total daily ICS dose (µg, shown as metered doses)					
	Low	Medium	High			
BDP (pMDI, standard particle, HFA)	100 – 200	> 200 - 400	> 400			
BDP (pMDI, extrafine particle, HFA)	50 – 100	> 100 - 200	> 200			
Budesonide (DPI)	100 – 200	> 200 - 400	> 400			
Budesonide (nebulised)	250 – 500	> 500 - 1000	> 1000			
Fluticasone propionate (DPI)	50 – 100	> 100 - 200	> 200			
Fluticasone propionate (pMDI, standard particle, HFA)	50 – 100	> 100 - 200	> 200			
Fluticasone furoate (DPI)	50	50	N.A.			
Mometasone furoate (pMDI, standard particle, HFA)	100	100	200			
Ciclesonide (pMDI, extrafine particle, HFA)	80	> 80 - 160	> 160			
Children aged ≥ 12 y	ears old					
BDP (pMDI, standard particle, HFA)	200 – 500	> 500 – 1000	> 1000			
BDP (DPI or pMDI, extrafine particle, HFA)	100 – 200	> 200 - 400	> 400			
Budesonide (DPI, or pMDI, standard particle, HFA)	200 - 400	> 400 - 800	> 800			
Ciclesonide (pMDI, extrafine particle, HFA)	80 – 160	> 160 - 320	> 320			
Fluticasone furoate (DPI)	1	00	200			
Fluticasone propionate (DPI)	100 – 250	> 250 - 500	> 500			
Fluticasone propionate (pMDI, standard particle, HFA)	100 – 250	> 250 - 500	> 500			
Mometasone furoate (DPI)	Depends on DPI device - see product information					
Mometasone furoate (pMDI, standard particle, HFA)	200	- 400	> 400			

BDP: beclomethasone dipropionate; DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; ICS: inhaled corticosteroid; LABA: long-acting  $\beta_2$ -agonists; N.A.: not applicable; pMDI: pressurised metered dose inhaler; ICS by pMDI should preferably be used with a spacer.

Adapted from Global Strategy for Asthma Management and Prevention (2024 update).<sup>9</sup>

#### 5.3.3 Side effects of asthma medications

Side effects of asthma medications are often overlooked during clinic visits for asthma monitoring (Table 5). Long-term use of ICS in low to moderate doses is predominantly safe with minimal side effects.<sup>61</sup> Children on high-dose ICS require close monitoring for growth and adrenal suppression. Other minor side effects that may be present are oral thrush and hoarseness of voice, which can be treated.<sup>9,58</sup> In general, all asthmatic children must have their growth (especially height) monitored during clinic visits.<sup>9,58</sup>

Table 5. Asthma medications and its adverse effects.

Medications	Adverse effects
ICS i.e. budesonide, fluticasone, beclomethasone, ciclesonide	<ul> <li>Perioral candidiasis, dysphonia</li> <li>Long-term high-dose use increases risk of systemic steroid side effects, i.e. adrenal suppression, glaucoma, osteoporosis and cataracts</li> </ul>
SABA i.e. salbutamol, terbutaline	<ul> <li>Tremor, tachycardia, palpitations, headaches, cramps, hypokalaemia</li> </ul>
ICS-LABA i.e. beclomethasone-formoterol, fluticasone-salmeterol, budesonide- formoterol	<ul> <li>LABA component can cause tachycardia, headache or cramps</li> <li>LABA should not be used without ICS, due to potential serious adverse outcomes</li> </ul>
Leukotriene modifier i.e. montelukast	<ul> <li>Sleep disturbance, behavioural change, neuropsychiatric disorder</li> </ul>
Long-acting muscarinic receptor antagonists i.e. tiotropium	• Urinary retention, excessive dry mouth

ICS: inhaled corticosteroids; LABA: long-acting  $\beta_2$ -agonists; SABA: short-acting  $\beta_2$ -agonists.

Adapted from Quirt J, et al. Allergy Asthma Clin Immunol. 2018; Sharma S, et al. 2022; Abosamak NR, Shahin MH. Beta2 receptor agonists and antagonists; US FDA. Singulair.<sup>62,65</sup>

Long-term asthma control and follow up

#### 6.1 Assessment of asthma control

The level of asthma control is the extent to which asthma features can be observed in the patient, or have been reduced or resolved by treatment. There are two domains of asthma control:<sup>9</sup>

• Symptom control

6

Control of future risk of adverse outcomes/exacerbations

Having risk factors increases patients' risk of exacerbations even with wellcontrolled asthma (Table 6).<sup>9</sup> Asthma control, adherence and inhaler technique must be assessed at every clinic visit.<sup>9</sup>

**Table 6.** Assessment of asthma control and risk factors for poor asthma outcomes inchildren aged 6 years and above.

A. Asthma symptom control	L	evel of asth.	ma symptom	o control
In the past 4 weeks, has the patient had:		Well- controlled	Partly controlled	Uncontrolled
• Daytime asthma symptoms > 2x a week?	Yes □ No □			
• Any night waking due to asthma?	Yes □ No □	None of	1-2	3-4
<ul> <li>SABA reliever needed for symptoms</li> <li>&gt; 2x a week? (excluding pre-exercise use)</li> </ul>	Yes □ No □	these	of these	of these
• Any activity limitation due to asthma?	Yes □ No □			

#### B. Risk factors for poor asthma outcomes

#### Risk factors for exacerbations:

Uncontrolled asthma symptoms

- Medications: High SABA use, inadequate ICS, poor adherence, incorrect inhaler technique
- Comorbidities: Obesity, chronic rhinosinusitis, GERD, confirmed food allergy
- Exposures: Smoking, allergen exposure if sensitised, air pollution
- Psychosocial: Major psychological or socio-economic problems

**Table 6.** Assessment of asthma control and risk factors for asthma outcomes in children aged 6 years and above. (*cont'd*)

#### B. Risk factors for poor asthma outcomes

- Lung function: Low FEV, (especially < 60% predicted), high bronchodilator reversibility</li>
- Type 2 inflammatory markers: Blood eosinophils, elevated FeNO
- Exacerbation history: Ever intubated or in intensive care unit for asthma, ≥ 1 severe exacerbation in last 12 months

#### Risk factors for developing persistent airflow limitation:

- · History: Preterm birth, low birth weight and greater infant weight gain
- Medications: Lack of ICS treatment
- Exposures: Tobacco smoke, noxious chemical
- Investigations: Low initial FEV, blood eosinophilia

#### Risk factors for medication side effects:

- Systemic: Frequent OCS, long-term and high-dose ICS
- Local: High-dose or potent ICS, poor inhaler technique

FeNO: fractional exhaled nitric oxide; FEV; i forced expiratory volume in one second; GERD: gastroesophageal reflux disease; ICS: inhaled corticosteroids; OCS: oral corticosteroids; SABA: short-acting  $\beta_2$ -agonists.

Adapted from Global Strategy for Asthma Management and Prevention (2024 update).<sup>9</sup>

Progression to the next level of treatment (step-up) is indicated when asthma control cannot be achieved at the current treatment level, provided that medication is used correctly.<sup>9</sup> Refer to Tables 7 and 8 for the initiation of long-term management of asthma based on asthma symptom severity.

## 6 | Long-term asthma control and follow up

 Table 7. Algorithm for the initiation of long-term management of asthma in children aged

 6-11 years old, based on asthma symptom severity.

Step	Step 1	Step 2	Step 3	Step 4	Step 5				
Symptom	Symptoms < 2x a week	Symptoms 2 - 5 days a week	Symptoms on most days, or waking with asthma $\ge 1x$ a week	Symptoms on most days, or waking with asthma ≥ 1x a week, and low lung function	Persistent symptoms despite correct inhaler technique and good adherence				
Preferred controller	Low-dose ICS taken whenever SABA taken	Daily low- dose ICS	Low dose ICS-LABA OR Medium dose ICS OR Very Iow dose ICS- formoterol MART	Medium- dose ICS- LABA OR Low-dose ICS- formoterol MART Refer for expert advice	Refer for phenotypic assessment ± Higher- dose ICS-LABA or add-on therapy, e.g. anti-IgE, anti-IL4Rα, anti-IL5				
Other controller options	-	Daily LTRA† OR Low-dose ICS taken whenever SABA taken	Low-dose ICS + LTRA†	Add tiotropium OR Add LTRA†	As a last resort, consider add-on low- dose OCS (consider side effects)				
Reliever	As-needed SA	As-needed SABA (or low-dose ICS-formateral reliever for MART in Steps 3 or 4)							

<sup>†</sup>If prescribing LTRA, note concerns about potential neuropsychiatric effects.

SABA (or low-dose ICS-formaterol for MART) can be taken as reliever as-needed at all steps. ICS: inhaled corticosteroid; IgE: immunoglobulin E; ILS: interleukin 5; LABA: long-acting β<sub>2</sub>-agonists; LTRA: leukatriene receptor antagonists; MART: maintenance and reliever therapy; OCS: oral corticosteroid; SABA: short-acting β<sub>2</sub>-agonists.

Adapted from Global Strategy for Asthma Management and Prevention (2024 update).<sup>5</sup>

## 6 | Long-term asthma control and follow up

 Table 8. Algorithm for the initiation of long-term management of asthma in children aged

 12 years old and above, based on asthma symptom severity.

Step		Step	01&2	Step 3	Step 4	Step 5	
Symptom		Symptoms < 3 - 5 days a week and normal (or mildly reduced) lung function		Symptoms on most days, or waking with asthma ≥ 1x a week, or low lung function	Daily symptoms or waking with asthma ≥ 1x a week, and low lung function, or recent exacerbation	Persistent symptoms despite correct inhaler technique and good adherence	
Track 1	Preferred controller	As-needed-only low-dose ICS-formoterol (AIR-only)		Low-dose maintenance ICS- formoterol (MART)	Medium- dose maintenance ICS- formoterol (MART)	Add-on LAMA Refer for phenotypic assessment ± biologic therapy Consider high-dose ICS- formoterol (MART)	
	Reliever	As-needed low-dose ICS-formoterol (AIR)					
Track 2	Alternative controller	Take ICS whenever SABA taken	Low-dose maintenance ICS	Low-dose maintenance ICS-LABA	Medium/ high-dose maintenance ICS-LABA	Add-on LAMA Refer for phenotypic assessment ± biologic therapy Consider high-dose ICS- formoterol	
	Reliever	Reliever As-needed			ded ICS-SABA		

<sup>†</sup>If prescribing LTRA, note concerns about potential neuropsychiatric effects.

AIR: anti-inflammatory reliever; ICS: inhaled corticosteroid; LABA: long-acting  $\beta_2$ -agonists; MART: maintenance and reliever therapy; SABA: short-acting  $\beta_2$ -agonists.

