# PAPP Clinical Practice Guidelines for Pediatric Asthma 2021

Philippine Academy of Pediatric Pulmonologists, Inc.

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PAPP Clinical Practice Guidelines for Pediatric Asthma 2021



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**Consensus Panel**

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We would like to thank Antonio and Ma. Asuncion Batoy, of Bohol Province, for their valuable perspective as a family with asthma in a rural setting. We dedicate this Philippine Clinical Practice Guideline to Filipino families with asthma.

# Message from the PAPP President

**Nepthalie R. Ordonez, MD, FPPS, FPAPP**

**The Philippine Academy of Pediatric Pulmonologists is honored and delighted to bring to fore the PAPP Clinical Practice Guideline for Pediatric Asthma 2021.**

**It has been almost 20 years now since the last pediatric asthma guideline was published in 2002. We are proud and excited to share with you the hard work accomplished by the PAPP Asthma Committee headed by Dr. Rozaida Villon, together with the dedicated brilliant minds of her members who have devoted their valuable time and efforts to come up with this manuscript in spite of the ongoing pandemic.**

**The guideline has fully considered the fast-paced changes, breakthroughs and evidence-based recommendations from the different internationally accepted asthma guidelines and merged them with the local setting, so that it will be more relevant to our pediatric practice.**

**Coming up with a guideline update is actually very tedious, expensive and time consuming, yet, despite the odds, our academy remains rooted to our goal of saving our children's lungs through sharing the expertise to all physicians in the practice of childcare. It is our hope that this guideline will help you in your decisions and in your approach in managing an asthmatic child.**

**May God bless the intentions of our hearts, and the work of our hands.**

# Message from the PAPP Immediate Past President

**Regina M. Canonizado, MD, MHA, FPPS, FPAPP**

**The healthcare profession will always be faced with everyday challenges in the diagnosis and management of bronchial asthma. As pediatricians, we have in our hands, volumes of scientific publication which we get to turn into, but we have been wanting in recommendations and guidelines endorsed by our own societies and experts several years after our very first national asthma guideline. It is along this line that we really recognize and highly appreciate the hard work of the PAPP Committee on Childhood Asthma and everyone involved in coming up with this much awaited Clinical Practice Guidelines for Pediatric Asthma. We hope this will have its own space in every clinician's go-to references and help in making the Filipino child breathe better through adherence to standardized pediatric and pulmonary healthcare practices. Let's all "SAVE OUR CHILDREN'S LUNGS."**

# Message from the PAPP Asthma Committee Chairperson

**Rozaida Villon, MD, FPPS, FPAPP**

**Greetings! Asthma in children is the most common chronic disease consistently inflicting a burden on health and finances. The increase in prevalence of asthma among children and adolescents were noted particularly in low to middle income countries, including the Philippines.**

**The Philippine Consensus for the Management of Childhood Asthma was first published in 2002 and there have been no formal nor interim updates since then. After almost two decades, the Asthma Committee of the PAPP then decided to launch this project to rewrite a new version in the form of a CPG which is evidence based.**

**The development of this CPG in this time of COVID 19 pandemic was not an easy task. However, the Asthma Committee was deeply bound to carry out its promise to provide up to date recommendations and evidence in the field of childhood asthma.**

**The PAPP CPG for Pediatric Asthma 2021 aims to be a comprehensive and updated guideline for the prevention, diagnosis, treatment and management and education for asthma in patients aged 18 years old and below. The primary target users of these guidelines are physicians who are directly involved in the care of children and adolescents with asthma.**

**PAPP would like to acknowledge the support of the Philippine Pediatric Society through its president, Dr. Jocelyn A. Eusebio. I would like to express my sincerest gratitude to 101 Health Research (Evidence Review Experts) for their notable and substantial participation in the appraisal, recommendations, and analysis of the manuscript. Utmost thanks as well to the consensus panel from different key stakeholders for their valuable inputs in the CPG.**

**The PAPP Asthma Committee would also like to acknowledge the full support given to us by the present board members headed by our President, Dr. Nepthalie Ordoñez.**

**In line with the PAPP mission statements, the committee's objectives, it is our hope that clinicians will be guided in the management of asthma thus improving the health of the Filipino children. Lastly, we encourage the dissemination and implementation of the treatment strategies and recommendations of this updated clinical practice guidelines.**

**Thank you.**

# Table of Contents

# Overview of the Asthma CPG

## Executive Summary

**Rationale.** Asthma is a chronic airway inflammatory condition associated with hyperresponsiveness and variable expiratory airflow limitation. It is a heterogeneous disease that may initially present across younger and older pediatric age groups.

In the Philippines, the previous consensus-based guideline on pediatric asthma was published in 2002. An update of this guideline is needed because:

(1) The diagnosis of pediatric asthma remains challenging because cough and wheezing are common symptoms in children;

(2) There have been major changes in asthma diagnostics and therapeutics in the past two decades;

(3) Increasing prevalence of asthma due to environmental and lifestyle changes, with pronounced impact on developing countries;

(4) Impact of uncontrolled asthma on quality of life, financial burden, and risk of asthma-related deaths;

(5) Evolving local health systems and transitioning into universal health care; and

(6) Growing evidence on primary and secondary prevention.

**What is new in this guideline.** This Philippine CPG answers nine key questions, and provides 6 *de novo* recommendations, 32 adapted recommendations, 40 adopted recommendations, and 11 Good Practice Statements. The type of recommendation, strength of recommendation, certainty of the evidence, and evidence summaries are indicated for each recommendation.

In Chapter 1, the diagnosis of asthma provides guidance for clinical evaluation of children unable to perform spirometry, and diagnosis in the context of patients with or without previous controller medications, and scenarios where spirometry may not be readily available.

In Chapter 2, the diagnosis and management of acute exacerbations in the home, ambulatory settings, emergency department, and inpatient settings are given. The use of a written asthma action plan, importance of severity classification, and clear understanding of treatment algorithms are emphasized in this chapter.

In Chapter 3, a major change in the long-term management of asthma is the use of inhaled corticosteroids as the primary controller and strategies to decrease overreliance on short acting beta-2 agonists (SABA). Assessing asthma control versus severity is highlighted. Questions on the use of fractionated exhaled nitric oxide, sputum eosinophil count, antibiotics, systemic corticosteroids and inhaled CS in exacerbations, Vitamin D supplementation, immunotherapy, and omalizumab are answered considering current evidence.

In Chapter 4, evidence-based recommendations were presented for lifestyle and non-pharmacologic measures related to primary and secondary prevention. This includes breastfeeding, immunization, air pollutants, environmental tobacco smoke, e-cigarettes, and stress reduction. Specific patient education points are also given.

In Chapter 5, guidance is given for exercise-induced bronchoconstriction, athletes, and preparing for surgery.

**Objectives.** The PAPP Clinical Practice Guidelines for Pediatric Asthma 2021 aims to be a comprehensive and updated guideline for the prevention, diagnosis, treatment and management, and education for asthma in patients aged 18 years old and below. It is the general objective of this CPG to provide pediatricians and healthcare professionals with a trustworthy guideline for the diagnosis and management of Filipino children and adolescents with asthma. The primary target users of this guideline are physicians who are directly involved in the care of children and adolescents with asthma.

**Methods.** The development of the CPG involved the Philippine Academy of Pediatric Pulmonologists, Inc. as its Lead CPG Developer, a full multi-disciplinary Consensus Panel, independent Evidence Review Experts (ERE) and Medical Writers, and a third-party organization for consensus panel, stakeholder mapping, and COI management. In the selection of global asthma guidelines for adaptation, AGREE-II evaluation was performed. The recommendations from GINA and BTS were mapped according to the specific sub-questions or sub-sections.

The primary method for guideline development was that of GRADE-ADOLOPMENT. This allowed varying levels of recommendations: adoption (without substantial modification from previously published guidelines), adaptation (with modification to suit local context), and *de novo* recommendations. 'Adolopment' of the recommendations entailed appraisal of the references of selected guidelines as well as independent literature search and certainty appraisal by the ERE. After the initial draft of the CPG was presented to the Consensus Panel, the draft underwent several e-Delphi rounds. Recommendations were also classified into the following types: (i) Evidence-based Recommendation, (ii) Consensus-based Recommendation, (iii) Clinical pathway or classification, or (iv) Good Practice Statement. The strength of recommendations was evaluated whether these are strong recommendations, conditional recommendations, or weak recommendations. This CPG also appraised the evidence base coming from the adapted guidelines, updated with the ERE's independent review of systematic reviews or latest evidence, as either very low, low, moderate, or high.

The methods are written in more detail in Part 2 of this document.

**Community and equity considerations.** Questions raised during the initial plenary presentation are answered in this Appendix. An extensive literature search on peer-reviewed and published Philippine based studies on pediatric asthma was done and synthesized in Part 1 of this document, and cited in the recommendations, when applicable.

**Funding.** The development of this Clinical Practice Guideline is fully funded by the Philippine Academy of Pediatric Pulmonologists, Inc.

# Summary of Recommendations

| No. | Recommendation | Type | Method | Strength | Certainty |
|---|---|---|---|---|---|
| **KEY QUESTION 1. WHAT ARE THE CLINICAL SIGNS AND SYMPTOMS TO DIAGNOSE ASTHMA?** | | | | | |
| 1a | The diagnostic approach to asthma in children <6 years is clinical: based on the overall picture of symptom patterns, risk factors, response to therapeutic trials, and exclusion of alternate diagnoses. | Clinical pathway | Adapted | Strong | N/A |
| 1b.1 | Lung function tests, specifically spirometry, are suggested with proper performance guidance among cooperative patients less than 6 years old. | Consensus based | Adapted | Conditional | N/A |
| 1b.2 | Plain chest radiography is suggested to be performed in asthma to assist in the exclusion of other diagnoses. | Consensus based | Adapted | Conditional | N/A |
| 1b.3 | Allergic sensitization tests are not required in the diagnosis of asthma, but it is an adjunct when allergen immunotherapy is being considered. | Evidence based | Adapted | Conditional | N/A |
| 1c | The criteria for the diagnosis of asthma in older children and adolescents (6 to 18 years old) is based on two key diagnostic features: a history of variable respiratory symptoms and confirmed variable expiratory airflow limitation. | Evidence based | Adapted | Strong | High |
| 1d.1 | Clinical pathway for the diagnostic approach for initial presentation of respiratory symptoms in patients 6-18 years old who are steroid naïve (Algorithm 1) | Clinical pathway | Adapted | Conditional | N/A |
| 1d.2 | Clinical pathway for the diagnostic approach for patients 6-18 years old on controllers, with variable respiratory symptoms, and without variable airflow limitation (Algorithm 2) | Clinical pathway | Adapted | Conditional | N/A |
| 1d.3 | Clinical pathway for the diagnostic approach for patients 6-18 years old on controllers, with few respiratory symptoms, with normal pulmonary function tests, and no variable airflow limitation (Algorithm 3) | Clinical pathway | Adapted | Conditional | N/A |
| 1d.4 | Clinical pathway for the diagnostic approach for patients 6-18 years old on controllers, persistent shortness of breath, and persistent airflow limitation (Algorithm 4) | Clinical pathway | Adapted | Conditional | N/A |
| **KEY QUESTION 2. WHAT ARE THE SIGNS AND SYMPTOMS OF AN ACUTE EXACERBATION?** | | | | | |
| 2a | If there is any risk factor for asthma-related death present, the patient must seek immediate medical care during the exacerbation. | Consensus based | Adopted | Strong | N/A |
| 2b | Physicians must recommend the specific treatment strategies once modifiable risk factors have been identified. | Consensus based | Adapted | Strong | N/A |

| No. | Recommendation | Type | Method | Strength | Certainty |
|---|---|---|---|---|---|
| 2c | An asthma exacerbation severity may be classified as mild, moderate, severe, or life threatening based on their activity level, respiratory rate, cardiac rate, pulse oximetry, and lung function, if evaluated. In children below 6 years old, no distinction is made between severe and life-threatening groups. | Clinical classification | Adapted | Strong | N/A |
| **KEY QUESTION 3. WHAT IS THE MANAGEMENT OF ASTHMA IN AN ACUTE EXACERBATION?** | | | | | |
| 3a | Healthcare professionals should provide patients and families with an individualized written asthma action plan (WAAP) for self-management or home-based management of exacerbations. The WAAP must be regularly reviewed and updated. | Evidence based | Adapted | Strong | Low |
| 3b.1 | Clinical pathway for the management of asthma in acute exacerbation in children below 6 years old in an outpatient or ambulatory setting (Algorithm 5) | Clinical pathway | Adopted | Strong | N/A |
| 3b.2 | Clinical pathway for the management of asthma in acute exacerbation in 6-18 years old in an outpatient or ambulatory setting (Algorithm 6) | Clinical pathway | Adopted | Strong | N/A |
| 3c | Asthma exacerbations that are severe and life-threatening are medical emergencies which need to be appropriately managed in an acute care setting like the emergency department. | Clinical pathway | Adapted | Strong | N/A |
| 3d | Hospital admission should be considered when the patient has any of the following clinical criteria:<br>1. use of more than 6-8 SABA puffs in the previous 24 hours<br>2. PEF 50% to 75% of personal best<br>3. history of severe exacerbations warranting ICU admission<br>4. hospital admission or previous exacerbation for the past 12 months<br>5. child in whom other considerations suggest that admission may be appropriate, such as psychosocial problems in child or parent/caregiver, physical disability or learning difficulties, exacerbation despite adequate dose of oral steroids pre-presentation, presentation at night, or in a remote location or without transportation/communication | Consensus based | Adapted | Conditional | N/A |
| 3e.1 | Clinical pathway for the management of asthma in acute exacerbation in children below 6 years old in a hospital setting. | Clinical pathway | Adopted | Strong | High |
| 3e.2 | Clinical pathway for the management of asthma in acute exacerbation in 6-18 years old in a hospital setting. | Clinical pathway | Adopted | Strong | High |

| No. | Recommendation | Type | Method | Strength | Certainty |
|---|---|---|---|---|---|
| 3f | A patient admitted for asthma may be discharged when the patient has reasonably fulfilled the following clinical criteria:<br>1. O2 saturation at room air >94%<br>PEF >75%<br>2. No signs of respiratory distress<br>3. Been on discharge medication for 12 to 24 hours<br>4. Stable on a 4-hourly inhaled treatment<br>5. Able to demonstrate inhaler use correctly<br>6. Understand treatment prescribed and signs of worsening asthma<br>7. Patient has his/her own written asthma action plan (WAAP), and the family understands how to use it | Consensus based | Adapted | Conditional | N/A |
| **KEY QUESTION 4. WHAT IS THE PHARMACOLOGICAL MANAGEMENT FOR ASTHMA OR SUSPECTED ASTHMA PATIENTS?** | | | | | |
| 4a | Low-dose ICS or controller treatment should be initiated once asthma is confirmed in adolescents (12-18 years old). This can be delivered with regular daily treatment or as-needed ICS-formoterol whenever needed for symptom relief. | Evidence based | Adopted | Strong | High |
| 4b | For patients three years old and below, the preferred device for asthma treatment is a pressurized metered dose inhaler (MDI) plus a dedicated spacer with a face mask, while the alternate option is that of a nebulizer and face mask. For patients four to five years old, the preferred device is a pressurized MDI plus dedicated spacer with mouthpiece, while the alternate option is a nebulizer with mouthpiece or face mask. | Evidence based | Adopted | Strong | High |
| 4c.1 | Step 1: Patients less than 6 years with infrequent viral wheezing should be provided with inhaled SABA for relief of symptoms. If SABA is used more than twice a week for a month, a trial of controller medication may be considered. In children with intermittent viral-induced wheezing and no interval symptoms, inhaled SABA is insufficient, intermittent high-dose ICS may be considered* | Consensus based | Adopted | Conditional | N/A |
| 4c.2 | Step 2: If the symptom pattern is consistent with asthma, and asthma symptoms are not well-controlled or with ≥3 exacerbations/year; or when the symptom pattern is not consistent with asthma but wheezing episodes requiring SABA occur frequently (≥3 per year), the preferred controller option is daily low dose ICS, to be given for at least 3 months. | Evidence based | Adopted | Strong | High |
| 4c.3 | Step 3: For patients diagnosed with asthma and whose symptoms are not well-controlled on daily low-dose ICS, consider doubling the initial low dose of ICS and re-assess the patient after 3 months. Another option is low dose ICS with LTRA. | Evidence based | Adopted | Conditional | Low |

| No. | Recommendation | Type | Method | Strength | Certainty |
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| 4c.4 | Step 4: For asthma patients who are not well-controlled on daily double low-dose ICS, refer the patient to an asthma specialist and consider further investigation. | Consensus based | Adopted | Conditional | N/A |
| 4d.1 | A clinical pathway for the pharmacological treatment of children 6-11 years old with asthma, wheezing, or suspected asthma is adopted from GINA 2021. The KQ4 pathway provides a preferred track (Track 1) with the following recommendations:<br><br>Step 1: For children 6-11 years with symptoms less than twice a month, the preferred controller option is low dose ICS whenever SABA is taken. Similar to Recommendation 4a, SABA-only treatment is no longer recommended. | Evidence based | Adopted | Strong | Low |
| 4d.2 | Step 2: If symptoms are twice a month or more, the preferred controller option is daily low dose ICS with as-needed SABA as reliever. | Evidence based | Adopted | Strong | High |
| 4d.3 | Step 3: If with troublesome asthma symptoms most days, waking due to asthma once a week or more despite Step 2 controller treatment, or with any risk factors (KQ 5), there are 3 preferred controller options: medium dose ICS with as needed SABA, low dose ICS - LABA with as needed SABA, very low dose ICS – Formoterol as maintenance and reliever therapy (MART therapy). | Evidence based | Adopted | Strong | High (i, ii)<br>Low (iii) |
| 4d.4 | Step 4: If the patient initially presents with severely uncontrolled asthma, or has an acute exacerbation, or is not adequately controlled by low-dose maintenance ICS-LABA with as-needed SABA the preferred controller option is medium dose ICS – LABA with as needed SABA or low dose ICS-formoterol MART. | Evidence based | Adopted | Conditional | Low |
| 4d.5 | Step 5: If the patient has persistent symptoms and exacerbations despite Step 4 medications, refer for expert assessment, add-on therapy, and phenotyping, as applicable. | Consensus based | Adopted | Conditional | N/A |
| 4e.1 | A clinical pathway for the pharmacological treatment steps of adolescents 12-18 years old with asthma, wheezing, or suspected asthma is adopted from GINA 2021 with two tracks. The primary difference between the two tracks is in the choice of the as-needed reliever drug for symptom relief, taking into consideration the patient's preference and adherence issues.<br><br>ICS-formoterol (Track 1) should be given as the as-needed reliever drug across all Steps 1-5 for adolescents. If ICS-formoterol is not available, not affordable, or not preferred by a patient with no exacerbations on current therapy, SABA (Track 2) may be given as the alternate reliever drug. | Evidence based | Adopted | Conditional | Low |

| No. | Recommendation | Type | Method | Strength | Certainty |
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| 4e.2 | Steps 1 and 2: For adolescents with mild symptoms, or less than 4-5 days a week:<br><br>TRACK 1: As-needed low-dose ICS-formoterol should be given, with a maximum dose of 72 mcg/day for budesonide-formoterol, or 48 mcg/day for beclomethasone-formoterol.<br><br>TRACK 2: Low dose ICS taken whenever SABA is taken may be an option if ICS-formoterol is not available or affordable. For Step 2, daily low dose maintenance ICS, is the preferred approach. Low dose ICS whenever SABA is taken, daily LTRA, or allergen immunotherapy (KQ 6) may be considered. | Evidence based | Adopted | Conditional | High |
| 4e.3 | Step 3: For adolescent patients with symptoms on most days, or waking with asthma once a week or more:<br><br>TRACK 1: Low dose maintenance ICS-formoterol should be given as both maintenance and reliever treatment (MART) but should not be used as a reliever for those taking ICS with a different LABA.<br><br>TRACK 2: Maintenance ICS-LABA with as-needed SABA. Other options include increasing ICS to medium dose, low dose ICS plus LTRA, low dose ICS plus sustained-release theophylline, or allergen immunotherapy (KQ 6). | Evidence based | Adopted | Conditional | High (Track 1)<br>Low<br>(Track 2) |
| 4e.4 | Step 4: For patients with daily symptoms or waking with asthma once a week or more and low lung function:<br><br>TRACK 1: The maintenance treatment with ICS-formoterol may be increased to medium dose if deemed necessary. However, the reliever is still low-dose ICS formoterol.<br><br>TRACK 2: Alternatively, medium dose ICS-LABA with as-needed SABA can be considered if maintenance and reliever therapy is not available. Other options are long-acting muscarinic antagonists (LAMA) such as tiotropium bromide. However, before considering adding LAMA, the ICS dose should be increased first to medium dose or treatment be switched to MART with ICS-formoterol. Allergen immunotherapy, medium dose ICS plus LTRA, and medium dose ICS plus sustained-release theophylline may also be considered. | Evidence based | Adopted | Conditional | Low |
| 4e.5 | Step 5: Consider high dose ICS and other add-on asthma medications depending on the assessment of the asthma specialist. | Consensus based | Adopted | Conditional | N/A |
| 4f | Children and adolescents should be referred to an asthma specialist for the following indications: (cont) | Consensus based | Adopted | Conditional | N/A |

| No. | Recommendation | Type | Method | Strength | Certainty |
|---|---|---|---|---|---|
| 4f | difficulty confirming the diagnosis of asthma, or presence of asthma complications or sub-types, persistent or uncontrolled asthma, risk of asthma-related death, and side effects due to asthma medications. | Consensus based | Adopted | Conditional | N/A |
| 4g | A clinical pathway for difficult-to-treat asthma patients for use is proposed for both primary and specialist care. | Clinical pathway | Adopted | Conditional | N/A |
| 4h | Fractionated exhaled nitric oxide (FeNO) can be used as an adjunct to guide treatment in children and adolescents. | Evidence based | De novo | Weak | Low |
| **KEY QUESTION 5. HOW DO WE EVALUATE CONTROL OF SYMPTOMS IN ASTHMA?** | | | | | |
| 5a | The regular use of patient-reported and family-assessed symptom tools is recommended to monitor and evaluate the control of asthma. | Evidence based | Adapted | Conditional | Low |
| 5b.1 | The use of a peak expiratory flow meter is recommended as an adjunct in long-term monitoring. | Consensus based | Adapted | Conditional | N/A |
| 5b.2 | Spirometry is not routinely required to assess asthma control. Normal spirometry results do not definitively indicate control of asthma. | Consensus based | Adapted | Conditional | N/A |
| 5c | Asthma severity may be classified as mild, moderate, or severe based on the level of treatment required to control symptoms and exacerbations. This is based on a retrospective assessment when a step down has been attempted to find the minimum effective level of treatment that keeps them symptom-free after several months of controller treatment. | Clinical classification | Adopted | Strong | N/A |
| **KEY QUESTION 6. WHAT ARE THE INDICATIONS TO CONSIDER USE OF ANTIBIOTICS / SYSTEMIC CORTICOSTEROIDS / VITAMIN D / IMMUNOTHERAPY IN CHILDREN WITH ASTHMA?** | | | | | |
| 6a | The routine use of antibiotics in the management of asthma exacerbations is not recommended. Antibiotics are indicated only when there is evidence of a concomitant bacterial lung infection. | Evidence based | Adapted | Strong | Low |
| 6b.1 | Systemic corticosteroids should be given as early as possible to manage acute asthma exacerbations, in concordance with the exacerbations management algorithms. Treatment with oral or intravenous corticosteroids may be individualized to the number of days necessary to achieve improvement. Tapering of the dose is not necessary if the systemic steroid administration is less than 14 days. | Evidence based | Adopted | Strong | Low |
| 6b.2 | Inhaled corticosteroids may be added to systemic corticosteroids in the Emergency Department for (cont) | Evidence based | De novo | Weak | Low |

| No. | Recommendation | Type | Method | Strength | Certainty |
|---|---|---|---|---|---|
| 6b.2 | pediatric patients with moderate to severe asthma exacerbations to reduce hospitalizations. | Evidence based | De novo | Weak | Low |
| 6c | Vitamin D supplementation may be added as an adjunct in asthmatic children on corticosteroids to reduce acute asthma exacerbations. | Evidence based | De novo | Weak | Very low |
| 6d | Immunotherapy is conditionally recommended for specific subpopulations of children or adolescents with difficult-to-treat allergic asthma. | Evidence based | De novo | Conditional | Moderate (safety)<br>Low (effectiveness) |
| 6e | Omalizumab may be given as an add-on therapy for children ages 6 years old and above with uncontrolled severe allergic asthma. | Evidence based | De novo | Weak | Very low |
| **KEY QUESTION 7. WHAT ARE THE EVIDENCE-BASED NON-PHARMACOLOGIC AND LIFESTYLE FACTORS THAT MAY BE RECOMMENDED FOR PRIMARY AND SECONDARY PREVENTION OF ASTHMA IN CHILDREN AND ADOLESCENTS?** | | | | | |
| 7a.1 | Pregnant patients must avoid exposure to air pollutants, including prenatal smoking. | Evidence based | Adapted | Strong | High |
| 7a.2 | Breastfeeding should be encouraged for all families. | Evidence based | Adapted | Strong | High (overall health)<br>Low (asthma prevention) |
| 7a.3 | Exposure to environmental tobacco smoke, aerosols from e-cigarettes, and air pollutants should be avoided to prevent respiratory symptoms | Evidence based | Adapted | Strong | High |
| 7a.4 | Immunization should be completed, and given on time. | Evidence based | Adapted | Strong | High (overall health)<br>Very low (asthma prevention) |
| 7a.5 | Weight reduction is recommended in obese patients to promote general health and to reduce subsequent respiratory symptoms consistent with asthma. | Evidence based | Adapted | Strong | Moderate |
| 7a.6 | Maternal distress during pregnancy or psychosocial stress during the child's early years should be mitigated. | Evidence based | Adapted | Strong | Low |
| 7b.1 | Asthmatics and families of children with asthma should be offered appropriate support to stop smoking cigarettes and/or e-cigarettes. | Evidence based | Adapted<br>De novo for e-cigarettes | Strong | Moderate (e-cigarettes) to high (cigarettes) certainty |
| 7b.2 | Patients or carers must be advised to avoid exposing the patient with asthma to unfavorable environmental conditions. This includes extreme weather conditions, poor air quality, volcanic ash, high pollen or mold counts. | Consensus based | Adapted | Strong | N/A |

| No. | Recommendation | Type | Method | Strength | Certainty |
|---|---|---|---|---|---|
| 7b.3 | Asthmatics who are on oral or inhaled corticosteroids may receive immunization as scheduled. | Evidence based | Adapted | Strong | High (overall health)<br>Low (asthma prevention) |
| 7b.4 | Encourage people with asthma to engage in regular, tolerable physical activity and provide advice on prevention of exercise-induced bronchoconstriction (see KQ 9). | Consensus based | Adopted | Strong | N/A |
| 7b.5 | Weight reduction interventions, including dietary and exercise-based programs, is recommended in overweight and obese patients to improve asthma control. | Evidence based | Adapted | Moderate | N/A |
| 7b.6 | Encourage patients with asthma to consume a diet high in fruit and vegetables. | Evidence based | Adapted | Strong | High (overall health) Low (asthma prevention) |
| 7b.7 | Review with the patient or family if emotional stress contributes to asthma symptoms. Encourage patients to identify goals and strategies to deal with emotional stress if it makes their asthma worse. | Consensus based | Adapted | Strong | N/A |
| **KEY QUESTION 9. WHAT ARE THE PREVENTIVE AND TREATMENT MEASURES RECOMMENDED FOR PEDIATRIC ASTHMA PATIENTS INVOLVED IN SPORTS, AND IN SURGERY?** | | | | | |
| 9a.1 | Appropriate training and sufficient warm-up prior to vigorous physical activity for all children and adolescents is recommended to reduce the incidence and severity of exercise-induced bronchoconstriction. | Evidence based | Adopted | Strong | High |
| 9a.2 | Regular controller treatment with inhaled corticosteroids is recommended for asthmatic children and adolescents because it confers protection against exercise-induced bronchoconstriction, in accordance with other recommendations of this guideline (see KQ 4). | Evidence based | Adopted | Strong | High |
| 9a.3 | Prior to exercise, the asthmatic child or adolescent should take SABA or LABA. However, patients with mild asthma who are already on ICS-formoterol can use the same medication and do not need to be prescribed with an additional SABA pre-exercise. | Evidence based | Adopted | Conditional | Moderate |
| 9a.4 | When breakthrough exercise-induced bronchoconstriction occurs, the physician must review control of symptoms (KQ 5), consider stepping up controller use (KQ4), review and teach inhaler technique and adherence (KQ 4, KQ 8). Acute exacerbations will follow the recommendations given in KQ 3. | Evidence based | Adapted | Strong | Specified in the various key questions' recommendations. |
| 9b.1 | Athletic children and adolescents with asthma should, as much as possible, avoid training in environments | Consensus based | Adopted | Strong | N/A |

| No. | Recommendation | Type | Method | Strength | Certainty |
|---|---|---|---|---|---|
| 9b.1 | with extreme cold or extreme heat, or with air pollutants and allergens. | Consensus based | Adopted | Strong | N/A |
| 9b.2 | Athletic children and adolescents with asthma should be maintained on adequate anti-inflammatory controller therapy like ICS to reduce overreliance on beta-2 agonists (SABA) to avoid the development of tolerance. The same treatment steps and principles provided in KQ 3 and KQ 4 apply to athletes. | Consensus based | Adopted | Strong | Provided in KQ 3 and KQ 4. |
| 9c.1 | For elective surgeries, good asthma control should be achieved before the surgery. This especially applies for patients with severe asthma, uncontrolled symptoms, recent exacerbations, or persistent airflow limitations. The same recommendations given in KQ 3 for acute exacerbations and KQ 4 for long-term management apply to pediatric patients preparing for surgery. | Evidence based | Adopted | Strong | Given in KQ3 and KQ4. |
| 9c.2 | Elective surgeries may be performed 4 to 6 weeks after the last asthma exacerbation, in accordance with Recommendation 9c.1 and the PAPP Position Statement on Preoperative Evaluation (as of June 2021). | Consensus based | Adopted | Conditional | N/A |
| 9c.3 | For emergency surgeries, the risks of proceeding without first achieving good asthma control should be weighed against the need for immediate surgery. | Consensus based | Adopted | Conditional | N/A |
| 9c.4 | Regular controller therapy should be maintained throughout the perioperative period. The same treatment recommendations from KQ 4 apply. | Evidence based | Adopted | Strong | N/A |
| 9c.5 | Patients taking long-term high dose ICS or who have received OCS for more than 2 weeks during the previous 6 months should receive hydrocortisone perioperatively as they are at risk of adrenal crisis in the context of surgery. | Consensus based | Adopted | Strong | N/A |
| 9c.6 | In accordance with the PAPP Position Statement on Preoperative Evaluation (as of June 2021), we suggest the following risk reduction strategies for pediatric patients with asthma undergoing surgery: (see 9c.6.1 to 9c.6.3) | Consensus based | Adopted | Conditional | N/A |
| 9c.6.1 | For well controlled asthma, use of inhaled beta-2 agonist (SABA) 1-2 hours before surgery. | Consensus based | Adopted | Conditional | N/A |
| 9c.6.2 | For partly controlled asthma, use inhaled corticosteroids with inhaled beta-2 agonist (LABA or SABA) one week before surgery, and inhaled SABA 1-2 hours before surgery | Consensus based | Adopted | Conditional | N/A |
| 9c.6.3 | For poorly controlled asthma, use of systemic corticosteroids for 3 to 5 days prior to surgery, and inhaled beta-2 agonist (SABA) 1-2 hours before surgery. | Consensus based | Adopted | Conditional | N/A |

**Note: There are no Recommendations for Key Question 8. KQ8 has Good Practice Statements.**

# Summary of Good Practice Statements

| Key Question | Number and statement |
|---|---|
| 1 | **Good Practice Statement 1.1**<br><br>The following are questions that can be used to elicit features suggestive of asthma:<br>1. Does your child have wheezing?<br>2. Does your child wake up at night because of coughing, wheezing, or "difficulty breathing," "heavy breathing," or "breathlessness"?<br>3. Does your child have to stop running, or play less hard, because of coughing, wheezing or "difficult breathing," "heavy breathing," or "shortness of breath"?<br>4. Does your child cough, wheeze, or get "difficult breathing," "heavy breathing," or "shortness of breath" when laughing, crying, playing with animals, or when exposed to strong smells or smoke?<br>5. Has your child ever had eczema, or been diagnosed with an allergy to foods?<br>6. Has anyone in your family had asthma, hay fever, food allergy, eczema, or any other disease with breathing problems? |
| | **Good Practice Statement 1.2**<br><br>Asthma predictive tools must be appraised and validated locally before being adapted in practice. |
| 2 | **Good Practice Statement 2.1**<br><br>Healthcare professionals and families should identify triggers that may be present in the asthmatic child or adolescent's environment or lifestyle. Advice on prevention or mitigation of exposure to these triggers should be offered. |
| | **Good Practice Statement 2.2**<br><br>Healthcare professionals should determine whether the asthmatic child or adolescent is at risk for asthma-related death.<br><br>See Table 4.1 for these risk factors. |
| | **Good Practice Statement 2.3**<br><br>Healthcare professionals and families should identify modifiable risk factors present in the asthmatic child or adolescent's environment and lifestyle to prevent exacerbations. |
| | **Good Practice Statement 2.4**<br><br>In children and adolescents with signs and symptoms of an exacerbation (e.g., wheezing, coughing, breathlessness, activity limitation), a brief focused history and targeted physical examination should be performed expeditiously without delay in the concurrent initiation of urgent therapy. All findings and interventions should be prompt and properly documented in the medical record. Refer to Table 5.1. |
| 4 | **Good Practice Statement 4.1**<br><br>The following must be taken into consideration when reviewing response and adjusting treatment:<br>1. Any step-up or step-down of asthma treatment is considered a therapeutic trial. Response to asthma treatment should be reviewed within 1-3 months and every 3-12 months thereafter, depending on their initial level of control, response to treatment and level of engagement in self-management.<br>2. After an exacerbation or flare-up, patients are advised to follow up within a week. |

3. It is recommended to continue treatment for at least 3 months to establish its effectiveness in achieving good asthma control, since full benefit may only be noted after 3-4 months.
4. For children below 5 years of age, asthma-like symptoms remit in a large proportion. Thus, regular assessment should be done to determine whether an asthma controller remains necessary.
5. Symptom control, presence of risk factors, frequency of exacerbations and side effects of medications are the essential parameters that must be assessed during the duration of treatment. Furthermore, adherence to medication, inhaler technique and patients' preference, goals and satisfaction must be reviewed by the health care provider during each visit.

**Good Practice Statement 4.2**

Due to the long-term use of pharmacologic agents, patients and families must be trained how to independently adjust the use of their medications based on their written asthma action plan (WAAP) and know when to contact their physician for major treatment decisions. The essential components of effective guided asthma self-management include self-monitoring of symptoms and/or peak flow, a clear and updated WAAP, and a regular review by physicians of the patient's asthma control, treatment, and skills in using asthma devices. These are discussed extensively in KQ 3 and KQ 5.

**5** **Good Practice Statement 5.1**

Physicians and healthcare providers should know whether the patient is at risk for asthma-related adverse outcomes. These adverse outcomes pertain to having exacerbations, persistent airflow limitation, and side effects from medications. The assessment of risk factors must be done at diagnosis of asthma, and at least every 1 to 2 years, particularly for patients with exacerbations. When applicable and feasible, measure FEV1 at the start of treatment, after 3 to 6 months for personal best lung function, and periodically for ongoing risk assessment (see Section 18).