Adapted from Global Strategy for Asthma Management and Prevention (2024 update).<sup>9</sup>

#### 6 | Long-term asthma control and follow up

The flow of asthma management is shown in Figure 1. When asthma control is achieved for at least three months, a reduction (step-down) from the current treatment level should be considered.<sup>9</sup> ICS should be adjusted to the minimum dose required to maintain asthma control.<sup>9</sup> Stepping down the treatment too far or rapidly can increase the risk of exacerbations, even if symptoms appear well-managed.<sup>9,66</sup> Gradually decreasing ICS doses by 25-50% every three months is generally feasible and safe for most patients.<sup>9,67</sup> Additionally, evidence indicates that effectively treating associated sinusitis and allergic rhinitis aids in the control of childhood asthma.<sup>7</sup>



Figure 1: Management flow of asthma.

The 5C evaluation, summarised below, is an easy-to-use and thorough evaluation for children with poorly controlled asthma prior to stepping up asthma treatment.

- 1. Correct diagnosis of asthma
- 2. Compliance evaluation

- 3. Correct inhaler technique
- 4. Continuous exposure to triggers
- 5. Comorbidities and contributing factors assessment

#### 6.2 Achieving and maintaining asthma control

Monitoring of asthma control includes regular patient assessment using monitoring tools available i.e. clinical, lung function, bronchial hyperresponsiveness and inflammatory markers (Tables 6 and 9). Objective assessment using clinical questionnaire and lung function test (peak flow or spirometry, depending on availability) should be done for each patient whenever possible. Asthma follow-ups should be done every 2-6 months depending on asthma severity (control status), age, phenotype and risk for exacerbations.

Monitoring tools	≥ 4 years and < 6 years	6 years
Clinical		
Clinical symptoms	+	+
Childhood asthma control test (C-ACT)	+	+
Asthma Control Questionnaire (ACQ)	-	+
Asthma exacerbations	+	+
Asthma Quality of Life Questionnaire (QoLQ)	-	+
Lung function tests		
Peak expiratory flow (PEF)	+/-	+
Flow volume curve, bronchodilator response	+/-	+
Bronchial hyperresponsiveness		
Exercise	+/-	+
Inflammatory markers		
Fraction exhaled nitric oxide (FeNO)	+	+

Table 9. Monitoring tools for asthma in children.

+: Possible -: Not possible +/-: Might be possible Adapted from Pijnenburg MW, et al. Resp J. 2015.<sup>47</sup>

#### 7.1 Difficult-to-treat asthma

"Difficult-to-treat asthma" is defined as persistent symptoms and/or frequent asthma attacks despite prescribing high dose controller treatment (i.e. GINA step 4 or 5).<sup>9</sup> In many cases, asthma may appear to be difficult-to-treat because of modifiable factors such as incorrect diagnosis, incorrect inhaler technique, poor adherence, presence of comorbidities and contributory factors (Table 10) and persistent exposure to allergens.<sup>9,68-70</sup> Children with difficult-to-treat asthma should be referred to paediatricians or paediatric respiratory physicians for further evaluation. Refer to the algorithm on approach to difficult asthma in Figure 2.

Table 10. Comorbidities and contributing factors.

- Rhinosinusitis/nasal polyps
- Allergic rhinitis
- Eczema
- Food allergy
- Psychological factors: Personality trait, symptom perception, anxiety, depression
- Vocal cord dysfunction
- Cardiac disease
- Obesity
- Obstructive sleep apnoea
- Bronchiectasis
- Hormonal influences: Premenstrual, menarche, thyroid disorders
- Gastroesophageal reflux disease (symptomatic)
- Drugs: Aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), β-adrenergic blockers, angiotensin converting enzyme inhibitors (ACE-inhibitors)
- Environmental: smoke, allergen exposures

Adapted from GINA 2023; Abul et al., 2019; Ramratnam et al., 2017; British Guidelines on the management of asthma, 2019; 9:48-70



Figure 2: Algorithm for approach to difficult asthma in children.

#### 7.2 Severe asthma

31

There is a small yet significant group of children with severe asthma. Prevalence estimates of severe asthma vary significantly depending on the diagnostic criteria used, ranging from 2.1% to 10%.<sup>71</sup>

Severe asthma is defined as asthma that remains uncontrolled despite adherence to optimised treatment with high-dose ICS-LABA and management of other contributory factors to prevent it from becoming uncontrolled, or asthma that worsens when high-dose treatment is decreased.<sup>60</sup> Inherent in the definition of severe asthma is the exclusion of individuals who present with "difficult-to-treat" asthma in whom the appropriate 5C evaluation and management vastly improves their current condition (Figure 3).<sup>9,69,70,72</sup>



Figure 3: Algorithm for approach to difficult asthma in children.

Severe asthma is sometimes referred to as 'severe refractory asthma' since it is defined by being relatively refractory to high dose inhaled therapy. However, with the advent of biologic therapies (Table 11), the word 'refractory' is no longer appropriate. Having one or both of the following criteria qualifies a patient as having uncontrolled severe asthma:<sup>72</sup>

- Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma).
- Frequent exacerbations (≥ 2/year) requiring OCS, or serious exacerbations (≥ 1/year) requiring hospitalisation.

**Table 11.** Options for add-on biologic therapy for patients with uncontrolled severe asthma despite optimised maximal therapy.

Class	Name	Age	Asthma indication	Side effects
Anti-IgE	Omalizumab (SC)	≥ 6 years	Severe allergic asthma	Systemic allergic/ hypersensitivity reactions, arthralgia
Anti-IL5	Mepolizumab (SC)	≥ 6 years	Severe eosinophilic asthma	Systemic allergic/ nonallergic reactions
Anti-IL5R	Benralizumab (SC)	≥ 12 years	Severe eosinophilic asthma	Systemic allergic/ hypersensitivity reactions

**Table 11.** Options for add-on biologic therapy for patients with uncontrolled severe asthma despite optimised maximal therapy. (*cont'd*)

Class	Name	Age	Asthma indication	Side effects
Anti-IL4R	Dupilumab (SC)	≥ 6 years	Severe eosinophilic/ type 2 asthma, or maintenance OCS	Systemic allergic/ hypersensitivity reactions, eosinophilia
Anti- TSLP	Tezepelumab (SC)	≥ 12 years	Severe asthma	Systemic allergic/ hypersensitivity reactions

IgE: immunoglobulin E; IL5: interleukin-5; IL5R: interleukin-5 receptor; IL4R: interleukin-4 receptor; TSLP: thymic stromal lymphopoietin.

Adapted from Global Strategy for Asthma Management and Prevention (2024 update); Zaazouee MS, et al. Front Pharmacol. 2022; Menzies-Gow A, et al. Lancet Respir Med. 2023.<sup>9,73,74</sup>

Severe asthma in children is a highly heterogeneous disorder with multiple clinical phenotypes.<sup>70</sup> Identifying certain characteristics that can help determine severe asthma phenotypes help guide targeted therapies and may predict treatment response. These patients should be referred to paediatric respiratory physicians for further evaluation and management. Minimal investigations for asthma phenotyping include blood eosinophil, total and specific IgE for allergens/skin prick test and fractional exhaled nitric oxide (FeNO).<sup>9</sup>

#### 7.3 Exercise-induced bronchoconstriction (EIB)

EIB is characterised by acute airway narrowing that occurs as a result of exercise. EIB occurs in a substantial proportion of patients with asthma, however it may also occur in individuals without a known diagnosis of asthma.<sup>75</sup> EIB is also a common feature of poorly controlled asthma.

The diagnosis of EIB is established by changes in lung function provoked by exercise, not based on symptoms. The difference between the pre-exercise FEV<sub>1</sub> value and the lowest FEV<sub>1</sub> value recorded within 30 minutes after exercise is expressed as a percentage of the pre-exercise value. The criterion for the percent fall in FEV<sub>1</sub> used to diagnose EIB is  $\geq 10\%$ .<sup>75</sup>

#### Recommended treatment

33

Treatment can be divided into pharmacologic and non-pharmacologic treatment, as summarised in Table  $12.^{75}$ 

#### Table 12. Recommended treatment for EIB.

Pharmacologic treatment	Non-pharmacologic treatment
$\begin{array}{l} \mbox{Administration of an inhaled short-acting}\\ \beta_2\mbox{-}agonists (SABA) or low-dose\\ \mbox{ICS-formoterol 5-20 minutes before exercise.} \end{array}$	Warming up 10-15 minutes before exercise to induce a refractory period.
Optimise/step up controller therapy for better asthma control.	Manoeuvre to pre-warm and humidify the air during exercise (e.g. breathing through the nose, face mask or scarf).
	Avoid exercising during ambient air pollution (e.g. haze), or extreme weather.

EIB: exercise-induced bronchoconstriction.

Adapted from Parsons JP, et al. Am J Respir Critic Care Med. 2013; Global Strategy for Asthma Management and Prevention (2024 update).<sup>9,75</sup>

# 8 Inhaler devices

Many children with asthma often use their inhalers incorrectly, resulting in minimal or no therapeutic benefit from their prescribed treatment.<sup>76</sup> To ensure better asthma control, it is important to provide thorough initial training on proper inhaler use, followed by repeated checks to confirm the child can demonstrate the correct technique.<sup>77</sup> Correct inhaler technique and good adherence to inhalers are important in achieving asthma control.<sup>77</sup>

Common inhaler devices used by children are summarised in Table 13. Pressurised metered dose inhaler (pMDI) therapy via spacer is as efficacious as nebuliser therapy.<sup>78</sup> Inhalation technique using pMDI via a spacer can either be a single-breath technique (need to hold the breath for 10 seconds) or tidal breathing technique (5-10 breaths).<sup>79</sup> Home nebuliser therapy is discouraged.

Children aged 0-6 years	• pMDI + spacer with facemask.
	• pMDI + spacer with mouthpiece (preferred).
	• pMDI + spacer with facemask.
Children aged > 6 years	• Dry powder inhaler (if the child has sufficient inspiratory flow).
	<ul> <li>Breath actuated inhaler (&gt; 7 years)</li> </ul>

Table 13. Inhaler devices recommended for children of different ages.

pMDI: pressurised metered dose inhaler.

35

Adapted from Van Aalderen WM, et al. NPJ Prim Care Respir Med. 2015.80

# Asthma in preschool children (5 years and younger)

Wheezing is a very common occurrence in young children. Approximately half of them have experienced a wheezing episode before 6 years of age.<sup>81</sup> However, determining if the wheeze is due to asthma or viral illnesses in this age group is very difficult due the heterogeneous nature of its clinical presentation, progression of disease and response to treatment.<sup>82</sup> In addition, wheezing in young children may be due to a variety of underlying airway and childhood disorders, or a number of interactions between genetic factors and the environment.<sup>83</sup>

#### 9.1 Wheeze classification

Classifying wheeze phenotypes in young children aims to guide treatment and predict progression of disease. There are two wheeze phenotypes classification:<sup>9,83</sup>

#### Symptom-based classification

- Episodic (viral) induced wheeze (EVW) Wheezing in discrete episodes associated with viral respiratory tract infections and no symptoms between episodes. Children with episodic wheeze are well between episodes.<sup>83</sup>
- Multiple-trigger wheeze (MTW) Wheezing both in discrete episodes and between episodes, with numerous triggering factors including viral colds, smoke, allergens, laughing, crying, exercise.<sup>83</sup>

However, symptom-based phenotypes were found to be inconsistent, limiting its usefulness in guiding treatment.  $^{\rm 82}$ 

#### Time trend-based classification

The landmark Tucson Birth Cohort study describes the temporal wheeze phenotype as follows:<sup>83</sup>

- Early transient wheeze Wheezing only during the first 3 years of life.<sup>83</sup>
- Persistent wheeze Wheezing beginning in early life and persisting up to school age.<sup>83</sup>
- Late-onset wheeze Beginning to wheeze after the age of 3 years.<sup>83</sup>

Although these temporal-based wheeze phenotypes have been expanded in further studies, its usefulness remains impractical in clinical situations.<sup>83</sup>

#### 9.2 Diagnosis of asthma

A definitive diagnosis of asthma in young children is challenging as the clinical symptoms are also commonly encountered in children with no asthma and other diseases.<sup>84</sup>

An asthma diagnosis in children 5 years and younger can often be based on:9

- Symptom patterns (recurrent episodes of wheeze, cough, breathlessness [typically manifested by activity limitation], and nocturnal symptoms or awakenings).
- Presence of risk factors for development of asthma, such as family history of atopy, allergic sensitisation, allergy or asthma, or a personal history of food allergy or atopic dermatitis.
- Therapeutic response to controller treatment.
- Exclusion of alternate diagnoses.

The likelihood for a definite diagnosis of asthma can be therefore made based on clinical symptom pattern, family history and physician findings (Table 14).<sup>9</sup>

Table	14. Probability	of asthma	diagnosis in	children 5	years or younger.
					/ / / /

Probability of Asthma	Not Probable	Probable	Very Probable
Duration of asthma symptoms (cough, wheeze and heavy breathing) with respiratory tract infections	< 10 days	> 10 days	> 10 days
Number of asthma symptom episodes per year	2-3 episodes/ year	> 3 episodes/ year, or severe episodes and/or night worsening	> 3 episodes/ year, or severe episodes and/or night worsening
Asthma symptoms between episodes	No	Yes	Yes
Asthma symptoms with exercise/laughing and playing	No	No	Yes
Atopy	No	No	Yes
Family history of asthma/atopy	No	No	Yes

Adapted from Global Strategy for Asthma Management and Prevention (2024 update).<sup>9</sup>

A positive family history of allergic disease or the presence of atopy/allergic sensitisation in children with recurrent wheeze may predict the likelihood of evolving into atopic asthma and its risk may be determined by the modified Asthma Predictive Index (mAPI)(Table 15).<sup>85</sup> The mAPI requires four or more wheeze episodes per year with at least 1 major criterion OR 2 minor criteria.<sup>85</sup>

Table 15. Probability of asthma diagnosis in children 5 years or younger.

Major criteria	Minor criteria
Parental history of asthma (diagnosed by a physician).	Eosinophilia greater than or equal to 4%.
Atopic eczema (diagnosed by a physician).	Wheezing unrelated to colds (reported by parents).
Aeroallergen sensitisation.	Allergic sensitisation to food, i.e. milk, egg, peanuts.

Adapted from Huffaker MF, et al. Ann Allergy Asthma Immunol. 2014.85

#### 9.3 Investigations and differential diagnoses of asthma

While it is often difficult to obtain objective assessments in children 5 years and younger, there are several tests that can be used as adjuncts in the diagnosis of asthma.<sup>9,68,86</sup>

#### Chest X-ray

While chest X-ray is rarely indicated in diagnosing asthma, it should be ordered when red flags are present (Table 16) to rule out structural airway abnormalities (e.g. congenital lobar hyperinflation, vascular ring), chronic infections (pulmonary tuberculosis), chronic suppurative lung disease or bronchiectasis, inhaled foreign body, or other diagnoses. Red flags in clinical history and physical examination that are suggestive of diagnosis other than asthma should prompt referral to the paediatrician for more detailed investigations.<sup>9,68</sup>

#### Allergic sensitisation tests

Skin prick testing or allergen-specific immunoglobulin E tests are two modalities to check for allergic sensitisation. Allergic sensitisation is present in most children with asthma once they are 3 years and above. However, the absence of sensitisation to common aeroallergens does not rule out asthma. Allergic sensitisation is the best predictor for persistent asthma.<sup>9</sup>

#### Lung function test

38

As most children 5 years and younger are unable to perform repeatable expiratory manoeuvres, lung function testing is not a major objective assessment in this age group.<sup>9,68</sup>

## 9 | Asthma in preschool children (5 years and younger)

Table 16. Red flags in children with wheeze and possible diagnosis.

Red Flags	Possible Diagnosis
History	
Neonatal/very early onset of symptoms	<ul> <li>Structural airway abnormalities (e.g. tracheomalacia, tracheal stenosis)</li> <li>Interstitial lung disease</li> </ul>
Respiratory symptoms worsened after feeds or associated with vomiting	<ul> <li>Gastroesophageal reflux disease</li> <li>Laryngeal cleft</li> <li>H-type tracheo-oesophageal fistula, swallowing incoordination, chronic aspiration syndrome</li> </ul>
Daily chronic wet cough (> 4 weeks duration)	Suppurative lung disease (protracted bacterial bronchitis/chronic suppurative lung disease/ bronchiectasis, cystic fibrosis, pulmonary tuberculosis)
Recurrent pneumonia	Immunodeficiency
Sudden onset of symptoms	Foreign body aspiration
Physical examination	
Fixed monophonic wheeze/stridor	<ul> <li>Congenital structural bronchial disease (e.g. tracheal stenosis)</li> <li>Tracheal/bronchial compression (vascular ring/ sling, enlarged cardiac chamber from heart failure, enlarged lymph node from tuberculosis)</li> </ul>
Focal or asymmetry lung signs	<ul> <li>Congenital lung malformation (e.g. congenital lung hyperinflation, congenital pulmonary airway malformation (CPAM))</li> <li>Foreign body aspiration</li> </ul>
Cardiovascular signs	Congenital heart disease
Finger clubbing	Bronchiectasis, cystic fibrosis, cyanotic congenital heart disease
Hypoxaemia outside the context of viral infection	<ul><li>Interstitial lung disease</li><li>Congenital heart disease</li></ul>
Failure to thrive	Unlikely asthma; look for other red flags for an alternative diagnosis
No obvious triggers for symptoms (e.g. viral upper respiratory tract infection)	Unlikely asthma; look for other red flags for an alternative diagnosis
Failure to respond to asthma medications (despite adherence and correct technique)	Unlikely asthma; look for other red flags for an alternative diagnosis

Adapted from Bush A. African J Respir Med. 2016; Ducharme FM, et al. Paediatr Child Health. 2015; Global Strategy for Asthma Management and Prevention (2024 update).<sup>987,88</sup>

#### 9.4 Management of asthma in children aged 5 years and younger

The goals of asthma management in preschool children are similar to those of older age groups, i.e. to achieve good, long-term symptom control and maintain normal activities, also to reduce future risks of exacerbation, impaired lung function and development, and medication side effects.<sup>9</sup> Good asthma control can be achieved through careful assessment, adjustment of medications and review of treatment response.<sup>9,82</sup> An overview of the diagnosis and management of asthma in children aged 5 years and below is shown in Figure 4.



**Figure 4**: Overview of the diagnosis and management of asthma in children under 5 years and younger.

#### 9.5 Treatment for asthma in children aged 5 years and younger<sup>9</sup>

#### **Reliever therapy**

- Inhaled short-acting β<sub>2</sub>-agonists (SABA): pMDI salbutamol as needed (as per action plan).
- Oral bronchodilator is not recommended due to its slower onset of action and higher risk of side effects.

#### **Controller therapy**

- ICS: Daily low-dose ICS is recommended as the initial preferred treatment to control asthma in young children. ICS should be given for at least 2-3 months to establish its effectiveness. The recommended ICS dose for children aged 5 years old and below are shown in Table 17.
- Montelukast (leukotriene receptor antagonist): An alternative anti-inflammatory
  agent to ICS. Montelukast is available in several forms, including tablets, chewable
  tablets, and oral granules. Parents should be advised that montelukast is known to
  possibly cause neuropsychiatric side effects (e.g. behaviour and mood changes)
  and sleep disturbances, and to immediately stop the medication and alert their
  healthcare providers if they notice such adverse events.<sup>65</sup>
- Combination of inhaled ICS/long-acting β<sub>2</sub>-agonists (LABA): Insufficient data on the safety and efficacy in those less than 4 years old.

ICS	Low total daily dose (µg)	Age group with adequate safety and effectiveness data
BDP (pMDI, standard particle, HFA)	100	Ages 5 years and older
BDP (pMDI, extrafine particle, HFA)	50	Ages 5 years and older
Budesonide nebulised	500	Ages 1 year and older
Fluticasone propionate (pMDI, standard particle, HFA)	50	Ages 4 years and older
Fluticasone furoate (DPI)	Not sufficiently studied in children aged 5 years old and below	
Mometasone furoate (pMDI, standard particle, HFA)	100	Ages 5 years and older
Ciclesonide (pMDI, extrafine particle, HFA)	Not sufficiently studied in children aged 5 years old and below	

 Table 17. Low daily ICS doses for children aged 5 years old and below.

BDP: beclomethasone dipropionate; DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; ICS: inhaled corticosteroid; pMDI: pressurised metered dose inhaler.

Adapted from Global Strategy for Asthma Management and Prevention (2024 update).<sup>9</sup>

A stepwise approach is recommended for long-term management of asthma in this age group to achieve good control (Table 18).<sup>9,68,87,89</sup> Assessment of asthma control and risk factors for asthma outcomes in children aged 5 years and below follows Table 19.