**7** **Good Practice Statement 7.1**

Households of patients with asthma, especially with allergic comorbidities, should reduce exposure to house dust mites. This includes multifaceted house dust mite control measures, regular cleaning of the home using damp cloths to remove settled dust, weekly change of beddings and pillowcases, and making the bedroom tidy and simple through minimizing clutter including curtains, rugs, carpets, books, wallpapers, and stuffed toys.

**8** **Good Practice Statement 8.1**

Primary care health professionals should teach patients and families on the following points: (i) transitioning to self-management among adolescents, (ii) identification of asthma triggers, (iii) manifestations of acute exacerbations, (iv) initial home and school remedies for asthma, (v) when to go to a hospital, and (vi) effective use of asthma devices/gadgets to ensure adherence to medications.

Adapted from BTS 2019[1] and GINA 2021[2]

Note: There are no Good Practice Statements for KQs 3, 6, and 9

## Summary of Tables

# Summary of Figures

## Summary of Algorithms

## List of Frequently Used Abbreviations

| | |
|---|---|
| **ACT** | Asthma Control Test |
| **ACQ** | Asthma Control Questionnaire |
| **ADAPTE** | Collaboration group for adaptation of guidelines |
| **AGREE-II** | Appraisal of Guidelines for Research and Evaluation II |
| **AIT** | allergen immunotherapy |
| **API** | asthma predictive index |
| **BD** | bronchodilator |
| **BPT** | bronchoprovocation testing |
| **BTS** | British Thoracic Society |
| **BUD-FORM** | budesonide-formoterol |
| **c-ACT** | Childhood Asthma Control Test |
| **COI** | Conflict of interest |
| **COPD** | chronic obstructive pulmonary disease |
| **COVID-19** | Coronavirus disease 2019 |
| **CPG** | Clinical Practice Guidelines |
| **cpm** | cycles per minute |
| **CS** | corticosteroid |
| **DOH** | Department of Health |
| **EIB** | exercise-induced bronchoconstriction |
| **ERE** | Evidence Review Expert |
| **ERS** | European Respiratory Society |
| **FeNO** | fractional exhaled nitric oxide |
| **FEV1** | forced expiratory volume in one second |
| **FVC** | forced vital capacity |
| **GINA** | Global Initiative for Asthma |
| **GRADE** | Grading of Recommendations Assessment, Development and Evaluation |
| **ICS** | inhaled corticosteroids |
| **ICU** | intensive care unit |

| | |
|---|---|
| **KQ** | key question |
| **LABA** | long-acting beta 2 agonist |
| **LAMA** | long-acting muscarinic antagonists |
| **LMIC** | Low to Middle Income Countries |
| **LTRA** | leukotriene receptor antagonist |
| **MART** | maintenance and reliever therapy |
| **MDI** | metered dose inhaler |
| **NSAIDS** | non-steroidal anti-inflammatory drugs |
| **OCS** | oral corticosteroid |
| **OPD** | outpatient department |
| **PAPP** | Philippine Academy of Pediatric Pulmonologists |
| **PC20** | provocative concentration of bronchoconstrictor (e.g. methacholine) required to cause a 20% fall in FEV1 |
| **PD20** | provocative dose of bronchoconstrictor (e.g. methacholine) required to cause a 20% fall in FEV1 |
| **PEF** | peak expiratory flow |
| **PICU** | Pediatric Intensive Care Unit |
| **PM10** | particulate matter 10 micrometers |
| **pMDI** | pressurized metered dose inhaler |
| **PPS** | Philippine Pediatric Society |
| **PSAAI** | Philippine Society of Allergy, Asthma and Immunology |
| **PTB** | Pulmonary Tuberculosis |
| **RCT** | randomized controlled trial |
| **QoL** | Quality of Life |
| **RSV** | respiratory syncytial virus |
| **SABA** | short-acting beta 2 agonist |
| **SCIT** | subcutaneous immunotherapy |
| **SLIT** | sublingual immunotherapy |
| **SpO2** | oxygen saturation measured by a pulse oximeter |
| **UA** | upper airway |
| **URTI** | upper respiratory tract infection |

| | |
|---|---|
| **WAAP** | written asthma action plan |
| **WHO** | World Health Organization |

# Part I. Introduction

The PAPP Clinical Practice Guidelines for Pediatric Asthma 2021 aims to be a comprehensive and updated guideline for the prevention, diagnosis, treatment and management, and education for asthma in patients aged 18 years old and below. Specifically, it covers the diagnosis of asthma, treatment of asthma to control symptoms and minimize risk, asthma education and skills training, management of worsening asthma and exacerbations, primary and secondary prevention, and risk evaluation.

*Increasing prevalence of asthma pronounced in LMICs and urban settings*

The burden of asthma affects all ages worldwide and can result in mortality and reduced quality of life. According to the Global Burden of Disease (GBD) study in 2016, there were 339.4 million people estimated to be affected by asthma, which also relates to the increase in age-standardized prevalence by 3.6% over a period of 10 years.[1] Among children, asthma is the most common chronic disease consistently inflicting a burden on health and finances. The increase in prevalence of asthma among children and adolescents were noted particularly in Low-Middle Income Countries (LMICs).[2] The International Study of Asthma and Allergies in Childhood (ISAAC) surveyed around 1.2 million children from 233 centers from 98 countries and their results show that globally, asthma prevalence among 13 to 14 years old was at 14.1% and among 6 to 7 years old was at 11.7%.[3] Additionally, between the ISAAC Phase One and Phase Three periods of survey, asthma symptoms were reported to have globally increased from 11.1% to 11.6% in children and from 13.2% to 13.7% in adolescents.[2] The increase in prevalence is particularly pronounced in urban settings, indicative of the role of environmental exposures in the development of childhood asthma.[2] Locally, the PPS have a Pediatrics Disease Registry Program wherein all admitted pediatric cases in member training hospitals submit monthly cases based on diagnosis. For bronchial asthma, included in the registry are a total of 40,359 cases across all pediatric age groups from 2006 to March 2022.[4]

Risk factors for childhood asthma are either genetic or non-genetic in nature. Genetic susceptibility has been known as evidenced in twin studies and scientists have identified genetic variants influencing risk. Non-genetic factors are largely environmental such as exposure to tobacco smoke, air pollution, the presence of mold and dampness, animals, and obesity to name a few. Recently, maternal stress and environmental risk have been reported to be positively correlated with low birthweight, asthma and/or allergy history in the mother and/or father, chronic bronchitis history in the mother, and primary education in the mother and/or father.[7] and allergen profile in house dust from homes of allergic and non-allergic subjects were significantly different from the Growing Up in Singapore Towards Healthy Outcomes (GUSTO) cohort.[8] An ecological study by Li, et al showed a one-degree Celsius increase in temperature variation between neighboring days (TVN) was found to be associated with a 4.2% increase in hospital visits for childhood asthma.[9]

In low-middle income countries (LMICs), children diagnosed with asthma suffer a higher disease burden, wherein it has been one of the main causes of hospitalization especially in children under the age of five years. Hence, the statement from the 2018 Global Asthma Report considers the potential of hospitalization due to asthma as an indirect indicator of efficacy of care. They also noted that in Europe, hospital admission due to asthma was at 0.6%. Although it is a relatively low proportion in hospital admission, the incidence of hospital admission among children with asthma are higher.[1,10]

*Direct and indirect economic burden of pediatric asthma*

Asthma continues to be a significant source of indirect and direct global economic burden. Direct costs such as diagnostic tests, physician consults, and medication is a burden carried by most patients, especially among those without health insurance. Indirect costs are exemplified by the loss of productivity, working day loss, and school day loss. Costs accrued from asthma are also classified into a third category - the intangible costs. This refers to impairment in quality of life, limitation of physical activities and school performance, and psychological effects.[2]

The components of asthma burden differ between continents. North America and Europe reported medication as the largest component of direct costs, while Middle East and Southeast Asia reported outpatient costs, physician consults,

and ER visits as the major components.[1] This difference may be partially due to the status of government healthcare and their allocation of revenue for asthma prevention and management between regions. Among children and adolescents with asthma, direct costs are high compared to those without asthma, and these costs increase according to asthma severity. Generally, 50-80% of the economic burden of asthma are direct costs.[11] As for indirect costs, absenteeism from school is higher among older children and there is an additional loss when at least one caregiver losses working days to take care of the child.[12] Intangible costs, in comparison, cannot be quantified. However, the burden is still considerable in both the quality of life (QoL) of the child and their caregiver. It considers the actual distress and suffering experienced by individuals resulting from having asthma due to its exacerbations and complications. In a study relating asthma severity with QoL of children, their results show that children with uncontrolled asthma had a poorer QoL in comparison to those with controlled asthma. However, in terms of psychosocial well-being, children with asthma are equally affected with no relation to their symptom control.[13]

*Consequences of asthma beyond the pediatric years*

Other metrics of asthma burden are lifelong outcomes, such as increased risk for Chronic Obstructive Pulmonary Disease (COPD), morbidity, and mortality. This translates to the lifelong disease burden of asthma. In the 2015 GBD, the overall asthma accounted for 1.1% of the global estimate of DALYs per 100,000 of all causes and was the 14$^{th}$ highest ranked cause of global Years Lived with Disability (YLDs) at all ages.[15] The report claims that asthma, second to COPD, is the most important respiratory disease in consideration of disease burden through YLDs and DALYs.

*Morbidity and mortality*

Mortality from asthma, however, is relatively low for all ages.[2] This is considerably due to the preventive aspect of death from asthma with proper management, particularly in preventing acute attacks. In 2016, the GBD estimated around 420,000 people in the world died secondary to asthma, more than 1000 per day; this contributes to only 1% of all deaths in most countries.[1] Mortality rates increased from mid-childhood to old age, the majority after middle age, which might be confounded by an existing comorbidity during adulthood. Based on the World Health Organization (WHO) Mortality Database in 2017, among low- and middle- income countries, from the period of 2011 to 2015, the Philippines ranked third in age-standardized deaths for asthma per million population. The trend in death rates has fallen from 2001-2005 to 2011-2015 by half and this was reflected among ages 5 to 34 years old.[1,17] From the ISAAC Phase One findings, they noted a significant positive correlation between asthma mortality in children and the prevalence of severe asthma symptoms among six to seven year old children across 29 countries and 13 to 14 years old children across 38 countries.[1,3] This finding further adds to the significance of updating the CPG for asthma.

*Literature review of Philippine studies on pediatric asthma*

A scoping search and review of related literature of local studies on pediatric asthma was conducted and a combination of different search strategies and keywords were done. We used the following search engines: HERDIN, EBSCO, MEDLINE, Google Scholar, Scopus, and others (see Appendix 2B for search strategy and yield). These topics on pediatric asthma were grouped into (a) diagnostics and its modalities, (b) disease severity, exacerbations, and control, (c) primary and secondary prevention measures, and (d) health promotion and education. The search yielded only 15 useful studies with full texts available.

For the diagnostics and investigative procedures involving lung function tests in the pediatric age group, researchers from the Philippine Children's Medical Center led by the group of Dela Cruz et al in 2017 conducted a study on the tidal breathing analysis, TBA, as a possible tool in diagnosing asthma from age six months to 5 years old. Due to the established difficulty in the application of spirometry in this age group, they conducted the study on 146 asthmatic and non-asthmatic children. They measured the TBA before and 15 minutes after the administration of 250 ug of salbutamol via nebulization. Their results revealed that baseline $t_{PEF}/t_E$ and $V_{PEF}/V_E$ can readily distinguish asthmatics from non-asthmatic children only for 2 years old and below. They suggest that by using the TBA the cut off point to be used were 32.259 $t_{PEF}/t_E$ for and 34.500 for $V_{PEF}/V_E$.[18]

Another study was conducted at PCMC by Columna and Cabanilla in 2019 exploring the possibility of utilizing bronchodilator challenge test using tidal rapid thoraco-abdominal compression technique to diagnose the disease among infants aged 6 to 24 months who were observed to have recurrent wheezing. This was a modification step on the bronchodilator challenge published in the standards released by the ERS and ATS in 2000. The maneuver was adapted from the studies done by Lai et al in 2015 and Jones et al in 2000 when these two groups of researchers tried to establish the normal values for respiratory functions for infants in Taiwan and USA.[19] In this local study, the bronchodilator agent used was a single dose of 400 mcg salbutamol MDI delivered via spacer. Baseline and 15 min post inhalation, Maximum flow and functional residual capacity, V' max FRC, were all determined. The study results revealed that significant difference in the bronchial dilation, based on V' max FRC after the challenge, was noted among infants with recurrent wheezing fulfilling the asthma predictive index scoring compared to normal infants, *p-value* 0.047.[19] However, changes from baseline after challenge was not significant between comparison groups.

For acute exacerbation and control of the disease, the pediatricians in the allergy and immunology group at the University of Santo Tomas conducted a study to determine whether being exposed and sensitive to common allergen worsens the status of exacerbation or asthma severity among children aged 5 years old and below. In 2003, Vicencio and Andaya studied that allergic sensitization and wheezing are often discernable during infancy stage. They investigated if sensitivity to kapok, *D. pteronyssinus*, *D. farina*, cat, dog, mixed feathers, Bermuda grass, mixed molds, cockroach, and Acacia has a relationship on how severe would asthma be in children of this age group. Their results revealed that the prevalence of skin test reactivity to inhalant allergens was almost half, 34% among asthmatic children aged 2 and that it increases with age, *p-value* 0.004.[20] However, there was no significant association between skin test reactivity to identified allergens and severity of asthma.

Investigations were also performed if there were other risk factors or comorbidities that affect the severity of exacerbations encountered by asthmatic patients. Obesity and history of breastfeeding are two of the most explored possible risk factors. In a retrospective cohort study of 303 children aged 5 to 18 years old seen at the ER due to asthma exacerbation by De Vera et al in 2016, results revealed that the prevalence of overweight and obese children were 21% and 28% respectively. Hence, there was no significant difference between obese and non-obese children in reference to the severity of their exacerbation [LR, 0.879; 95%CI 0.42-0.42; P= .88].[21] As for breastfeeding, Butalid et al in 2013 found in their study that among children aged 5 to 7 years old, those who were bottle fed had higher incidence of asthma compared to the breastfed respondents, p-value <.001.[22]

For prevention and treatment, Dr Miguel Noche in 1990 explored the possible use of ketotifen in the prevention of exacerbation among pediatric asthma patients. They found out that the drug was effective compared to the placebo, p-value <.05 with the peak flow meter recording 20 to 60% improvement in FEV.[23] Other papers were not accessible in the local search engines.

In addition to studies conducted in PCMC, they also tried to explore the treatment options for asthmatic children. Estrera et al in 2017 studied the safety and efficacy of oral ICS for controlling moderate and persistent asthma in the 6 to 15 years old age group.[24] In consideration of cost and access, they performed RCT among 40 patients newly diagnosed with the disease. Outcomes of interest include effect on daytime and nighttime cough, need for bronchodilators, limitation of activity, FEV1, PEFR, and control. There was no significant difference found between the two arms.[24] But the reverse was seen when inhaled and intravenous SABA were studied in an RCT trial by Garin and Barzaga in 1992. Their study revealed that at the 15, 30 and 45 minutes mark post giving of medications, the inhalation group had significantly higher asthma severity index, p-value .03, ,02, and .03 , respectively.[25]

Cepeda et al in 2009 conducted a double-blind placebo RCT on the adjunct supplementation of zinc on bronchial asthma as evaluated by their sputum eosinophil levels and asthma control test among pediatric patients.[26] Twelve weeks of supplementation of 20 mg/day zinc was given to experimental group. Notably both groups had lower sputum eosinophil count post supplementation, but the zinc group had significant decrease p-value =.029 but no difference between group and from baseline asthma control test within each group were determined.[26] They proposed that the supplementation may have decreased airway inflammation among asthmatic patients.

In Key Question 5 (KQ5) of this CPG, local studies on the validation of patient-reported asthma control tools are cited accordingly.

We recognize that local pediatric asthma research outputs have been either (1) conducted but not published in a peer reviewed journal and (2) published in journals not indexed in the search engines used in the search. In future updates of this CPG, we welcome peer-reviewed and published Philippine-based studies.

**Rationale for the development of the pediatric asthma CPG**

A clinical practice guideline for pediatric asthma is needed because of the following reasons:

a. Challenges in diagnosis and monitoring

Respiratory symptoms such as cough and wheezing are common in children, and there are several "mimics" of asthma. Wheezing is identified as a common clinical problem among the pediatric age group, especially during infancy. In American Thoracic Society documents, 34% of children had at least one episode of wheezing before reaching 3 years old. It can signify either (1) early onset asthma; (2) diminished airway function; or (3) innate immune responses.[27] Therefore, a definitive and systematic method is necessary to capture the correct diagnosis and give the optimal treatment.

Spirometry, the gold standard for asthma diagnosis, is impracticable for very young children. Spirometry has been identified as the gold standard in asthma diagnosis, however many clinicians do not routinely use this in diagnosing their suspected asthma patients in children due to limited access to the machine, problems with interpretation of results, and difficulty of performing the protocol since it requires effort-dependent lung maneuvers.[28, 29, 30] There are also emerging tests such as FeNO4 and oscillometry.[29-33] The Philippine Academy of Pediatric Pulmonology had previously released recommendations on pediatric pulmonary function testing[34] and will be releasing an update to their proceedings on Pediatric Pulmonary Function Testing in mid-2022.

b. Underuse, misuse, or overuse of asthma devices

The effectiveness of asthma management is a result of interplay among: finding the device best suited for a patient; ability of the clinician to give instructions on the importance of performing the correct technique in using the device; and the reception and acceptability of the patient in using the device.[36-38] Despite international recommendations that device such as spacers be used to maximize drug delivery, particularly for the use of pediatric metered dose inhalers (MDIs), in addition to little knowledge and education about asthma as a disease entity, under-utilization was noted in various countries, including high-income countries such as the United Kingdom and Canada, at 10% and 46% respectively.[36] Misuse of devices was also reported among pediatric patients which often resulted to poor compliance and, concomitantly, control of the disease. Spacers and valved holding chambers with facemasks are often advised among pediatric patients. However, if the facemask is large relative to the size of the child's face, the inadequate seal leads to poor or varied dosage delivery.[36] This example of improper device use is associated with lack of asthma education, irregular clinic follow ups, and three or more visits to emergency department (ED) due to severe asthma exacerbations.[37]

c. A new group of long acting beta-agonists, long acting muscarinic antagonists, and advances on immunomodulators and immunotherapy in asthma management

There is emerging research on long-acting beta-agonists (LABAs) and immunomodulators. The identification of the sub-phenotypes under severe refractory asthma, which were characterized by different clinical and physiological features reflecting separate immunopathologies, necessitated research on a new generation of LABAs, role of LAMAs as a treatment additive, immunomodulators, and immunotherapy in the arsenal of asthma management and treatment.[39] The recently identified ultra-long acting LABAs include indacaterol, carmoterol, olodaterol, vilanterol and abediterol, which are currently undergoing clinical trials.[40, 41]

Research on immunomodulators and immunotherapy targeting each phenotype are currently ongoing.[47] Allergen Immunotherapy, or AIT, is continuously being investigated and evaluated for its safety and effectivity based on their routes of delivery among pediatric age groups: subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT).[48-50] Although proven to be an effective adjunct in the treatment of asthma in adults, long term effects and safety of House Dust Mite Sublingual Immunotherapy (HMD-SLIT) tablets are being investigated among children and adolescents.[48] Benralizumab, mepolizumab, omalizumab and reslizumab are four of the immunomodulators that have shown potential in the management of asthma, and its safety and efficacy for children are being studied.[50]

d. Chronicity of the illness and implication on families and lifestyle

As a chronic respiratory illness, asthma imposes a considerable burden of accrued expenditures in terms of regular or emergency consults, medications, and preventive measures. Precautions for daily home and school activities, such as sports and care of pets and the need to routinely monitor asthma control have direct and indirect effects, not just on the child, but on the immediate caregiver and the rest of the family, as their lifestyle is constrained by medications and frequent precautions that can curtail their day-to-day activities. A study using the Pediatric Quality of Life Inventory Family Impact module on parents of children with asthma showed that additional difficulties such as anxiety and financial hardships, waking with asthma symptoms one or more nights a week, regular use of symptom reliever medication and female gender were independently associated with lower QoL.[52] They also found lower socioeconomic status of the family and exposure to molds increased the odds for a lower QoL.

e. Update of the 2002 PAPP asthma guidelines

The last formal guideline was released in 2002,[53] and there have been no updates since then.

f. Opportunity for national dissemination and implementation

In 2018, DOH Secretary Francisco Duque released Administrative Order (AO) 2018-0019, entitled *Guidelines on the Institutionalization and Implementation of the National Clinical Practice Guidelines Program.*[54] This AO provided the framework for quality assurance of CPGs and standardization in all processes from planning to implementation, whether they are produced by DOH or externally (i.e. medical societies.) It mandated the formation of the National Guideline Clearinghouse, which shall appraise guidelines prior to endorsement to the Secretary of Health for approval. Once approved by the DOH, it shall be used to guide clinical practice and policy development of pertinent clinicians and payers of healthcare.

# Part II. Objectives

## End-users of the guideline

The primary target users of this guideline are physicians who are directly involved in the care of children and adolescents with asthma. This includes general and subspecialist pediatricians, family medicine physicians, school physicians, surgeons and anesthesiologists, general practitioners, and public health doctors. Owing to the broad scope and preventive nature of several of the recommendations, we aim for this CPG to be useful for pediatric asthma patients and their families, (2) schools, (3) health promotion initiatives, (4) hospital and clinic administrators, (5) policymakers in the Department of Health, Philippine Health Insurance Corporation, local government units, and (6) related guideline developers.

## Target population to whom the guideline is meant to be applied

This guideline is applicable to asthma patients ages 18 years and below, and their families.

## Objectives of the Guidelines

General Objective

To provide pediatricians and healthcare professionals with a trustworthy guideline for the diagnosis and management of Filipino children and adolescents with asthma

Specific Objectives

a. To provide evidence-informed and context-specific recommendations for commonly encountered questions relating to Filipino children and adolescents with asthma
b. To ensure methodological rigor and timeliness in the adaptation of global pediatric asthma guidelines, combined with the best available evidence suitable and equitable for the Philippine setting

## Equity in the guidelines

Integral to the objectives is to ensure that the guidelines promote equity in the care of the Filipino child with asthma. Abiding with the WHO's declaration that "the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition," the proponents of this CPG revision, updating and adaptation, that equity, human rights, gender and other social determinants of health considered in each step of the CPG conceptualization, re-formulation and revision. Recommendations developed with reduction of health inequalities as one of its major considerations. For asthma, this focus on equity will be to ensure that the recommendations are practicable and acceptable in various settings (primary vs tertiary care, urban vs rural, geographically isolated and disadvantaged areas) in the Philippines, with special considerations on access to medicines, human health resources, gadgets, and technology.

Each group involved in this guideline development, especially the Lead CPG provider, ensured to integrate equity in critical aspects in the CPG development, namely: topic selection; planning the CPG revision and updating; setting up of technical working groups; conflict of interest; key questions formulation; evidence retrieval and synthesis; evidence assessment; recommendation proposal; publication in relevant scientific media; and adaptation, implementation, and evaluation. Answers to frequently asked questions raised during the first plenary session presenting the CPG are also reported in this guideline version.

## Scope and Limitation

This CPG covered key issues ranging from prevention, lifestyle, diagnosis, primary care, and management of severe asthma, for asthma patients aged 18 years and below in the Philippines.

This guideline is limited to pediatric asthma and shall not include the definitive diagnosis, treatment, or management of mimics of asthma and cardiac wheezing, asthma care in adults, and general prenatal care of pregnant teenagers with asthma. The guideline also does not take into consideration economic evaluations and health technology assessment.

# Part III. Guideline Development Working Groups

The following are the groups involved in the development and approval of this CPG:

## Lead CPG Developer and Steering Committee

The Lead CPG Developer is the Philippine Academy of Pediatric Pulmonologists (PAPP), Inc. The PAPP is the national accrediting and training professional medical society for the subspecialty of pediatric pulmonology in the Philippines. The specific Steering Committee is the Asthma Committee of the PAPP, Inc.

The Executive Board of the PAPP has appointed Dr. Rozaida Villon and Dr. Charito delos Santos as co-chairpersons of the Asthma Committee. Dr. Villon, Dr. Delos Santos, and the members of the Asthma Committee were responsible for the overall governance of the CPG, including identifying the qualifications and areas of expertise of who will compose the Asthma Consensus Panel and the Evidence Review Experts.

## Consensus Panel (CP)

The DOH requires that a Consensus Panel be composed of "10 to 15 multi-sectoral representatives from healthcare practitioners, patients, advocates, methodologists, and DOH representatives who can influence the uptake of CPG recommendations." The Consensus Panel was selected through a formal Stakeholder Mapping process.

The Consensus Panel for this Pediatric Asthma CPG consisted of representatives from the following organizations:

a. Philippine Academy of Pediatric Pulmonologists, Inc.
b. Philippine Pediatric Society
c. Department of Health
d. Philippine Society of Allergy, Asthma, and Immunology
e. Philippine College of Emergency Medicine
f. Philippine Academy of Family Physicians
g. Philippine Society of Pediatric Anesthesiologists
h. Philippine Society of Public Health Physicians
i. Association of Municipal Health Officers of the Philippines
j. Philippine Alliance of Patient Organizations

The Consensus Panel was consulted on the content of the guidelines in terms of (1) relevance of the questions for the CPG and (2) feasibility and acceptability of the recommendations shortly after the first draft of the guidelines were produced. The management of the consensus process and evaluation of conflict of interest (COI) assessment was performed by an independent management body (Healthcare Policy and Practice Management, Inc.). All members of the Consensus Panel were offered an honorarium for participation, to be received once the consensus process was completed. All meeting costs were covered by the PAPP. Each panel member submitted a signed personal declaration of conflict of interest prior to inclusion in panel meetings.

## Evidence Review Experts (ERE) and Medical Editors

The Lead CPG Developer has procured the technical assistance of an independent Philippine research company, 101 Health Research, to perform the following tasks: (1) searching and retrieval of relevant evidence-based journal articles, reviews and sources; (2) evaluating the retrieved evidence by calculating the quality scores, or similar such appraisals; (3) writing the protocol and the manuscript; (4) giving feedbacks on all assessments; and (5) reviewing the draft guideline before sending it out for external reviews and consultations with independent bodies.

# Part IV. Methods

## Priority setting for key clinical questions

A series of round table discussions were convened within the PAPP Asthma Committee to formulate key clinical questions. The key questions were discussed in detail through an extensive series of consultations with PAPP, an in-depth interview with a family with asthma based in Baclayon, Bohol, and a Municipal Health Officer based in Samar. These face-to-face meetings were performed shortly before the pandemic set in. After the onset of the pandemic, all meetings and communications were conducted through email and online meeting platforms.

On approval by the lead CPG Developer, the ERE proceeded to perform an initial scoping search of guidelines at that time. The international guidelines that were considered for reference and review include:

a. Philippine Academy of Pediatric Pulmonology Clinical Practice Guideline for the Management of Pediatric Asthma 2002[53]
b. Global Initiative for Asthma (GINA) 2018-2021 updates[1]
c. National Asthma and Prevention Program 2018[55]
d. PRACTALL (EAACI and AAAI) 2007[56]
e. British Thoracic Society/Scottish Intercollegiate Guideline Network British Guideline on Management of Asthma 2019[57]
f. Asthma, Allergy and Immunology Research[41, 58]
g. Japanese Guideline for Childhood Asthma 2017[59]
h. Asthma and Respiratory Foundation NZ Child and Adolescent Asthma Guidelines: A Quick Reference Guide 2017[60]
i. National Institute for Health and Care Excellence (NICE): Asthma: Diagnosis, Monitoring and Chronic Asthma Management Guideline 2017[61]
j. European Respiratory Society Clinical Practice Guidelines and Task Force Reports[29, 30, 34, 41]
k. American Thoracic Society Clinical Practice Guidelines[27, 28, 31]
l. Korean Asthma Guideline 2014[62]
m. Singapore CPG Management of Asthma 2008[63]
n. 2014 Malaysia Childhood Asthma CPG Consensus Statement[64]
o. Saudi Arabia Pediatric Asthma CPG 2019[65]

## Comprehensive literature search

Based on the Key Issues and Questions formulated by the Lead CPG Developer for aspects of Diagnosis, Assessment, Treatment, Education, Prevention, and Others, the Evidence Review Experts retrieved literature on the topic using a combination of MeSH and free text search keywords. We covered publications from 2009 to 2021; covering pediatric age group from birth to 18 years old; written in English or in English translations from any language; developed in any country but with special preference for Asia and LMICs; and produced by professional medical societies, academe, or governments.

There were four main rounds of literature search to cover various study types. The first round was specific to clinical practice guidelines; that is, we had searched for all published pediatric asthma related guidelines. The second round was specific to pediatric asthma-related systematic reviews and similar evidence synthesis forms. The third round was specific to original research (RCTs, cohort, cross-sectional, case-control, descriptive, qualitative) to look for new research articles that may not have been covered by previously published CPGs and systematic reviews, especially for *de novo* recommendations. The fourth round of literature search was for pre-prints and for gray literature, if appraised to be applicable. Due to the varied types of research and policy documents for, we used a combination of different search strategies. We used HERDIN, MEDLINE, Google Scholar, and Epistemonikos as our primary search engines (see Appendix).

The general approach in determining the CPG questions and their specific search strategies is that of the Population, Intervention, Professionals, Outcomes, and Health Care Setting and Context (PIPOH) approach.

**Box 1. PIPOH Approach for formulation of the CPG questions**

| PIPOH | Example |
|---|---|
| Population | Age 0-18 years, male or female, with or suspected to have bronchial asthma |
| Intervention | Prevention, Diagnosis, Treatment, Maintenance |
| Professionals | Healthcare professionals |
| Outcomes | Resolution of acute asthma attack or return to baseline or normal lung function, control of symptoms, prevention of recurrence of acute attacks |
| Health Care Setting and Context | Outpatient and inpatient settings<br>Emergency Room settings<br>Community and school settings<br>Philippines, LMIC context, devolved health system with a relatively large importance of private service providers |

Following the previously postulated PIPOH, we searched for guidelines and relevant literature using the Population, Intervention, and Outcome (PIO) model. Figure 1 shows the proposed search key terms, following the research question: "*What are the current techniques for the assessment, diagnosis, treatment, control of Bronchial Asthma among the Pediatric age group?*"

The boxes below each search category exemplified search topics or keywords to be used in gathering relevant evidence-based documents. These were refined during the search process to ensure all possible sources were exhausted. A variety of search strategies such as using exact phrases, truncation, wildcard creation, adjacency, subject headings, citations, and Boolean logic were utilized in this manner.

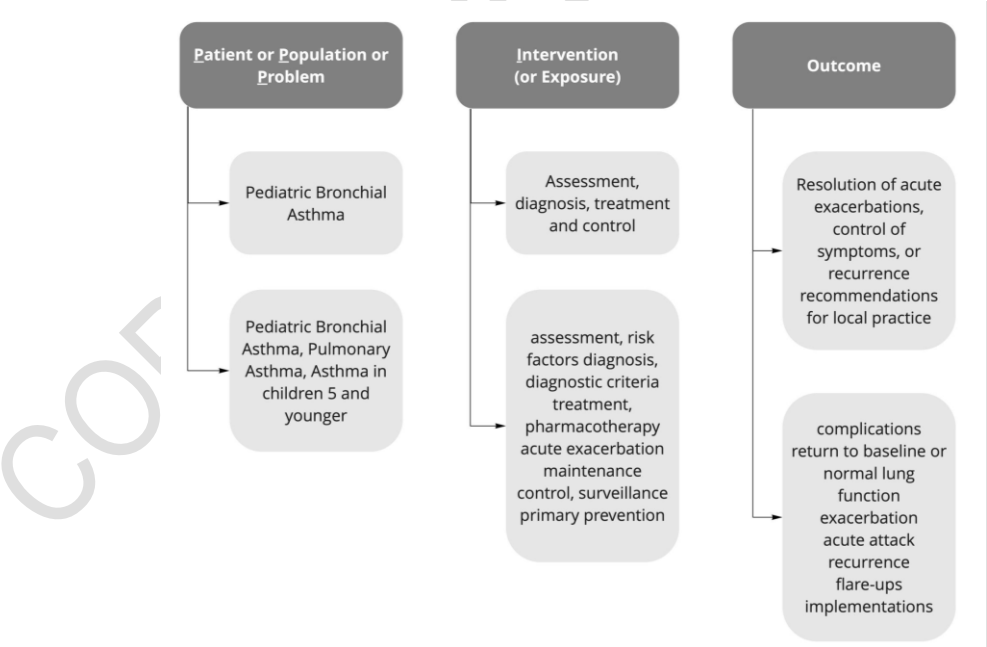


**Figure 1. Search Strategy following the PIO model**

Depending on the nature of the health questions, various research question framework approaches were utilized for the literature search, see Box 2.

**Box 2. Approaches to formulating the Health Questions for Literature Search**

| | Definition | Types of research |
|---|---|---|
| **PICO/PIO** | Population, intervention, comparison, outcome | Interventional/experimental research |
| **PECO/PEO** | Population, exposure, comparison, outcome | Observational/epidemiological studies |
| **PIRT** | Population, index test, reference test, and target condition | Diagnostics and agreement studies |
| **SPICE** | Setting, perspective, phenomenon of interest, comparison, and evaluation | For exploratory 'how' or 'why' questions |
| **CMO** | Context, mechanism, outcome | Qualitative research, HPSR (health policy and systems research) |

## Mapping of key questions and guidelines for adaptation

The ERE conducted a comprehensive literature search for all published asthma guidelines and determined whether the guidelines directly answered the identified key questions in the CPG protocol. From an initial list of 15 guidelines, a total of four guidelines were considered for adaptation: GINA, BTS, New Zealand, and Japan. The ERE and PAPP conducted an AGREE-II workshop and appraised the four guidelines, and this further narrowed down the list to GINA and BTS.
Through a series of virtual focus group discussions, we determined whether the recommendations from GINA and BTS directly answered our key questions. When key questions were of a general nature (also known as a background question), the CPG Developers determined more specific sub-questions (known as foreground questions). The recommendations from GINA and BTS were mapped according to the specific sub-questions or sub-sections.

## Appraisal of guidelines and recommendations

Each asthma guideline and supplementary articles resulting from the search were screened and appraised using the Appraisal of Guidelines for Research Evaluation II, AGREE II Instrument.[55] Its previous version, the AGREE Instrument, was first published in 2003 by a group of international guideline developers and researchers, the AGREE Collaboration, to aid in the assessment of the quality of guidelines, defined as the confidence that potential biases of guideline development have been addressed adequately and that the recommendations are both internally and externally valid and are feasible in practice. It is a 23-item tool consisting of six quality domains. It deals with judgment of methods used in the development of the guideline, the elements of the final recommendations, and the factors that are connected to their acceptance.

An AGREE-II workshop was conducted by 101 Health Research with members of the PAPP Asthma Committee.