**Table 18.** Algorithm for long-term management of asthma or recurrent wheeze in children5 years and younger.

Step	Step 1	Step 2	Step 3	Step 4
Symptom	Intermittent asthma symptoms (Infrequent viral wheezing episodes with no or minimal interval symptoms/ unlikely asthma)	Persistent asthma symptoms or frequent or severe wheezing episodes	Asthma symptoms not well- controlled on low-dose ICS <i>Review the 5C</i> <i>evaluation</i>	Asthma symptoms not well-controlled on medium-dose ICS or combination therapy (LTRA)
Preferred controller	N/A	Daily low-dose ICS (Diagnostic trial of 4-8 weeks)	Medium-dose ICS	Continue controller PLUS Refer respiratory specialist for assessment
Other controller options	Consider intermittent short course of ICS at onset of viral illness	Daily LTRA OR Intermittent short course of ICS at onset of respiratory illness	Low-dose ICS + LTRA (Consider paediatrician or family medicine specialist referral)	LTRA OR Increase ICS frequency OR Add intermittent ICS
Reliever	As-needed SABA			

ICS: inhaled corticosteroids; LTRA: leukotriene receptor antagonists; SABA: short-acting  $\beta_2$ -agonists. Adapted from Global Strategy for Asthma Management and Prevention (2024 update).<sup>9</sup>

Frequent wheezing episodes are commonly encountered in infants and young children who are being sent to nursery or day care ("nursery syndrome").<sup>87</sup> The severity of the episodes needs to be taken into account to avoid overtreatment or unnecessary treatment.<sup>87</sup> Consider to discontinue treatment if there is no benefit.<sup>9</sup>

## 9 | Asthma in preschool children (5 years and younger)

 Table 19. Assessment of asthma control and risk factors for asthma outcomes in children aged 5 years and below.

A. Asthma symptom control	Level of asthma symptom control			control
In the past 4 weeks, has the patient had:		Well- controlled	Partly controlled	Uncontrolled
• Daytime asthma symptoms for more than a few minutes, > 1x a week?	Yes □ No □			
• Any activity limitation due to asthma?	Yes □ No □			
<ul> <li>SABA reliever needed for symptoms &gt; 1x a week?</li> </ul>	Yes □ No □	None of these	1-2 of these	3-4 of these
<ul> <li>Any night waking or night coughing due to asthma?</li> </ul>	Yes □ No □			
B. Future risk for poor asthma outcomes				
Risk factors for asthma exacerbations within	the nex	t few months	5:	
Uncontrolled asthma symptoms				
<ul> <li>One or more severe exacerbations (ED attendance, hospitalisation, or course of OCS) in previous year</li> </ul>				
<ul> <li>The start of the child's usual 'flare-up' season (especially if autumn/fall)</li> </ul>				
• Exposures: Tobacco smoke, indoor or outdoor air pollution, indoor allergens (e.g. house dust mites, cockroaches, pets, mould), especially in combination with viral infection				
<ul> <li>Major psychological or socio-economic problems for child and family</li> </ul>				
<ul> <li>Poor adherence with ICS medication, or incorrect inhaler technique</li> </ul>				
Outdoor pollution (NO2 and particles)				
Risk factors for persistent airflow limitation:				
Severe asthma with several hospitalisations				
History of bronchiolitis				
Risk factors for medication side effects:				
<ul> <li>Systemic: Frequent courses of OCS, high-dose and/or potent ICS</li> </ul>				
<ul> <li>Local: Moderate - to high-dose or potent ICS, incorrrect inhaler technique, failure to protect skin or eyes when using ICS by nebuliser or spacer with face mask</li> </ul>				

ED: emergency department; ICS: inhaled corticosteroids; OCS: oral corticosteroids; SABA: short-acting  $\beta_2$ -agonists. Adapted from Global Strategy for Asthma Management and Prevention (2024 update).<sup>o</sup>

# 10 Management of acute asthma exacerbations in clinical setting

#### 10.1 Definition of asthma exacerbation/asthma attack

Asthma exacerbations or asthma attacks are episodes characterised by a progressive increase in symptoms of shortness of breath, cough, wheezing and chest tightness, or some combination of these symptoms.<sup>9</sup> It is also characterised by a progressive decrease in lung function as it represents a change from the patient's usual status that is sufficient to require a change in treatment.<sup>9</sup>

Exacerbations may occur in a patient with pre-existing asthma diagnosis or occasionally, as the first presentation of asthma. Severe exacerbations can be life-threatening and can occur in patients even with mild or controlled asthma.<sup>9</sup>

#### 10.2 Goals of treatment of acute asthma exacerbations

The goals of acute asthma exacerbation treatment are:<sup>24</sup>

- To relieve airway obstruction and hypoxaemia as quickly as possible.
- To prevent complications and death.
- To prevent further relapses.

#### 10.3 General principles in the treatment of acute asthma

The general principles in the treatment of acute asthma include:9,24,68,90

- Assessing severity (mild, moderate, severe or life-threatening) while starting bronchodilator treatment immediately.
- Administering oxygen therapy to maintain oxygen saturation of 94-98%.
- Completing observations and assessments (based on clinical priorities determined by baseline severity).
- Administering systemic corticosteroids within the first hour of treatment.
- Repeated reassessment of response to treatment and treatment decision (either continuing treatment or adding on treatments) until acute asthma has resolved or patient has been admitted to hospital or transferred to an intensive care unit.
- Apart from response to treatment, the availability of drugs and facilities at the particular clinic/hospital and the experience of the attending doctor are also important factors in treating acute asthma.

#### **10.4 First-line treatment for standard therapy**<sup>9,24,68,90</sup>

## 10.4.1 Short-acting β<sub>2</sub>-agonists (SABA)<sup>9,24,68,90</sup>

- SABAs are the first-line treatment for acute asthma and are the bronchodilators of choice. It should be administered rapidly after a quick history, physical examination and vital examination are done.<sup>24,68,90</sup>
- pMDI plus spacer is favoured as it is more efficient than nebuliser for bronchodilator delivery, and it is a preferred method for children with mild to moderate acute asthma.<sup>9</sup>
- In cases of severe and life-threatening acute asthma, the combination of SABA and SAMA via nebulisation (oxygen-driven) is recommended.<sup>24,68,90,91</sup>
- However, the use of nebulisers during a respiratory pandemic carries a high risk of transmitting viral infections because they generate aerosol droplets that can spread for several metres and remain airborne for more than 30 minutes.
- Parenteral SABA should be considered in children with severe or life-threatening exacerbations.<sup>68</sup> However, the side effects including tremor and hypokalaemia must be monitored closely. Serum lactate can be used to monitor parenteral salbutamol toxicity.<sup>68</sup>

#### 10.4.2 Inhaled short-acting muscarinic antagonists (SAMA)

#### Ipratropium bromide (IB)

- Ipratropium bromide should be added to SABA If symptoms are refractory to initial β<sub>2</sub>-agonist treatment.<sup>9,24,68,90-94</sup>
- Frequent doses of ipratropium bromide (every 20-30 minutes) used in addition to B<sub>2</sub>-agonists for the first hour may be continued for a maximum two hours of a severe asthma attack, and it is safe and efficacious.<sup>68</sup> Benefit of its use is more apparent in the most severe asthma exacerbation.<sup>93,94</sup> Subsequently, the ipratropium dose may be discontinued or tapered to four to six hourly.<sup>90</sup>
- Current guidelines suggest its role in children with asthma is limited to severe and life-threatening exacerbations.<sup>9,24,90,93</sup> IB has little effect on hospital admission but has a more concerning effect of increased risk of adverse events, justifying the reason why it should not be used in moderate asthma.<sup>92-94</sup>
- Precaution must be taken to avoid contact with eyes by using a well-fitted mask or covering the eyes.

#### **10.4.3 Controlled/titrated oxygen therapy**<sup>9,24,68,90</sup>

- Children with severe and life-threatening asthma or SpO<sub>2</sub> < 94% should receive oxygen.<sup>9</sup>
- This can be delivered via nasal prong (especially if using MDI SABAs) or face-mask oxygen.<sup>90</sup>
- If the patient is acutely distressed, give oxygen-driven nebulised bronchodilators.<sup>9</sup>
- The inhaled bronchodilators and oxygen are crucial in relieving hypoxia.<sup>90</sup>
- Oxygen therapy should be titrated against pulse oximetry to maintain SpO<sub>2</sub> 94-98% in children.<sup>9,90</sup> In patients hospitalised with an acute exacerbation, controlled or titrated oxygen therapy is associated with lower mortality and better outcomes.<sup>9</sup>
- Continuous SpO<sub>2</sub> monitoring is important as SpO<sub>2</sub> may drop during sleep.

#### 10.4.4 Corticosteroids (systemic, parenteral, oral, or nebulised)<sup>9,24,68,90</sup>

- Systemic corticosteroids are essential in the treatment of acute exacerbations of asthma to hasten the recovery and it should be given early within one hour. 9.24,68,90,95
- This can be administered via the oral or IV route. The oral route is preferred as it is quicker, less expensive and less invasive.<sup>9,24</sup>
- The parenteral route is indicated in children who are vomiting or unable to tolerate orally and children with severe or life-threatening acute exacerbations.<sup>9,24,90</sup>
- Oral and parenteral corticosteroid need at least four hours to produce clinical improvement.<sup>9</sup>
- They are usually given for 3-5 days for children and 5-7 days for adolescents (12 years and above). Weaning is unnecessary unless the course of steroid exceeds 14 days.<sup>9,24,68,90</sup>
- Consider nebulised corticosteroid together with SABA and SAMA every 20 minutes during the first hour of treatment in patients with severe asthma exacerbation.<sup>9</sup>
- Inhaled corticosteroids, usually used in combination with systemic corticosteroids, have been shown to relieve asthma attacks, reduce hospital admissions, were well-tolerated and had few side effects.<sup>16</sup>
- Theoretically, nebulised corticosteroids have a faster onset of action than systemic corticosteroids (1-2 hours vs. 4 hours). They also have more local effects on airways as it reduces bronchial mucosal swelling and bronchospasms with a better safety profile and reduced side effects.<sup>96</sup>

#### 10.5 Second-line/adjunct therapies

Second-line treatment should be initiated when there is no improvement or response to the first-line treatment, or if the patient is experiencing a severe or acute life-threatening exacerbation.

#### 10.5.1 Intravenous magnesium sulphate (IV MgSO<sub>4</sub>)<sup>9,24,68,90</sup>

- Consider IV MgSO<sub>4</sub> as first-line option for adjunct/second-line intravenous treatment of severe or life-threatening exacerbations.<sup>9,68,90</sup>
- It is safe and beneficial in severe acute asthma.

#### **10.5.2** Systemic β<sub>2</sub>-agonists (parenteral or subcutaneous)

- Intravenous β<sub>2</sub>-agonists: Consider IV salbutamol in severe or life-threatening exacerbations unresponsive to the initial inhaled treatment.<sup>9,68</sup>
- Consider subcutaneous terbutaline in children with severe or life-threatening asthma with no IV access.

#### 10.5.3 Ventilatory support

- Consider early respiratory support with HFNC or NIV in severe acute asthma.
- Intubation and ventilation may be required in life-threatening asthma, or unresponsive to escalation of medical therapies.

Drug doses that are used for the management of acute asthma are shown in Table 20.

Table 20. Drug dosages in acute exacerbation.

Drugs	Formulation	Dosage
Bronchodilator		
1. SABA (short-actin	ig β <sub>2</sub> -agonists)	
Salbutamol	MDI + spacer	<ul> <li>≤ 6 years: 4-6 puffs</li> <li>&gt; 6 years : 8-10 puffs</li> </ul>
	Nebuliser solution 5 mg/ mL	<ul> <li>May administer every 20 min x 3</li> <li>0.15 mg/kg</li> <li>≤ 5 years: 2.5 mg</li> <li>&gt; 5 years: 5 mg</li> <li>Consider neat nebulised salbutamol in life-threatening asthma</li> </ul>
	Intravenous	<ul> <li>Single bolus 5-15 μg/kg over 10 minutes then 1-5 μg/kg/min thereafter</li> </ul>

Table 20. Drug dosages in acute exacerbation. (cont'd)

Drugs	Formulation	Dosage
Terbutaline	Nebuliser solution 10 mg/ mL, 2.5 mg/ mL or 5 mg/ mL respule	<ul> <li>0.2-0.3 mg/kg/dose or</li> <li>&lt; 20 kg: 2.5 mg/dose</li> <li>&gt; 20 kg: 5.0 mg/dose</li> </ul>
	Subcutaneous	• 5-10 µg/kg/dose (maximum 0.5 mg)
2. SAMA (short-actin	ng muscarinic antagonists [a	nti-cholinergic])
Ipratopium bromide (used in combination with SABA)	Nebuliser solution 250 µg/mL	<ul> <li>&lt; 6 years: 125-250 µg 4-6 hourly</li> <li>≥ 6 years: 250-500 µg 4-6 hourly</li> <li>May administer every 20 minutes x 3 in the first hour of nebulised ipratropium</li> </ul>
	MDI + spacer (inhaler)	<ul> <li>&lt; 6 years : 4 puffs every 20 minutes x 3</li> <li>≥ 6-12 years: 4-8 puffs every 20 minutes x 3</li> <li>≥ 12 years: 8 actuations every 20 minutes x 3 in the first hour</li> <li>1 puff = 20 µg</li> </ul>
3. Magnesium sulphate* (MgSO4)	Intravenous	<ul><li>Magnesium sulphate 50%,</li><li>0.1 mL/kg (50 mg/kg) IV over 20 minutes</li></ul>
4. Corticosteroids		
Prednisolone (preferably morning dose)	Oral	<ul> <li>1-2 mg/kg/day x 3-5 days</li> <li>Maximum daily dose: <ul> <li>20 mg prednisolone for children under 2 years of age</li> <li>30 mg for children aged 2-5 years</li> <li>40 mg for children 6-11 years</li> <li>50 mg for children 12 years and older</li> </ul> </li> </ul>
Hydrocortisone	IV	<ul><li> 4-5 mg/kg/dose 6-hourly</li><li> Maximum per dose: 100 mg</li></ul>
Methylprednisolone	IV	<ul> <li>1 mg/kg/dose 6-hourly on day 1, 12-hourly on day 2, and then daily</li> </ul>
Dexamethasone	PO	<ul> <li>0.6 mg/kg/dose (maximum 16 mg) OD for 1-2 days</li> </ul>
	Intramuscular	• 0.3-0.6 mg/kg/dose (maximum 15 mg)
Budesonide**	Nebulised	• 0.5 mg/dose x 3 doses within first 1 hour (maximum daily dose is 2 mg

IV: intravenous; OD: once daily; PO: per oral; SABA: short-acting  $B_2$ -agonists; SAMA: short-acting muscarinic antagonists (anti-cholinergic). \*IV MgSO<sub>4</sub>: the concentration of MgSO<sub>4</sub> needs to be < 20% if given via peripheral line. If using MgSO<sub>4</sub> 50% concentration, dilute at least 3 times. The diluent is either normal saline or dextrose 5% or dextrose saline. \*\*Can be mixed with SABA and SAMA solutions.

Adapted from Global Strategy for Asthma Management and Prevention (2024 update); National Asthma Council Australia. Australian Asthma Handbook–Quick Reference Guide; Grant EK, et al. Pediatrics. 2014; Alangari AA, et al. Chest. 2014; 9207,98

#### 10.6 Paediatric Asthma Score and Asthma Clinical Pathway

The Paediatric Asthma Score (PAS) is a valuable validated clinical tool used to assess the severity of asthma exacerbation in children (Table 21).<sup>99,100</sup> It is a standardised method that can ensure consistency in evaluation and management across different healthcare settings. The PAS incorporates objective measurements such as respiratory rate, oxygen saturation, and use of accessory muscles. The PAS when combined with Asthma Clinical Pathway, can assist healthcare providers in the evaluation and management of asthma exacerbations in children, offering benefits such as standardisation, objectivity, early recognition of severity, treatment guidance, monitoring response to treatment, communication, documentation, and education. The Asthma Clinical Pathway using PAS for the management of acute asthma in

The Asthma Clinical Pathway using PAS for the management of acute asthma in children is shown in Figure 5.

Table 21. Paediatric Asthma Score.

• Use in children aged 2-18 years with asthma exacerbation to guide inpatient, outpatient and emergency department management.

Variable	1 Point	2 Points	3 Points
RR			
2-3 years	≤ 34	35-39	> 40
4-5 years	≤ 30	31-35	> 36
6-12 years	≤ 26	27-30	> 31
>12 years	≤ 23	24-27	> 28
Oxygen requirements	> 95% on room air	90-95% on room air	<90% on room air or any supplemental oxygen
Retraction	None or intercostal	Intercostal and substernal	Intercostal, substernal and supraclavicular
Dyspnoea	Speaks in sentences	Speaks partial sentences	Speaks in single words or short phrases or grunt
Auscultation	Normal breath sounds to end-expiratory rhonchi only	Expiratory rhonchi	Inspiratory and expiratory rhonchi to disminished breath sounds

• No need to use PEF or FEV,.

#### Interpretation

Paediatric asthma score (PAS)	Severity of exacerbation
5-7	Mild
8-11	Moderate
12-15	Severe

RR: respiratory rate.

Reprinted from Kelly CS, et al. Ann Allergy Asthma Immunol. 2000 with permission.<sup>99</sup>

#### Give systemic corticosteroid Vital signs & PAS every 20 min Lethargy, cyanosis, decreasing respiratory effort and/or rising IV MgSO4/IV salbutamol Administer 100% oxygen AS SOON AS POSSIBLE Arrange for PICU/PHDW 20min X 3 back to back/ (DO NOT OVER VENTILATE) (Give SC Terbutaline if no IV + steroid stat and every + ipratropium bromide respiratory failure Life-threatening Nebulised salbutamol (within 20 min of triage) Support ventilation Consider ABG test cardiopulmonary To assess STAT Continuous monitoring continuous admission access) 00 CXR MDI salbutamol + ipratropium bromide Complete all of the above within 60 min Continue with salbutamol + ipratropium N MgSO<sub>A</sub>/IV salbutamol/SC Terbutaline Administer oxygen to maintain SpO<sub>3</sub> Nebulised salbutamol + ipratropium to move to "life-threatening respiratory Vital signs & PAS every 20-30 min stat and every 20 min X 3 (via spacer) every 20 min X 3 (MDI + spacer OR neb) bromide + steroid stat and every (Give SC Terbutaline if no IV access) Continuous cardiopulmonary Give oral/IV corticosteroid AS SOON AS POSSIBLE IV MqSO "/IV salbutamol PHDW/PICU admission If PAS remained the same Severe (within 20 min of triage) If PAS improving (8-11) Consider ABG test failure pathway" monitoring If PAS increase 20 min X 3 94-98% of triage AC AND If PAS reduced (5-7) to consider every 20 min (via spacer) X 3 Give oral corticosteroid AS If PAS increase (12-15) to move If PAS remained the same (PAS 8-11) to consider admission to Short course prednisolone MDI salbutamol stat and Vital signs & PAS every move to "severe pathway" Administer oxygen to maintain SpO, 94-98% Complete all of the above inhaler; PAS: Paediatric Asthma Score; PHDW: paediatric high dependency ward; Provide discharge plan nebulised salbutamol SOON AS POSSIBLE ABG: arterial blood gas: CXR: chest X-ray: IV: intravenous: MDI: metered dose (within 60 min of triage) within 60 min of triage Moderate 30-60 min to "severe pathway" PICU: paediatric intensive care unit; PRN: as-needed; SC: subcutaneous. discharge • Short course prednisolone If PAS increase (8-11) to move MDI salbutamol stat and Vital signs & PAS every Complete all of the above If PAS remained the same or less (PAS 5-7) to consider Provide discharge plan nebulised salbutamol to "moderate pathway" within 60 min of triage every 60 min PRN corticosteroid (oral) (via MDI and spacer) PAS 5-7) 60min Mild Give systemic discharge AC

Figure 5: Acute asthma management pathway in children aged 2-18 years using the Paediatric Asthma Score.

to move to "moderate pathway"

#### Management of acute asthma exacerbations in clinical setting 10

.

#### 10.7 Therapies not recommended for acute exacerbation<sup>9,24,68,90</sup>

- Antibiotics Unless the patients are suspected to have concurrent pneumonia (fever, purulent sputum or radiographic evidence of pneumonia) or other bacterial infections.
- Intramuscular (IM) adrenaline Indicated as add-on therapy of acute exacerbations associated with anaphylaxis and angioedema. It is not otherwise routinely recommended.
- Antihistamines May be indicated for acute treatment of anaphylaxis and angioedema.
- Sedatives Generally should be avoided especially in young children as it may cause drowsiness and hypoventilation/apnoea.
- Mucolytics Not recommended as it may worsen cough.
- Nebulised hypertonic saline Not recommended as it causes bronchoconstriction.
- Chest physiotherapy Not recommended as it may cause patient discomfort and bronchospasm.

#### 10.8 Role of chest x-ray in acute exacerbation<sup>9</sup>

Chest X-ray is not routinely recommended but is indicated in the following circumstances:

- Suspected pneumothorax or pneumomediastinum (i.e. presence of subcutaneous emphysema).
- Lung collapse or consolidation.
- Life-threatening asthma not responding to treatment satisfactorily.
- Requirement for ventilation.
- Suspected foreign body inhalation

The need for chest X-ray must **not** compromise emergency medical treatment.