The AGREE II instrument steps in appraisal: Screening to Recommendation

a. Search strategy and selection of evidence

The ERE members evaluated the source guidelines' search strategy based on their inclusion/ exclusion criteria in reference selection; the relevance and extensiveness of the databases searched; the search strategies utilized; and the number of references identified, included and excluded.

b. Appraising consistency between selected evidence, its interpretation, resulting and recommendations

The ERE members reviewed each guideline's evidence tables and judged for consistency and clinical relevance of the primary study results reported; presence of heterogeneity of the studies; whether the recommendations were supported

by data from the studies included; methods used to determine level of evidence and justification of its recommendation; comparability of the subjects in each study reviewed and included in the guideline; considerations pertaining to the balance between risks and benefits; and processes used by the guideline in defining its recommendation.

c. Assessment of the acceptability and adaptability of recommendations

The Lead CPG Developer and the ERE members determined if the guideline's recommendations should be put into practice; and if it is feasible in practice. Assessment will be done by determining if the population described in the guideline is comparable or similar enough to the population to which the adapted guideline will be applied to; if it will be compatible with targeted patients' views and preferences; if the interventions are available for use in the context of the local setting; if the necessary skills and levels of expertise for implementation are available; if there will be obstacles and constraints in the targeted health care setting that can serve as hurdle to the implementation of the proposed guideline; if the recommendation is compatible with the culture and values of the targeted population; and if the benefits to be gained from its implementation make it worth implementing.

## Declaration and management of conflicts of interest

Stakeholder mapping and conflict of interest (COI) declaration was supervised by an independent consensus panel management team (HPPM, Inc). After stakeholders were identified, we sent official letters of invitations for them to be part of the Consensus Panel. Those who had accepted also underwent COI declaration. The Consensus Panel convened for a virtual onboarding conference.

All members of the Lead CPG Developer, Consensus Panel, Evidence Review Experts, and Medical Writers are obliged to disclose all possible and actual conflicts of interests. Such COI includes intellectual, academic and/or financial types, and is particularly critical for those involved in preparation of systematic reviews, formulation of recommendations, and/or drafting the actual CPG. The disclosure of all possible COIs that have existed four (4) years prior to her/his acceptance of the invitation and/or participation in the CPG development project. All mentioned above signed the Declaration of Conflict of Interest form, in the format required by the Department of Health. Identified and declared conflicts of interest stated by each member were assessed, evaluated, and managed by an independent management group (HPPM, Inc) in accordance with the prescribed policies adapted from the Manual for Clinical Practice Guideline Development of the Department of Health-Philippines.



## Funding

The evidence review, stakeholder mapping, and consensus panel activities of the Asthma Clinical Practice Guideline was entirely funded by the Philippine Academy of Pediatric Pulmonologists, Inc.

## Evidence to Recommendations

*Consensus Panel eDelphi*

The initial draft of the CPG was presented to the Consensus Panel, and the draft underwent several e-Delphi rounds. The comments of the Consensus Panel members were summarized and analyzed by the Evidence Review Experts (101) and the CP Management Team (HPPM). Major points were referred to and resolved by the Asthma Committee, while minor points were resolved by 101 and HPPM.

*GRADE-ADOLOPMENT*

Concomitantly, GRADE-ADOLOPMENT was performed by both the ERE and the Asthma Committee.[66] In GRADE-ADOLOPMENT, recommendations are either adopted, adapted, or developed de novo. Generally, recommendations that have long been established and practiced without any variation (e.g., use of beta2 agonists) are adopted without substantial modification from the original guidelines. Recommendations which may have variation in practice and required equity considerations for low resource settings are adapted to suit local contexts and provide alternatives. Important questions which were not covered directly by GINA and BTS led to de novo recommendations. De novo recommendations were made based on systematic reviews and appraisal of current literature.

Recommendations were then classified into the following types: (i) Evidence-based Recommendation, (ii) Consensus-based Recommendation, (iii) Clinical pathway or classification, or (iv) Good Practice Statement. Evidence-based recommendations were made for questions that covered interventions, diagnostics, prognosis, or harm; and for which the recommendation was made based on existing evidence. This evidence may be based on the references cited by GINA or BTS, or from an independent systematic review appraised by the ERE which may be newer than GINA or BTS references. Consensus-based recommendations were provided for common decision-making points of healthcare professionals, patients, or families as they navigate diagnosis, prevention, and treatment, and for which no or little evidence may be available or feasible. Clinical pathways or classification refer to complex recommendations that involve several steps and various interventions, depending on precedent conditions and response to treatment; these may be evidence-based, consensus-based, or a combination of evidence and consensus. Lastly, Good Practice Statements were given to emphasize practice points that support CPG recommendations, or boost prevention or education, for patients and their families. This classification of recommendations was applied in previously published guidelines such as the DOH-WHO Leprosy Clinical Practice Guidelines,[68] and by Australian government guidelines.[69]

*Strength of recommendations*

The **strength of recommendations** was evaluated whether these are *strong recommendations, conditional recommendations,* or *weak recommendations. Strong recommendations* are given when most clinicians and stakeholders would want to implement the action, and/or most patients would prefer to receive the action, and/or there is moderate to high certainty of evidence, and/or the recommendation may be used as a quality criterion or performance indicator. *Conditional recommendations* are given when most clinicians and stakeholders recognize that different choices will be appropriate for different patients, and/or patient preferences may vary, and/or policymaking will require debates, and/or implementation may be different across settings. Certainty of evidence may range from very low to high. For practical purposes, we gave a conditional rating for recommendations which stakeholders may feel strongly for, but have several clinical requirements, or where it may only be applicable with a specific subset of the asthma population. *Weak recommendations* are very similar to conditional recommendations, but typically have very low to low certainty of evidence rather than contextual considerations. Conditional or weak recommendations mandate shared decision making between healthcare providers and patients, while strong recommendations are typically prescribed by healthcare providers. This rating of recommendations is adapted from the GRADE guidelines (Box 3).[70]

*Certainty appraisal*

This CPG also appraised the evidence coming from either GINA/BTS or our independent review of systematic reviews or latest evidence. We appraised the *certainty* of evidence as either very low, low, moderate, or high. Certainty may also be referred to as quality of the evidence, confidence in the effect estimate, and strength of the evidence across various guidelines. However, we would like to make the distinction that our certainty evaluation begins with quality of evidence but may be downgraded or upgraded depending on various factors. In the GRADE methodology, RCTs start as high, observational studies as low; then downgraded for risk of bias, imprecision, indirectness, inconsistency, publication bias; upgraded for magnitude of effect, dose response, and effect of plausible confounding factors. Certainty ratings were given for evidence-based recommendations. Consensus-based recommendations and clinical pathways may or may not have certainty ratings, as applicable. Certainty ratings do not apply to Good Practice Statements. For recommendations that were labeled as having Evidence A in GINA or BTS, we conducted rapid scoping reviews and if there were no major changes in findings as that from GINA/BTS, we adopted these ratings as having high certainty; for ratings of Evidence B and below, we conducted an independent review and certainty appraisal.

Thus, for every recommendation, there must be:

- Recommendation statement and number (e.g., Recommendation 1a)
- Method: adapt, adopt, or de novo
- Type of recommendation: consensus-based, evidence-based, clinical pathway or classification, or good practice statement
- Strength of recommendation: strong, conditional, weak
- Certainty of evidence for evidence-based recommendations
- Evidence summary, and an explanation or caveats to the recommendation

**Box 3. Strength of recommendations**

| STRONG | CONDITIONAL | WEAK |
|---|---|---|
| When most clinicians and stakeholders would want to implement the action, | When most clinicians and stakeholders recognize that different choices will be appropriate for different patients, | When most clinicians and stakeholders recognize that different choices will be appropriate for different patients, |
| And/or most patients would prefer to receive the action | And/or patient preferences may vary, and/or policymaking will require debates, and/or implementation may be different across settings | And/or patient preferences may vary, and/or policymaking will require debates, and/or implementation may be different across settings |
| And/or there is moderate to high certainty of evidence | Certainty of evidence may range from very low to high. | Typically: due to very low to low certainty of evidence rather than contextual considerations. |
| And/or the recommendation may be used as a quality criterion or performance indicator | For practical purposes, we gave a conditional rating for recommendations which stakeholders may feel strongly for, but have several clinical requirements, or where it may only be applicable with a specific subset of the asthma population.<br><br>Conditional or weak recommendations mandate shared decision making, while strong recommendations are typically prescribed by healthcare providers. | |

Note: This rating of recommendations is based on GRADE.

## Pre-publication Review and Approval

This draft of the guideline is to be presented to the PAPP board and the Consensus Panel for further evaluation, recommendations and approval in a plenary meeting with asthma experts, pediatricians, and stakeholders. The proceedings or comments arising from plenary will be included in the final version of this clinical practice guidelines. The final version is to be approved by the board of the Philippine Academy of Pediatric Pulmonologists, Inc. Once approved, it will be submitted to the Philippine Pediatric Society and the Department of Health.

## Dissemination and Implementation

This CPG will be disseminated through peer-reviewed publications and presentations in relevant national conventions. Every user of this guideline as well as the members of this committee are highly encouraged to send in their experiences and comments with regards to the utilization of the recommendations listed here to the Philippine Academy of Pediatric Pulmonologists, Inc. for the CPG developer to make certain amendments and/or reviews if necessary. We also welcome

end-users to send us any scientific articles or updates regarding the evidence posted here to help us update and improve the guideline.

This guideline is due for updating and revisions every three years depending on the availability of new discoveries and advent of new diagnostics and treatment modalities in the field of asthma management in pediatrics locally and internationally.

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# PART V. CLINICAL PRACTICE GUIDELINES

## CHAPTER 1. DEFINITION AND DIAGNOSIS OF ASTHMA

Asthma is a chronic airway inflammatory condition associated with hyperresponsiveness and variable expiratory airflow limitation. It is a heterogeneous disease that may be present across younger and older pediatric age groups.

Generally, asthma is defined by a history of recurrent respiratory symptoms such as wheeze, shortness of breath, cough, and chest tightness. These symptoms vary in frequency and in intensity over time. The clinical presentation of asthma is reviewed more broadly over time and collectively as a group of signs and symptoms.

For this guideline, we present distinct approaches in the diagnosis of asthma for two age groups: a younger age group defined as below 6 years old, and an older group defined as 6 to 18 years old. For children below six, the inability to perform lung function precludes the documentation of variable airflow limitation and bronchial hyperresponsiveness. It is also in this age group where viral induced recurrent wheezing is common, making it difficult to decide if an event is an initial presentation of asthma.

In both age groups, a structured clinical assessment and ruling out of age-appropriate differential diagnoses are essential in the diagnosis of asthma. A structured clinical assessment includes the child's medical history and physical examination, family history, typical predisposing factors, historical risk factors and response to asthma therapy.

Considering the resource limited settings in the Philippines, this guideline presents algorithms to assist primary care physicians in the approach to the diagnosis of asthma in the pediatric population.

In the Philippines, asthma is known as hika (Tagalog), hubak (Cebuano), hapo (Hiligaynon), and usól, hápo' (Bikolano).

### KEY QUESTION 1. WHAT ARE THE CLINICAL SIGNS AND SYMPTOMS TO DIAGNOSE ASTHMA?

**Dr. Ma. Victoria Jalandoni-Cabahug**

*What are the clinical signs and symptoms to diagnose asthma in children below 6 years old and children 6 years old and above?*

**Section 1. Approach to the diagnosis of asthma in children below 6 years old**

**Recommendation 1a**

The diagnostic approach to asthma in children <6 years is clinical: based on the overall picture of symptom patterns, risk factors, response to therapeutic trials, and exclusion of alternate diagnoses.

Clinical pathway adapted from GINA 2021[1] and BTS 2019[2]
Strong recommendation

Recurrent wheezing in children less than six years old is common, and this is typically induced by viral infections. The heterogeneity of etiology of wheezing in this age group makes it difficult to definitively diagnose the child as having asthma. This is especially true during the first episodes, especially of children less than 2 years of age, where viral infections can occur six to eight times per year. It is challenging to differentiate whether wheezing associated with a respiratory viral infection is an isolated event, or due to childhood asthma in evolution.

Presented herein is a probability-based approach, adapted from the GINA 2021[1] guidelines in making a diagnosis of asthma in children below 6 years old.

**Table 1.1 Approach to the diagnosis of asthma in children below 6 years old, according to patterns of respiratory symptoms (adapted from GINA 2021[1])**

| SYMPTOM PATTERN | | | |
|---|---|---|---|
| **Duration of symptoms** | Symptoms of coughing, wheezing, heavy breathing for **<10 days** during upper respiratory tract infections | Symptoms of coughing, wheezing, heavy breathing for **>10 days** during upper respiratory tract infections | Symptoms of coughing, wheezing, heavy breathing for **>10 days** during upper respiratory tract infections |
| **Frequency of symptoms** | **2 to 3 episodes** per year | **>3 episodes** per year<br><br>**OR** severe episodes and/or night worsening | **>3 episodes** per year<br><br>**OR** severe episodes, and/or night worsening |
| **Symptoms between episodes** | **No symptoms** | Between episodes, the child may have **occasional** cough, wheeze, or heavy breathing | Between episodes, the child has cough, wheeze, or heavy breathing during play or when laughing<br><br>Known to have allergic sensitization, atopic dermatitis, food allergy, or family history of asthma |
| **Proportion of young children with asthma** | **Few** have asthma | **Some** have asthma | **Most** have asthma |
| **Asthma category** | **Less likely** to be asthma<br><br>**Hindi pa maituturing** na hika | Asthma **suspect**<br><br>**Maaaring** may hika | **More likely** to be asthma<br><br>**Malamang** may hika |

**Section 1.1. Components and clinical features considered in strengthening the basis for making a diagnosis of asthma in children below six years old**

### 1.1.1 Component 1

**Symptom patterns (recurrent episodes of wheeze, cough, breathlessness typically manifested by activity limitation) and nocturnal symptoms or awakenings**

Cough is typically recurrent or persistent and dry. It is usually worse at night and may be accompanied by wheezing and breathing difficulties. Wheezing is likewise recurrent and may be heard audibly and occurs often during sleep. Typical triggers of these episodes are vigorous activity, laughing, crying or exposure to tobacco smoke and air pollutants/irritants. They may exhibit limitations in physical activity (e.g., during running, playing, or laughing) and tire out more easily than other children of the same age.

### 1.1.2 Component 2

**Presence of risk factors** for development of asthma, such as family history (especially first-degree relatives) of atopy, allergic sensitization, allergy or asthma, allergic rhinitis or a personal history of food allergy or atopic dermatitis.

### 1.1.3 Component 3

**Therapeutic response to controller treatment**

A therapeutic trial with low dose ICS and as needed SABA, results in clinical improvement during the 8-12 weeks of controller treatment and worsening of symptoms when treatment is ceased or discontinued.

The child is first placed on low dose ICS and as-needed SABA over 8-12 weeks. During this time, daytime symptoms, nighttime symptoms, and frequency of wheezing and exacerbations must be documented to evaluate whether the child is responding to treatment. If there is marked clinical improvement during treatment, and deterioration when treatment is stopped, this is supportive of a diagnosis of asthma. A possible repeat trial may be done to be more definite in the diagnosis.

### 1.1.4 Component 4

**Exclusion of alternate diagnosis**

The following table presents clinical findings and alternate (differential) diagnoses commonly encountered in this age group (Table 1.2).

**Table 1.2 Common differential diagnoses for children below 6 years old adapted from BTS 2019[2]**

| Condition | Signs and symptoms |
|---|---|
| **Bronchiolitis** | • Coughing<br>• Decrease in appetite<br>• Fever<br>• Runny nose<br>• Sneezing<br>• Wheezing<br>• In very young infants with respiratory syncytial virus (RSV), the only symptoms may be irritability, decreased activity, and breathing difficulties |
| **Bronchopulmonary dysplasia** | • History of premature birth and prolonged mechanical ventilation<br>• Symptoms since birth |
| **Congenital heart disease** | • Cardiac murmur<br>• Cyanosis when eating<br>• Failure to thrive<br>• Hepatomegaly<br>• Poor response to asthma medications<br>• Tachycardia<br>• Tachypnea |
| **COVID-19[3*]** | • Fever<br>• Cough<br>• Difficulty breathing<br>• Colds<br>• Decreased appetite<br>• Vomiting<br>• Abdominal pain<br>• Watery stools<br>• Loss of smell and loss of taste<br>• Sore throat<br>• Muscle pain<br>• Seizure<br>• Headache<br>• Rash |

| | |
|---|---|
| **Foreign body aspiration** | • Abrupt, severe cough and/or stridor during eating or play<br>• Focal lung signs<br>• Recurrent chest infections and cough |
| **Gastroesophageal reflux** | • Coughing during feeding<br>• Poor response to asthma medications<br>• Recurrent chest infections<br>• Vomiting after large feeds |
| **Immune deficiency** | • Failure to thrive<br>• Recurrent fever and multiple respiratory and non-respiratory infections |
| **Parasitic infections of the lung** | • Cough<br>• Wheezing<br>• Lives in areas with high prevalence of parasitism |
| **Protracted bacterial bronchitis** | • Persistent 'wet' or *mahalak* cough<br>• Poor response to asthma medications |
| **Recurrent viral upper respiratory tract infections** | • Cough and colds for <10 days, and<br>• No symptoms between infections |
| **Tracheomalacia** | • Harsh cough<br>• Noisy breathing when crying or eating or during URTI<br>• Poor response to asthma medications<br>• Retractions<br>• Symptoms since birth |
| **Tuberculosis** | • At least 2 weeks duration of cough and/or wheezing<br>• History of TB exposure<br>• Unexplained fever<br>• Unexplained weight loss |
| **Vascular ring** | • Noisy breathing<br>• Poor response to asthma medications |

**Section 1.2. Eliciting features suggestive of asthma in children below 6 years old**

**Good Practice Statement 1.1**

The following are questions that can be used to elicit features suggestive of asthma:

1. Does your child have wheezing?
2. Does your child wake up at night because of coughing, wheezing, or "difficulty breathing," "heavy breathing," or "breathlessness"?
3. Does your child have to stop running, or play less hard, because of coughing, wheezing or "difficult breathing," "heavy breathing," or "shortness of breath"?
4. Does your child cough, wheeze, or get "difficult breathing," "heavy breathing," or "shortness of breath" when laughing, crying, playing with animals, or when exposed to strong smells or smoke?
5. Has your child ever had eczema, or been diagnosed with an allergy to foods?
6. Has anyone in your family had asthma, hay fever, food allergy, eczema, or any other disease with breathing problems?

The questions enumerated have been adapted from GINA 2021.[1] These questions can be modified for cross-cultural validity and translated to the local dialect.

**Section 1.3. Adjuncts to assist in the diagnosis of asthma in children below 6 years old**

*Should the following tests be used in the diagnosis of asthma in children below 6 years old?*

**Recommendation 1b**

1b.1 Lung function tests, specifically spirometry, are suggested with proper performance guidance among cooperative patients less than 6 years old.

Consensus-based recommendation adapted from GINA 2021[1]
Conditional recommendation

Generally, lung function tests are neither feasible nor reproducible in very young children. This is due to the inability of children below 6 years to perform a reliable spirometry (reproducible expiratory maneuvers) or a bronchial provocation test. Certainty of evidence cannot be graded due to the inherent lack of studies because of the inability of young children to perform these tests.

Lung function tests, specifically spirometry utilization for children 5-6 years, is conditionally recommended when it is feasible with proper performance guidance, as this is an important component in making the diagnosis of asthma. Technical challenges due to the capability of this age group may be barriers to the quality of spirometry results as far as its reproducibility is concerned. This taken into consideration is the limitation of strongly considering this to be done on a routine basis.

1b.2 Plain chest radiography is suggested to be performed in asthma to assist in the exclusion of other diagnosis.

Consensus-based recommendation adapted from GINA 2021[1]
Conditional recommendation

This is a conditional recommendation because while chest radiography has no role in the diagnosis of asthma, it is a common requirement for the diagnosis of alternate conditions which may mimic asthma. As an example, a plain radiograph may assist in ruling out structural abnormalities or chronic infections like PTB or foreign body aspiration in a young child with wheezing. The certainty of evidence cannot be graded because the basis of the recommendation is on exclusion rather than diagnosis itself.

1b.3 Allergic sensitization tests are not required in the diagnosis of asthma, but it is an adjunct when allergen immunotherapy is being considered.

Evidence-based recommendation adapted from GINA 2021[1]
Conditional recommendation

Tests for allergic sensitization refer to skin prick testing or blood testing for serum allergen-specific IgE. These are useful to document specific triggers and are a prerequisite for allergen immunotherapy among difficult-to-treat asthma patients. Certainty of evidence cannot be graded because the basis of the recommendation is on the appropriateness of use rather than diagnosis itself. Refer to KQ6 for more information on allergen immunotherapy.

**Good Practice Statement 1.2**

Asthma predictive tools must be appraised and validated locally before being adapted in practice.

GINA 2021 cites Asthma Predictive Index from the Tucson Children's Respiratory study, which was conducted among children living in Arizona in 1989, and where ethnic groups were not mentioned.[4] However, this tool aims to predict children who will have persistent symptoms and does not differentiate asthma from non-asthma per se. A recent systematic review by Colicino et al in 2019 showed that childhood asthma predictive tools, including API, had poor predictive accuracy with performance variation in sensitivity and positive predictive values.[5]

**Section 2. Approach to the diagnosis of asthma in the 6 to 18 year old group**

The diagnosis of asthma in older children and adolescents in terms of the characteristic respiratory symptom patterns do not differ significantly from that of children below six years old. In addition to clinical assessment, lung function tests are more feasible and reproducible in older children and adolescents. The criteria for evidence of variable airflow limitation and documentation of bronchodilator reversibility can apply in this age group. It is ideal to perform lung function tests when available before treating with controller therapies.

In low resource settings with limited pulmonary function laboratories or spirometry facilities, the approach to the diagnosis of asthma with the assistance of such diagnostic testing is a challenge. The following algorithms presented may guide the primary care physician in the approach to the diagnosis of asthma despite the lack of such diagnostic tests.

Making the initial diagnosis of asthma in this age group is based on identifying both (1) a characteristic pattern of respiratory symptoms, such as wheezing, shortness of breath (or dyspnea), chest tightness or dry cough and (2) variable expiratory airflow limitation.

Whenever possible, it is strongly recommended for all patients to document variable expiratory airflow limitation or obstruction before starting maintenance treatment as evidence in support of the diagnosis of asthma.

**Section 2.1 Diagnostic criteria for older children and adolescents**

**Recommendation 1c**

The criteria for the diagnosis of asthma in older children and adolescents (6 to 18 years old) is based on two key diagnostic features: a history of variable respiratory symptoms and confirmed variable expiratory airflow limitation.

Evidence-based recommendation adapted from GINA 2021[1] and BTS 2019[2]
Strong recommendation, high certainty of evidence

The specific diagnostic criteria for this age group are shown on Table 2.1. Lung function tests are feasible and reproducible in older children and adolescents and have long been validated as the reference standards for pulmonary diagnosis.

**Table 2.1 Criteria for making the diagnosis of asthma in older children and adolescents (ages 6 to 18 years)**

| Diagnostic Feature | Criteria for Diagnosis |
|---|---|
| **First, a history of variable respiratory symptoms** | |
| **Wheeze, shortness of breath, chest tightness and cough.** | • Usually more than one type of respiratory symptom<br>• Occurs variably over time and vary in intensity<br>• Often worse at night or on waking<br>• Often triggered by exercise, laughter, allergens, cold air<br>• Often appears or worsens with viral infections |
| **Second, confirmed variable expiratory airflow limitation, any of the following** | |
| **Documented expiratory airflow limitation** | • At a time when $FEV_1$ is reduced, confirm that $FEV_1/FVC$ is reduced (usually >0.90) |
| **Documented excessive variability in lung function (one or more of the tests below)** | • The greater the variations, or the more occasions where excess variation is seen, the more confident the diagnosis. If initially negative, tests can be repeated during symptoms or in the early morning. |
| **Positive BD reversibility test (more likely to be positive if BD medication is withheld before test: SABA ≥4 hrs, LABA≥15 hrs)** | • Increase in $FEV_1$ of >12% predicted |
| **Excessive variability in twice-daily PEF over 2 weeks** | • Average daily diurnal PEF variability >13% |
| **Positive exercise challenge test** | • Fall in $FEV_1$ of >12% predicted, or PEF >15% |
| **Excessive variation in lung function between visits (good specificity but poor sensitivity)** | • Variation in $FEV_1$ of >12% in $FEV_1$ or >15% in PEF between visits (may include respiratory infections) |

***BD:** bronchodilator

***Variability:** refers to improvement and/or deterioration of symptoms and lung function which may occur over the course of one day (diurnal variability, day to day, or seasonally*).

***Reversibility:** may be referred to as 'responsiveness' in some texts, refers to rapid improvement in $FEV_1$ or PEF, measured within minutes after inhalation of short acting B2 agonist or a more sustained improvement over a duration of time after the initiation of controller treatment such as ICS.

***Variability computation** Diurnal PEF variability = $\frac{[\text{Day's highest PEF} - \text{Day's PEF lowest}]}{[\text{average of day's highest and lowest PEF}] \times 100}$

++ the average of each day's value, diurnal PEF variability, is computed for 1-2 weeks.



**Section 2.2 Diagnostic approach for asthma diagnosis in <u>different clinical scenarios</u> for ages 6 to 18**

A patient who comes in for asthma assessment in this age group may or may not have been started on medications. In low resource settings, lung function tests may not always be available. We present four algorithms for the diagnostic approach of common clinical scenarios: for patients who are steroid-naïve, or already on controllers. Among those on controllers, they may present with minimal or persistent symptoms, or with or without variable airflow limitation.

**Recommendation 1d**

In settings where lung function tests are not readily available, or when older children and adolescents come in with varying symptoms and medications, we suggest the following clinical pathways:

1d.1 Clinical pathway for the diagnostic approach for initial presentation of respiratory symptoms in patients 6-18 years old who are steroid naïve (Algorithm 1)

1d.2 Clinical pathway for the diagnostic approach for patients 6-18 years old on controllers, with variable respiratory symptoms, and without variable airflow limitation (Algorithm 2)

1d.3 Clinical pathway for the diagnostic approach for patients 6-18 years old on controllers, with few respiratory symptoms, with normal pulmonary function tests, and no variable airflow limitation (Algorithm 3)

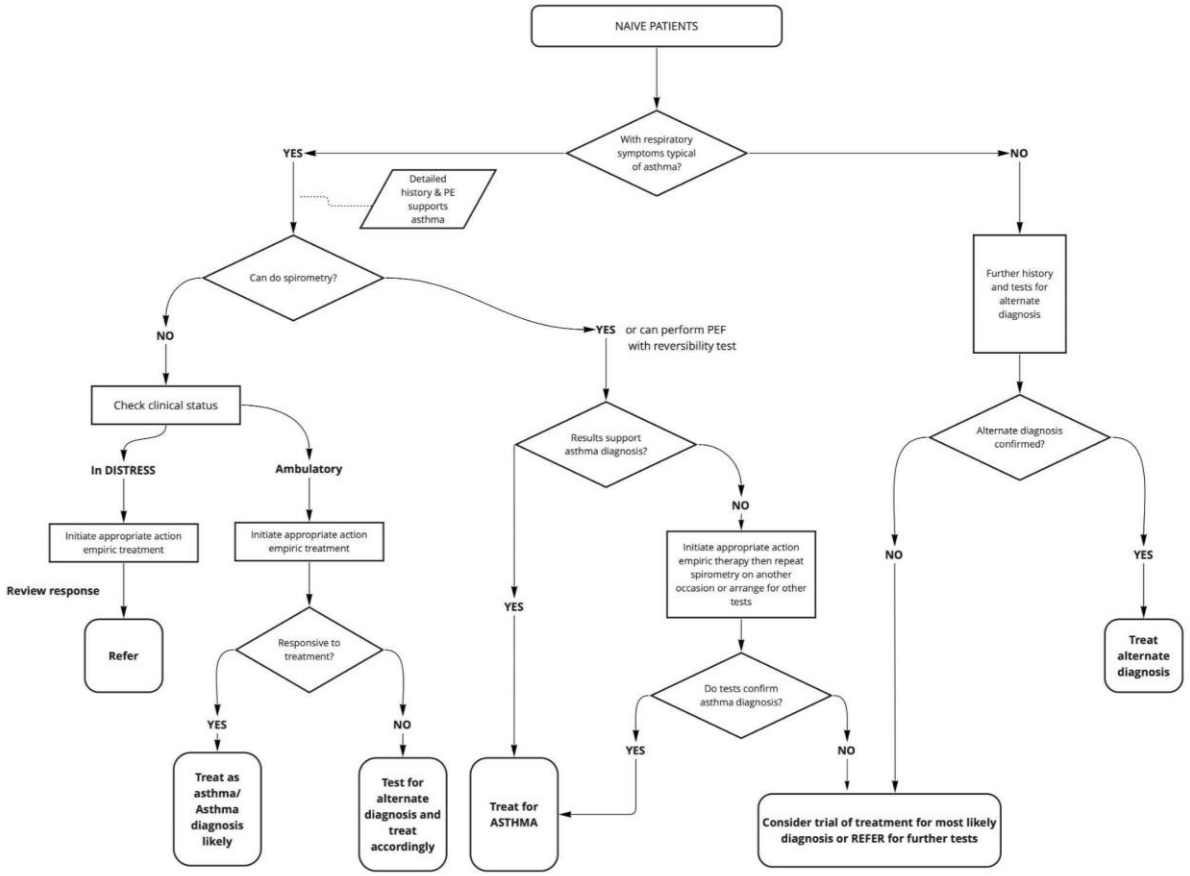
1d.4 Clinical pathway for the diagnostic approach for patients 6-18 years old on controllers, persistent shortness of breath, and persistent airflow limitation (Algorithm 4)

Clinical pathways adapted from GINA 2021[1]
Conditional recommendation

These consensus-based clinical pathways are given conditional recommendation ratings because these are alternative diagnostic pathways for clinical scenarios when lung function tests are not available, or when the patient has already been started on steroids or controller treatment. While the content is substantially similar to GINA, this guideline dissects the text from GINA and presents it in a sequential decision-making process. This guideline further differentiates between patients who are steroid naïve versus already on controllers; and options for when lung function testing is not available. This is because it is common in practice to receive older children and adolescents who are already on controllers (i.e., inhaled corticosteroids), but in whom asthma has not been diagnosed. This critical shift in the approach to diagnosis underwent several focus group discussions and consensus panel reviews.

**Algorithm 1. Diagnostic approach for initial presentation of respiratory symptoms in patients who are steroid naive**

This algorithm illustrates how to assess a patient suspected to have asthma and who have not been on any steroid medication. This stresses the importance of ensuring that a good review of medication intake and its effect on the patient is taken as part of the initial assessment. The algorithm starts with the critical step of determining if the respiratory symptoms are typical of asthma (see Table 1.1), whereas if it is not, an alternate diagnosis should be determined and treated. For those with identified typical asthma symptoms, the left arm of the algorithm will be the guide on the next steps to be done and in which scenarios treatment can be started, an asthma diagnosis can be determined, or if further referral to a specialist is required.




**Algorithm 1. Clinical pathway for the diagnostic approach for initial presentation of respiratory symptoms in patients 6-18 years old who are steroid naïve**

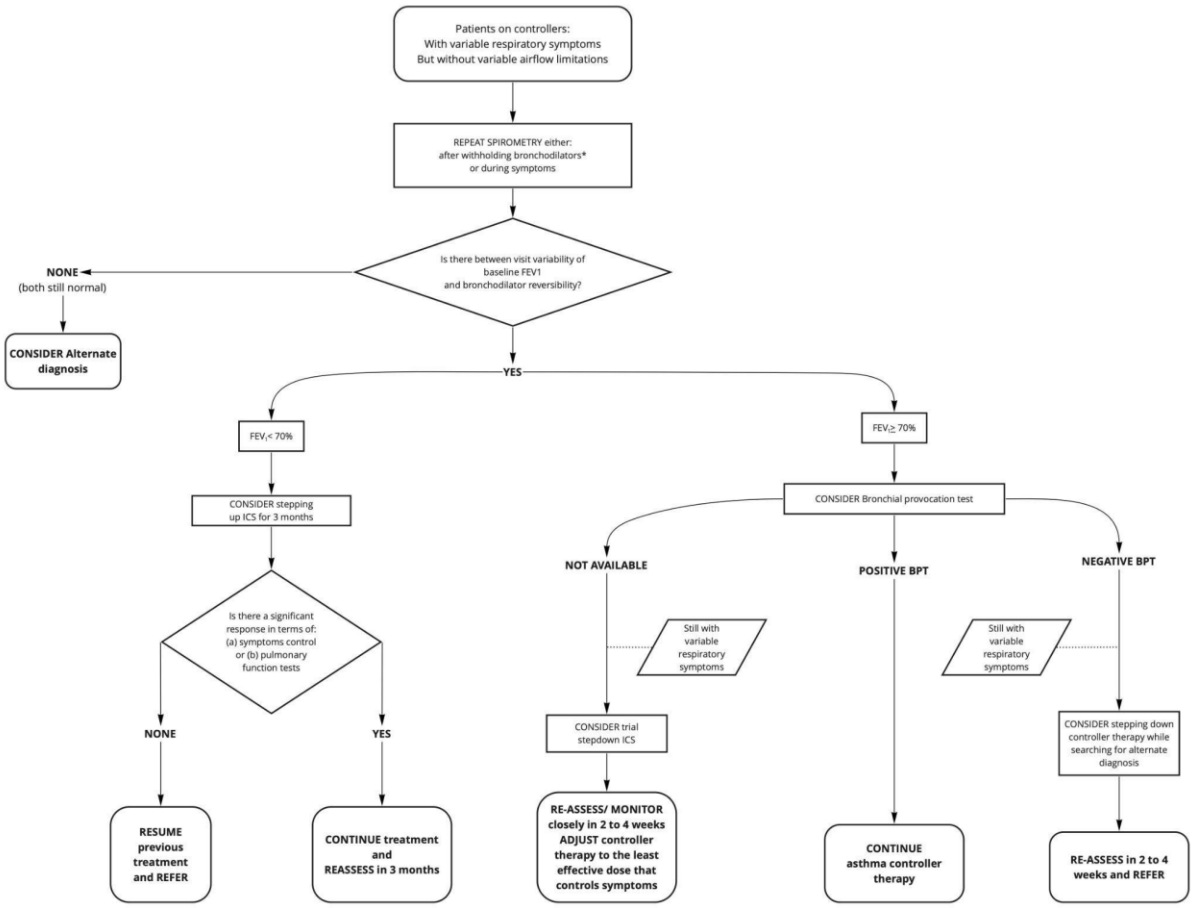
**Approach for confirming the diagnosis of asthma in patients already taking controller treatment (ages 6-18)**

The process of confirming the diagnosis in patients already on controller treatment depends on the patient's symptoms and lung function. If the diagnosis of asthma cannot be confirmed, it would be advisable to refer the patient to a specialist.

The following algorithms show the diagnostic approach for asthma diagnosis in patients on controller treatment. In the Philippine setting where lung function testing is not always available, an alternative pathway is presented. In all situations however, it is always recommended to document variable airflow limitation by performing lung function tests, specifically spirometry, to document the diagnosis of asthma.

**Algorithm 2: Patient on controllers, whose current status is <u>with variable respiratory symptoms BUT without variable airflow limitation</u>**

For those already on controllers, but still with variable respiratory symptoms and without variable airflow limitations, this algorithm starts with repeating the spirometry either after withholding bronchodilator use or during symptomatic episodes. When spirometry results are normal, an alternate diagnosis should be determined. For those with abnormal findings on spirometry, two decision arms are available depending on the $FEV_1$ findings (below OR equal or above 70%). The succeeding steps per arm will lead to either continuing or adjusting asthma controller therapy and/or reassess after some time OR refer to a specialist if an asthma diagnosis is still not confirmed.