#### 10.9 Blood gases

Blood gas measurements should be considered if there are life-threatening features not responding to treatment. Normal or raised partial pressure of carbon dioxide (PaCO<sub>2</sub>) levels are indicative of worsening asthma.<sup>9</sup>

## 10.10 Management of acute asthma exacerbations

- Mild exacerbation can be usually treated at home if the parents/caregivers are prepared and the patient has a personal asthma action plan.<sup>9</sup>
- Moderate or severe exacerbations require treatment at a healthcare facility.<sup>9</sup>
- Asthma exacerbation requires prompt treatment.
- A patient with brittle asthma, a history of ICU admissions for asthma or parents who are either uncomfortable or unable to manage the child's acute exacerbation should be admitted to hospital.<sup>68</sup>

#### **10.11 Respiratory support and safe transfer**

Acute presentation of asthma can be very dynamic. In some rare occasions, there may be an initial clinical improvement with treatment before a rapid deterioration.<sup>101</sup> Hence, it is crucial to recognise severe or life-threatening asthma prior to transfer from the emergency department or ward to the acute care area, so that prompt treatment can be initiated to improve oxygenation and ventilation.<sup>101</sup>

In cases requiring respiratory support, the choice of respiratory support includes oxygen therapy, high-flow nasal cannula (HFNC), non-invasive ventilation (NIV) (e.g. continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BiPAP]) and invasive mechanical ventilation. HFNC and NIV are preferred methods of respiratory support compared to assisted invasive ventilation. Invasive mechanical ventilation may lead to possible complications, e.g. tension pneumothorax or overinflated lungs, causing loss of cardiac output.<sup>102-103</sup>

However, in life-threatening asthma, intubation and invasive mechanical ventilation, if required, should **NOT** be delayed.<sup>9</sup> The choices of sedation agent in preparation for intubation are:

- 1. Ketamine (preferred because of its bronchodilators properties)
- 2. Midazolam (an option because of its wide availability)

Avoid the use of morphine and atracurium, which are both associated with histamine release.  $^{\rm 58}$ 

If intubated, the recommended mechanical ventilation settings are:

- 1. Low respiratory rate (to avoid breath stacking and auto-positive end expiratory pressure (PEEP)  $^{\rm 104}$
- 2. PEEP of 4-6 cmH<sub>2</sub>O
- 3. Peak inspiratory pressure (PIP) of  $< 35 \text{ cmH}_2\text{O}$

Transfer to the acute care area should only be done when the patient's haemodynamic status is stable. Safe transfer of patients with severe or lifethreatening exacerbation of bronchial asthma can be complex. A good understanding of complications particularly associated with intubation and mechanical ventilation would improve the patient's outcome.

Requirements for safe transfer include:

- 1. Pre-transfer optimisation of the patient's blood pressure, heart rate and SpO<sub>2</sub>
- 2. Competent accompanying personnel
- 3. Functional and appropriately sized equipment
- 4. Sufficient supplies (medications/oxygen/batteries)
- 5. Effective communication along with teamwork

Shared decision to transfer should be made by both the referring and receiving teams, with the most experienced clinician providing guidance.

During transfer, common complications that may occur include hypotension and severe bronchospasm with acute hypercarbia. Hence, fluid resuscitation with or without inotropic support and effective nebulisation on respiratory support are important to maintain stability throughout the journey.

A sample checklist for transferring patients with severe or life-threatening exacerbation of bronchial asthma is shown in Table 22, whereas preparation of accompanying personnel and medications are detailed in Table 23. Refer to algorithm in Figure 6 for pre-transfer emergency ventilation management and stabilisation.

**Pre-departure During transfer** On arrival □ Ensure that primary team □ Continuous close monitoring, □ Ensure respiratory and referral has been made including vital signs haemodynamic stability □ Ensure that all imaging and Documentation of the □ Handover of patient to point-of-care investigations vital signs/events and the receiving team have been reviewed interventions □ Ensure that medications have □ Ensure effective nebulisation been served on respiratory support □ Brief team on care plan and disposition

Table 22. Preparation checklist for transfer.

□ Update caregivers and address concerns, including consent

## 10 | Management of acute asthma exacerbations in clinical setting

#### Table 22. Preparation checklist for transfer. (cont'd)

Pre-departure	During transfer	On arrival
□ Identify personnel escorting the patient (see Table 23)	Maintenance of sedation of choice if intubated	
<ul> <li>Alert and ensure that the receiving Intensive Care Unit (ICU) team is ready</li> </ul>		
Transfer patient onto a portable monitor		
Reassess vital signs prior to departure		
□ Check the cardiac monitor		
$\hfill\square$ Ensure that airway is secured		
Ensure that the oxygen tank is full or adequate for transfer		
□ Check the ventilator settings (if on ventilator) and ensure that the battery is charged, and tubing is well-connected		
Ensure that IV lines are functioning	1	
<ul> <li>Ensure that medications are served and sufficient for the duration of transfer (see Table 23)</li> </ul>		
Ensure that emergency drugs are prepared and any infusion pump used is charged (any inotropes/vasopressor needs to be prepared beforehand, if necessary)		
<ul> <li>Ensure that the patient is secured on the transport trolley/stretcher</li> </ul>		
<ul> <li>Ensure that a portable resuscitation kit is available for transport</li> </ul>		
Ensure all documentations are brought along for transport		

Adapted from Advanced Paediatric Life Support (APLS) 7<sup>th</sup> edition; Paediatric Emergency Department, Hospital Tunku Azizah. Transfer checklist 2024; Paediatric Emergency Department, Hospital Tunku Azizah. Interfacility transfer monitoring form 2024; Hospital Tunku Azizah. Referral and Transfer Policy 2024.<sup>105-108</sup>

## 10 | Management of acute asthma exacerbations in clinical setting

and they

55

 Table 23. Pre-departure preparation of accompanying personnel and medications.

Accompanying personnel	Medication
Most competent personnel deemed appropriate and essential for transfer	□ Sedation (if intubated and ventilated) IV ketamine 10-40 µg/kg/min <i>OR</i> IV midazolam 1-4 µg/kg/min
<ul> <li>At least 1 personnel capable of airway management and paediatric resuscitation (if available):</li> <li>1 medical officer</li> <li>1 paramedic</li> </ul>	□ Acute asthma medications (Refer to Table 20)



Figure 6: Algorithm for pre-transfer emergency ventilation management and stabilisation.

#### 10.12 Discharge planning and follow-up

- Children can be discharged when stable on four-hourly inhaled bronchodilators, that can be continued at home.<sup>68</sup>
- They must be clinically stable, able to eat and sleep well, and achieve PAS  $\leq 7.68$
- SpO<sub>2</sub> should be > 94% in room air.<sup>68</sup>
- Post-bronchodilator PEF and/or FEV, should be > 70% of best or predicted values.
- Arrange follow-up by primary care services within two weeks or earlier with a written asthma action plan.
- Arrange follow-up in a paediatric asthma clinic within one to two months.<sup>68</sup>
- Arrange referral to a paediatric respiratory specialist if it was a life-threatening exacerbation.

# 11 Asthma action plan (AAP)

An AAP is a written asthma plan that outlines a symptom-guided self-management plan for the individual patient.<sup>109</sup> Objectives are to prevent prolonged and severe asthma exacerbations, adverse patient outcomes and morbidity. In addition, it will help reduce subsequent healthcare services utilisation.

Evidence shows that using AAPs can reduce hospital admissions, emergency department visits, unscheduled visits to the doctor, school absences and nocturnal awakenings.<sup>110</sup> It is recommended for all children with asthma, especially those with partly or uncontrolled asthma, a history of severe exacerbation, uncontrolled asthma and high-risk asthma patients.<sup>24,109</sup>

## 11.1 What should the AAP entail?

It should include basic information about the child, and their doctor's contact detail. It may also include the contact details of the patient's carer or emergency contact person.<sup>109</sup>

Other information to include in the AAP is as below:<sup>24,109</sup>

- 1. Controller therapy, including doses and frequency of treatment.
- 2. List of danger signs, and when and how to seek urgent medical help.
- 3. Outline for the patient and/or their carer to recognise asthma exacerbation symptoms and signs.
- 4. Instruction on steps to be taken in response to asthma exacerbation.

A sample of an AAP is shown in Figure 7 below.

## 11 | Asthma action plan (AAP)

#### PELAN TINDAKAN ASMA (ASTHMA ACTION PLAN)

X Allow

Nama Hospital

NAMA PESAKIT	RAWATAN ASMA BERDASAKAN ZON:
TARIKH	1. ZON HIJAU bermakna guna ubat PENCEGAH (Preventer)
	2. ZON KUNING bermakna guna ubat PENCEGAH DAN PELEGA (Reliever)

3. ZON MERAH

bermakna dapatkan bantuan dari doktor

#### ZON HIJAU

Tanda anak anda SIHAT	Gunakan ubat PENCEGAH setiap hari		
<ul> <li>Pernafasan biasa nafas tidak laju</li> </ul>	UBAT PENCEGAH	SEDUTAN/MAKAN	KEKERAPAN
<ul> <li>Tiada batuk atau nafas berbunyi</li> </ul>			
<ul> <li>Boleh bermain dan bersekolah</li> </ul>			
<ul> <li>Tidur lena pada waktu malam</li> </ul>	Jika ada tanda asma semasa bersenam	Sebelum bersenam	

#### ZON KUNING

Tanda anak TIDAK SIHAT	Sambung ubat PENCEGAH seperti di atas dan tambahkan ubat PELEGA		
<ul> <li>Batuk pada waktu</li> </ul>	UBAT PELEGA	SEDUTAN	KEKERAPAN
maiam			
<ul> <li>Batuk yang berterusan</li> </ul>			
<ul> <li>Nafas laju dari biasa</li> </ul>			
<ul> <li>Bunyi berdehit (wheezing)</li> </ul>			

#### ZON MERAH

KECEMASAN	Guna ubat PENCEGAH SEPERTI BIASA D	AN PELEGA dan jumpa	doctor dengan segera
<ul> <li>Ubat pelega tidak berkesan</li> </ul>	UBAT PELEGA	SEDUTAN	KEKERAPAN
<ul> <li>Pernafasan susah dan cepat</li> </ul>			Setiap 15 minit
<ul> <li>Bibir kebiruan/ kehitaman</li> </ul>			sehingga anda tiba di HOSPITAL
<ul> <li>Anak anda nampak keletihan dan sukar bercakap</li> </ul>			BERDEKATAN

Tandatangan :

Nama Doktor :

Adapted from Ministry of Health Malaysia and Malaysian Thoracic Society.<sup>111</sup>

Figure 7: Sample of an Asthma Action Plan for paediatric patients (in Bahasa Malaysia).

#### 11.2 What to do with the AAP?

The AAP must be kept in an obvious place that is easy to see and access, e.g. sticking the plan on the refrigerator or the family noticeboard. Parents should also provide a copy of the AAP to the school teacher, nursery, babysitter/childcare centre and family members.<sup>24</sup> Regular review of the AAP is important, as it may change over time depending on the child's asthma control status.<sup>24,47</sup>

- Ministry of Health Malaysia. National Health and Morbidity Survey 2023 Key Findings and Technical Report. Available at https://iku.nih.gov.my/nhms.
- International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J.* 1998;12:315-35.
- Azizi BHO. Respiratory symptoms and asthma in primary school children in Kuala Lumpur. Acta Paediatr Japan. 1990;32:183-7.
- Norzila MZ, Haifa AL, Deng CT, Azizi BHO. Prevalence of childhood asthma and allergy in an inner city Malaysian community: intra-observer reliability of two translated international questionnaire. Med J Malaysia. 2000;55:33-9.
- Surdi Roslan MJ, Mohd Johari MN, Abdul Mubing NM, Harif Fadzilah H. Sociodemographic profile of childhood asthma among children in Selangor-Malaysia. Paediatr Res. 2011;70:557.
- 6. Serebrisky D, Wiznia A. Pediatric asthma: a global epidemic. Ann Glob Health. 2019;85(1):6.
- 7. Bousquet J, Van CP, Khaltaev N. Allergic rhinitis and its impact on asthma. J Allergy Immunol. 2001;108:S147-334.
- Asher MI, Montefort S, Björkstén B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet. 2006;38(953):733-43. Erratum in: Lancet. 2007;370(95593):1128.
- Global Strategy for Asthma Management and Prevention (2024 update). Available at https://ginasthma.org/wp-content/ uploads/2024/05/GINA-2024-Main-Report-WMS-1.pdf. Accessed on 10 May 2024.
- Saglani S, Malmstorm K, Pelkonen AS, et al. Airway remodelling and inflammation in symptomatic infants with reversible airflow obstruction. Am J Respir Crit Care Med. 2005;171:722-72.
- Bacharier LB, Boner A, Carlsen K-H, et al. Diagnosis and treatment of asthma in childhood: a PRACTALL consensus report. Allergy. 2008;63:5-34.
- 12. Trivedi M, Denton E. Asthma in children and adults—what are the differences and what can they tell us about asthma? Front Pediatr. 2019;7:256.
- 13. Lai CK, De Gui TS, Kim YY, et al. Asthma control in Asia Pacific region: the asthma insights and reality in Asia-Pacific Study. J Allergy Clin Immunol. 2003;111:263-8.
- Wong G, Gunasekera K, Hong J, Hsu J. AlRIAP 2: childhood asthma control in Asia according to the Global Initiative for Asthma (GINA) criteria. J Allergy Clin Immunol. 2008;121(2):S95.
- Chan PWK, Norzila MZ. Prescribing patterns for childhood asthma treatment in general practice. Med J Malaysia Medical. 2003;58:475-81.
- Edmonds ML, Camargo CA Jr, Pollack CV Jr, Rowe BH. Early use of inhaled corticosteroids in the emergency department treatment of acute asthma. Cochrane Database Syst Rev. 2003;(3):CD002308. Update in: Cochrane Database Syst Rev. 2012;12:CD002308.
- 17. Chong J, Haran C, Chauhan BF, Asher I. Intermittent inhaled corticosteroid therapy versus placebo for persistent asthma in children and adults. Cochrane Database Syst Rev. 2015;2015(7):CD011032.
- Academy of Medicine of Malaysia. Clinical practice guidelines for the management of childhood asthma 2014. Available at shttps://www.mts.org.my/resources/CPG\_ChildhoodAsthma.pdf. Accessed on 18 January 2023.
- Reddel HK, Taylor DR, Bateman ED, et al. An official American Thoracic Society/European Respiratory Society statement: asthma control and exacerbations: standardizing endpoints for clinical asthma trials and clinical practice. Am J Respir Crit Care Med. 2009;180(1):59-99.
- Becker A, Berube D, Chad Z, et al. Canadian pediatric asthma consensus guidelines 2003 (updated to December 2004). CMAJ. 2005;172:S12-4.
- 21. Bousquet J, Kjellman NIM. Predictive value of tests in childhood allergy. J Allergy Clin Imunol. 1986;78:1019-22.
- 22. Marchant JM, Masters B, Taylor S, et al. Evaluation and outcome of young children with chronic cough. Chest. 2006;129:1132-41.
- Chang AB, Glomb WB. Guidelines for evaluating chronic cough in pediatrics: ACCP evidence-based clinical practice guidelines. Chest. 2006;129(1):260S-83S.
- 24. National Heart, Lung, and Blood Institute (NHLBI). Guidelines for the Diagnosis and Management of Asthma (EPR-3), 2007.
- 25. Mueller GA, Eigen H. Pediatric pulmonary function testing in asthma. Pediatr Clin North Am. 1992;39(6):1243-58.
- 26. Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005;26(5):948-68.
- Chan EY, Dundas I, Bridge PD, Healy MJ, McKenzie SA. Skin-prick testing as a diagnostic aid for childhood asthma. Pediatr Pulmonol. 2005;39:558-62.
- Baraldi E, Dario C, Ongaro R, et al. Exhaled nitric oxide concentrations during treatment of wheezing exacerbations in infants and young children. Am J Respir Crit Care Med. 1999;159:1284-8.

#### 2024 Consensus Statement Fourth Edition

and the second

- 29. Moeller A, Franklin P, Hall GL, et al. Inhaled fluticasone dipropionate decreases levels of nitric oxide in recurrent wheezy infants. Pediatr Pulmonol. 2004;38:250-5.
- Ministry of Health Malaysia. Respiratory medication therapy adherence clinic protocol: asthma/COPD (adult & pediatric). Second edition. Available at https://www.pharmacy.gov.my/v2/sites/default/files/document-upload/book.-protocolrespiratory-2.6-ver(2\_0.pdf. Accessed on 20 January 2023.
- Richter DC, Joubert JR, Nell H, Schuurmans MM, Irusen EM. Diagnostic value of post-bronchodilator pulmonary function testing to distinguish between stable, moderate to severe COPD and asthma. Int J Chron Obstruct Pulmon Dis. 2008;3(4):693-9.
- Child Health BC Provincial Asthma Guideline Pediatric Asthma Education Checklist. Available at https://www.google. com/search?q=Childhood+asthma+education+checklist&sxsf=APwXEddA\_Htu1\_oUf6cRrBfVs7mUhf4ePw:1680169977 013&source=Inms&tbm=isch&sa=X&ved=2ahUKEwjngZH1sIP-AhXWcGwGHX\_UAOSQ\_AUoAXoECAEQAw&biw=130 8&bih=770&dpr=0.9#imgrc=PmF0PO-1IAkw4M. Accessed on 30 March 2023.
- 33. Fadzil A, Norzila MZ. Parental asthma knowledge. Med J Malaysia. 2002;57(4):474-81.
- Hachim MY, Alqutami F, Hachim IY, et al. The role of systems biology in deciphering asthma heterogeneity. Life. 2022;12(10):1562.
- Farber HJ, Groner J, Walley S, Nelson K. Protecting children from tobacco, nicotine, and tobacco smoke. Pediatrics. 2015;136(5): e1439-67.
- He Z, Wu H, Zhang S, et al. The association between secondhand smoke and childhood asthma: a systematic review and meta-analysis. Pediatr Pulmonol. 2020;55(10):2518-31.
- Burke H, Leonardi-Bee J, Hashim A, et al. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. Pediatrics. 2012;129(4):735.
- Feleszko W, Ruszczyński M, Jaworska J, Strzelak A, Zalewski BM, Kulus M. Environmental tobacco smoke exposure and risk of allergic sensitisation in children: a systematic review and meta-analysis. Arch Dis Child. 2014;99(11):985-92.
- Bao Y, Chen Z, Liu E, Xiang L, Zhao D, Hong J. Risk factors in preschool children for predicting asthma during the preschool age and the early school age: a systematic review and meta-analysis. Curr Allergy Asthma Rep. 2017;17(12):85.
- 40. Zacharasiewicz A. Maternal smoking in pregnancy and its influence on childhood asthma. ERJ Open Res. 2016;2(3).
- Cook DG, Strachan DP. Parental smoking and prevalence of respiratory symptoms and asthma in school age children. Thorax. 1997;52(12):1081.
- Khreis H, de Hoogh K, Nieuwenhuijsen MJ. Full-chain health impact assessment of traffic-related air pollution and childhood asthma. Environ Int. 2018;114:365.
- 43. Azizi BHO, Henry RL. The effects of indoor environmental factors on respiratory illnesses in primary school children in Kuala Lumpur. Int J Epidemiology. 1991;20:144-50.
- Azizi BHO, Zulkifli I, Kassim MS. Indoor air pollution and asthma in hospitalised children in a tropical environment. J Asthma. 1995;32:413-8.
- 45. Platts-Mills TAE, Rakes GP, Heymann PW. The relevance of allergen exposure to the development of asthma in childhood. J Allergy Clin Immunol. 2000;105:S503-8.
- Morgan WJ, Crain EF, Gruchalla RS, et al. Results of a home-based environmental Intervention among urban children with asthma. N Engl J Med. 2004;351:1068-80.
- 47. Pijnenburg MW, Baraldi E, Brand PL, et al. Monitoring asthma in children. Eur Resp J. 2015;45(4):906-25.
- 48. O'Connor GT. Allergen avoidance in asthma: what do we do now? J Allergy Clin Immunol. 2005;116:26-30.
- Sicherer SH, Sampson HA. Food allergy: a review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. J Allergy Clin Immunol. 2018;141(1):41-58.
- 50. Bird JA, Burks AW. Food allergy and asthma. Prim Care Respir J. 2009;18(4):258-65.
- Jackson DJ, Gern JE, Lemanske Jr RF. The contributions of allergic sensitization and respiratory pathogens to asthma inception. J Allergy Clinl Immunol. 2016;137(3):659-65.
- Westergren T, Fegran L, Nilsen T, Haraldstad K, Kittang OB, Berntsen S. Active play exercise intervention in children with asthma: a PILOT STUDY. BMJ Open. 2016;6(1):e009721.
- Egan KB, Ettinger AS, Bracken MB. Childhood body mass index and subsequent physician-diagnosed asthma: a systematic review and meta-analysis of prospective cohort studies. BMC Pediatr. 2013;13(1):121.
- Forno E, Weiner DJ, Mullen J, et al. Obesity and airway dysanapsis in children with and without asthma. Am J Respir Crit Care Med. 2017;195(3):314.
- 55. Wright AL, Holberg CJ, Taussig LM, Martinez FD. Factors influencing the relation of infant feeding to asthma and recurrent wheeze in childhood. *Thorax.* 2001;56:192-7.
- Kramer MS, Matush L, Vanilovich I, et al. Effect of prolonged and exclusive breast feeding on risk of allergy and asthma: cluster randomised trial. BMJ. 2007;335(7624):815.
- Lodge CJ, Tan DJ, Lau MX, et al. Breastfeeding and asthma and allergies: a systematic review and meta-analysis. Acta Paediatr. 2015;104(467):38.