**Algorithm 2. Clinical pathway for the diagnostic approach for patients 6-18 years old on controllers, with variable respiratory symptoms, but without variable airflow limitation**

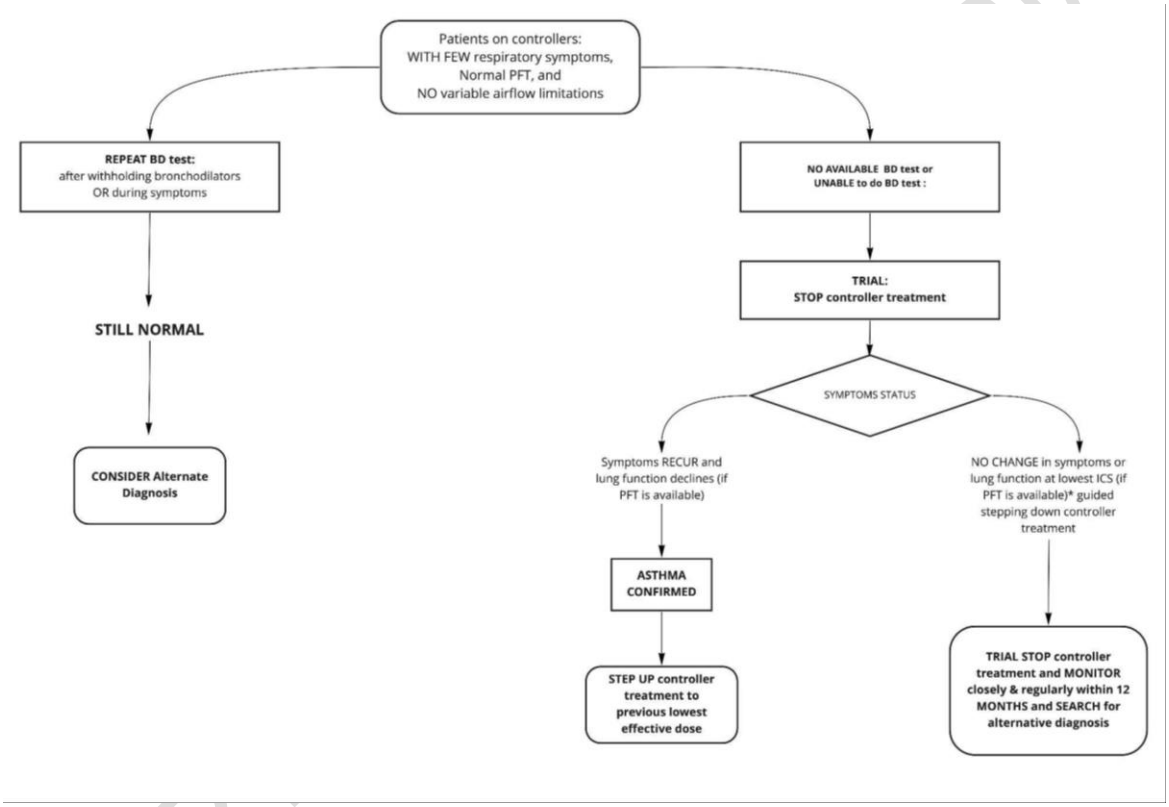
**After withholding SABA for 4 hours or LABA for 12 to 24 hours*

**Algorithm 3. Patient on controllers, whose current status is one with few respiratory symptoms, normal PFTs, AND no variable airflow limitation.**

As for children or adolescents who are on controllers and still with few respiratory symptoms but have normal PFT and have no variable airflow limitations, this algorithm offers two decision arms to help arrive at confirming an asthma diagnosis.

If a bronchodilator test (BD) is feasible, repeat the test either after withholding bronchodilators or during a symptomatic episode. A normal result will lead you to consider an alternate diagnosis.

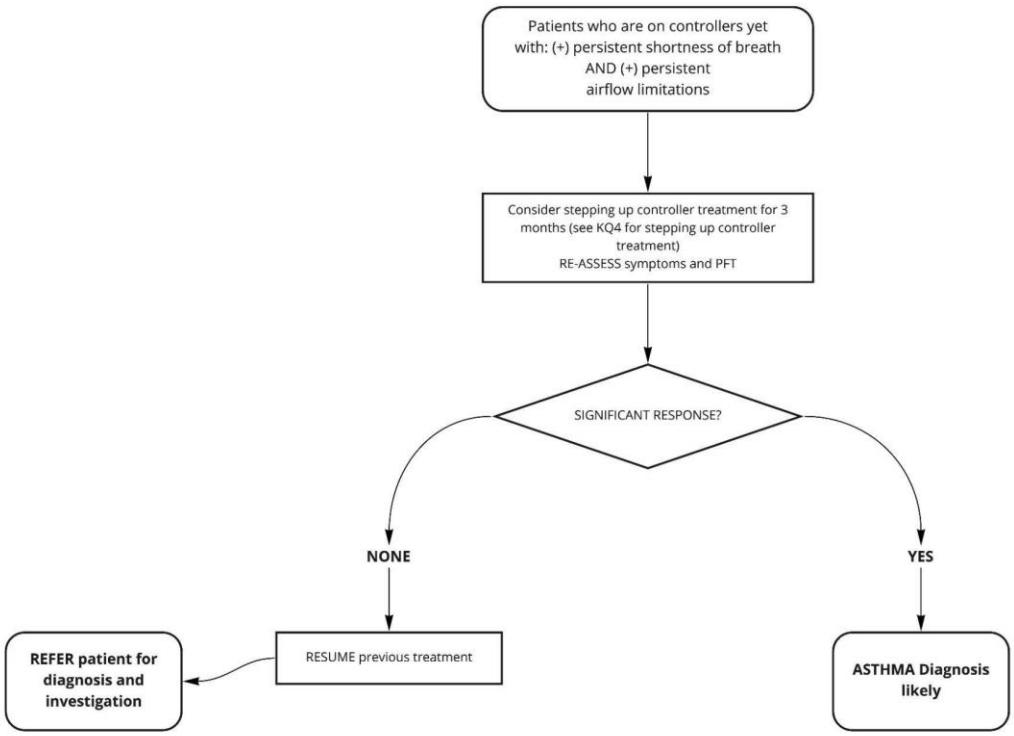
The other arm is stepping down the ICS controller that the patient is on and observing for symptoms and repeating PFT if feasible. This can either confirm the diagnosis of asthma or proceed to a trial of discontinuing the controller therapy and monitoring the patient while assessing for an alternate diagnosis.




**Algorithm 3. Clinical pathway for the diagnostic approach for patients 6-18 years old on controllers, with few respiratory symptoms, with normal pulmonary function tests, and no variable airflow limitation**

**Algorithm 4. Patient whose current status is one with Persistent Shortness of Breath AND Persistent Airflow Limitation**

Lastly, among patients who are on controllers, but persistently experiencing shortness of breath and airflow limitation, this algorithm shows us that stepping up controller treatment should be considered. A significant response of improved symptoms and pulmonary function test (PFT) findings will lead us to an asthma diagnosis, while the opposite response will lead us to resume previous treatment therapy and refer the patient to a specialist.




**Algorithm 4. Clinical pathway for the diagnostic approach for patients 6-18 years old on controllers, persistent shortness of breath, and persistent airflow limitation**

**Section 2.3 Guide in stepping down controller therapy to help confirm the diagnosis of asthma in older children and adolescents (6-18 years)**

**A. Assess**

Assess the patient's status and level of asthma control and lung function. If there are red flags on risk of exacerbation (see KQ2 and KQ3), supervise closely with the step down. Patients should have a stable clinical status (i.e., no respiratory infection, good seasonal conditions, no life stressors) during step down. Provide parents with a Written Asthma Action Plan (WAAP) and educate them formally and thoroughly on its use. Refer to KQ3 for an example of a WAAP.

**B. Adjust**

Instruct parents how to reduce the controller drug (ICS) by 25-50% or how to stop the add-on drugs (e.g., LABA, LTRA). Monitor closely with a follow up visit in 2-4 weeks or sooner if symptoms worsen. Educate patients to recognize worsening symptoms (see KQ8).

**C. Review Response**

Follow up and repeat assessment of asthma control and lung function in two to four weeks. If symptoms increase or variable airflow limitation is confirmed after stepping down asthma medication/ therapy, asthma is confirmed, and controller medications should be reverted to the lowest effective dose that keeps the patient symptom-free. If after stepping down to low dose controller treatment, symptoms do not worsen and/or there is still no evidence of airflow limitation, consider stopping controller treatment. Review asthma control and lung function tests in 2-3 weeks with close supervision, and follow up over the next 12 months.

## Section 2.4 Differential diagnosis in the 6 years to 18 years old group

There are various differential diagnoses for older children ages 6-11 years, and adolescents 12-18 years, and across 6-18 years. Listed below (Table 2.2) are the considerations for alternate differential diagnoses in this age subgroups.

**Table 2.2 Differential diagnosis among 6 to 18 years old**

| Age | Symptoms | Condition |
|---|---|---|
| 6 to 11 years | Sneezing, itching, blocked nose, throat-clearing | Chronic upper airway (UA) cough syndrome |
| | Sudden onset of symptoms, unilateral wheeze | Inhaled foreign body |
| | Recurrent infections, productive cough | Bronchiectasis |
| | Recurrent infections, productive cough, sinusitis | Primary ciliary dyskinesia |
| | Cardiac murmurs | Congenital heart disease |
| | Preterm delivery, symptoms since birth | Bronchopulmonary dysplasia |
| | Excessive cough and mucus production, GI symptoms | Cystic fibrosis |
| 12 and older | Sneezing, itching, blocked nose, throat-clearing | Chronic UA cough syndrome |
| | Dyspnea, inspiratory wheezing (stridor) | Inducible laryngeal obstruction |
| | Dizziness, paresthesia, sighing | Hyperventilation, dysfunctional breathing |
| | Productive cough, recurrent infections | Bronchiectasis |
| | Excessive cough and mucus production | Cystic fibrosis |
| | Cardiac murmurs | Congenital heart disease |
| | Shortness of breath, family history of early emphysema | Alpha1-antitrypsin deficiency |
| | Sudden onset of symptoms | Inhaled foreign body |
| All ages | Chronic cough, hemoptysis, dyspnea; and/or fatigue, fever, anorexia, weight loss | Tuberculosis |
| | Fever, cough, dyspnea, loss of appetite or energy, anosmia, dysgeusia, diarrhea, rash | COVID-19 |

## Section 3. Asthma Phenotypes

Asthma phenotypes refer to recognizable clusters of asthma patients that share similar demographic, clinical, or pathophysiological characteristics. Among patients with more severe asthma, there are phenotype-guided treatments. However, there is limited evidence on whether these phenotypes are associated with treatment response. Further research is underway in understanding the gap in knowledge in the clinical applicability of this phenotypic classification in asthma. For the more common clinical phenotypes of asthma identified, see Table 3.1

**Table 3.1 Most common clinical phenotypes of asthma**[1]

| Asthma Phenotype | |
|---|---|
| **Allergic asthma** | ● Most easily recognized<br>● Often commences in childhood, associated with past and/or family history of allergic diseases<br>● Assessment of sputum before treatment often reveals eosinophilic airway inflammation<br>● Usually respond well to inhaled corticosteroid (ICS) treatment |
| **Non-allergic asthma** | ● Cellular profile of the sputum of these patients may be neutrophilic, eosinophilic or contain only a few inflammatory cells<br>● Often demonstrates less short-term response to ICS |
| **Adult-onset or late-onset asthma** | ● Some adults, particularly women, present with asthma for the first time in adult life<br>● Tend to be non-allergic, and often require higher doses of ICS or relatively refractory to corticosteroid treatment<br>● Occupational asthma should be ruled out |
| **Asthma with persistent airflow limitation** | ● Some with long-standing asthma develop airflow limitation that is persistent or incompletely reversible.<br>● Thought to be due to airway remodeling |
| **Asthma with obesity** | ● Some obese patients with asthma have prominent respiratory symptoms and little eosinophilic airway inflammation |

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# CHAPTER 2. RECOGNIZING AND MANAGING ACUTE EXACERBATIONS

An acute exacerbation refers to an episode of increasing severity and frequency of respiratory symptoms from the patient's usual status, such as cough, wheezing, shortness of breath, nocturnal awakenings, or chest tightness. It may also involve a progressive decrease in lung function (PEF or $FEV_1$). In the Philippine setting, parents are likely to report an increase in use of bronchodilators (i.e., nebulization or metered dose inhalers MDI).

Exacerbations occur either as a recurrent episode in children with previously diagnosed asthma, or as an initial presentation of asthma in a child. These may also be referred to as "acute severe asthma," "flare-up," "attacks," and "episodes." Whether the exacerbation is clinically observed or documented through lung function testing, it necessitates a change in current treatment.

## KEY QUESTION 2. WHAT ARE THE SIGNS AND SYMPTOMS OF AN ACUTE EXACERBATION?

**Dr. Consuelo Lu**
**Dr. Alfredo Bongo, Jr.**

**Section 4. Prevention of acute exacerbations by identifying triggers, risk factors, and risk for asthma-related death**

Note: The key question is on signs and symptoms of acute exacerbations, but the CPG developer and Consensus Panel agreed that identification of triggers, risk factors, and factors for asthma death are essential and clinically useful to include in this section.

### 4.1. Triggers of Acute Exacerbations

**Good Practice Statement 2.1**

Healthcare professionals and families should identify triggers that may be present in the asthmatic child or adolescent's environment or lifestyle. Advice on prevention or mitigation of exposure to these triggers should be offered.

To prevent exacerbations, it is important to identify triggers that may be present in the child's environment or lifestyle. Common triggers of asthma exacerbation include:

1. Viral respiratory infections
2. Allergen exposure (e.g., dust mites, cockroaches)
3. Food allergy as a trigger of wheezing bronchospasm from anaphylaxis
4. Outdoor air pollution, irritants, and environmental tobacco smoke
5. Seasonal changes
6. Poor adherence with ICS, and/or incorrect use of devices

### 4.2. Risk of Asthma-Related Death

**Good Practice Statement 2.2**

Healthcare professionals should determine whether the asthmatic child or adolescent is at risk for asthma-related death.

See Table 4.1 for these risk factors.

**Recommendation 2a**

If there is any risk factor for asthma-related death present, the patient must seek immediate medical care during the exacerbation.

Consensus-based recommendation adopted from GINA 2021[1]
Strong recommendation

It is likewise important to identify patients at risk for asthma-related death and these patients should be advised to seek immediate medical care early during the exacerbation. The same risk factors can increase a patient's risk for exacerbation (Table 4.1).

**Table 4.1 Factors that increase the risk of asthma-related death**

| | |
|---|---|
| **Major independent risk factors for flare ups** | • History of near-fatal asthma with intubation and mechanical ventilation<br>• Hospitalization or ER visit for asthma in the past year |
| **Medications** | • Currently using or having recently stopped using oral corticosteroids. The use of oral corticosteroids is a marker of event severity.<br>• Not currently on inhaled corticosteroids |
| **Uncontrolled asthma symptom and treatment factors** | • Over-use of SABAs, use of more than one canister of salbutamol (or equivalent) in one month<br>• Poor adherence with asthma medications<br>• Poor adherence with (or a lack of) a written asthma action plan |
| **Psychiatric disorder or psychosocial issues** | • Anxiety and/or depression in the child or adolescent, poverty |
| **Co-morbidity** | • Food allergy, history of anaphylaxis |

### 4.3. Independent and modifiable risk factors

**Good Practice Statement 2.3**

Healthcare professionals and families should identify modifiable risk factors present in the asthmatic child or adolescent's environment and lifestyle to prevent exacerbations.

**Recommendation 2b**

Physicians must recommend the specific treatment strategies once modifiable risk factors have been identified.

Consensus-based recommendation, adapted from GINA 2021[1]
Strong recommendation

Risk factors for asthma should be assessed at diagnosis, and periodically during follow-up visits. These factors increase the patient's possibility of an exacerbation even if asthma symptoms are few. Having one asthma flare-up increases the likelihood of experiencing another exacerbation within the next 12 months. Besides optimizing medications, identifying, and treating the patient's modifiable risk factors is important to reduce a patient's exacerbations. For any patient with a risk factor for exacerbation: assess symptom control, adherence to medications and proper use of inhalers or asthma devices, and exposure to triggers; consider stepping up therapy (see KQ 4); and prepare or update the written asthma action plan (see KQ 3).

Enumerated in Table 4.2 are independent and modifiable risk factors and the corresponding treatment strategies adapted from the 2021 GINA guidelines.[1] The treatment strategies are also discussed in more detail in succeeding sections.

**Table 4.2 Independent and modifiable risk factors for exacerbations and corresponding treatment strategy**

| Risk factor | Treatment strategy |
|---|---|
| **At least one severe exacerbation in the past 12 months** | • ICS-formoterol maintenance and reliever regimen reduces risk of severe exacerbations compared to a regimen where the reliever is SABA.<br>• Assess patient's symptom control and consider alternative controller regimen or stepping up of controller treatment<br>• Identify any avoidable triggers for exacerbation |
| **Exposure to tobacco smoke** | • Encourage smoking cessation by patient or family<br>• Consider stepping up ICS dose if asthma is uncontrolled |
| **Low $FEV_1$, especially if <60% predicted** | • Consider giving high dose ICS and/or 2 weeks OCS for 3 months then reassess the patient. There are three options: high dose ICS for 3 months, 2 weeks OCS, or high dose OCS for 3 months and 2 weeks OCS<br>• Exclude other lung diseases (i.e. COPD)<br>• Refer to a specialist in pediatric asthma |
| **Obesity** | • Encourage patient to follow weight reduction strategies<br>• Distinguish if symptoms are due to asthma vs deconditioning, mechanical restriction, and/or sleep apnea<br>• Refer to a specialist in pediatric asthma |
| **Major psychological problems** | • Help patients distinguish between symptoms of anxiety versus asthma<br>• Refer to a specialist in pediatric asthma |
| **Major socioeconomic problems** | • Prescribe the most cost-effective ICS-based regimen |
| **Confirmed food allergy** | • Appropriate food avoidance<br>• Injectable epinephrine, if necessary.<br>• Refer for expert advice |
| **Allergen exposure if sensitized** | • Consider stepping up of controller treatment<br>• Advise patient regarding simple avoidance strategies<br>• Refer for expert advice |
| **High SABA use (>1 canister per month)**<br>**Inadequate ICS**<br>**Not prescribed ICS** | • Check inhaler technique by having the patient and parents demonstrate how they deliver SABA<br>• Check compliance to controller |
| **Risk factors for medication side effects:**<br>**Systemic: Frequent OCS, long term, high dose &/or potent ICS**<br>**Local: high dose or potent ICS, poor inhaler technique** | • Indication for referral for expert advice |

## Section 5. Identifying acute exacerbations and severity

### 5.1 Initial assessment of exacerbation severity

**Good Practice Statement 2.4**

In children and adolescents with signs and symptoms of an exacerbation (e.g., wheezing, coughing, breathlessness, activity limitation), a brief focused history and targeted physical examination should be performed expeditiously without delay in the concurrent initiation of urgent therapy. All findings and interventions should be prompt and properly documented in the medical record. Refer to Table 5.1.

**Table 5.1 Assessing asthma exacerbation severity in pediatric asthma**

| | |
|---|---|
| **History** | • Timing of onset and cause (if known) of the present exacerbation<br>• Severity of asthma symptoms, including any limitation of activity and exercise or interrupted sleep<br>• Any symptoms of anaphylaxis: wheezing, feeling lightheaded, breathing difficulties, tachycardia, clammy skin, confusion and anxiety, and losing consciousness<br>• Any risk factor for asthma-related death (Table 4.1)<br>• All current reliever and controller medications: doses, devices prescribed, adherence pattern, any recent dose changes, and response to current therapy |
| **Physical examination** | • Signs of exacerbation severity (Table 5.2) and vital signs (e.g., temperature, pulse rate, respiratory rate, blood pressure); level of consciousness, ability to complete sentences, use of accessory muscles, wheeze<br>• Complicating factors (e.g., anaphylaxis, pneumonia, pneumothorax)<br>• Signs of alternative conditions that could explain acute breathlessness (e.g., cardiac failure, inducible laryngeal obstruction, inhaled foreign body, pulmonary edema) |
| **Objective assessment** | • Pulse oximetry: Oxygen saturation level <90% signals the need for aggressive therapy<br>• Perform peak expiratory flow (PEF) in patients older than 5 years |

### 5.2 Severity classification of asthma exacerbation

In this section, the adaptation to the severity classification was performed by further specifying the normal reference ranges for vital signs per age group. A tabular summary is provided to demonstrate that for younger children, the management for severe and life-threatening exacerbations are the same. Meanwhile, for older children and adolescents, it is life-threatening exacerbations that require immediate ICU care.

**Recommendation 2c**

An asthma exacerbation severity may be classified as mild, moderate, severe, or life threatening based on their activity level, respiratory rate, cardiac rate, pulse oximetry, and lung function, if evaluated. In children below 6 years old, no distinction is made between severe and life-threatening groups.

Clinical classification adapted from GINA 2021[1]
Strong recommendation

An exacerbation ranges from mild to moderate, severe, or life-threatening depending on signs and symptoms (see Table 5.2). Depending on severity and presence of risk factors for asthma-related death, the management of asthma exacerbation may be managed at home, in a primary care setting, or may require referral to an emergency care facility (see KQ3).

**Table 5.2 Clinical presentation and classification of asthma exacerbation**

| Parameters/ Classification | Age < 6 years old | | | Ages 6-18 years old | | | |
|---|---|---|---|---|---|---|---|
| | Mild | Moderate | Severe/ Life-threatening | Mild | Moderate | Severe | Life-threatening |
| Activity/ Sensorium | Able to talk | | Breathless, unable to talk, confused, or drowsy | Able to talk | Able to talk only in phrases | Breathless or unable to talk | Drowsy, confused |
| Respiratory rate, cpm | No increase in RR | <40/min | >40/min | No increase in RR | <30/min | >30/min | Proceed or triage immediately to an acute care facility or Emergency Department |
| Cardiac rate, cpm | 100-120/min | <140/min | >140/min | 100-120/ min | 100-120/ min | >125/ min | |
| Pulse oximetry | >95% | >92% | <92% | 95% | 90-95% | <90% | |
| Lung Function | NA | | | >50% of personal best | | 30% to 50% of personal best | |

* In order to classify to a higher classification, at least 1 parameter should be present.
* WHO Resting Respiratory rate (Normal for age):[2]
  - 1 month – 12 months = < 50 per min
  - 1 – 5 years old = < 40 per min
  - 6 – 10 years old = < 30 per min
  - 11 – 18 years old = < 20 per min
* Harriet Lane reference range for cardiac rate:
  - 0-3 months = 110-160
  - 3-6 months = 100-150
  - 6-12 months = 90-130
  - 1-3 yrs = 80-125
  - 3-6 yrs = 70-115
  - 6-12 yrs = 60-100
  - >12 yrs = 60-100

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## KEY QUESTION 3. WHAT IS THE MANAGEMENT OF ASTHMA IN AN ACUTE EXACERBATION?

**Dr. Gerarda Ember Afable**

*What is the management of asthma in acute exacerbations in children and adolescents in the following settings:*

- *Management in the home*
- *Outpatient, ambulatory, or primary care settings*
- *Emergency Department*
- *Hospital setting*

The objectives of treatment of asthma exacerbations are the rapid relief of airway obstruction and hypoxemia, to decrease inflammatory pathophysiology, and to prevent relapse. The basic principles in treating asthma exacerbation are as follows:

1. Controlled flow oxygen supplementation to correct hypoxemia
2. Vigorous bronchodilation through repeated administration of inhaled bronchodilator (SABA) to reverse bronchoconstriction which will manifest as improvement in symptoms and lung function
3. Early introduction of systemic corticosteroids to address inflammation
4. Timely initiation of ICS-containing controller treatment

**Section 6. Self-management or home-based management of exacerbations with a written asthma action plan**

**Recommendation 3a**

Healthcare professionals should provide patients and families with an individualized written asthma action plan (WAAP) for self-management or home-based management of exacerbations. The WAAP must be regularly reviewed and updated.

Evidence-based recommendation
Adapted from GINA 2021[1] and BTS 2019[2]
Strong recommendation, low certainty of evidence

An effective asthma self-management education includes individual monitoring of symptoms and/or lung function, as well as a written asthma action plan with regular review by a healthcare professional.

A written asthma action plan (WAAP) includes specific instructions on how to recognize and respond appropriately to worsening of asthma symptoms. Individualized instructions on how to adjust reliever and controller medications are included. Directives on when and how to access medical care and a follow up with their physician are indicated. This written asthma action plan must be reviewed and modified regularly. An English version of the WAAP is provided in Table 6 below, while a Filipino version is provided in the Appendix.

After a self-managed asthma flare-up, patients are still advised to notify their doctors. The follow-up visit within a week will include assessment of symptom control, identification of risk factors and exposure to triggers, and an update of their written asthma action plan. However, if asthma symptoms continue or progress, patients are advised to call and see their doctors immediately.

Evidence Summary:

In the study by Wong SS. et al in 2013, they showed that WAAPs did not provide significant differences in patients' unscheduled doctor visits,[3] the groups compared were composed of 39.5% with controlled asthma against 60.5% with partly/uncontrolled asthma..[3] Additionally, in another study by Lakupoch et al (2018) where WAAPs improved children's outcomes through decreasing ER visits and unscheduled OPD visits, admission days, and school absence days, the population comprised of 78% patients with moderate to severe asthma.[4] The study mentions how characteristics of the

WAAP are an important factor in asthma outcomes.[4] Furthermore, the WAAP's impact can be understood as a way to use clear communication principles which improve asthma counseling quality.[5]
WAAPs is an integral part of asthma education, which a study found useful for children with partly controlled asthma.[6] WAAPs were also found to be effective in the pediatric emergency department when combined with standard discharge instructions, through an educational session with the patient and their family.[7]

Besides being a part of clear communication and education efforts, why WAAPs were seen to be effective can also be explained by providers being more likely to prescribe inhaled corticosteroids in the study group with WAAPs compared to the group with discharge instructions alone.[7] Keep in mind that WAAPs can be effective, given that the communication strategy is appropriate for the patients and their families with an overall effort to educate and that the appropriate treatment strategies are well indicated.

**Table 6. Symptom Based Written Asthma Action Plan (WAAP)**

**ASTHMA ACTION PLAN**

Name _____

Phone _____

Action plan updated: M_____/DD_____/YYYY_____

Bring this action plan to your doctor/nurse at each visit.

| | YOUR DOCTOR | IN AN EMERGENCY, CALL (OR CALL AN AMBULANCE IMMEDIATELY.) | YOUR EMERGENCY CONTACT PERSON |
|---|---|---|---|
| NAME | | | |
| PHONE | | | |

**GREEN ZONE (GO): Asthma is well controlled.**

| | |
|---|---|
| Does not wake up at night due to cough<br>Able to do normal activity (asthma does not limit activities including exercise)<br>No symptoms of asthma flare-up<br>Compliant with asthma medications | Resting Respiratory rate (Normal for age):<br>1month–12 mos. = ≤ 50 per min<br>1 - 5 years old = ≤ 40 per min<br>6- 10 years old = ≤ 30 per min<br>11 - 18 years old = ≤ 20 per min<br><br>If available: Peak flow between ____ and ____L/min |

**ACTION**

1. Continue daily asthma medications and monitor.
2. _____
3. _____
4. _____

Follow up with your doctor as scheduled.

**YELLOW ZONE (Caution): Mild-Moderate Flare-up, Asthma is getting worse.**

| | |
|---|---|
| Wakes up at night due to asthma<br>Unable to do normal activities<br>Increased asthma symptoms (chest tightness, shortness of breath, cough; audible wheeze)<br>Needs reliever medications more often than usual | Resting RR ____ breaths/min to ____ bpm<br>** depends on age of the patient (MD to specify)<br><br>If available: Peak flow between ____ and ___ L/min |

**ACTION**

- Continue daily asthma control medications **PLUS RESCUE MEDICATIONS. Monitor.**

**RESCUE MEDS (Instruction)**

**Step 1:** _____ puffs SABA MDI (+/- spacer) as needed.

☐ OR SABA nebulization (if nebulizer available), with 1 SABA nebule via face mask/mouthpiece.

OR for 12 years old and above: Increase ICS/formoterol dose with a maximum of 72mcg formoterol per day.

**Step 2:** Check resting RR after 10 minutes of giving the medication.

**Step 3:** Repeat SABA treatment if needed, up to 3 times, with an interval of 20 minutes between doses, then see clinical response and follow instructions below.

| | |
|---|---|
| **GOOD RESPONSE if**<br>Resting RR: ≤ ___ breaths/min<br>Wheezing improved.<br>Response to SABA lasts at least 4 hours (without feeling the need of another puff/ nebulizations due to shortness of breath within 4 hours.) | Continue:<br>1. SABA nebulization or MDI puffs via spacer ___ puffs every 4 hours for ____ days.<br>☐ For 12 yrs. and above, ICS/formoterol as reliever; maximum of 72mcg formoterol per day<br>2. If on maintenance medication, increase ICS to _____ puffs 2x/day for ___ days. |
| **POOR RESPONSE**<br>Resting RR: > _____ breaths/min<br>Symptoms remain marked despite rescue medications given | Proceed to Red Zone for management |

Notify your doctor for further instructions.

**RED ZONE (Danger): Severe Flare-up, Asthma symptoms are severe.**

| | |
|---|---|
| Often wakes up at night due to asthma<br>Usual activity severely limited<br>Very short of breath<br>Symptoms are present >24 hrs.<br>Needs reliever medication more often than every 3-4 hours | Resting RR > _____ cpm<br>** depends on the age of the patient (MD to specify)<br><br>Poor response to YELLOW ZONE action |

**ACTION**

- **Continue daily asthma control medications PLUS RESCUE MEDICATIONS. Monitor.**

**RESCUE MEDS (Instruction)**

**Step 1:** _____ puffs SABA MDI (+/- spacer) every hour.

☐ OR SABA nebulization (if nebulizer available), with 1 SABA nebule via face mask/mouthpiece

☐ OR for 12 years old and above: Increase ICS/formoterol dose maximum: 72mcg formoterol/day.

**Step 2:** Check resting RR after 5 - 10 minutes of giving the medication.

**Step 3:** Repeat SABA treatment up to 3 times, with an interval of 20 minutes between doses.

**Step 4:** Start Prednisone/ Prednisolone (__mg/ml), give ___ml NOW then see clinical response and follow instructions below.

| | |
|---|---|
| **POOR RESPONSE if**<br>Resting RR: > _____ breaths/min<br>Symptoms remain marked despite rescue medications given | Continue:<br>1. SABA nebulization or MDI ___ puffs every 20 mins for ____ hours and/or<br>2. For 12 yrs. and above, ICS/Formoterol as reliever; maximum 72mcg formoterol. |

Contact MD/Emergency Number ASAP. Go to the nearest Emergency Department..

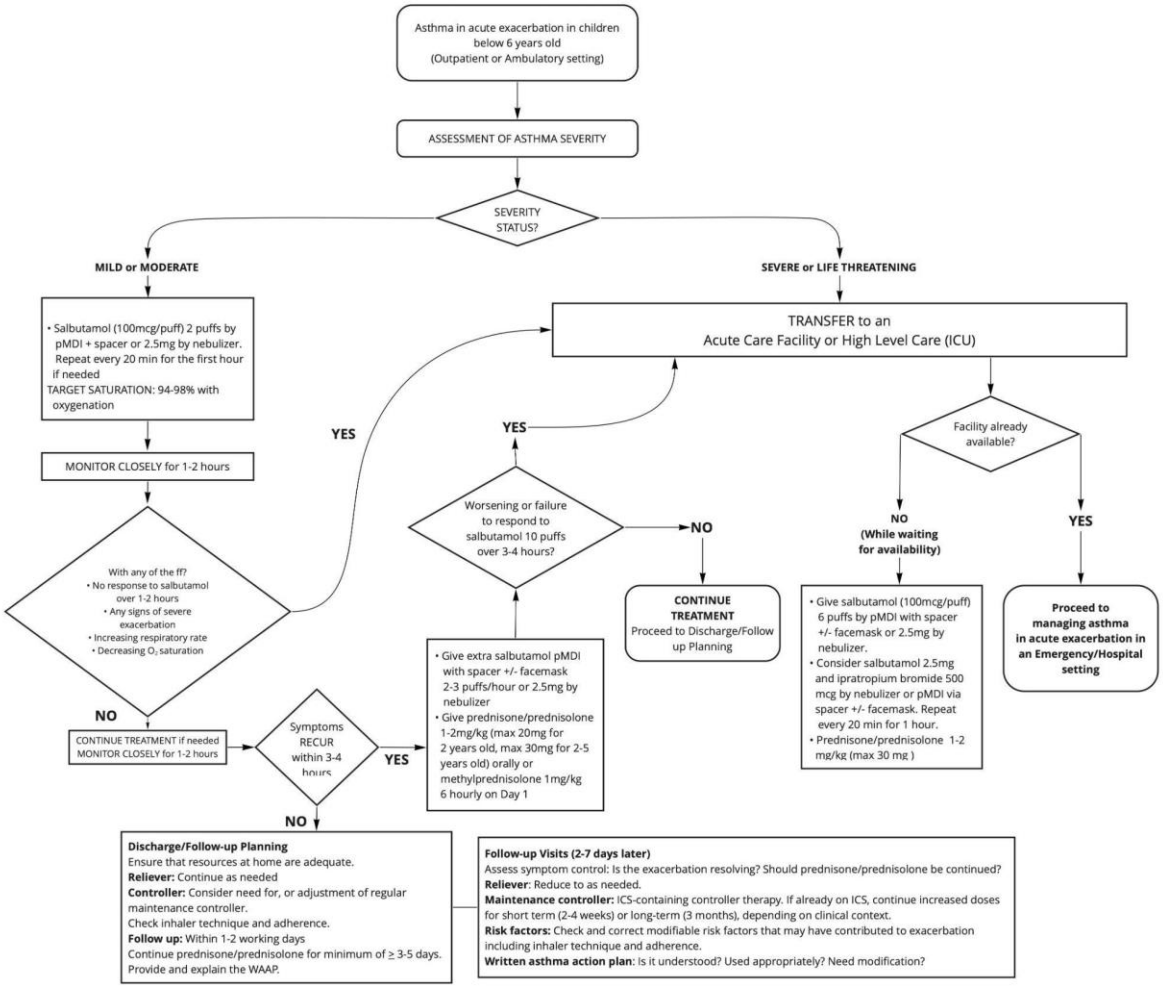
## Section 7. Management of asthma exacerbations in primary care

Triaging of patients with exacerbations should be promptly done. Milder exacerbations can usually be treated in a primary care setting, depending on resources, facilities, and expertise. Severe or life-threatening exacerbation should be directed to an urgent care facility, where continued therapy and monitoring are undertaken.