- 58. British National Formulary 78—September 2019 to March 2020. London; BMJ Group and Pharmaceutical Press; 2019.
- O'Byrne P, Fabbri LM, Pavord ID, Papi A, Petruzzelli S, Lange P. Asthma progression and mortality: the role of inhaled corticosteroids. Eur Resp J. 2019;54(1):1900491.

--

- 60. Drotar D, Bonner MS. Influences on adherence to pediatric asthma treatment: a review of correlates and predictors. J Dev Behav Pediatr. 2009;30:574-82.
- 61. Anuradha KWDA, Prematilake GLDC, Batuwita BAUI, et al. Effect of long term inhaled corticosteroid therapy on adrenal suppression, growth and bone health in children with asthma. BMC Pediatr. 2019;19(1):1-6.
- 62. Quirt J, Hildebrand KJ, Mazza J, et al. Asthma. Allergy Asthma Clin Immunol. 2018;14(Suppl 2):50.
- 63. Sharma S, Hashmi MF, Chakraborty RK. Asthma medications. 2022. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–.
- 64. Abosamak NR, Shahin MH. Beta2 receptor agonists and antagonists. In: StatPearls [Internet] 2023 Feb 27. StatPearls Publishing.
- US FDA. SINGULAIR<sup>®</sup> (montelukast sodium). Available at https://www.accessdata.fda.gov/drugsatfda\_docs/ label/2012/021409s036lbl.pdf. Accessed on 15 March 2024.
- 66. FitzGerald JM, Boulet LP. The CONCEPT trial: a 1-year , multicentre, randomized double blind dummy comparison of a stable dosing regimen of salmeterol/fluticasone propionate with an adjustable maintenance dosing regimen of formoterol/budesonide in adults with persistent asthma. *Clin Thor.* 2005;27:393-406.
- 67. Hagan JB, Samant SA, Volcheck GW, et al. The risk of asthma exacerbation after reducing inhaled corticosteroids: a systematic review and meta-analysis of randomized controlled trials. Allergy. 2014;69(4):510-6.
- British Thoracic Society and Scottish Intercollegiate Guidelines Network (SIGN). British Guidelines on the management of asthma, May 2006, revised June 2019.
- 69. Abul MH, Phipatanakul W. Severe asthma in children: evaluation and management. Allergol Int. 2009;68:150-157.
- 70. Ramratnam SK, Bacharier LB, Guilbert TW. Severe asthma in children. J Allergy Clin Immunol Pract. 2017;5(4):889-98.
- 71. Pijnenburg MW, Fleming L. Advances in understanding and reducing the burden of severe asthma in children. Lancet Respir Med 2020;8:1032-1044.
- Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J. 2014;43:343-73.
- Zaazouee MS, Alwarraqi AG, Mohammed YA, et al. Dupilumab efficacy and safety in patients with moderate to severe asthma: a systematic review and meta-analysis. Front Pharmacol. 2022;13:992731.
- Menzies-Gow A, Wechsler ME, Brightling CE, et al. Long-term safety and efficacy of tezepelumab in people with severe, uncontrolled asthma (DESTINATION): a randomised, placebo-controlled extension study. Lancet Respir Med. 2023;11(5):425-38.
- Parsons JP, Hallstrand TS, Mastronarde JG, et al. An official American Thoracic Society clinical practice guideline: exerciseinduced bronchoconstriction. Am J Respir Critic Care Med. 2013;187:1016-27.
- Gillette C, Rockich-Winston N, Kuhn JA, Flesher S, Shepherd M. Inhaler technique in children with asthma: a systematic review. Acad Pediatr. 2016;16(7):605-15.
- Capanoglu M, Dibek Misirlioglu E, Toyran M, Civelek E, Kocabas CN. Evaluation of inhaler technique, adherence to therapy and their effect on disease control among children with asthma using metered dose or dry powder inhalers. J Asthma. 2015;52(8):838-45.
- van Geffen WH, Douma WR, Slebos DJ, Kerstjens HA. Bronchodilators delivered by nebuliser versus pMDI with spacer or DPI for exacerbations of COPD. Cochrane Database Syst Rev. 2016;8:CD011826.
- Malaysian Thoracic Society. The Malaysian Thoracic Society recommendations on inhalational therapy during the COVID-19 pandemic. Available at https://mts.org.my/download/MTS\_Recommendations\_on\_Inhalational\_Therapy\_ During\_COVID19\_Pandemic.pdf. Accessed on 2 April 2024.
- Van Aalderen WM, Garcia-Marcos L, Gappa M, et al. How to match the optimal currently available inhaler device to an individual child with asthma or recurrent wheeze. NPJ Prim Care Respir Med. 2015;25(1):1-7.
- 81. Martinez FD, Wright AL, Taussig LM, et al. Asthma and wheezing in the first six years of life. New Engl J Med. 1995;332(3):133-8.
- Brand PL, Caudri D, Eber E, et al. Classification and pharmacological treatment of preschool wheezing: changes since 2008. Eur Respir J. 2014;43(4):1172-7.
- Brand PL, Baraldi E, Bisgaard H, et al. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. Eur Respir J. 2008;32(4):1096-110.
- 84. Ducharme FM, Tse SM, Chauhan B. Diagnosis, management, and prognosis of preschool wheeze. Lancet. 2014;383(9928):1593-604.
- Huffaker MF, Phipatanakul W. Utility of the Asthma Predictive Index in predicting childhood asthma and identifying disease-modifying interventions. Ann Allergy Asthma Immunol. 2014;112(3):188-190.

 Pedersen SE, Hurd SS, Lemanske RF, Jr., et al. Global strategy for the diagnosis and management of asthma in children 5 years and younger. Pediatr Pulmonol. 2011;46(1):1-17.

- 87. Bush A. Recent advances in the management of preschool wheeze. African J Respir Med. 2016;11(2):7-11.
- Ducharme FM, Dell SD, Radhakrishnan D, et al. Diagnosis and management of asthma in preschoolers: a Canadian Thoracic Society and Canadian Paediatric Society position paper. Paediatr Child Health. 2015;20(7):353-61.
- 89. Chavasse RJ, Kerr M. Asthma in children. Medicine. 2016;44(5):281-6.
- 90. National Asthma Council Australia. Australian Asthma Handbook–Quick Reference Guide, Version 1.0. 2014.
- Plotnick LH, Ducharme FM. Combined inhaled anticholinergic agents and beta-2-agonists for initial treatment of acute asthma in children. Cochrane Database Syst Rev. 2000;2:CD000060.
- Vézina K, Chauhan BF, Ducharme FM. Inhaled anticholinergics and short-acting beta-agonists versus short-acting beta2agonists alone for children with acute asthma in hospital. Cochrane Database Syst Rev. 2014;7:CD010283.
- Wyatt E, Borland M, Doyle S, Geelhoed G. Metered dose inhaler ipratropium bromide in moderate acute asthma in children: a single blinded randomised controlled trial. J Paediatr Child Health. 2015;51:192-8.
- 94. Colin VEP, Noel EC. The current role of ipratropium bromide in an acute exacerbation of asthma. J Paediatr Child Health. 2015;51:751-2.
- Rowe BH, Spooner C, Ducharme F, Bretzlaff J, Bota G. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database Syst Rev.* 2001;1:CD002178.
- Horvath G, Wanner A. Inhaled corticosteroids: effects on the airway vasculature in bronchial asthma. Eur Respir J. 2006; 27:172–87.
- 97. Grant EK, Matthew PG, Andrea KM, et al. Dexamethasone for acute asthma exacerbations in children: a meta-analysis. Pediatrics. 2014,133(3):493-9.
- Alangari AA, Malhis N, Mubasher M, et al. Budesonide nebulization added to systemic prednisolone in the treatment of acute asthma in children: a double-blind, randomized, controlled trial. Chest. 2014;145(4):772-8.
- Kelly CS, Andersen CL, Pestian JP, et al. Improved outcomes for hospitalized asthmatic children using a clinical pathway. Ann Allergy Asthma Immunol. 2000;84(5):509-16.
- Jose JK, Namboodiripad A. Validation of the Paediatric Asthma Score (PAS) in evaluation of acute exacerbation of asthma in children. J Nepal Paediatr Soc. 2023;43(1):95-8.
- 101. Maselli DJ, Peters JI. Medication regimens for managing acute asthma. Respi Care. 2018;63(6):783-96.
- 102. Hsu CW, Sun SF. latrogenic pneumothorax related to mechanical ventilation. World J Crit Care Med. 2014;3(1):8.
- Kumar AK, Anjum F. Ventilator-induced lung injury (VILI) [Updated 2022 Dec 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563244/
- Chanques G, Kress JP, Pohlman A, et al. Impact of ventilator adjustment and sedation-analgesia practices on severe asynchrony in patients ventilated in assist-control mode. Crit Care Med. 2013;41(9):2177-87.
- Advanced Life Support Group, Stephanie Smith (Editor). Advanced Paediatric Life Support (APLS) 7th edition. John Wiley & Sons (Wiley-Blackwell); 2023.
- 106. Paediatric Emergency Department, Hospital Tunku Azizah. Transfer checklist 2024.
- 107. Paediatric Emergency Department, Hospital Tunku Azizah. Interfacility transfer monitoring form 2024.
- 108. Hospital Tunku Azizah. Referral and Transfer Policy 2024.
- PORTAL MyHEALTH. Asthma Action Plan. Available at http://www.myhealth.gov.my/en/asthma-action-plan/. Accessed on 29 March 2023.
- Gibson PG, Powell H, Wilson A, et al. Self-management education and regular practitioner review for adults with asthma. Cochrane Database Syst Rev. 2002;3:CD001117.
- Ministry of Health Malaysia and Malaysian Thoracic Society. Asthma Kidz Education Programme. Available at https://www. infosihat.gov.my/images/media\_sihat/lain\_lain/pdf/Carta%20Selak%20Program%20Pendidikan%20Kidz%20Asthma.pdf. Accessed on 31 March 2023.

# Acknowledgement

This clinical practice guideline was developed with the support of an unconditional educational grant provided to the Malaysian Thoracic Society by AstraZeneca, Sanofi, and GlaxoSmithKline. Representatives of these entities were not involved in any aspect of the deliberation process, content development, or editorial review of this document.