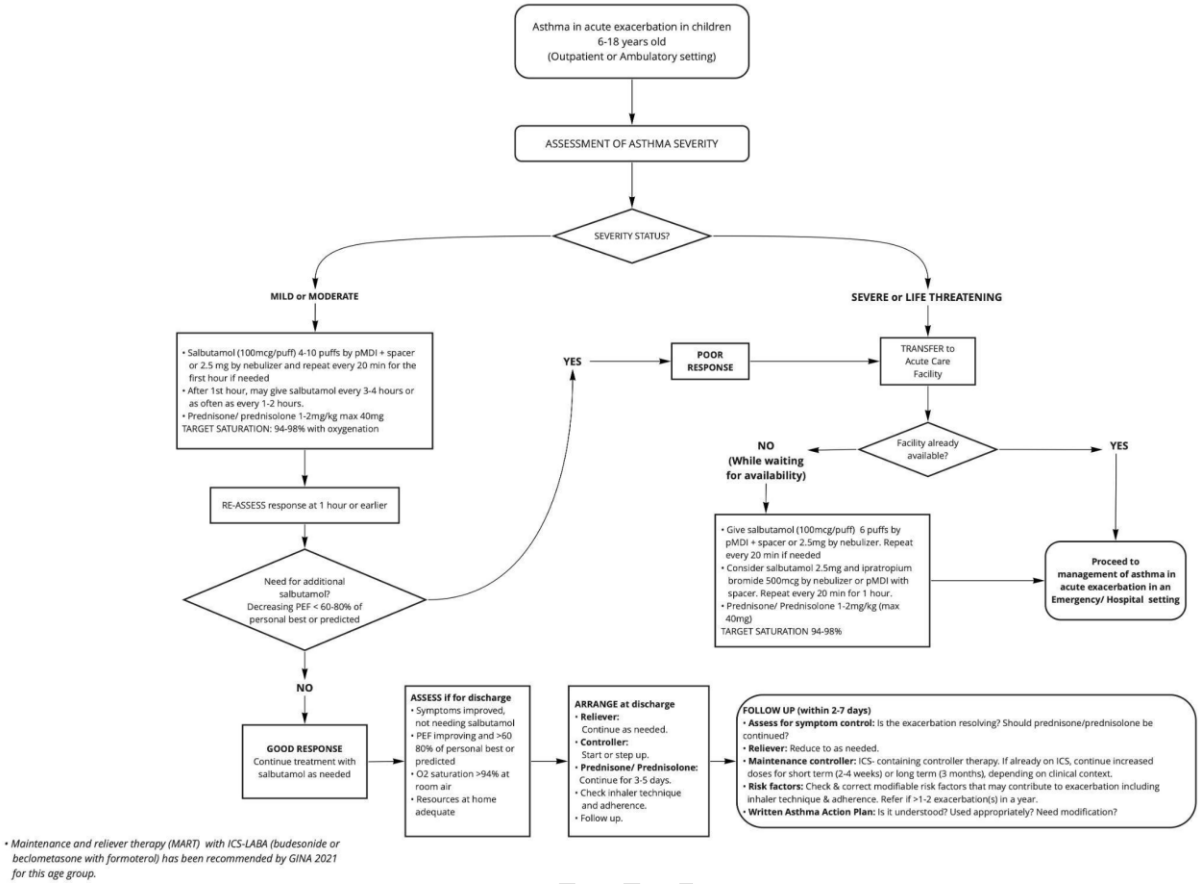
**Recommendation 3b**

3b.1 Clinical pathway for the management of asthma in acute exacerbation in children below 6 years old in an outpatient or ambulatory setting (Algorithm 5)
3b.2 Clinical pathway for the management of asthma in acute exacerbation in 6-18 years old in an outpatient or ambulatory setting (Algorithm 6)

These clinical pathways adopted from GINA 2021 are given strong recommendation ratings.[1] The safety and effectiveness of the medicines described in these pathways have long been established.




**Algorithm 5. Management of asthma in acute exacerbation in children below 6 years in an outpatient or ambulatory setting**




**Algorithm 6. Management of asthma in acute exacerbation in 6-18 years old in an outpatient or ambulatory setting**



## Section 8. Management of asthma exacerbations in the emergency department

**<u>Recommendation 3c</u>**

Asthma exacerbations that are severe and life-threatening are medical emergencies which need to be appropriately managed in an acute care setting like the emergency department.

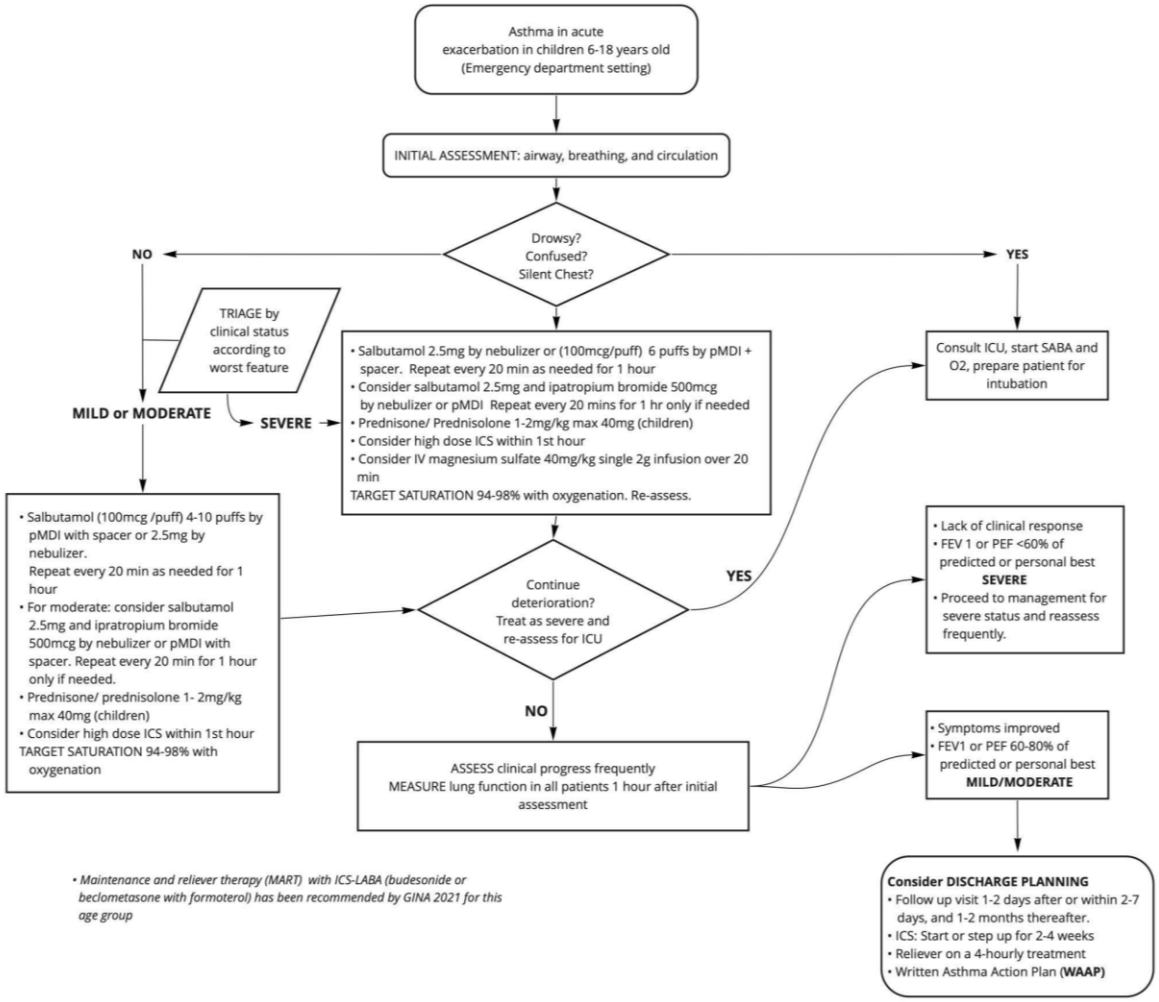
Clinical pathway adapted from GINA 2021[1]
Strong recommendation

**Indications for immediate transfer to hospital among below 6 years group:**
If any of the following are present, immediate transfer to hospital is advised (adopted from GINA 2021, Box 6-10, p159[1]):

1. At initial or subsequent assessment
    a. Child is unable to speak or drink
    b. Cyanosis
    c. RR >40/min
    d. O2 sat <92% at room air
    e. Silent chest on auscultation

2. Lack of response to initial bronchodilator treatment
    a. Lack of response to 6 puffs inhaled SABA (2 separate puffs, repeated 3 times) over 1 to 2 hours
    b. Persistent tachypnea despite three consecutive administrations over 1-2 hours of inhaled SABA, even if child shows other clinical signs of improvement
3. Social environment that limits delivery of acute treatment, or parent/caregiver unable to manage acute asthma at home.

Inhaled SABA and oxygen should be continued during transfer to maintain oxygen saturation at 94 to 98%. Systemic corticosteroids should be initiated.




**Algorithm 7. Management of asthma in acute exacerbation in 6-18 years old in an Emergency Department setting**

## Section 9. Management of asthma exacerbations in the hospital setting

### 9.1 Criteria for admission to ward

The decision to admit a patient for asthma considers the severity of the asthma exacerbation, response to treatment, the underlying risks for asthma-related death, presence of complex comorbidities, and social context, such as access to healthcare facilities and ability of the household to manage asthma. The criteria for hospital admission is in Recommendation 3d.

**Recommendation 3d**

Hospital admission should be considered when the patient has any of the following clinical criteria:

1. use of more than 6-8 SABA puffs in the previous 24 hours
2. PEF 50% to 75% of personal best
3. history of severe exacerbations warranting ICU admission
4. hospital admission or previous exacerbation for the past 12 months
5. child in whom other considerations suggest that admission may be appropriate, such as psychosocial problems in child or parent/caregiver, physical disability or learning difficulties, exacerbation despite adequate dose of oral steroids pre-presentation, presentation at night, or in a remote location or without transportation/communication

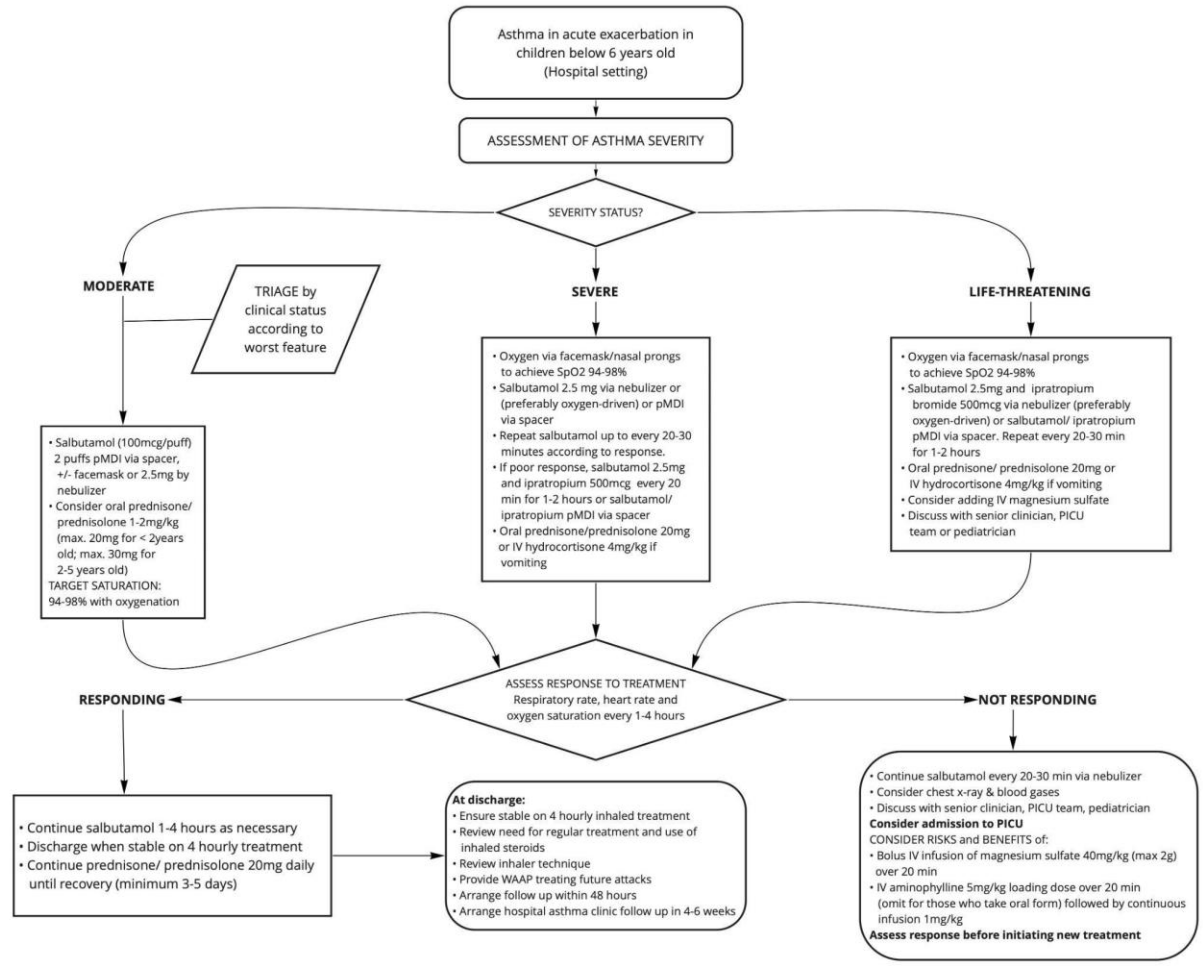
Consensus-based recommendation, adapted from GINA[1] and BTS[2]
Conditional recommendation

**Recommendation 3e**

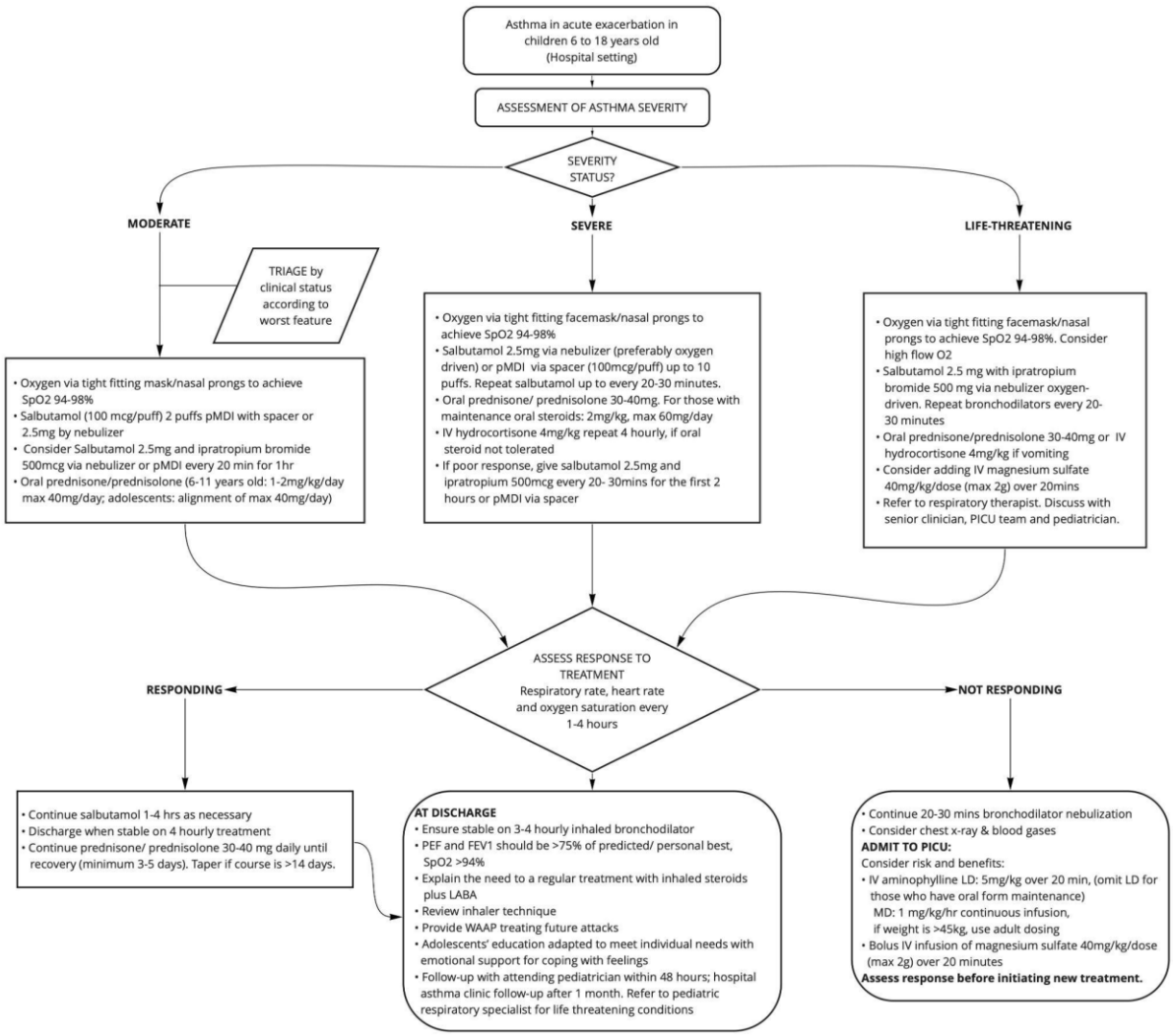
3e.1 Clinical pathway for the management of asthma in acute exacerbation in children below 6 years old in a hospital setting (Algorithm 8)

3e.2 Clinical pathway for the management of asthma in acute exacerbation in 6-18 years old in a hospital setting (Algorithm 9)

These clinical pathways adopted from GINA 2021 and BTS 2019 are given strong evidence-based recommendation ratings.[1] The safety and effectiveness of the interventions described in these pathways have long been established, hence rated as having high certainty of evidence.




**Algorithm 8. Management of asthma in acute exacerbation in children below 6 years in a hospital setting**




**Algorithm 9. Management of asthma in acute exacerbation in 6-18 years old in a hospital setting**

## Section 9.2. Criteria for discharge from hospital

**Recommendation 3f**

A patient admitted for asthma may be discharged when the patient has reasonably fulfilled the following clinical criteria:

1. O2 saturation at room air >94%
2. PEF >75%
3. No signs of respiratory distress
4. Been on discharge medication for 12 to 24 hours
5. Stable on a 4-hourly inhaled treatment
6. Able to demonstrate inhaler use correctly
7. Understand treatment prescribed and signs of worsening asthma
8. Patient has his/her own written asthma action plan (WAAP), and the family understands how to use it

Consensus-based recommendation adapted in BTS[2]
Conditional recommendation

**Section 10. General Principles on the Management of Asthma Exacerbations for Children and Adolescents (adopted from GINA[1])**

The treatments outlined below are administered concurrently and regular assessment of response to therapy with appropriate adjustments in treatment is expeditiously performed to achieve rapid improvement.

1. **Oxygen Therapy**
   - Delivery mode preferred is via nasal cannula or an age-appropriate fitted mask.
   - Pulse oximetry should be used to guide oxygen target saturations, but its unavailability should not preclude oxygen therapy.
   - In severe exacerbations, controlled low flow oxygen therapy is the choice even in the absence of a pulse oximeter
   - Target oxygen saturations: for age 6-11 years: 94-98% ; older adolescents : 93-95%
   - Oxygen saturations less than 92% in children is a predictor of the need for hospitalization while less than 90% warrants aggressive therapy.
   - If oxygen is required, an oxygen driven nebulizer may also be used as an alternative delivery mode with a proper mask/mouthpiece.

2. **Inhaled Short Acting Beta -2 Agonists**
   - Patients with asthma not on controller medications should be started on regular ICS-containing treatment. This is because as-needed SABA-only asthma treatment is less effective in preventing progression to severe exacerbation requiring OCS than patients who use low dose ICS-formoterol reliever either with or without daily maintenance controller. As-needed SABA-only asthma treatment is no longer advised.
   - When given, inhaled SABA therapy, delivery via pMDI-spacer is the most cost effective and has similar improvement in lung function as delivery via nebulizer.[1] There is limited evidence in administering continuous versus intermittent nebulization. In the more severe exacerbations, it may be preferred over pMDI-spacer.
   - Dose: 100mcg 4-6 puffs every 20 minutes as needed for the first hour, may increase to 6-10 puff every 20 minutes in severe cases (above 6 years old); 100 mcg 2 puffs every 20 minutes as needed for first hour, give extra 2-3 puffs per hour if symptoms recur after 3-4 hours (ages below 6 years old)
   - In moderate to severe exacerbations, when response to initial salbutamol nebulization/pMDI is insufficient, ipratropium combination can be added for 3 consecutive doses.
   - On choosing an inhaler device: pMDI plus dedicated spacer with face mask (0-3 years), pMDI plus dedicated spacer with mouthpiece (4-5 years).
   - If inhalation is not possible, an IV bolus of terbutaline 2 mcg/kg can be given over 5 minutes, followed by continuous infusion of 5 mcg/kg/hour. Children should be monitored and dose adjusted according to clinical improvement and side-effects.
   - Inhaler technique and adherence must be thoroughly reviewed and reiterated. Reliever inhaler must be taken only as needed and not routinely.

3. **Systemic Corticosteroids**
   - Systemic corticosteroids are utilized in all but the mildest exacerbations across all age groups as it speeds the resolution of the exacerbation and prevents relapse and should be given within the first hour of presentation.
   - In the ER setting its expedient utilization is in the following situations:
     - Initial SABA treatment does not achieve lasting symptom improvement
     - The exacerbation developed while already taking OCS
     - Past history of previous exacerbations requiring OCS
   - Route of delivery: equal effectiveness whether oral or intravenous. Oral is preferred due to its faster, less costly, and less invasive administration. Intravenous is the option only if the patient persists to vomit, is intubated or too dyspneic to swallow.

- For children with moderate exacerbations who fail to respond to bronchodilator therapy after the first hour with worsening of symptoms and for those with severe exacerbations, a course of oral corticosteroids is warranted.
- Dose: Prednisone/prednisolone 1-2 mg/kg/day, maximum 20 mg/day (under 2 years old), 30mg/day (ages 2-5 years), 40 mg/day (6 years old and above); or IV methylprednisolone 1mg/kg 6-hourly on day 1; or IV dexamethasone 0.6mg/kg/day divided into 3-4 hours for 2 days (ages below 6 years)
- Duration: 3-5 days is sufficient for most of the children
- Patients are not required to taper oral corticosteroids if these were taken for only 14 days or less

**4. Inhaled Corticosteroids**

- On discharge for home: patients should be given regular ICS-containing treatment to prevent future severe exacerbations and hospitalizations, as well as to reduce the risk of asthma related deaths.
- For children not previously on ICS, an appropriate dose of a controller drug, depending on their asthma level of control is started and continued under the guidance of an asthma specialist.
- If 3 months of low dose ICS fails to control symptoms or if exacerbations occur, stepping up by doubling the initial low dose of ICS (medium dose) is the best option for ages below 6 years.
- Dose: High dose beclomethasone 1,600 mcg/day divided into four doses over the day for 5-10 days may reduce the need for oral corticosteroids.

**5. Combination ICS-LABA**

- As a controller and reliever medication, increasing the as-needed dose of the combined rapid-onset LABA (formoterol) and low dose ICS (budesonide or beclomethasone) when asthma worsens improves asthma symptom control, and addresses the on-going inflammation at its onset. It reduces the risk of severe exacerbations requiring oral corticosteroids and hospitalizations compared with SABA-only treatment or daily same or higher dose ICS plus as-needed SABA.
- Maximum dose: 48mcg formoterol (beclomethasone-formoterol) 72 mcg formoterol (budesonide-formoterol) in 24 hours
- There is insufficient evidence on its safety and efficacy for young children < 4 years old.

**6. Ipratropium Bromide**

- In the ER, across all ages for moderate to severe asthma, treatment with a single ICS-LAB inhaler is effective in improving asthma symptom control and reduces exacerbations; while the use of combination inhaled SABA and ipratropium was associated with fewer hospitalizations and greater improvement in lung function. For those hospitalized, however, there is no additional benefit in adding it to in-hospital treatment, such as in decreasing length of hospitalization.

**7. Magnesium Sulfate**

- Magnesium sulfate is not routinely given for acute exacerbations. It is an add-on treatment in the first hour to the standard of treatment with nebulized SABA and ipratropium bromide in acute severe asthma exacerbations (O2 saturations below <92%). Magnesium sulfate IV in a single dose of 40-50 mg/kg (maximum 2 grams) by slow infusion (20-60 minutes) is given. When administered in severe exacerbations, it reduces hospitalization in a proportion of patients.
- The role of magnesium sulfate in the less than 5 years of age is still not established due to the paucity of studies in this age group.

**8. Leukotriene Receptor Antagonists**

- There is limited evidence to support its use in the ER setting

## Section 10.1 Diagnostic Tests (adopted from GINA[1])

A. Lung Function Measurement: When possible and available, it is recommended to perform PEF or FEV1; in children however, this may be non-reproducible. Lung function ideally should be monitored after SABA therapy is started. Additional treatment should be given until PEF or FEV1 reaches a plateau or has returned to the patient's previous best. An assessment can then be made whether to discharge or transfer to an acute care facility. Schedule for a follow up clinic check-up in 2-7 days later.
B. Arterial Blood Gases are not routinely required and may be done in instances where there is poor response to initial vigorous treatment or for those deteriorating.
C. Chest X-ray is not routinely recommended and is only performed when complications of asthma, such as pneumothorax or when other coexisting diagnosis is suspected.

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# CHAPTER 3. PRINCIPLES OF LONG-TERM MANAGEMENT IN ASTHMA

Asthma management consists of the following components: pharmacologic management, non-pharmacologic strategies for prevention and symptom control, and self-management (or parental management) with asthma education and skills training. Pharmacologic management is extensively discussed in Key Question 4, while non-pharmacologic strategies and self-management are covered in Key Questions 6, 7, and 8. Meanwhile, the control of asthma is covered in Key Question 5. Across these components, a strong partnership with effective communication should be forged between the patients' families and their healthcare providers.

In this section, we also discuss recommendations on the indications for referral to asthma specialists and on the management of the difficult to treat asthmatic patients.

The long-term goals of asthma management are adopted from GINA 2021[1]:

1. To achieve good control of symptoms and maintain normal activity levels
2. To minimize risk of asthma related deaths, exacerbations, persistent airflow limitation and side effects
3. To provide the patient and caregivers with suitable information and training to manage their asthma in partnership with their health care providers.

Asthma control and management entails regular shared decision making. Healthcare providers must consider patients, caregivers, and families as partners in this long-term relationship. The pharmacological recommendations for asthma are given as treatment steps, but it is important to individualize and adjust management to the patient's needs and preferences. Treatment of modifiable risk factors, comorbidities, and non-pharmacologic approaches should be considered parallel to pharmacologic treatment (see KQ 2, KQ 6, KQ 7).

The personalized control-based asthma management approach is described as the Assess-Adjust-Review cycle (Figure 2). The overall management is viewed as a continuous cycle that involves assessment, adjustment of treatment and review of patient's response in both symptom control and future risk of exacerbation by a healthcare provider. When deciding on asthma management, discuss with the patient, caregiver, and family on their preferred treatments for symptoms control and risk reduction. The dialogue should also include any features present that predict differences in their future risk or treatment response. The presence of any modifiable risk factors or comorbidities that may affect outcomes, their goals, beliefs and concerns about asthma and medication should be relayed and explained to them. Reviewing the inhaler technique for correctness and importance of adherence, and costs of treatment of the patient should also be stressed. For population-level medication choices for asthma policies, the preferred medication for each step in the treatment steps should be based on evidence of efficacy, effectiveness, safety, availability, and cost.

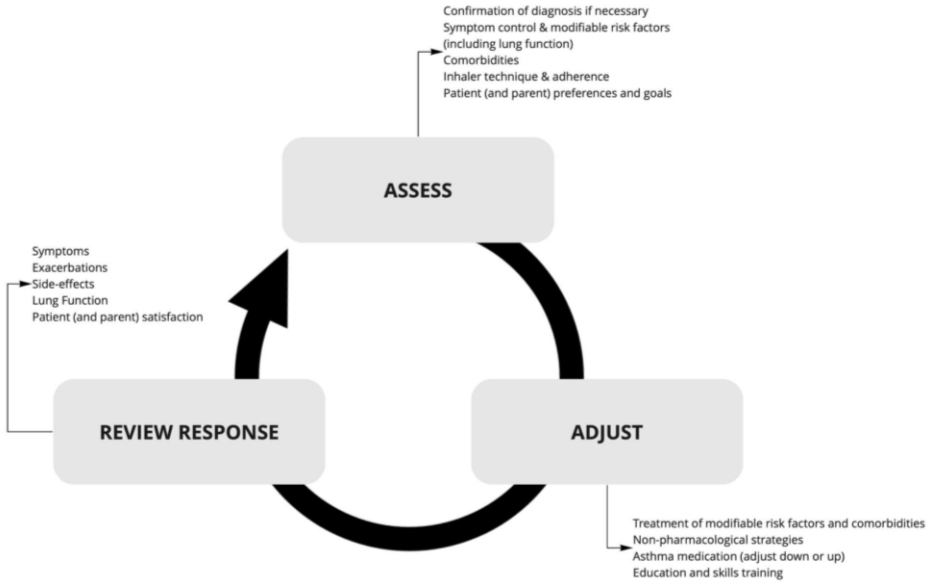


**Figure 2. Assess-Adjust-Review cycle**

# KEY QUESTION 4. WHAT IS THE PHARMACOLOGICAL MANAGEMENT FOR ASTHMA OR SUSPECTED ASTHMA PATIENTS?

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### Section 11. Pharmacological management for children and adolescents with asthma or suspected asthma

### Section 11.1. Categories of Asthma Medications

The pharmacological options for long term treatment of asthma fall into the following three main categories:

1. Controller (maintenance) medications are used to reduce airway inflammation, control symptoms, and decrease future risks of exacerbations and decline in lung function. Examples are inhaled corticosteroids (ICS) and inhaled corticosteroids with long-acting beta agonists (ICS-LABA).
2. Reliever (rescue) medications are provided to all patients for as-needed relief of breakthrough symptoms during worsening asthma or exacerbations. Examples of these relievers are low-dose beclomethasone-formoterol, budesonide-formoterol, and short acting beta agonists (SABA, such as salbutamol). These are also being used to prevent exercise-induced bronchoconstriction.
3. Add-on therapies for patients with severe asthma may be considered when patients have persistent symptoms and/or exacerbations despite optimal treatment with high dose controller medications (e.g., high dose ICS plus LABA or LTRA), and treatment of modifiable risk factors.

A major change in recommendation for asthma management in adolescents is emphasized in GINA 2021, and we hereby adopt this recommendation:[1]

**Recommendation 4a**

Low-dose ICS or controller treatment should be initiated once asthma is confirmed in adolescents (12-18 years old). This can be delivered with regular daily treatment or as-needed ICS-formoterol whenever needed for symptom relief.

Evidence-based recommendation adopted from GINA 2021[1]
Strong recommendation, high certainty of evidence

GINA 2021 makes this major change in recommendation based on earlier publications, which showed that early initiation of low-dose ICS in asthmatic patients results in greater short-term and long-term improvement in lung function than those whose symptoms have been present for 2-4 years and are not prescribed with ICS.[1]

Additional evidence review:

A newer meta-analysis by Crossingham (2021) includes five randomized controlled trials enrolling 9657 participants (ages 12 and up) with mild asthma found symptom-driven, as-required use of fast-acting β2 agonist (FABA)/ICS compared with reliever-only treatment reduced severe exacerbations requiring oral corticosteroids intake, and rates of emergency admission to hospital.[2] This supports GINA's recommendation away from SABA-only treatment for Step 1.

### Section 11.2. Pharmacological treatment steps according to age groups <6 years, 6-11 years, and 12 and above

Once asthma treatment has commenced, ongoing treatment decisions will be based on a personalized cycle of assessment, adjustment of treatment and review of the response as seen above. The following tables/diagrams present the pharmacological treatment steps per age group.

The following clinical pathways for the pharmacological treatment steps are **adopted** entirely from GINA 2021 without substantial modification.[1]

### 11.2.1 Starting treatment in children less than 6 years old

**Recommendation 4b**

For patients three years old and below, the preferred device for asthma treatment is a pressurized metered dose inhaler (MDI) plus a dedicated spacer with a face mask, while the alternate option is that of a nebulizer and face mask. For patients four to five years old, the preferred device is a pressurized MDI plus dedicated spacer with mouthpiece, while the alternate option is a nebulizer with mouthpiece or face mask.

Evidence-based recommendation adopted from GINA 2021[1]
Strong recommendation, high certainty of evidence

The basis of the recommendation of GINA 2021 for the choice of asthma devices for young children is a systematic review by Castro-Rodriguez et al (2004) comparing the effectiveness of pressurized MDI with valved holding chamber versus nebulization in delivering salbutamol.[3] In 2020, this systematic review was updated by the same group of authors which showed a significant reduction in the pulmonary index score or PIS (mean difference [MD], -0.63; 95% CI, -0.91 to -0.35; I2 = 0%; p < .00001), and a significantly smaller increase in HR (better; MD -6.47; 95% CI, -11.69 to -1.25; I2 = 0%; p = .02) when salbutamol was delivered through metered dose inhaler with spacer, than when it was delivered through nebulization.[4]

Note: Refer to the following websites endorsed by GINA 2021 for instructions: https://www.inhalers4u.org/ and information on https://ginasthma.org/.

**Recommendation 4c**

A clinical pathway for the pharmacological treatment steps of children less than 6 years old with asthma, wheezing, or suspected to have asthma is adopted from GINA 2021 with the following recommendations:[1]

4c.1 Step 1: Patients less than 6 years with infrequent viral wheezing should be provided with inhaled SABA for relief of symptoms. If SABA is used more than twice a week for a month, a trial of controller medication may be considered. In children with intermittent viral-induced wheezing and no interval symptoms, if inhaled SABA is insufficient, intermittent high-dose ICS may be considered*

Consensus-based recommendation adopted from GINA 2021
Conditional recommendation

*For Step 1: Intermittent high dose ICS can be an option if the physician is confident that the family and the patient will be able to adhere to instructions, properly use the device, and follow-up regularly. Inappropriate treatment with high dose ICS may lead to side effects.

GINA 2021 based this recommendation on expert panel consensus due to paucity of evidence for infrequent wheezing in this age group.[1] Since acute bronchiolitis is an important differential in this age group, GINA also cites a 2014 Cochrane systematic review that SABA is not effective for wheezing due to acute bronchiolitis.[5]

4c.2 Step 2: If the symptom pattern is consistent with asthma, and asthma symptoms are not well-controlled or with ≥3 exacerbations/year; or when the symptom pattern is not consistent with asthma but wheezing episodes requiring SABA occur frequently (≥3 per year), the preferred controller option is daily low dose ICS, to be given for at least 3 months.

Evidence-based recommendation adopted from GINA 2021[1]
Strong recommendation, high certainty of evidence

Evidence review:

In children 5 years and younger, a low dose ICS is advised as the initial treatment in controlling asthma on a regular daily basis and it must be given for at least 3 months for it to be effective.[6, 7, 8] Systematic review on pre-schoolers with asthma or recurrent wheezing was done wherein ICS use on a daily basis was more efficient in controlling the exacerbations than the regular LTRA monotherapy.[9] An ICS (as needed or episodic)[10, 11] may be used in pre-school children with interval asthma symptoms and asthma described with frequent wheezing (viral-induced). However, a trial of regular daily low dose ICS should be started prior. The result on exacerbation risk is the same for regular daily low dose and episodic high dose ICS.[8] GINA 2021 further states that if asthma is not controlled in Step 2, consider alternate options for Step 2 before stepping-up to Step 3.[1]

4c.3 Step 3: For patients diagnosed with asthma and whose symptoms are not well-controlled on daily low-dose ICS, consider doubling the initial low dose of ICS and re-assess the patient after 3 months. Another option is low dose ICS with LTRA.

Evidence-based recommendation
Conditional recommendation, low certainty of evidence.

Evidence review:

In a systematic review by Kaiser et al, twenty-two studies, with 4550 enrolled subjects, were reviewed. Among the fifteen of these studies (N=3278) included in this review, they compared ICS to placebo. Analysis revealed reduced exacerbations when daily medium-dose ICS were utilized (risk ratio [RR] 0.70; 95% CI, 0.61-0.79, NNT, 9). Similarly, the subgroup analysis performed in eight studies (N=2505) involving children with persistent asthma exhibited reduction of exacerbation (RR 0.56, 95% CI, 0.46-0.70; NNT, 11).[8]

In one study with 202 subjects analyzed in the same systematic review and meta-analysis by Kaiser et al, revealed that low dose ICS budesonide daily regimen, even if frequency was doubled during mild exacerbation, when compared with montelukast, significantly reduce exacerbations (RR 0.59; 95% CI 0.38-0.92; P=.02).[8]

In a network meta-analysis by Zhao et al (2015) which included 35 trials, comprising 12 010 patients,[12] based on both primary and secondary outcomes, combined ICS and LABA was ranked first in effectiveness (OR 0.70, 95% CI: 0.52–0.97 and OR 1.23, 95% CI: 0.94–1.61, respectively, compared with low-dose ICS).[12] Low-dose ICS, medium- or high dose ICS and combined ICS and LTRA strategies were comparable in effectiveness. ICS monotherapies, and ICS + LABA and ICS + LTRA strategies were similarly safe.[12] However, there is insufficient evidence on the safety and effectiveness of combination of ICS-LABA for young children.

4c.4 Step 4: For asthma patients who are not well-controlled on daily double low-dose ICS, refer the patient to an asthma specialist and consider further investigation.

Consensus-based recommendation adopted from GINA 2021[1]
Conditional recommendation

This pathway offers alternative controller options (Figure 3) if the recommendations cannot be met. In this age group, the safety and efficacy of ICS-LABA has not been established, for which we cannot make a recommendation. Lastly, if leukotriene antagonists (LTRA) are prescribed, physicians must counsel parents on the risk of neuropsychiatric events (i.e., impact on sleep and behavior).

| | STEP 1 | STEP 2 | STEP 3 | STEP 4 |
|---|---|---|---|---|
| CONSIDER THIS STEP FOR CHILDREN WITH: | Infrequent viral wheezing<br>No or few interval symptoms | Symptom pattern CONSISTENT with asthma, and asthma symptoms not well-controlled or with >/=3 exacerbations/year<br><br>Symptom pattern NOT CONSISTENT with asthma but wheezing episodes requiring SABA occur frequently (>/=3 per year). | Asthma diagnosis, and asthma not well controlled on low dose ICS | Asthma not well controlled on double ICS |
| PREFERRED INITIAL CONTROLLER | | Daily 'low dose ICS' | Double 'low dose' ICS | Continue controller & refer for Specialist assessment<br><br>Add:<br>• LTRA or<br>• Further increase ICS dose/ frequency or add a low dose oral corticosteroids for a few weeks or<br>• LABA in combination with ICS for >/= 4 years old<br>• intermittent high dose ICS at onset of respiratory illnesses to the regular daily ICS |
| OTHER CONTROLLER OPTIONS | | Daily LTRA or intermittent short courses of ICS at onset of respiratory illness<br><br>Give DIAGNOSTIC TRIAL for 3 months and consider specialist referral. | Low dose ICS + LTRA<br><br>Consider specialist referral | |
| RELIEVER | As needed inhaled short-acting beta2-agonist (SABA) | | | |
| STARTING DOSE (low total daily dose in mcg) | **BEFORE STEPPING UP:** review inhaler technique and adherence, treat modifiable risk factors and check for alternative diagnosis. | | | |
| | | Beclometasone dipropionate (pMDI, standard particle): 100mcg (5 years and older)<br>Budesonide nebule: 500mcg (1 year and older)<br>Fluticasone propionate (pMDI): 50mcg (4 years and older) | | |
| SAFETY | Data on the efficacy and safety of ICS-LABA in children <4 are insufficient.<br>LTRA – patients should be counselled about the risk of neuropsychiatric events (i.e., impact on sleep and behavior) | | | |

**Figure 3. Treatment steps for children below 6 years old**

### 11.2.2 Starting treatment in children 6-11 years old

**Recommendation 4d**

A clinical pathway for the pharmacological treatment of children 6-11 years old with asthma, wheezing, or suspected asthma is adopted from GINA 2021. The KQ4 pathway provides a preferred track (Track 1) with the following recommendations:

4d.1 Step 1: For children 6-11 years with symptoms less than twice a month, the preferred controller option is low dose ICS whenever SABA is taken. Similar to Recommendation 4a, SABA-only treatment is no longer recommended.

Evidence-based recommendation
Strong recommendation, low certainty of evidence

Evidence review:

This recommendation adopted from GINA 2021 was indirectly deduced from trials of adolescents.[17,18] Similar to Recommendation 4a, a newer systematic review from Crossingham 2021 (n = 9657) showed that: Compared with as-required FABA alone, as-required FABA/ICS reduced exacerbations requiring systemic steroids (OR 0.45, 95% CI 0.34 to 0.60, 2 RCTs, 2997 participants, high-certainty evidence), equivalent to 109 people out of 1000 in the FABA alone group experiencing an exacerbation requiring systemic steroids, compared with 52 (95% CI 40 to 68) out of 1000 in the FABA/ICS as-required group.[2] FABA/ICS as required may also reduce the odds of an asthma-related hospital admission or emergency department or urgent care visit (OR 0.35, 95% CI 0.20 to 0.60, 2 RCTs, 2997 participants, low-certainty evidence).[2] Therefore, certainty was downgraded to a low rating due to indirectness of the evidence because of the older age groups studied.

4d.2 Step 2: If symptoms are twice a month or more, the preferred controller option is daily low dose ICS with as-needed SABA as reliever.

Evidence-based recommendation
Strong recommendation, high certainty of evidence[4]

Evidence review:

In an RCT study by Martinez et al in 2011[17] involving 843 children, they have noted that compared to the placebo group, those who were randomized to daily low dose ICS (28%, 95% CI 18-40, P=.03), combined 2x daily low ICS dose with beclomethasone plus rescue albuterol(31%, 95% CI 21-43, p=.07), and 2x daily placebo with beclomethasone plus albuterol as rescue (35%, 95% CI 24-47, p=.07) were noted to have fewer episodes of exacerbation. The occurrence of treatment failure was also high among those in the placebo group (twice daily placebo with placebo + albuterol as rescue) at 28% (95% CI 14-43). This was given an Evidence A rating by GINA.

Additionally, a systematic review by Zhang et al (2019) demonstrated a dose-response in the use of ICS as a controller. Their results showed that doubling the dose of maintenance inhaled corticosteroids in mild pediatric asthma (n = 1074, 4 studies) was shown to decrease the odds of an acute exacerbation requiring systemic corticosteroids (pooled OR 0.91, 95% CI 0.67 to 1.25 compared to stable dose).[19] This was originally graded as moderate certainty due to the RCTs having varying follow-up periods and age groups, but was upgraded due to a dose-response reduction with quadruple dosing (OR 0.74, 95%CI 0.62 to 0.88).[19]

4d.3 Step 3: If with troublesome asthma symptoms most days, waking due to asthma once a week or more despite Step 2 controller treatment, or with any risk factors (KQ 5), there are 3 preferred controller options: medium dose ICS with as needed SABA, low dose ICS - LABA with as needed SABA, very low dose ICS – Formoterol as maintenance and reliever therapy (MART therapy).

Evidence-based recommendation
Strong recommendation, high certainty of evidence for (i, ii), and low certainty for (iii).

Evidence review:

In the systematic review by Adams et al in 2006, they reported that all ICS demonstrate dose response relationship as these were evaluated based on efficacy.[20] However, it is the low to moderate dosage range of these drugs whose effects were found to be beneficial among those with mild to moderate asthma severity.[20] Moreover, only small increments of improvement of control were seen in the studies that utilized high doses of fluticasone accompanied with increased incidence of side effects.[20] In the case of patients who have severe asthma and are dependent on oral steroids, it is more beneficial to decrease the oral steroids dosage compared with giving high dose fluticasone. These findings were replicated in the more recent study by Vaessen-Verberne et al in 2010 where they compared the effectiveness of SABA +

LABA versus LABA alone.[21] All arms exhibited improvement during the prescribed treatment period and no significant difference in between groups (adjusted mean difference [FP-SFP]2.6%; 95% CI, -8.1- 13.4).[21] No differences in terms of exacerbation rates, adverse events or growth. These studies were appraised by GINA as Evidence A.

In the trial using SMART therapy, Bisgaard et al in 2006 noted that SMART (single ICS-formoterol maintenance and reliever therapy) increased the time interval to first exacerbation episode when compared to fixed dose budesonide, p=.02 and fixed dose combination of budesonide/ formoterol, p<.001.[22] Rates of exacerbations needing hospitalization or medical intervention, mild exacerbation days and awakening were significantly lower among patients who were under the SMART arm.[22]

4d.4 Step 4: If the patient initially presents with severely uncontrolled asthma, or has an acute exacerbation, or is not adequately controlled by low-dose maintenance ICS-LABA with as-needed SABA the preferred controller option is medium dose ICS – LABA with as needed SABA or low dose ICS-formoterol MART.

Evidence-based recommendation
Conditional recommendation, low certainty of evidence

Evidence review:

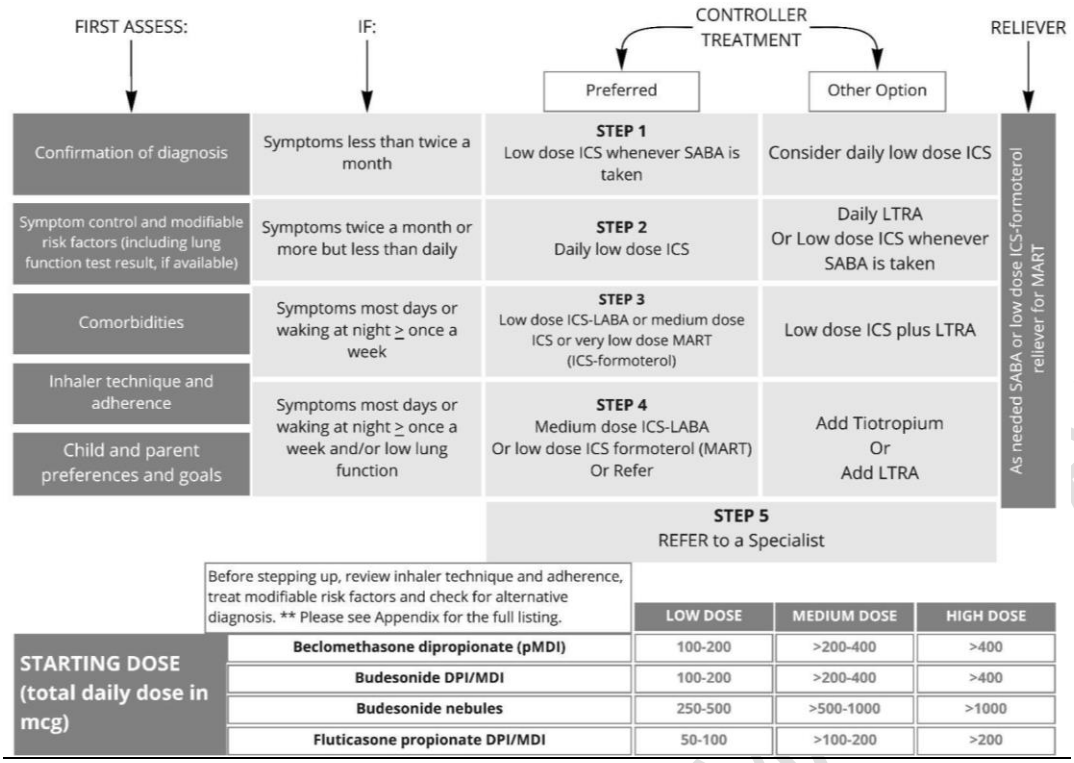
In the systematic review and meta-analysis by Zhou et al in 2021, eight of the studies reviewed comparing salmeterol + fluticasone vs montelukast + fluticasone as controllers reported clinical effective rate.[23] Moreover, based on daytime and night-time asthma scores, the salmeterol + fluticasone group showed significantly higher full controlled level (RR 1.51; 95% CI 1.24-1.85; I2= 0; P<.001).[23] This arm also showed significant improvement in night time asthma score after 12 weeks treatment.[23]

4d.5 Step 5: If the patient has persistent symptoms and exacerbations despite Step 4 medications, refer for expert assessment, add-on therapy, and phenotyping, as applicable.

Consensus-based recommendation
Conditional recommendation

For Steps 4 and 5, GINA 2021 also suggests a short course of oral corticosteroids for patients presenting with severely uncontrolled asthma.

This pathway offers Track 2 alternative controller options (Figure 4) if the recommendations cannot be met. If leukotriene antagonists (LTRA) are prescribed, physicians must counsel parents on the risk of neuropsychiatric events (i.e., impact on sleep and behavior).




* Very low dose: BUD-FORM 100/6 mcg

**Figure 4. Clinical pathway for the pharmacological treatment of children 6-11 years old with asthma, wheezing, or suspected asthma**

### 11.2.3 Asthma treatment in adolescents 12 years and above:

**Recommendation 4e**

A clinical pathway for the pharmacological treatment steps of adolescents 12-18 years old with asthma, wheezing, or suspected asthma is adopted from GINA 2021 with two tracks. The primary difference between the two tracks is in the choice of the as-needed reliever drug for symptom relief, taking into consideration the patient's preference and adherence issues.

TRACK 1 and TRACK 2:

4e.1 ICS-formoterol (Track 1) should be given as the as-needed reliever drug across all Steps 1-5 for adolescents. If ICS-formoterol is not available, not affordable, or not preferred by a patient with no exacerbations on current therapy, SABA (Track 2) may be given as the alternate reliever drug.

Evidence-based recommendation
Conditional recommendation, low certainty of evidence

The recommendation by GINA to extend ICS-formoterol as an as-needed reliever drug to Step 1 was based on reports that patients with few interval asthma symptoms can have severe exacerbations,[24] and that there is a paucity in the safety and efficacy of SABA-only treatment. However, this recommendation has also been criticized by other experts.[25]

Note that for the age group 12-18 years old, the controller was given as Recommendation 4a, to highlight this major change in GINA.

4e.2 Steps 1 and 2: For adolescents with mild symptoms, or less than 4-5 days a week:

TRACK 1: As-needed low-dose ICS-formoterol should be given, with a maximum dose of 72 mcg/day for budesonide-formoterol, or 48 mcg/day for beclomethasone-formoterol.

TRACK 2: Low dose ICS taken whenever SABA is taken may be an option if ICS-formoterol is not available or affordable. For Step 2, daily low dose maintenance ICS, is the preferred approach. Low dose ICS whenever SABA is taken, daily LTRA, or allergen immunotherapy (KQ 6) may be considered.

Evidence-based recommendation
Conditional recommendation, high certainty of evidence

In the RCT study done by O'Bryne et al in 2018[26] involving patients with mild asthma and an open label study by Beasley et al in 2019,[27] low dose budesonide- formoterol combination can significantly reduce exacerbation by 64% compared to SABA alone. In addition, this low dose combination regimen produced noninferior results compared to regular ICS[26, 28] and when used as an as needed medication among mild asthmatic patients in decreasing risk or occurrence of severe exacerbations.[27,] As for average dosing, RCTs reviewed, if used as an as needed treatment, it can be given in a lower average ICS dose[29,30,31,32] and > 2x a day dosing can lower the short-term risk of severe exacerbation. Therefore, timing of use of ICS-formoterol is important.[33,34]

SABA-only treatment is not recommended in this age group because some studies suggest that over-use of SABA (≥ 3 canisters per year) is associated with increased risk of severe exacerbations and mortality. This new set of recommendations seek to minimize patient reliance on SABA.

4e.3 Step 3: For adolescent patients with symptoms on most days, or waking with asthma once a week or more:

TRACK 1: Low dose maintenance ICS-formoterol should be given as both maintenance and reliever treatment (MART) but should not be used as a reliever for those taking ICS with a different LABA.

TRACK 2: Maintenance ICS-LABA with as-needed SABA. Other options include increasing ICS to medium dose, low dose ICS plus LTRA, low dose ICS plus sustained-release theophylline, or allergen immunotherapy (KQ 6).

Evidence-based recommendation
Conditional recommendation
High certainty of evidence for Track 1 and low certainty for Track 2

For Track 1: Using low dose ICS-formoterol as maintenance and reliever treatment is the preferred Step 3 management for adolescents. Combination options include budesonide-formoterol or beclomethasone- formoterol. For patients with ≥1 exacerbations in the previous year, this type of MART lowers episodes and gives equivalent levels of disease control like low-dose ICS. This is the opposite when a fixed dose of ICS-LABA is used as maintenance treatment or a higher ICS dose with both additional as needed SABA.[35,36,37,38,39] In papers by Cates et. al. in 2013[35] and Demoly P. et al in 2009,[40] for those without any history of previous exacerbation, MART with ICS-formoterol also significantly reduced severe exacerbations using a lower average dose of ICS. Maximum recommended dose for formoterol is 72mcg metered dose for budesonide-formoterol combinations and 48 mcg metered dose for beclomethasone-formoterol combination. ICS-formoterol cannot be a reliever medication for those using different ICS -LABA maintenance regimens since safety and efficacy evidence for this use is insufficient.

For Track 2: According to the review by Cates et al in 2018 and study by Busse et al 2018, addition of LABA to the maintenance ICS + needed SABA in an inhaler form gives additional improvements in symptoms and lung function with noticeable decrease in the risk of exacerbations if compared with same dose of ICS.[41,42] However, utilizing LABA as a

reliever gives only minute improvement.[41,43] For Step 3 maintenance treatment, among the various approved combinations of ICS-LABA inhalers, fluticasone furoate-vilanterol and budesonide-formoterol in separate studies compared to usual care exhibited effectiveness for asthma control in a real environment set up but there was no difference in reduction of risk among the other formulations.[44,45]

4e.4 Step 4: For patients with daily symptoms or waking with asthma once a week or more and low lung function:

TRACK 1**:** The maintenance treatment with ICS-formoterol may be increased to medium dose if deemed necessary. However, the reliever is still low-dose ICS formoterol.

TRACK 2: Alternatively, medium dose ICS-LABA with as-needed SABA can be considered if maintenance and reliever therapy is not available. Other options are long-acting muscarinic antagonists (LAMA) such as tiotropium bromide. However, before considering adding LAMA, the ICS dose should be increased first to medium dose or treatment be switched to MART with ICS-formoterol. Allergen immunotherapy, medium dose ICS plus LTRA, and medium dose ICS plus sustained-release theophylline may also be considered.

Evidence-based recommendation
Conditional recommendation, low certainty of evidence

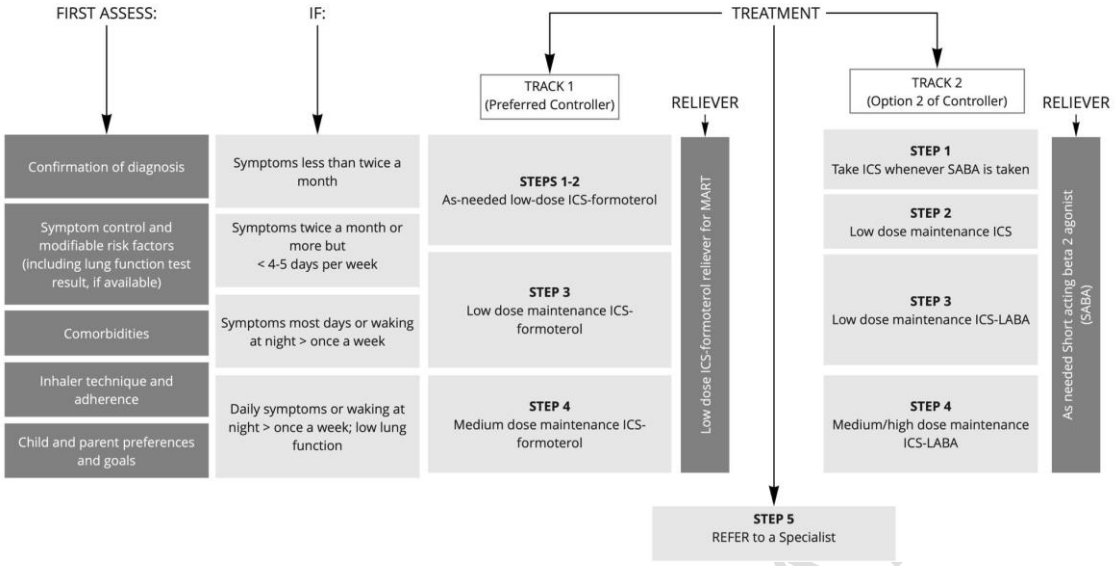
Using a combination of ICS-formoterol as maintenance and reliever treatment can reduce exacerbations among asthmatic adolescents compared to utilizing maintenance ICS LABA at the same dose or higher doses of ICS.[46] This combination induced significant reduction in risk of exacerbation among patients with a history of severe attacks. However, the MART regimen also conferred a significantly more effective effect than conventional best practice treatments in studies performed in real-world environments.[47] As for the alternative step 4 treatment or track 2, it must be considered that for this group individual ICS responsiveness varies. Degree of asthma control differs in each patient when low dose ICS-LABA was used even if the patient is compliant and performs good, accepted inhaler technique. For these patients, they might benefit from medium dose ICS-LABA plus as needed SABA.[48]

4e.5 Step 5: Consider high dose ICS and other add-on asthma medications depending on the assessment of the asthma specialist.

Consensus-based recommendation
Conditional recommendation

During asthma treatment, prescribed controller medication may be stepped up or down along one track, using the same reliever medication OR it can be switched between tracks but following the reliever medication for that particular 'track.'

**Starting treatment in adolescents 12 years old and above:**




| STARTING DOSE (total daily dose in mcg) | Before stepping up, review inhaler technique and adherence, treat modifiable risk factors and check for alternative diagnosis. ** Please see Appendix for complete list of dosages | LOW DOSE | MEDIUM DOSE | HIGH DOSE |
|---|---|---|---|---|
| | **Budesonide DPI** | 200-400 | >400-800 | >800 |
| | **Fluticasone propionate** | 100-250 | >250-500 | >500 |
| | **Mometasone propionate** | 200-400 | 200-400 | >400 |

**Figure 5. Clinical pathway for the pharmacological treatment of children 12-18 years old with asthma, wheezing, or suspected asthma**

**Section 11.3. Reviewing response and adjusting treatment**

**Good Practice Statement 4.1**

The following must be taken into consideration when reviewing response and adjusting treatment:

1. Any step-up or step-down of asthma treatment is considered a therapeutic trial. Response to asthma treatment should be reviewed within 1-3 months and every 3-12 months thereafter, depending on their initial level of control, response to treatment and level of engagement in self-management.
2. After an exacerbation or flare-up, patients are advised to follow up within a week.
3. It is recommended to continue treatment for at least 3 months to establish its effectiveness in achieving good asthma control, since full benefit may only be noted after 3-4 months.
4. For children below 5 years of age, asthma-like symptoms remit in a large proportion. Thus, regular assessment should be done to determine whether an asthma controller remains necessary.
5. Symptom control, presence of risk factors, frequency of exacerbations and side effects of medications are the essential parameters that must be assessed during the duration of treatment. Furthermore, adherence to medication, inhaler technique and patients' preference, goals and satisfaction must be reviewed by the health care provider during each visit.

**Section 11.4 When and how to STEP DOWN asthma treatment:**

The aim of the health care provider is to find the patient's minimum effective asthma treatment. Due to cost or concerns regarding prolonged steroid use, most patients tend to experiment by discontinuing the prescribed controller. It is important to encourage patients to continue their controller medication despite symptom control or absence of exacerbation. To minimize risk of SABA-only treatment, an alternative is to cease maintenance ICS and switch to as-needed ICS-formoterol for 12 years old and above.

Once good asthma control is achieved for 3 months and lung function has significantly improved or reached a plateau (if spirometry is not done), asthma treatment can be reduced without loss of asthma control.

The following are the general principles and guidelines of stepping down treatment once asthma is well-controlled:

1. A written asthma action plan with updated instructions for how and when to revert to their previous level of treatment should be provided.
2. Prior to stepping down treatment, factors such as timing, presence of risk factors and patient's preference should be considered.
    a. Choose an appropriate time wherein the patient has no respiratory infection, is not travelling, or is not pregnant.
    b. Identify the patient's risk factors. Some risk factors are associated with higher risks of exacerbation after step-down (i.e., ER visit in the previous 12 months or low baseline $FEV_1$) thus, close monitoring is advised while on a step-down therapeutic trial.
    c. Engage the patient in the process and provide clear instructions
3. Reducing ICS doses by 25-50% of the current dose at 3-month intervals is feasible and safe for most patients
4. Do not completely withdraw ICS unless needed temporarily to confirm diagnosis. If stepping down of asthma medication is done too quickly, exacerbation risk may significantly increase even if symptoms are controlled.
5. Remind the patient to have sufficient medication available to resume their previous dose, if necessary.
6. Monitor response to treatment based on symptom control and/or PEF, and schedule a follow-up visit.

| | STEP 5 | STEP 4 | | | STEP 3 | | | STEP 2 | |
|---|---|---|---|---|---|---|---|---|---|
| **Current Treatment** | Since referral for asthma management is advised for this group, decision for stepping down depends on the assessment of the specialist. | Moderate to high dose ICS-LABA | Medium dose ICS-formoterol as MART | High dose ICS plus second controller | Low dose ICS-LABA maintenance | Low dose ICS-formoterol as MART | Medium or high dose ICS | Low dose ICS | Low dose ICS or LRTA |
| **STEP DOWN to this treatment** | | Continue ICS-LABA with 50% reduction in ICS component | Reduce maintenance ICS-formoterol to low dose and continue as-needed low dose ICS-formoterol reliever | Reduce ICS by 50% and continue second controller | Reduce ICS-LABA to once daily | Reduce maintenance ICS-formoterol to once daily and continue as-needed low dose ICS-formoterol reliever | Reduce ICS dose by 50%<br><br>Adding LTRA may allow ICS dose to be stepped down | Once daily dosing or switch to:<br><br>As-needed low dose ICS-formoterol for children 12 yrs and above<br><br>OR<br><br>ICS taken whenever SABA is taken | Switch to As-needed low-dose ICS formoterol for children 12 yrs and above |

**Figure 6. Step-down strategy for different controller treatments (adapted from GINA 2021[1])**

## Section 12. Indications for Referral to a Specialist

**Recommendation 4f**

Children and adolescents should be referred to an asthma specialist for the following indications: difficulty confirming the diagnosis of asthma, or presence of asthma complications or sub-types, persistent or uncontrolled asthma, risk of asthma-related death, and side effects due to asthma medications.

Consensus-based recommendation, adopted from GINA 2021[1]
Conditional recommendation

This is considered a conditional recommendation in view of varying resource settings, availability of a specialist, quality of healthcare delivery systems, and overall clinical context.

While most patients with asthma can usually be managed in primary care, some clinical situations warrant referral for expert advice regarding diagnosis and or management. Below are the indications for considering referral for expert advice, where available (Table 12.1):

**Table 12.1 Indications for referral to a specialist**

| | |
|---|---|
| **Difficulty confirming the diagnosis of asthma** | • Patient has symptoms of chronic infection, or features suggesting a cardiac or other non-pulmonary causes.<br>• Diagnosis is unclear even after a trial of therapy with ICS or systemic corticosteroids<br>• Patients with features of both asthma and COPD, if there is doubt about priorities of treatment |
| **Suspected occupational asthma** | • Refer for confirmatory testing and identification of sensitizing or irritant agents, specific advice about eliminating exposure and pharmacological treatment. |
| **Persistent or severely uncontrolled asthma or frequent exacerbations** | • Patient's symptoms remain uncontrolled, the patient has ongoing exacerbations or low lung function despite correct inhaler technique and good adherence with step 4 treatment. Before referral, depending on the clinical context, identify and treat modifiable risk factors and comorbidities<br>• Patient has frequent asthma-related health care utilization (e.g., multiple ED visits or urgent primary care visits) |
| **Any risk factors for asthma-related death** | • Near-fatal asthma attack (ICU admission, or mechanical ventilation for asthma) at any time in the past<br>• Anaphylaxis or confirmed food allergy in a patient with asthma |

| | |
|---|---|
| **Evidence of, or risk of, significant treatment side-effect** | • Patients with significant side-effects from treatment<br>• Need for long-term oral corticosteroid use<br>• Frequent courses of oral corticosteroid (e.g., two or more courses a year) |
| **Symptoms suggesting complications or sub-types of asthma** | • Aspirin-exacerbated respiratory disease; allergic bronchopulmonary aspergillosis |
| **Additional reasons for referral in children 6-11 years** | • Doubts about diagnosis of asthma (i.e., respiratory symptoms are not responding well to treatment in a child who was born prematurely)<br>• Symptoms or exacerbations remain uncontrolled despite medium dose ICS with correct inhaler technique and good adherence<br>• Suspected side-effects of treatment (e.g., growth delay)<br>• Asthma and confirmed food allergy<br>• Safeguarding concerns |

*ED: emergency department
*ICS: inhaled corticosteroids
*ICU: intensive care unit

**Section 13. Difficult to treat asthma and severe asthma in adolescents**

Difficult-to-treat and severe asthma is based on the concept of uncontrolled asthma. **Uncontrolled asthma** includes one or both of the following:

1. Poor symptom control is characterized by frequent symptoms or reliever use, with limitation of activity and night awakening due to asthma.
2. Frequent exacerbations (≥2 per year) requiring OCS, or serious exacerbations (≥ 1 per year) requiring hospitalization

**Difficult to treat asthma** is asthma that is uncontrolled despite being on medium or high dose ICS with a second controller (usually a LABA) or with a maintenance low dose OCS, or that requires high dose treatment to maintain good symptom control and reduce the risk of exacerbations.

**Severe asthma** is a subset of difficult to treat asthma. It refers to asthma that remains uncontrolled despite adherence with maximally optimized therapy, treatment, and management of contributory risk factors or one that worsens when high dose ICS treatment is decreased. Asthma is not considered severe if it markedly improves when non-pharmacologic factors, such as inhaler technique and adherence, are addressed.

The most common issues that need to be excluded before a diagnosis of difficult to treat/severe asthma can be made are:

1. Poor inhaler technique (present in up to 80% of patients)
2. Poor adherence to medication (present in up to 75% of patients)
3. Incorrect diagnosis of asthma, with symptoms due to alternative conditions (e.g., cardiac failure)
4. Comorbidities or complicating conditions, such as rhinosinusitis, gastroesophageal reflux, obesity, and obstructive sleep apnea
5. Ongoing exposure to sensitizing or irritant agents in the home or school environment

Patients with difficult asthma should be systematically and carefully evaluated to include the following: 1) confirmation of the diagnosis of asthma, 2) identification of the mechanism of persisting symptoms, and 3) assessment of adherence to therapy. This assessment should be facilitated through a multidisciplinary team, if available in the local setting.

**Recommendation 4g**

A clinical pathway for difficult-to-treat asthma patients for use is proposed for both primary and specialist care.

Clinical pathway adopted from GINA 2021[1]
Conditional recommendation

Below is a clinical pathway which provides information to general practitioners and specialists about what should be considered in each phase of diagnosis and management of difficult to treat and severe asthma. After 3 to 6 months of reviewing response and asthma is still uncontrolled despite optimized therapy, further assessment and management should be done preferably by multidisciplinary teams, if available. In local settings, such teams may include a primary care physician or pediatrician, pediatric pulmonary specialist, and allergologist-immunologist.

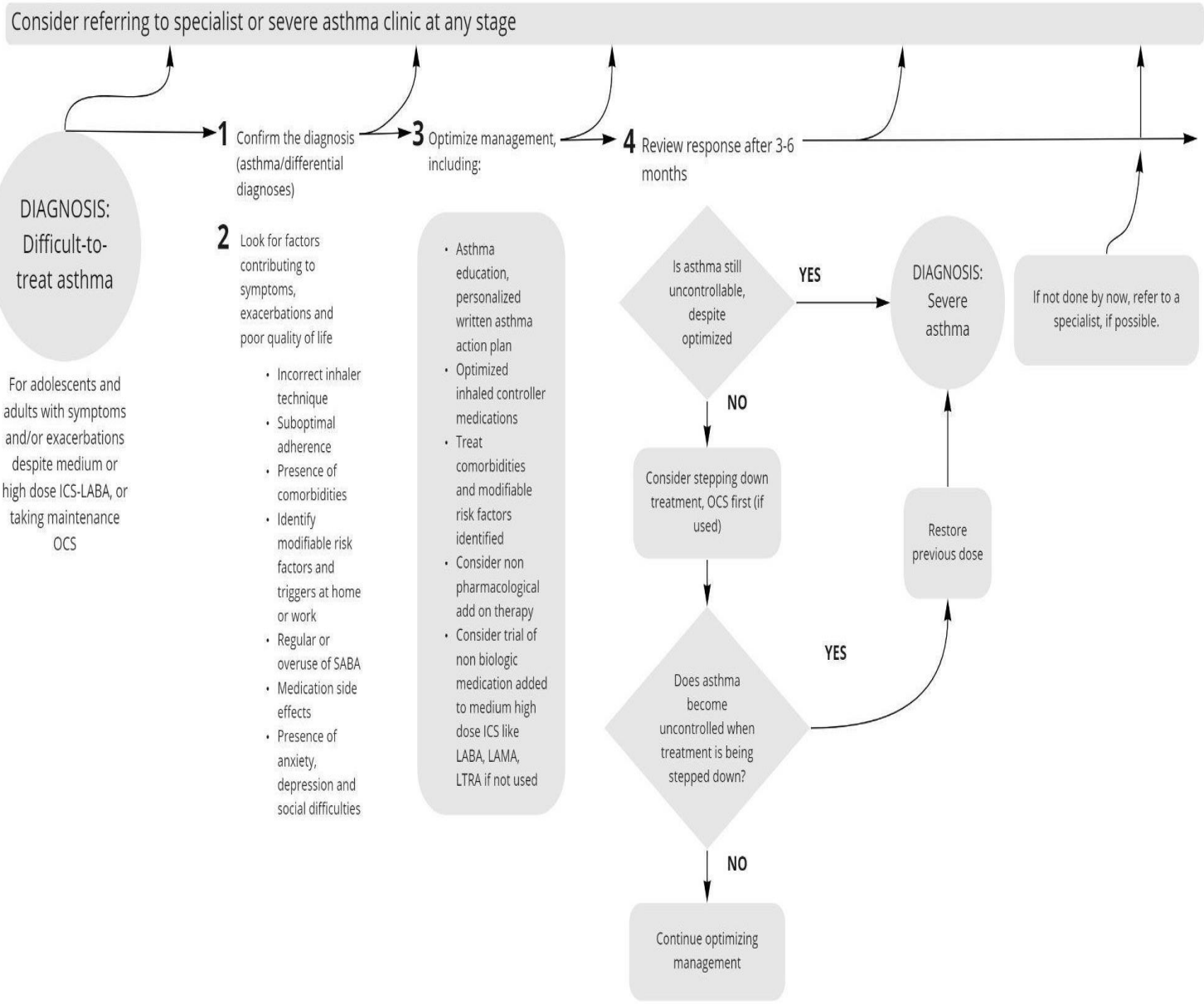



**Figure 7. Clinical pathway for difficult-to-treat asthma patients for use is proposed for both primary and specialist care**

**Section 14. Training in guided asthma self-management**

**Good Practice Statement 4.2**

Due to the long-term use of pharmacologic agents, patients and families must be trained how to independently adjust the use of their medications based on their written asthma action plan (WAAP) and know when to contact their physician for major treatment decisions. The essential components of effective guided asthma self-management include self-monitoring of symptoms and/or peak flow, a clear and updated WAAP, and a regular review by physicians of the patient's asthma control, treatment, and skills in using asthma devices. These are discussed extensively in KQ 3 and KQ 5.

**Section 15. Alternative strategies which have been evaluated for adjusting asthma treatment**

*Should we use FeNO as an adjunct to guide treatment in children and adolescents with asthma?*

**Recommendation 4h.**

Fractionated exhaled nitric oxide (FeNO) can be used as an adjunct to guide treatment in children and adolescents.

Evidence-based recommendation. De novo.
Weak recommendation. Low certainty of evidence.

Evidence summary:

Currently, GINA 2021 does not provide any recommendation for FeNO-guided treatment. A pre-print of a systematic review and meta-analysis accepted for publication of 23 RCTs comprising 2723 pediatric patients showed that children showed that FENO-guided asthma management helped reduce the numbers of children with asthma exacerbations (risk ratio (RR) 0.73, 95% confidence interval (CI) 0.63 to 0.84; P < 0.0001) and exacerbation frequency (standardized mean difference (SMD) -1.57, 95% CI -2.25 to -0.88; P < 0.00001).[13] Other older systematic reviews on the use of FeNO for monitoring in childhood asthma reported equivocal results.[14, 15]

*Should we use sputum eosinophil count as an adjunct to guide treatment in children and adolescents with asthma?*

A Cochrane systematic review by Petsky et al in 2017 stated that there is insufficient evidence on tailoring asthma medications based on sputum eosinophilia in children.[16] As such, this guideline is likewise unable to make a recommendation.

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## KEY QUESTION 5. HOW DO WE EVALUATE CONTROL OF SYMPTOMS IN ASTHMA?

**Dr. Maria Corazon Avanceña**

Physicians or healthcare providers evaluating asthma control in children and adolescents must assess two domains: (1) symptom control and (2) future risk of adverse outcomes or exacerbations.[1]

Poor asthma control is a burden to patients and their caregivers. The goal of asthma management is to use the minimum dose of maintenance medication to achieve asthma control. In low-resource settings like in many parts of the country, financial ability to sustain long-term asthma control should be part of the assessment. It is vital to look at social determinants that can negate medical efforts to control asthma.

It is important to explain to patients what asthma control means. For patients and their families, control is often perceived as the quick relief of symptoms after the use of reliever medications. This may mislead them into complacency and place them at increased risk for exacerbations. Identifying patients with poor asthma control allows the proper advice on increasing frequency of follow up, initiating or increasing controller or maintenance medication, individualizing asthma action plans, avoiding triggers, avoiding use of unnecessary medications such as antibiotics, and addressing concerns on inhaled corticosteroid treatment.

Symptom control is evaluated through patient or caregiver-reported outcome questionnaires. In Section 16, commonly used and previously validated categorical and numerical tools for asthma symptoms are presented. In general, these tools inquire about daytime and nighttime symptoms, frequency of SABA use, and activity limitation.

Parallel to evaluating symptom control, the healthcare provider must also be aware if the patient is at risk for exacerbations and similar adverse outcomes. In Section 17, factors that increase risk for adverse outcomes are enumerated. These factors include comorbidities, history of exacerbations, inhaler techniques, and adherence to medications.

Sections 16 and 17 deal with patient-reported and family-assessed evaluations to review asthma control, while Section 18 covers the utility of objective measurements through lung function tests.

Asthma control should be differentiated from asthma severity. Severity is only assessed after the level of treatment required to control the symptoms has been achieved. Poor symptom control may be due to improper inhaler technique, and not due to severe asthma, and may be immediately addressed. Conversely, patients who may have proper inhaler use may still have severe asthma, for which pharmacologic management may need to be stepped up. The assessment of severity is discussed in Section 19.

### Section 16. Evaluating symptom control

*Among children and adolescents with asthma, should patient-reported or family-assessed symptom tools be used to monitor and evaluate whether asthma is controlled?*

**Recommendation 5a**

The regular use of patient-reported and family-assessed symptom tools is recommended to monitor and evaluate the control of asthma.

Evidence-based recommendation adapted from GINA[1]
Conditional recommendation, low certainty of evidence

Asthma symptoms typically vary in intensity and frequency over time, and these constitute a significant burden to patients and caregivers. Poor symptom control is strongly associated with an increased risk of asthma exacerbations. It is important to therefore assess symptom control on a regular basis and at every opportunity in patient encounters.

There are various tools developed to assess symptom control, classified as simple screening, *categorical*, and *numerical*. Most of these have been developed and validated for adults and adolescents, but fewer for younger children. What these tools have in common is that they ask about symptoms over the past four weeks in terms of frequency of daytime symptoms, nighttime symptoms such as awakening due to asthma, frequency of short acting beta 2 agonist (SABA) use, and limitations in activity.

Parents and caregivers may describe children to be irritable, easily tired, or moody. These observations may also be symptoms of uncontrolled asthma. Children and adolescents may already have airflow limitation even before they explicitly complain of difficulty of breathing or before they require reliever therapy. When evaluating control of symptoms, it is equally important to ask both parents or caregivers, and the patients themselves.

Simple screening tools can be used to quickly identify patients who need more detailed assessments in primary care settings. This guideline adopts the GINA symptom screening tool, which is presented below.

**Table 16.1 GINA Symptom Screening Tool**

| **A. Assessment of Symptom Control** | |
|---|---|
| **In the past 4 weeks, has the patient had:**<br>**Daytime symptoms more than twice/week?**<br>**□ Yes**<br>**□ No** | **Level of Asthma Symptom Control**<br>**(how many "yes" ticked)**<br><br>**0: Well Controlled**<br>**1 to 2: Partially controlled**<br>**3 to 4: Uncontrolled** |
| **SABA reliever needed more than twice/week?**<br>**□Yes**<br>**□ No** | |
| **Any night waking due to asthma?**<br>**□Yes**<br>**□ No** | |
| **Any activity limitation due to asthma?**<br>**□Yes**<br>**□ No** | |

If a patient requires a more detailed assessment, the healthcare provider may use symptom control tools such as the ACT, c-ACT, and ACQ-5. These are widely used and extensively validated internationally, but more studies are needed to translate and validate asthma control tools for children and adolescents in the Philippine setting.

1. ACT for adolescents

A concise patient-reported evaluation of asthma symptoms, the Asthma Control Test (ACT), is a validated tool that assesses the impairment domain of asthma control and detects poorly controlled asthma in adults and in adolescents above 12 years old.[2] It is composed of five questions about frequency of manifestations of asthma and use of rescue medication for the past four weeks. Each question has five choices with corresponding scores of 1 to 5. The sum of scores would give the total ACT score, which can be interpreted from 5 (poorest asthma control) to 25 (optimal asthma control). An ACT score of > 19 indicates well-controlled asthma.[3]

In a local study by Mendoza et al (2007), results showed that ACT < 20 is 92.3% sensitive and 90.5% specific, with an area under the curve (AUC) of 0.972 using FEV1 as a reference standard to detect uncontrolled asthma in Filipino adults. The

positive and negative predictive values were 98% and 79%, respectively.[4] ACT therefore, may be utilized to evaluate asthma severity even in the absence of a spirometer or a peak flow meter in outpatient cases.

2. c-ACT for children

The Childhood Asthma Control Test (c-ACT) is composed of seven questions about the past four weeks. This questionnaire is divided into two parts, with the first and second parts being filled up by the child and by the parent or caregiver, respectively. The first part is composed of four questions regarding perception of asthma control, limitation of activities, coughing and awakenings at night. Every question corresponds to four possible answers (0 to 3) using a visual analogue scale. The second part is composed of three questions such as daytime complaints, daytime wheezing, and awakenings at night. Every question corresponds to six possible answers (0 to 5).[2]

ACT has been validated for use by children 4 to 11 years of age in other countries. Like the ACT, the c-ACT score is the total sum of the scores, from 0 the poorest asthma control to 27 the optimal asthma control. A score of less than or equal to 19 also indicates uncontrolled asthma.[5]

3. Asthma Control Questionnaire (specifically ACQ-5) for adolescents

There are several versions of the ACQ but GINA 2021 explicitly prefers ACQ-5 because the evaluation of other versions is still ongoing.[1] Unlike the ACT that asks about symptoms over a four-week recall period, the ACQ asks about symptoms from the past 7 days. It consists of five questions: nighttime awakening, symptoms upon waking up, activity limitations, shortness of breath, and wheezing. Response options are on a 7-point scale from 0 point (no impairment) to 6 points (as maximum impairment). The final score is the average of the total scores for the five items, with higher scores indicating worse control.

Nguyen et al demonstrated the ACQ to be a valid and moderately responsive tool in assessing asthma control among pediatric patients ages 6 to 17 years in a clinical trial. It provides an additional tool in assessing asthma control among children.[6] The main advantage of the ACQ is the similar psychometric characteristics in adults and children, permitting the use of a single instrument in clinical trials that includes both children and adults. In contrast, the c-ACT and ACT have different ranges, which make it difficult to analyze combined child and adult data.[6] A recent study by Khusial et al (2020) has also shown that online versions of ACQ are in good agreement with original paper versions; this demonstrates that the ACQ can be administered online and is a valid measurement tool.[7]

**Section 17. Risk factors for future adverse outcomes**[1]

*Among children and adolescents with asthma, what are the factors that increase risk of adverse outcomes or exacerbations?*

**Good Practice Statement 5.1**

Physicians and healthcare providers should know whether the patient is at risk for asthma-related adverse outcomes. These adverse outcomes pertain to having exacerbations, persistent airflow limitation, and side effects from medications. The assessment of risk factors must be done at diagnosis of asthma, and at least every 1 to 2 years, particularly for patients with exacerbations. When applicable and feasible, measure FEV1 at the start of treatment, after 3 to 6 months for personal best lung function, and periodically for ongoing risk assessment (see Section 18).

Evidence to support risk prediction in preschool children under 6 years of age is limited. Therefore, the succeeding risk factors are for pediatric patients ages six and above. Knowing these risk factors should prompt closer monitoring of asthma control.

Risk factors for exacerbations:

- **Medications:** high SABA use (associated with increased exacerbations and mortality if ≥ one 200 dose-canister per month); ICS not prescribed; poor adherence; incorrect inhaler technique
- **Comorbidities:** obesity; chronic rhinosinusitis; gastroesophageal reflux disease; confirmed food allergy; anxiety; depression; pregnancy; chronic mucus hypersecretion
- **Exposures:** smoking; tobacco smoke; allergen exposure if sensitized; air pollution; noxious chemicals; occupational exposures
- **Medical history:** ever intubated or admitted in an intensive care unit for asthma, or having at least one severe exacerbation in the last 12 months
- **Socio economic problems:** or poor access to healthcare
- **Lung function for older children and adolescents:** low $FEV_1$, especially if <60% predicted; high bronchodilator reversibility
- **Other tests** for adults and with limited evidence in children: sputum/blood eosinophilia, and elevated FeNO in allergic adults on ICS

Risk factors for developing persistent airflow limitation:

- Preterm birth, low birth weight, greater infant weight gain
- Lack of ICS treatment in patients who had a severe exacerbation

Risk factors for medication side-effects:

- Systemic: frequent oral corticosteroids; long-term, high dose and/or potent inhaled corticosteroids (ICS); also taking P450 inhibitors
- Local: high dose or potent ICS; poor inhaler technique

GINA 2021 provides the following specific questions in the assessment of asthma control in children 6-11 years old in Table 17.1.[1]

**Table 17.1 Specific guide questions for assessment of asthma control in children 6-11 years**

| Factors | Specific questions |
|---|---|
| **Asthma Symptom Control** | |
| **Day Symptoms** | • In the number of times per week or day, how often does the child have cough, wheeze, difficulty of breathing, or heavy breathing?<br>• What triggers the symptoms?<br>• How are they handled? |
| **Night Symptoms** | • Are there any coughing, awakenings, or tiredness during the day?<br>→ If the only symptom is coughing, consider other diagnoses such as rhinitis or GERD. |
| **Reliever Use** | • How often is reliever medication used?<br>→ Check date on inhaler or last prescription. Distinguish use of medications for pre-exercise (sports) and use for relief of symptoms. |
| **Level of Activity** | • What sports/hobbies/interests/ does the child have at school and in his spare time?<br>• How does his level of activity compare with his peers or siblings?<br>• How many days is the child absent from school?<br>→ Try to get an accurate picture of the child's day from the child without interruption from the parent or caregiver. |

| | |
|---|---|
| **Risk Factors for Adverse Outcomes** | |
| **Exacerbations** | • How do viral infections affect the child's asthma?<br>• Do symptoms interfere with school or sports?<br>• How long do symptoms last?<br>• How many episodes have occurred since their last check-up?<br>• Have you had any urgent doctor/emergency department visits?<br>• Do you have a written action plan? |
| **Lung Function** | → For asthma control, the key parameters for monitoring are $FEV_1$ and $FEV_1/FVC$ ratio. Plot these values as percent predicted to see trends over time, if available or applicable. |
| **Side-effects** | → Check the child's height at least yearly (poorly controlled asthma can affect growth and growth velocity may be lower in the first 1-2 years of ICS treatment).<br>→ Ask about frequency and dose of inhaled and oral corticosteroids. |
| **Treatment Factors** | |
| **Inhaler technique** | → Ask the child to demonstrate inhaler use.<br>→ Compare with device-specific checklists. |
| **Adherence** | • Is there any controller medication in the home at present?<br>• On how many days does the child use his controller in a week?<br>• Is it easier to remember to use it in the morning or evening?<br>• Where is the inhaler kept - is it in plain view to reduce forgetting?<br>→ Check date on inhaler. |
| **Goals/Concerns** | • Does the child or his parent or caregiver have any concerns about his asthma (such as fear of medication side-effects, interference with activity)?<br>• What are the child's/parent's/caregiver's goals for treatment? |
| **Comorbidities** | |
| **Allergic Rhinitis** | • Is there itching, sneezing, or nasal obstruction?<br>• Can the child breathe through his nose?<br>• What medications are being taken for nasal symptoms? |
| **Eczema** | • Is there sleep disturbance?<br>• Do you use topical corticosteroids? |
| **Food Allergy** | • Is the child allergic to any foods?<br>→ Confirmed food allergy is a risk factor for asthma-related death. |
| **Obesity** | → Check age-adjusted BMI.<br>→ Ask about diet and physical activity. |
| **Other Investigations (if needed)** | |
| **2-week diary** | → If no clear assessment can be made based on the above questions, ask the child or parent/caregiver to keep a daily diary of asthma symptoms, reliever use and peak expiratory flow (best of three) for 2 weeks. |
| **Exercise Challenge (laboratory)** | → Provides information about airway hyperresponsiveness and fitness.<br>→ Only undertake a challenge if it is otherwise difficult to assess asthma control. |

**Section 18. Lung function in monitoring asthma**

*Among children and adolescents with asthma, should we use lung function tests to evaluate control in asthma?*

**Recommendation 5b**

5b.1 The use of a peak flow meter is recommended as an adjunct in long-term monitoring.

5b.2 Spirometry is not routinely required to assess asthma control. Normal spirometry results do not definitively indicate control of asthma.

Consensus-based recommendations adapted from GINA 2021[1]
Conditional recommendations

In assessing asthma control, lung function tests are objective measurements to determine future risk of an exacerbation because it shows whether airflow obstruction is present. The specific parameters to be measured and monitored in asthma patients are $FEV_1$ and $FEV_1$/FVC on spirometry, and personal peak expiratory flow (PEF). Spirometry testing is done in tertiary centers while PEF may be done in primary care centers or at home with portable peak flow meters. However, for children below six years old, lung function testing usually cannot be reliably obtained with good reproducibility.

Children six years and above can perform spirometry and peak flow meter monitoring. Lung function tests are ideally measured before initiation of treatment, at three to six months after initiation of treatment, and at regular intervals in the long term. This is done to monitor for deterioration, improvement, and response to treatment.

A caveat in interpreting these lung function tests is that normal $FEV_1$ and $FEV_1$/FVC values do not automatically mean that asthma is controlled, nor do they rule out asthma exacerbations. Children with uncontrolled asthma may still present with normal lung function values between exacerbations. GINA 2021 states that lung function test results have not been shown to correlate well with asthma symptoms in children.[1] Abnormal spirometry results should be interpreted by specialists. This guideline does not require spirometry as a tool to differentiate between controlled and uncontrolled asthma.

Peak expiratory flow (PEF) monitoring provides families a reference point for the asthmatic's personal best and enables them to determine if PEF is markedly reduced (i.e., < 80% of personal best) providing information on asthma control. However, in a Cochrane systematic review of four trials (n = 355) symptom-based written action plans remain superior over PEF-based written action plans for preventing acute care visits.

This guideline therefore recognizes peak flow monitoring as good practice for long term monitoring; but changes in PEF are not required to differentiate controlled versus uncontrolled asthma. See Appendix for the reference ranges, how to interpret $FEV_1$, $FEV_1$/FVC, PEF, and what is personal best.

**Section 19. Assessing Asthma Severity**

**Recommendation 5c**

Asthma severity may be classified as mild, moderate, or severe based on the level of treatment required to control symptoms and exacerbations. This is based on a retrospective assessment when a step down has been attempted to find the minimum effective level of treatment that keeps them symptom-free after several months of controller treatment.

Clinical classification adopted from GINA 2021[1]
Strong recommendation

Asthma severity may change over the course of management and may change over months or even years. This should be explained to patients and their caregivers. The importance of obtaining an accurate medical history and empowering families with a clear understanding of asthma severity cannot be overly emphasized. They may underestimate severity due to perceptions based on the intensity or frequency of symptoms or the ease by which SABA brings quick relief of their symptoms. Patients may still be at risk of future exacerbations especially if not on controller medication (i.e., an ICS-containing regimen).

**Classification of asthma severity:**

**MILD**

1. Asthma that is well-controlled with Step 1 or Step 2 treatment (KQ4), that is, with as needed ICS-Formoterol alone, or with low-level maintenance/controller treatment, such as low dose inhaled corticosteroid or leukotriene receptor antagonist.
2. For patients on as-needed ICS-Formoterol, the frequency of use that should be considered to represent well controlled asthma has not been determined.
3. The previous terminology of "mild intermittent" and "mild persistent" are no longer used. GINA's distinction was not evidence-based but rather, on an untested assumption that patients with symptoms twice a week or less would not benefit from ICS.[1] However, patients with mild intermittent asthma can still have severe exacerbations, and this risk may be reduced by ICS-containing treatment.

**MODERATE**

Asthma that is well-controlled with Step 3 or Step 4 treatment (KQ4), that is with low or medium dose ICS-LABA.

**SEVERE**

1. Asthma that remains uncontrolled despite optimized treatment with high dose ICS-LABA, or asthma that requires high dose ICS-LABA to prevent it from becoming "uncontrolled."
2. According to GINA 2021, the European Respiratory Society and the American Thoracic Society Task Force on Severe Asthma considered that the definition of severe asthma should be reserved for "patients with refractory asthma and those in whom response to treatment of comorbidities, (such as chronic rhino sinusitis or obesity) is incomplete."[1]

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# KEY QUESTION 6. WHAT ARE THE INDICATIONS TO CONSIDER USE OF ANTIBIOTICS / SYSTEMIC CORTICOSTEROIDS / VITAMIN D / IMMUNOTHERAPY IN CHILDREN WITH ASTHMA?

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There is no cure for asthma. However, symptoms can be controlled, and exacerbations can be prevented and relieved. Other supportive therapies that can be offered to patients are available, but some may lack evidence to support its routine use in the management of asthma. Antibiotics, steroids, vitamin D supplementation, and immunotherapy are commonly given with asthma medications. In this section the role of these therapies in pediatric asthma are reviewed.

### Section 20. Antibiotics

*Should antibiotics be used in children to manage an acute asthma exacerbation? What are the indications to consider the use of antibiotics in pediatric asthma patients in acute exacerbations?*

**Recommendation 6a**

The routine use of antibiotics in the management of asthma exacerbations is not recommended. Antibiotics are indicated only when there is evidence of a concomitant bacterial lung infection.

Evidence-based recommendation adapted from GINA 2021[1] and BTS 2019[2]
Strong recommendation, low certainty of evidence

Majority of acute asthma attacks in children are triggered by viral infections. Thus, antibiotics are not indicated in its management.

The GINA 2021 and BTS 2019 guidelines do not support its routine use in acute asthma unless there is evidence of concomitant bacterial lung infection such as high-grade fever, radiographic evidence of consolidative pneumonia, and other supportive laboratory parameters (e.g., complete blood count and procalcitonin indicating bacterial infection or sepsis).[1, 2]

Furthermore, in a Cochrane systematic review by Normansell et al in 2018, the few studies included either have problems in the inclusion and exclusion criteria, or have variation in the methodological quality, making it difficult for the authors to compare them.[3] Upon evaluation for the quality of outcomes, they gave them grades ranging from moderate to very low quality due to suspicion of publication bias, indirectness in reporting, imprecision in the statistical analysis and poor methodology designs. This led to their conclusion that there is very limited evidence to demonstrate whether antibiotics improve symptoms or improve PEF in children in acute exacerbations.

### Section 21. Systemic Corticosteroids

*Should systemic corticosteroids be used in children to manage an acute asthma exacerbation?*

**Recommendation 6b.1**

Systemic corticosteroids should be given as early as possible to manage acute asthma exacerbations, in concordance with the exacerbations management algorithms. Treatment with oral or intravenous corticosteroids may be individualized to the number of days necessary to achieve improvement. Tapering of the dose is not necessary if the systemic steroid administration is less than 14 days.

Evidence-based recommendation
Adopted from GINA 2021[1] and BTS 2019[2]
Strong recommendation, low certainty of evidence

Steroid therapy early in the treatment of acute asthma attacks in children has been shown to reduce the need for hospital admission. Therefore, steroids should be given within an hour of presentation at the emergency department, for children and adolescents with worsening of symptoms despite initial SABA treatment, or despite having previously increased their reliever and controller medications prior to the emergency room visit.

Oral and parenteral steroids are known to have equal bioavailability and efficacy with the same onset of action. Other advantages of oral steroids compared to intravenous steroids are its ease with administration, less invasive, and less costly. Intravenous steroids should be reserved for patients with vomiting, or unable to tolerate oral medications. It may be considered for patients in severe exacerbation who are too dyspneic to swallow, and may require non-invasive ventilation or intubation.

The dose of prednisone/prednisolone for children is 1 to 2 mg/kg/day up to a maximum dose of 20 mg/day for below 2 years old, 30 mg/day for 2 to 5 years old, 40mg/day for 6-11 years old and 50 mg/day for 12-18 years old. Intravenous steroid (hydrocortisone) dose is 4mg/kg/dose given every 6 hours. Treatment with oral or intravenous corticosteroids of 3 to 5 days is usually sufficient, but the total duration of treatment may be individualized to the number of days necessary to achieve improvement. Tapering of the dose is not necessary if the systemic steroid administration is less than 14 days.

Dexamethasone may be considered as an alternative to prednisone in the emergency department. A systematic review and meta-analysis by Cai et al (2021) pooled 10 pediatric RCTs comparing dexamethasone and prednisone for acute exacerbation in the Emergency Department.[4] Their results showed reduction in vomiting in the dexamethasone arm compared to prednisone (n = 2226, pooled RR 0.29, 95% CI 0.18 to 0.48, p <0.00001), and no statistically significant difference in terms of hospital admission, return to ED, or hospital admissions after relapse.[4] However, the dexamethasone doses varied across the studies, from oral dexamethasone at 0.3 mg/kg to 0.6 mg/kg maximum of 12 mg, intramuscular route at 0.6 mg/kg maximum 15 mg, and nebulized dexamethasone at 1.5 mg/kg maximum of 45 mg.

*Are inhaled corticosteroids effective as an adjunct to systemic corticosteroids to reduce hospitalizations in pediatric asthma exacerbations at the Emergency Department?*

**Recommendation 6b.2**

Inhaled corticosteroids may be added to systemic corticosteroids in the Emergency Department for pediatric patients with moderate to severe asthma exacerbations to reduce hospitalizations.

Evidence-based recommendation. De novo.
Weak recommendation, low certainty of evidence

Evidence Summary:

This is a *de novo* recommendation, and there was no explicit recommendation from GINA 2021 and BTS 2019.

Sawanyawisuth 2020 included four RCTs (n = 1230), comparing ICS with SC versus placebo and SC-only for moderate to severe asthma in patients 18 years old and below, which showed a 25% reduction in odds for hospitalization (0.75, 95% CI 0.57-0.99, p = 0.04, $I^2$ 71%).[5] The ICS used in the trials was budesonide ranging from 1.5 mg to 3mg.[5] The RCTs had a baseline certainty rated as high but was downgraded due to imprecision (wide CI, small sample) and risk of publication bias (few studies).

Another meta-analysis by Li 2021 showed similar results, hence the low certainty of evidence was retained.[6] In Li's study, a total of 9 RCTs were included for the hospitalization outcome. Children receiving nebulized budesonide had 43% lower risk of being hospitalized (RR 0.57; 95% CI, 0.39; 0.85) compared with those receiving placebo.[6]

**Section 22. Vitamin D supplementation**

*Is Vitamin D supplementation safe and effective in children to reduce acute asthma exacerbations?*

**Recommendation 6c**

Vitamin D supplementation may be added as an adjunct in asthmatic children on corticosteroids to reduce acute asthma exacerbations.

Evidence-based recommendation. De novo.
Weak recommendation, very low certainty of evidence

Evidence Summary:

There is some evidence that vitamin D supplementation is safe and effective in reducing asthma exacerbations in children on corticosteroids. A recent systematic review and meta-analysis, which included four pediatric RCTs involving a total of 387 asthmatic children maintained on corticosteroids, showed a modest reduction in risk of exacerbations in the vitamin D supplementation arm (pooled RR 0.69, 95% CI 0.55-0.87).[7]

However, the vitamin D doses and follow up durations varied widely across the trials. Vitamin D doses used in the trials were: 100,000 IU/3.5 months, 4000 IU/day, 500 IU/day, 60,000 IU/month.[7] While the baseline rating was high certainty due to the use of RCTs, it was downgraded to very low certainty due to imprecision and potential for publication bias.

The definite dose for vitamin D as an adjunct in asthma cannot be established at this point because the RCTs used varying doses.

**Section 23. Immunotherapy for pediatric asthma**

For many patients with allergic asthma, conventional therapy may not completely control their symptoms. Therefore, it can be helpful to advise patients regarding different step-up treatments for difficult-to-control asthma. Immunotherapy in asthma may be defined as therapies that aim to modify the underlying immunologic mechanisms behind the allergic inflammation.

Specific allergen immunotherapy (AIT) is a serial administration of increasing dose of a specific allergen to which a patient tested positive on skin prick test or serum specific immunoglobulin E and to which exposure to that particular allergen aggravates asthma symptoms.[8] AIT addresses underlying allergic inflammation with the goal of immune tolerance. Immunotherapy is the only disease-modifying treatment for allergic asthma.

*Is immunotherapy safe and effective in the management of children and adolescents with asthma?*

**Recommendation 6d**

Immunotherapy is conditionally recommended for specific subpopulations of children or adolescents with difficult-to-treat allergic asthma.

Evidence based recommendation. De novo.
Conditional recommendation. The certainty of evidence for safety is moderate while the certainty of evidence for effectiveness is low.

For a patient to qualify for immunotherapy, he or she must have a positive skin test or serum IgE to the specific allergen, and in whom asthma has been reported to be triggered upon exposure to the specific allergen.
Evidence Summary:

For SCIT there is moderate certainty of evidence in decreasing long-term control medication
in children with dust mite allergies, and low to very low certainty for other outcomes such as quality of life, FEV1 improvement, systemic steroid use, short-term medication use.[9]

For SLIT there is low to very low certainty for decreasing long-term control medication, systemic steroid use, FEV1 improvement, and insufficient evidence for symptom control, quality of life, and short-term medication use; however, GINA 2021 recommended adding house dust mite SLIT at Step 2, 3, and 4 treatment for asthmatic patients with allergic rhinitis sensitized to house dust mite for 12 years old and above for as long as their FEV1 is more than 70%.[9] For both SCIT and SLIT, local and systemic reactions are common, while anaphylaxis is rare, for children and adolescents. A systematic overview of systematic reviews by Asamoah et al (2017) on AIT for allergic asthma that included studies in both adult and children demonstrated significant improvement in long-term medication use and symptom scores.[10] When added to conventional therapy, AIT can decrease symptoms, thus improving disease severity and medication requirements.[11] It offers protection against the development of new sensitizations, and consequently it decreases the risk of developing asthma for those with allergic rhinitis due to the atopic march.[11] Thus, immunotherapy is a possible treatment option in children with these disorders along with pharmacotherapy and allergen avoidance. Long-term effects of SCIT and SLIT have been reported to be maintained approximately 7–12 years after discontinuation of treatment.[12]

The addition of specific allergen immunotherapy is indicated in the following:

1. patients with allergic rhinitis/conjunctivitis or allergic asthma whose symptoms are inadequately controlled by medications or avoidance measures
2. patients who require high medication doses [ e.g. inhaled fluticasone propionate > 200 mcg/day in 6-11 years of age and >500mcg/day in adolescents (4)], multiple medications, or both to maintain control of their allergic disease
3. patients who developed adverse effects of medications or who want to avoid or reduce the long-term use or cost of medications

It must be emphasized that a patient's asthma must be controlled during administration of immunotherapy. There is no specific upper or lower age limit in pediatric patients for initiating allergen immunotherapy for as long as the patient's condition meets the stated indications above.[8] Immunotherapy can be safely initiated in young children less than 5 years of age who can communicate their symptoms, especially systemic reactions. Other factors to consider for patient selection are the absence of significant comorbid conditions and parents/patients' willingness to comply with the allergen immunotherapy regimen.

Allergen immunotherapy has two types available for clinical use, namely subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT).

SCIT involves subcutaneous injection of sterile allergen extracts. The initial build-up phase involves receiving injections in increasing amounts of allergen weekly, duration of which depends on the extract used and ranges from 1 to 12 months. Maintenance phase begins when the effective therapeutic dose is reached. The effective therapeutic dose is based on recommendations from a national collaborative committee in the United States called the Joint Task Force on Practice Parameters: Allergen Immunotherapy: a practice parameter third update, 2011.[8] Once the target maintenance dose is reached, the intervals between allergy injections can be increased up to 4 weeks. Immunotherapy treatment should be completed for a minimum of 3 to 5 years.

SLIT involves placement of allergens under the tongue either in lyophilized tablet form, or liquid drops and sprays. Unlike SCIT, there is no build-up phase in SLIT. A fixed dose of an allergen is given daily for 3 to 5 years instead.

Examples of allergen extracts available in the Philippines are house dust mites (*Dermatophagoides* spp and *Blomia tropicalis*), cockroach, grass and tree pollen and animal dander.
Adverse reactions associated with AIT can be local or systemic. Local reactions (LRs) are fairly common with both SCIT (erythema, pruritus, and swelling at the injection site) and SLIT (oropharyngeal pruritus, swelling, or both). Local and systemic reactions occur more frequently in patients who receive SCIT or SLIT than comparator groups in RCTs.[13, 14, 15]

In pediatric AIT trials, SCIT local reactions occur in 0% to 27% of patients; and approx 6.4 events per patient; versus none in comparator groups. SCIT systemic reactions occur in 6% to 17% patients or 0.7 to 1.1 events per patient versus 0% to 3% or approx 0.5-0.8 events per patient in comparator arms. Anaphylaxis is reported in 2% of its recipients.[9]

Meanwhile, SLIT local reactions occur in 0% to 35% of patients, at 0.35 to 5.2 events per patient versus 0% to 20% in comparator groups; and systemic reactions in 2% or 0.23 events per patient, versus 4.5% or 0.48 events per patient in comparator arms. No anaphylaxis reported in the RCTs for SLIT. Anaphylaxis for SCIT and SLIT have been documented in non-RCTs and case reports. [10, 13, 14, 15]

AIT via subcutaneous immunotherapy should only be administered at a medical facility by healthcare professionals with appropriate training since occasional reactions may require immediate therapy. Patients are observed in the physician's office for at least 30 minutes for systemic reactions. A systemic reaction is an adverse event involving organ-specific systems distant from the injection site, an example of which is anaphylaxis. On the other hand, with sublingual immunotherapy, the first dose is administered at the clinic. The rest of the daily dosing is administered at home. Patients are recalled every 1-2 months for monitoring and re-assessment.

**Section 24. Omalizumab**

*Should omalizumab be given as an add-on therapy for children ages 6 years old and above with uncontrolled severe allergic asthma to decrease acute exacerbations?*

**Recommendation 6e**

Omalizumab may be given as an add-on therapy for children ages 6 years old and above with uncontrolled severe allergic asthma.

Evidence-based recommendation. De novo.
Weak recommendation, very low certainty of evidence

Omalizumab is a human monoclonal antibody that binds to free human immunoglobulin E (Ig E) thus preventing its interaction with IgE receptors thereby interfering with cell activation and mediator release, decreasing allergic inflammation.[16] Currently it is the only biological drug available in the Philippines indicated as an add-on therapy in children from age 6 and above with uncontrolled severe allergic asthma.[17] It is given as a subcutaneous injection, every 2-4 weeks

in a hospital setting. The dose is based on age, pretreatment serum IgE levels (30-1,300 IU/mL) and body weight. Anaphylaxis is infrequent (≤0.2%).[18]

A recent systematic review (Henriksen 2020) reports that omalizumab appears safe and suggests that it may reduce exacerbations in children and adolescents; but the individual studies could not be pooled due to inherent clinical heterogeneity in outcomes measurement. There is insufficient evidence on its effect on lung function, asthma control, and quality of life.[19] Furthermore, the cost of omalizumab therapy can be an issue in the Philippines and further cost-effectiveness studies are necessary.

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# CHAPTER 4. EDUCATION AND PREVENTION OF ASTHMA

## KEY QUESTION 7. WHAT ARE EVIDENCE-BASED NON-PHARMACOLOGIC AND LIFESTYLE FACTORS THAT MAY BE RECOMMENDED FOR PRIMARY AND SECONDARY PREVENTION OF ASTHMA IN CHILDREN AND ADOLESCENTS?

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**Dr. Jacqueline Reyes-Rodolfo**

The recommendations were initially adapted from GINA 2021[1] and BTS 2019,[2] but the Evidence Review Experts team of this Philippine guideline further conducted an updated literature review and independent appraisal of evidence.

There are numerous triggers of asthma that may contribute to the presence of symptoms and exacerbations in asthmatic patients. Avoiding these triggers may help improve asthma and reduce the requirement for pharmacotherapy. There are several non-pharmacological interventions that are proposed to help prevent and control asthma. However, evidence of its effectiveness is difficult to establish, and more well-controlled studies are needed.

Prevention interventions may be classified into primary and secondary. Primary prevention refers to interventions introduced before the onset of disease and designed to reduce its incidence, while secondary prevention are interventions introduced after the onset of disease to reduce its impact.[2] The following are recommendations on primary and secondary prevention interventions for asthma. These recommendations should be part of patient or family education.

### Section 25. Primary prevention of childhood asthma

The development and persistence of asthma may be driven by gene-environment interactions. Those occurring early in life and in utero are the most important interactions. Data supporting the role of environmental risk factors in the development of asthma focus on nutrition, allergens, pollutants, microbes, and psychosocial factors.[1, 2]

**Recommendation 7a**

The following *primary prevention* measures are recommended:

7a.1 Pregnant patients must avoid exposure to air pollutants, including prenatal smoking.

Evidence-based recommendation
Strong recommendation, high certainty of evidence

The deleterious effects of maternal smoking and air pollutants impacts asthma and overall health of fetuses, neonates, and children is well studied. A systematic review by He et al in 2020, pooling 93 observational studies, showed the association of prenatal maternal tobacco exposure to doctor-diagnosed asthma (active smoking and doctor-diagnosed asthma, OR 1.26 95% CI 1.15-1.37, $I^2 = 62.8\%$, $p < 0.001$) and to wheezing symptoms (OR 1.36, 95% CI 1.19-1.54, $I^2 = 55.7\%$, $p < 0.001$).[3]

7a.2 Breastfeeding should be encouraged for all families.

Evidence-based recommendation
Strong recommendation
High certainty of evidence for overall health, low certainty for asthma prevention

Breastfeeding is encouraged for all its positive benefits on the child's nutrition and development. Furthermore, a systematic review of 42 observational studies by Xue 2021 suggests that the duration and exclusivity of breastfeeding are associated with a lower risk of asthma in children less than 7 years old.[4] Specifically, children with longer duration or more breastfeeding had lower odds of developing asthma (OR 0.84, 95% CI 0.75-0.93, $I^2 = 62.4\%$), while children with more exclusive breastfeeding versus less exclusive breastfeeding also had lower odds of asthma (OR = 0.81, 95% CI 0.72-0.91, $I^2 = 44\%$).[4]

### 7a.3 Exposure to environmental tobacco smoke, aerosols from e-cigarettes, and air pollutants should be avoided to prevent respiratory symptoms

Evidence-based recommendation,
Strong recommendation, high certainty

Environmental tobacco smoke has long been established as triggers of asthma and respiratory symptoms. For e-cigarettes, secondhand smoke from aerosols or ENDS have likewise recently shown to be associated with asthma symptoms and uncontrolled asthma. Alnajem 2020 reports increased prevalence of asthma symptoms (aPR 1.56, 95% CI 1.13-2.16) and uncontrolled asthma (aPR 1.88, 95% CI 1.35 to 2.62) in 1,565 adolescents in Kuwait. Bayly 2019 reports increased odds for an asthma exacerbation among adolescents ages 11-17 years with exposure to secondhand smoke to ENDS in 11,830 teenagers in the US. These studies were initially rated as low certainty, but was upgraded to moderate due to large magnitude of effect despite adjusting for covariates.

Air pollutants are well-documented triggers of respiratory symptoms; this extends to maternal exposure. Bettiol 2021 conducted a systematic review of traffic-related air pollution (TRAP) and development of wheezing or asthma in the first 1000 days of life with 21 birth cohort studies.[5] Across 10 birth cohorts, maternal exposure to particulate matter (PM) and nitric oxides (NOx) were consistently associated with asthma and wheezing in their offspring.[5] Across 20 birth cohorts, results suggest that early life exposure to traffic related air pollutants and wheezing. Pooling could not be achieved due to differences in measurement of exposures and outcomes.

Han et al (2021) conducted a systematic review and meta-analysis of 27 studies on TRAP and childhood asthma development. Various measurements of TRAP were assessed: PM2.5 (meta-OR=1.07, 95% CI:1.00-1.13), NO2 (meta-OR=1.11, 95% CI:1.06-1.17), Benzene (meta-OR: 1.21, 95% CI:1.13-1.29) and TVOC (meta-OR:1.06, 95% CI: 1.03-1.10).[6] Notably, higher associations between TRAP and childhood asthma were significantly higher in Asia than those in Europe and North America.[6]

### 7a.4 Immunization should be completed, and given on time.

Evidence-based recommendation
Strong recommendation
High certainty of evidence for overall health, very low certainty for asthma prevention

The effect of vaccination on asthma prevention is not directly measured in published literature. At most, influenza vaccination has shown to decrease flu complications in asthmatic patients.[7] However, immunization is encouraged for its positive benefits on prevention of complications of bacterial and viral infections, and for its overall public health impact.

### 7a.5 Weight reduction is recommended in obese patients to promote general health and to reduce subsequent respiratory symptoms consistent with asthma.

Evidence-based recommendation
Strong recommendation, moderate certainty

A meta-analysis of 18 studies found that being either overweight or obese was a risk factor for childhood asthma and wheeze, particularly in girls.[8] Weight reduction is recommended in obese patients to promote general health and to reduce subsequent respiratory symptoms consistent with asthma.[2]

7a.6 Maternal distress during pregnancy or psychosocial stress during the child's early years should be mitigated.

Evidence-based recommendation,
Strong recommendation, low certainty

Evidence shows that maternal psychosocial and psychological exposure to stress puts children at risk of asthma. An updated systematic review by Chen et al (2021) suggested that prenatal mental disorders, particularly depression, to be associated with childhood asthma (n = 6 studies, ES 1.146, 95% CI 1.054-1.245, p = 0.001, $I^2$ = 93.5%).[9] Another systematic review by Flanigan et al (2018) including 30 studies (> 6 million participants in total), showed that maternal exposure to major stressors, especially anxiety and depression, were associated with offspring wheeze (OR 1.34, 95% CI 1.16-1.54), asthma (OR 1.15, 95% CI 1.04-1.27), atopic eczema/dermatitis (OR 1.34, 95% CI 1.22-1.47), or allergic rhinitis (OR 1.30, 95% CI 1.04-1.62). This was particularly pronounced for exposures in the third trimester. As an example, death of a child (HR 1.28, 95% CI 1.10-1.48) or a spouse (HR 1.40, 95% CI 1.03-1.90) increased the risk of offspring asthma.[10] Van de Loo et al (2016) pooled 10 studies and showed that the prevalence of wheezing, asthma and other respiratory symptoms was higher in children of mothers who were had psychological stress during pregnancy than in mothers who did not (pooled OR 1.56 (95% CI 1.36–1.80).[11]

There is insufficient evidence for the following *primary prevention* measures, and therefore NO recommendation can be made for the following:[1, 2]

- Maternal diet and food allergen avoidance
- Maternal dietary intake of fish or seafood, or supplementation of fish oil
- Maternal supplementation of selenium or vitamin E[2]
- Maternal use of dietary probiotics[2]
- Modified infant milk formula
- Delay of introduction of solid food[1]
- Early introduction of 'allergenic' food[2]
- Vitamin D
- Avoidance of antibiotics or paracetamol[1]
- Pet ownership[2]

## Section 26. Secondary prevention of childhood asthma

**Recommendation 7b**

The following secondary prevention measures are recommended:

7b.1 Asthmatics and families of children with asthma should be offered appropriate support to stop smoking cigarettes and/or e-cigarettes.

Evidence-based recommendation, adapted from GINA 2021 and BTS 2019
De novo for e-cigarettes
Strong recommendation, moderate (e-cigarettes) to high (cigarettes) certainty

For e-cigarettes, three systematic reviews and meta-analyses published in 2021 (Xian 2021, Chaffee 2021, and Chand 2021) with observational studies totaling over 1 million adolescents and adults all consistently showed the association of current or former e-cigarette use with asthma symptoms.[12, 13, 14] Teenager users of e-cigarettes have a greater risk of developing asthma. Xian et al found a significant association between current (OR = 1.30, 95% CI = 1.17–1.45) and former (OR = 1.22, 95% CI = 1.08–1.39)) e-cigarette usage with asthma. When e-cigarettes were used in combination with traditional cigarettes, the association was further increased (OR 1.47 (95% CI = 1.13–1.91) and was even higher than that of users who used traditional cigarettes (OR = 1.33, 95% CI = 1.19–1.49). Promoting and educating e-cigarette users,

especially those with symptoms of wheezing, should be reinforced.[14] This was similar to the findings of Chand and Hosseinzadeh (2021), whose meta-analysis found a significant association between current e-cigarette use and asthma (pOR = 1.36, 95% CI 1.21–1.52) and ever e-cigarette use and asthma (pOR = 1.24 95% CI 1.13–1.36).[12] The odds of developing symptoms did not vary significantly with the type of device used however, the progression of symptoms is prominent among frequent e-cigarette users.[13] While the baseline rating was low certainty due to studies being observational in nature, it was upgraded to moderate due to the large magnitude of effect of e-cigarettes on symptoms.[12, 13, 14]

7b.2 Patients or carers must be advised to avoid exposing the patient with asthma to unfavorable environmental conditions. This includes extreme weather conditions, poor air quality, volcanic ash, high pollen or mold counts.

Consensus-based recommendation adapted from GINA[1]
Strong recommendation

Particulate matter could be categorized as either natural or anthropogenic (e.g. wind-blown dust, sea salt, volcanic ash, pollens, fungal spores, soil particles, products of forest fires and oxidation of biogenic reactive gases).[15] There were reports on increased risk of visits to emergency department due to asthma exacerbation in 3 to 18-year old children due to a short-term local exposure to these particulate matter.[16] Moreover, exposure to pollens (e.g. tree and ambient grass) is a significant trigger for asthma exacerbations in children that needs immediate medical attention.[17, 18]

7b.3 Asthmatics who are on oral or inhaled corticosteroids may receive immunization as scheduled.

Evidence-based recommendation
Strong recommendation
High certainty of evidence for overall health, low certainty for asthma prevention

Similar to 7a.4, the effect of vaccination on asthma prevention is not directly measured in published literature. At most, influenza vaccination has shown to decrease flu complications in asthmatic patients.[7] However, immunization is encouraged for its positive benefits on prevention of complications of bacterial and viral infections, and for its overall public health impact.

This recommendation follows general vaccination guidance. Specifically, asthmatics who are on inhaled corticosteroids or low-dose and less than 14 days oral corticosteroids may receive immunizations as scheduled. Corticosteroids, depending on dose and duration, can cause immunosuppression, which can lead to severe or fatal reactions during immunization with live, attenuated vaccines. Hence, those receiving large doses (20mgs or more daily or 2mg or more per kg body weight per day or prednisone) for 14 days or longer should not receive live vaccines. Rescheduling the vaccination and, if it outweighs the need for continued corticosteroid use, planning the weaning from steroid treatment, should be under physician guidance. While inactivated vaccines are safe (i.e., they cannot replicate) to administer in immunosuppressed individuals, guidance from the steroid prescribing physician should be sought, to determine the degree of immunosuppression present in the patient and if enough immune response will be mounted upon vaccination.[19]

7b.4 Encourage people with asthma to engage in regular, tolerable physical activity and provide advice on prevention of exercise-induced bronchoconstriction (see KQ 9)

Consensus-based recommendation
Strong recommendation
See KQ9 for more details on EIB

7b.5 Weight reduction interventions, including dietary and exercise-based programs, is recommended in overweight and obese patients to improve asthma control.[20, 21, 22]

Evidence-based recommendation
Strong recommendation, moderate certainty of evidence

Weight loss either or both via dietary modifications and/or exercise-based programs are considered essential in the management control of asthma diseases. Relationship between insulin resistance and lung function among obese pediatric patients with asthma was discussed in the paper of Filippo et al in 2018.[20] Their post hoc analysis showed that pulmonary parameters such as FEV1/FVC (p=.003), PEF (p=.005), FEF25 (p=.001) and FEF 50 (p=0.019) were significantly reduced among obese asthmatics compared to normal weight non asthmatic children.[20] However, no differences were noted among obese asthmatics versus normal weight asthmatic pediatric patients. Furthermore, although not significant, evidence pointed out that there was an inverse relationship between insulin resistance (calculated using homeostatic model assessment of insulin resistance- HOMA-IR) and all spirometry parameters. Significantly lower FVC were also noted among insulin resistant children (p=0.03).[20]

In the four studies included in the systematic review conducted by Okoniewski et al also in 2018 revealed that expiratory reserve volume (ERV) was decreased among children both with asthma and were obese.[21] Those who belonged in the treatment arm (dietary or exercise management), although not statistically significant, were reported to have improvements in this particular pulmonary function parameter.[21] In addition, one study in this particular pool reported that RV and RV/TLC significantly improved from baseline among subjects distributed in the dietary management intervention group (mean improvement, -0.4 L for RV and -6.9% for RV/ TLC).[21]

Such changes were also seen in the inflammatory markers, in the above-mentioned systematic review, as FENO decreased in correlation with decrease in their BMI z-score(r=0.46, p=0.034) and also reductions in CRP, IL-6, adiponectin and TNF. These findings were also similar to that finding of RCT performed by Al-Sharif et al in 2020 with added findings of increase in CD4 and CD8 cell count.[22]

7b.6 Encourage patients with asthma to consume a diet high in fruit and vegetables.

Strong evidence-based recommendation
High certainty of evidence for overall health, low certainty for asthma prevention

Half of the forty-one studies involving children and adolescents as subjects in the systematic review and meta-analysis completed by Hosseini et al in 2016 revealed that there was an inverse relationship with fruit and vegetable intake on asthma or asthma related symptoms.[23] Four in these studies reported that immune responses to intake of these food items among children has a protective effect on systematic or airway inflammation. Fruits and vegetables consumption analyzed in these studies were based on total fruit and vegetable intake in forms of fresh fruit only, citrus fruits plus vegetables, salads, and vegetables in cooked form.[23] Meanwhile, van Brakel et al in 2020 performed review and meta-analysis involving studies on nutritional interventions and asthma.[24] According to analyses of studies involving herbs (herbs, herbs mixture or extract), supplements, vitamin D3, Omega 3 FA and whole food items have reported simultaneous improvements either in asthma related outcomes or immunological parameters. However, due to conflicting results in each studies, further investigations were advised.[24]

7b.7 Review with the patient or family if emotional stress contributes to asthma symptoms.[25] Encourage patients to identify goals and strategies to deal with emotional stress if it makes their asthma worse.

Consensus-based recommendation
Strong recommendation

Studies find that stress, whether from individual, family, or community factors, negatively impact a child or adolescent's asthma symptoms. Chronic stress may be linked to atopic asthma in children and adolescents.[25] In a study on children with chronic asthma, negative life events were found to increase the risk of asthma attacks in the following weeks.[26] Adolescents with asthma who had an accumulation of stress had negatively impacted asthma outcomes including worse Quality of Life and asthma control, and increased ED visits whereas individual stressors comprised of poverty, neighborhood stress, and school stress.[25] Adverse social conditions impact asthma morbidity, through affecting physiologic systems and through altering health behaviors.[28]

There is insufficient evidence for the following *secondary prevention* measures in childhood asthma, and therefore no recommendation can be made at this point for the following:

- General avoidance of food and food chemicals, except when food allergy or food chemical sensitivity has been clearly demonstrated, typically through carefully supervised food challenges
- Vitamin C, Vitamin E, selenium, magnesium, fish oil, probiotics, general reduction of salt intake
- Air ionizers[2]
- Acupuncture[2]
- Manual therapy including massage and spinal manipulation[2]
- Herbal and traditional Chinese medicines[2]
- Homeopathy[2]
- Hypnosis[2]
- Air purifiers, air humidifiers, essential oils, and ultraviolet light (UVC) (not mentioned in GINA or BTS)

**Good Practice Statement 7.1**

Households of patients with asthma, especially with allergic comorbidities, should reduce exposure to house dust mites. This includes multifaceted house dust mite control measures, regular cleaning of the home using damp cloths to remove settled dust, weekly change of beddings and pillowcases, and making the bedroom tidy and simple through minimizing clutter including curtains, rugs, carpets, books, wallpapers, and stuffed toys.

**Use of house dust mite avoidance as adjuncts for secondary prevention of asthma**

House dust mite (HDM) has been documented as the most common airborne allergen triggers for respiratory allergies not only in the local setting but globally.[26, 27]

The use of multifaceted HDM control measures (HDM impermeable beddings, acaricides plus high-efficiency particulate air filters) to reduce exposure to house dust mites and improve asthma symptoms can be prescribed based on the following reasons:

1. HDM is the most predominant airborne allergen in the Philippines.[26, 27]
2. There is a strong connection of house dust mite exposure and triggering of asthma symptoms.[27, 28]
3. HDM avoidance measures are relatively available in the Philippine setting.

Despite the lack of high-quality trials,[33] avoidance of documented airborne allergen triggers as an intervention is considered practical advice for allergic patients with asthma. These strategies are prescribed for allergy patients, and subsequently asthma patients, to reduce triggers of allergic symptoms, and decrease medication needs.[34]

Regular cleaning and tidying the allergic and asthmatic patient's home should be advised to families. This includes weekly cleaning to remove dust, the use of damp cloths for cleaning to prevent the disturbance of settled dust, weekly change of beddings and pillowcases, and making the patient's room simple through minimizing the use of curtains, rugs, carpets, books, wallpapers, and stuffed toys.

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## KEY QUESTION 8. WHAT ARE THE ESSENTIAL POINTS THAT PRIMARY CARE PROFESSIONALS SHOULD TEACH FAMILIES ON THE CARE OF THE CHILD WITH ASTHMA?

**Dr. Grace Malayan**

**Good Practice Statement 8.1**

Primary care health professionals should teach patients and families on the following points: (i) transitioning to self-management among adolescents, (ii) identification of asthma triggers, (iii) manifestations of acute exacerbations, (iv) initial home and school remedies for asthma, (v) when to go to a hospital, and (vi) effective use of asthma devices/gadgets to ensure adherence to medications.

Adapted from BTS 2019[1] and GINA 2021[2]

The guidance for this key question adapts recommendations on patient and family education from both GINA 2021 and BTS 2019. Modifications to suit local contexts were done by group discussions and consensus.

Asthma, just like other conditions, should be discussed thoroughly with the patient, families, immediate caregivers, and school medical personnel.

Being a chronic and recurring condition, psychosocial issues may arise during treatment which may affect the pediatric patient's adherence to therapy.[3] Specifically, the fear of being unable to fit in, arising from limitations in activity or adherence to the use of gadgets even in school, should be recognized and managed.

Patients should be equipped with all the needed information about their condition. Patients and their families must be taught the following: self-management of adolescents, triggers, identifying exacerbations, home and school remedies, when to go to the hospital, and proper use of gadgets and adherence to medications.

### Section 27. Transitioning to Self-Management of Adolescents[1]

All patients with asthma or suspected to have asthma must be educated with certain core asthma information, management, and skills for effective use of asthma medication. Asthma education significantly reduced hospitalization, emergency department visits, outpatient clinic visits, and oral steroid use in a Korean setting.[4]

Non-adherence can arise when adolescents want to be responsible for taking their medication, but forget or become embarrassed to take it in front of their peers.[5] Physician-patient collaboration reduced non-adherence to asthma treatment due to general and adolescent-specific factors, which is an approach done through open communication with the patients and their families.[5] For young children, their parents/caregivers will be the focus of asthma education. During the initial visit, verbal information should be supplemented with written and visual representation regarding asthma and its treatment.

Since asthma is a chronic condition, patients may experience medication fatigue that may affect the psychosocial aspects of their lives. Patients and their families are described to be intentionally non-adherent to asthma treatment, through purposeful decisions on their regimen's components, as a way to "balance the burden of disease with the burden of treatment."[6] It is the adolescent population that is most likely prone to experience the psychosocial problems, thus it is encouraged that they should be empowered. Adolescents with asthma, who soon transition to adult care, experience physical and psychosocial changes, and an increased risk for depression and anxiety which can lead to non-adherence.[7] Adolescents in Alabama had asthma knowledge and social support have positive relationships with asthma self-management behaviors.[8] The support coming from their families, friends and doctors should always be guaranteed to ease possible mental health issues.

Adolescents will be eventually endorsed to an adult physician in the future; hence their current pediatricians, family physicians or healthcare providers should orient and prepare them properly.[9] For a successful transition of care to occur, adolescents should be empowered to be responsible for their own asthma and overall health. Parents should also be encouraged and guided to slowly handover the responsibility of asthma management to their own child. The specific knowledge, attitudes and skills that underpin independent self-management practices in adolescents with asthma are that they can:

1. Name and explain their condition
2. List their medications, treatments or other management practices (e.g. special diets if applicable)
3. Explain why each medication or management practice is necessary
4. Remember to take their medications most of the time
5. Answer questions asked of them by doctors or other healthcare professionals
6. Ask queries to their doctors or other healthcare professionals
7. Arrange (and cancel) appointments
8. Remember to purchase medications before it runs out
9. Develop the desire for their healthcare to be independent of their parents or caregivers
10. Prioritize their health over (some) other desires.

**Section 27.1 Psychosocial issues of adolescents with asthma**

Both published literature and local observations report that adolescents may find the use of asthma gadgets embarrassing to use in front of their peers, frustration over limitations in normal activities which may be indicated, or due to overly protective parents and caregivers.[5] They may also be anxious over the fear of dying or bear guilty feelings over the burden of their illness on the family. They are concerned that their teachers and other people around them may not know what to do if they have a bad asthma attack. A qualitative study found that children in Sweden felt like outsiders of everyday life, with feelings of deprivation, guilt, loneliness, anxiety, and fear.[10] Adolescents find reassurance from support from friends, especially those who also have asthma.

Below are the valuable factors that adolescents feel when delivering education about self-management:

1. There is no one-size-fits-all for asthma education of adolescents; it must be adapted to meet the individual needs of the adolescent. Management of asthma should be repeated and developed as understanding and experience increases and should include emotional support for coping with feelings.
2. Asthma education should be delivered by people that respect, engage, encourage, and motivate adolescents.
3. Educational materials or references, both written and oral, should be personalized rather than general. Use non-medical language that adolescents can understand.
4. Asthma education should be delivered in an appropriate and uninterrupted setting; make appropriate use of information technology.

**Section 28. Triggers**

Healthcare providers should explain that an important part of prevention of asthma attacks is through identifying and preventing triggers. While coughing and wheezing may happen anytime, it is these triggers that can further increase the severity of the asthma attacks.

Encourage the child, adolescent, and/or parents and caregivers to document what they observe to trigger asthma attacks through keeping an asthma diary and writing on the asthma action plan (WAAP).

Common triggers include environmental conditions such as weather changes, cold air, rains or winds, upper respiratory tract infections, exercise or vigorous physical activity, irritants such as tobacco smoke or poor air quality, and known or suspected allergens.

An extensive list of asthma triggers is given in Key Questions 1, 2, 3.

**Section 29. Manifestations of asthma exacerbation**

The asthmatic child or adolescent, with their families and caregivers, should be taught the early signs and symptoms of an acute asthma exacerbation which should prompt them to initiate management based on their written asthma action plan and seek medical consultation.

Teach the families to watch out for:

1. Increase in wheeze and shortness of breath
2. Fast breathing, alar flaring, intercostal, subcostal, supraclavicular retractions
3. An increase in coughing, especially while the child is asleep
4. Decreased activity, diminished energy, or reduced exercise tolerance
5. Impairment of daily activities, including feeding; agitation or irritability
6. A poor response to reliever medication
7. Oxygen saturation < 94% if a pulse oximeter is available at home
8. Peak flow <80% if the family has been properly trained in using peak expiratory flow meter monitoring

**Section 30. Initial home or school remedies (adapted from GINA 2021[2])**

In the event a child has an asthma attack at home, in school, or within a community setting, initial management should be administered immediately.

1. The health professional may administer 1 nebule 2.5 mg SABA via a mouthpiece or face mask OR a parent or caregiver may initiate two puffs of inhaled SABA (100 mcg per puff) via spacer. This may be repeated up to two more times at 20 minutes intervals if warranted (after reviewing the response).
2. The initial dose of SABA may be given by a pMDI with a spacer and mask or mouthpiece or an air-driven nebulizer; or, if oxygen saturation is less than 94%, by an oxygen-driven nebulizer. For most children, pMDI plus spacer is favored as it is more efficient than a nebulizer for bronchodilator delivery, and nebulizers can spread infectious particles. The initial dose of SABA is two puffs of salbutamol (100 mcg per puff) or equivalent, except in acute, severe asthma when six puffs should be given. When a nebulizer is used, a dose of 2.5 mg salbutamol solution is recommended, and infection control procedures should be followed. The frequency of dosing depends on the response observed over 1–2 hours.
3. For children with moderate-severe exacerbations and a poor response to initial SABA, GINA 2021[2] recommends nebulized ipratropium bromide, or 1-2 puffs, may be added every 20 minutes for 1 hour only. However, currently we do not have plain ipratropium for children. What is locally available as of writing are: salbutamol 2.5 mg plus ipratropium bromide 500 mcg nebule or an MDI salbutamol 120 mcg plus ipratropium bromide 21 mcg.
4. The healthcare provider may also consider giving an initial dose of oral prednisolone (GINA 2021[2] p 167) with a dose of 1–2 mg/kg up to a maximum 20 mg for children <2 years old and max of 30 mg for children 2–5 years. For children 6-11 years old: prednisolone is 1-2 mg/kg/day, or maximum of 40 mg/day, to be given for 3-5 days.
5. Children and adolescents whose symptoms are not controlled by up to 10 puffs of salbutamol via a pMDI and spacer should seek urgent medical attention.
6. If symptoms are severe, additional doses of bronchodilator should be given as needed whilst awaiting medical attention.

Note: Infection control protocols include proper handwashing before and after using the nebulizer. The nebulizing kit should not be shared with other patients, even if they are members of the same family. For COVID suspects, patients should be nebulized by the caregiver in an exclusive room with proper ventilation. The caregiver should be wearing proper protective gear (i.e., face masks).

**Section 31. Criteria when to refer to hospital[2]**

Teach the families that during an acute asthma exacerbation (or 'attack'), the child should be closely monitored by the parent/caregiver/health professional thoroughly, and referral to a hospital should be done immediately if:

1. The child is in acute cardiorespiratory distress, with one or a combination of the following clinical manifestations:
    a. Difficulty of breathing
    b. Unable to speak or drink, especially for < 5 years old
    c. Respiratory rate > 40 cpm, or above normal for age
    d. 02 sat <92% on room air
    e. Silent chest on auscultation
    f. Cyanosis
2. The child does not improve on initial bronchodilator treatment, or there is lack of response after 6 puffs of inhaled SABA (2 puffs repeated 3 times) over 1-2 hours
3. Persisting tachypnea despite three administrations of inhaled SABA, even if the child shows other clinical signs of improvement
4. The period of relief after doses of SABA becomes progressively shorter.
5. A child younger than 1 year requires repeated inhaled SABA over several hours.
6. A social environment that limits delivery of acute treatment (no asthma medications or gadgets available), or parent/caregiver unable to manage acute asthma at home

Important:

- During transfer to hospital, continue to give inhaled SABA, oxygen (if available) to maintain saturation 94–98%, and give prednisolone 1-2 mg/kg/day. For more than 6 years old, instead of SABA, ICS-formoterol as-needed for relief of symptoms in mild asthma, or as part of maintenance and reliever regimen with low dose budesonide or beclomethasone with formoterol may be an option. The maximum recommended dose of ICS- formoterol in a single day is a total of 48 mcg formoterol for beclomethasone-formoterol (36 mcg delivered dose), and 72 mcg formoterol for budesonide-formoterol (54 mcg delivered dose)
- Parents and caregivers must know how to count the respiratory rate. They should also know the normal respiratory rates: <60 breaths/minute in children 0–2 months; <50 breaths/minute in children 2–12 months; <40 breaths/minute in children 1–5 years.

**Section 32. Effective use of gadgets and adherence to medications[2]**

Skills training on the use of gadgets is an essential component in self-management and empowering families in the care of the asthmatic child. One of the most common causes of poor asthma control is the wrong use of asthma gadgets, leading to poor adherence to medications. The healthcare provider should ensure that the patient and their families know the proper use of the gadgets to be used through demonstration and return demonstration. This should be done on prescription and repeatedly during patient encounters. Visual aids such as pictograms attached to inhalers, short yet standardized demonstration and back-demonstration sessions, and inhaler-specific checklists have been shown to be effective in improving gadget use.

GINA 2021 estimated that up to 70% to 80% of patients are unable to use their inhalers correctly and reported that many healthcare providers do not know how to use nor how to teach the use of inhalers.[2] There is no one perfect inhaler, thus the choice of the inhaler type will depend on several factors. When used properly, respiratory medications are delivered more effectively and more safely to the airways than systemic medications.

GINA provides the Choose-Check-Correct-Confirm strategies to ensure effective inhaler device use.[2]

**CHOOSE:**

- The most appropriate inhaler device considering the patient's or family's preference: availability, age, skills, cost
- The use of a spacer for pMDIs to improve delivery of the medication, and to decrease side effects such as mouth sores (i.e., due to ICS)
- A type of inhaler device that is easy to use, appropriate for age, and without physical/anatomical barriers
- To limit the use of different inhaler types to minimize confusion in the use of the gadgets

**CHECK:**

- The inhaler technique at every check-up/opportunity
- Whether the patient can use the gadget properly; ask patients to show you how they use their inhalers
- If there are any errors using device-specific checklists

**CORRECT:**

- Show the patient and the family how to use the device correctly with a physical demonstration.
- Only consider an alternative device if the patient cannot use the inhaler correctly after several repeats of training
- Re-check inhaler technique frequently. After initial training, errors often recur within 4-6 weeks.

**CONFIRM:**

- Healthcare providers must confirm that they are able to demonstrate the correct technique for each of the inhalers that they prescribe
- Healthcare providers include nurses and pharmacists. In the Philippine context, primary care healthcare workers should be trained in the proper use of asthma gadgets.

** See Appendix for different types of inhalers, pictograms and checklists, or refer to https://www.inhalers4u.org/ and information on https://ginasthma.org/

**Preventing poor medication adherence**

Identify whether the patient or the family encounter any of the following contributing factors to poor medication adherence:

- Medication factors: difficulties in using the inhaler, burdensome regimen, use of multiple different inhalers
- Unintentional factors: misunderstood instructions, missed doses, absence of a daily routine, cost
- Intentional factors: perception that the treatment is not necessary, denial or anger towards asthma or its treatment, inappropriate expectations, concerns with side effects, concerns on tolerance or addiction, stigmatization, cultural or religious issues, cost, or dissatisfaction with the doctor.

**How to identify poor adherence in clinical practice**

Check the patient's date of the last controller medication, and the date and dose counter on the inhaler. If adherence may be an issue, encourage open dialogue with the patient and the family with a non-judgmental stance. Acknowledge that incomplete adherence is an issue.

Probe the family in a neutral manner with questions such as:

"Nahihirapan ka bang gamitin ang inhaler mo?
Gusto ko kayo/kita matulungan, para di ka atakihin ng hika mo. Maaari mong sabihin sa akin kung nais mong palitan ang gamot o inhaler mo."

**Section 33. Successful adherence interventions**

GINA 2021 cited studies of interventions that have increased adherence. These interventions included shared decision making on the choice of the medication and dosing, use of inhaler reminders, prescribing low-dose ICS once-daily instead of twice-daily, and home visits by a designated asthma nurse for a comprehensive asthma program.[2]

A systematic review showed that motivational interviewing may improve adherence to asthma medications.[11] Instead of traditional behavioral interventions which can come off as aggressive and confrontational, consider using motivational interviewing, which is a communication style that is collaborative and goal-centered. Motivational interviewing strengthens your patients' and their families' personal motivations to commit to a goal, by using their reasons for change within an accepting and compassionate therapeutic atmosphere.



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# CHAPTER 5. RISK EVALUATION

## KEY QUESTION 9. WHAT ARE THE PREVENTIVE AND TREATMENT MEASURES RECOMMENDED FOR PEDIATRIC ASTHMA PATIENTS INVOLVED IN SPORTS, AND IN SURGERY?

**Dr. Charito delos Santos**

### Section 34. Exercise-induced bronchoconstriction

Engaging in play is important for a child's normal social and physical development. However, children and adolescents with poorly controlled asthma often avoid strenuous activities or exercise to prevent exercise-induced bronchoconstriction. Physical activity triggers asthma symptoms in both young children and adolescents, characterized as worsening of symptoms and bronchoconstriction after cessation of exercise.

However, only a minority of adolescents referred for assessment of exercise-induced respiratory symptoms show objective evidence of exercise-induced bronchospasm. It is also important to consider that the symptoms of shortness of breath and wheezing on exercise may also be due to other conditions which include normal physiological exercise limitation due to obesity, poor physical fitness, vocal cord dysfunction, dysfunctional breathing, habit cough, and supraventricular tachycardia.

To prevent exercise-induced bronchoconstriction, the following are recommended:

**Recommendation 9a**

9a.1 Appropriate training and sufficient warm-up prior to vigorous physical activity for all children and adolescents is recommended to reduce the incidence and severity of exercise-induced bronchoconstriction.

Strong evidence-based recommendation adopted from GINA 2021[1]
High certainty of evidence

Stickland et al in 2012 pooled seven randomized controlled trials comparing maximum percent decrease in FEV1 and peak expiratory flow between warm-up versus no warm-up groups.[2] The participants benefited from warm-up across all forms, whether it was high intensity or variable intensity.[2] The authors concluded that an appropriate warm-up strategy is a short-term non-pharmacological approach to prevent EIB.[2]

9a.2. Regular controller treatment with inhaled corticosteroids is recommended for asthmatic children and adolescents because it confers protection against exercise-induced bronchoconstriction, in accordance with other recommendations of this guideline (see KQ 4).

Strong evidence-based recommendation adopted from GINA 2021[1]
High certainty of evidence

A Cochrane review by Koh et al (2007) pooled results from eight randomized controlled trials involving 162 participants (two trials involving adults and six involving children).[3] Combining results from the three parallel studies with at least 4 weeks duration of inhaled corticosteroids versus placebo, the use of inhaled corticosteroids significantly attenuated the percent fall index in forced expiratory volume in 1 second (WMD (fixed): 11.74%; 95% CI.: 10.06% to 13.42%).[3] The result from one crossover study with duration of inhaled corticosteroids of 4 weeks revealed significant attenuation of percent fall in forced expiratory volume in 1 second ( WMD 11.70%; 95% CI.: 7.51% to 15.90%) and the percent fall in peak expiratory flow ( WMD 11.50%; 95% CI.: 6.31% to 16.69%). As such, the authors concluded that inhaled corticosteroids compared to placebo used for 4 weeks or more before exercise testing significantly reduced exercise-induced bronchoconstriction.[3>]

The consensus panel for this Philippine guideline raised concerns on the effect of chronic use of inhaled corticosteroids. Zhang conducted a systematic review to assess the impact of inhaled corticosteroids on growth in children, yielding 37 studies for inclusion.[4] Of these 37 studies, 21 showed that having severe or uncontrolled asthma per se can also impair a child's growth and development.[4] In one of the trials with 23 participants included in the systematic review and meta-analysis done by Axelsson et al in 2019, they reported that compared to fluticasone + beclomethasone, fluticasone given alone at an equivalent dose was associated with significant greater linear growth velocity [MD 0.81 cm /year, 95% CI 0.46-1.16]. Two studies that they also analyzed for this review, with 359 subjects, reported that fluticasone, when compared to budesonide at an equivalent dose, have less suppressive effect on growth when measured by change in height on a 5 to 12 months period [MD 0.97cm, 95%CI 0.62-1.32]. But, no significant difference in terms of linear growth velocity was noted between fluticasone and budesonide, given at equal doses [MD 0.39 cm/year, 95% CI 0.94-1.73].[5] Randomized controlled trials showed a small mean reduction in linear growth (−0.91 cm/year for beclomethasone, −0.59 cm/year for budesonide, and −0.39 cm/year for fluticasone) in the first year of treatment with inhaled corticosteroids in prepubertal children with persistent asthma, and were "likely to be molecule- and dose-dependent."[4] In both reviews, the authors concluded that the benefits of controlling asthma far outweigh the risk of a relatively small suppression in growth.

9a.3 Prior to exercise, the asthmatic child or adolescent should take SABA or LABA. However, patients with mild asthma who are already on ICS-formoterol can use the same medication and do not need to be prescribed with an additional SABA pre-exercise.

Evidence-based recommendation adopted from GINA 2021[1]
Conditional recommendation, moderate certainty

The quick onset of action of SABAs and LABAs make them commonly used medications before exercise, with several studies showing their effectiveness.[6] This is a conditional recommendation because tolerance to the protective effect of SABAs and LABAs against EIB will develop among those who regularly uses these drugs more than once daily leading to underuse of inhaled corticosteroids for EIB.[3, 7]

Stakeholders asked about the specific time for pre-exercise SABA or LABA. GINA 2021 does not specify the time per se. This will depend on the specific SABA or LABA's onset of action and duration of action.

9a.4 When breakthrough exercise-induced bronchoconstriction occurs, the physician must review control of symptoms (KQ 5), consider stepping up controller use (KQ4), review and teach inhaler technique and adherence (KQ 4, KQ 8). Acute exacerbations will follow the recommendations given in KQ 3.

Strong evidence-based recommendation, adapted from GINA 2021.[1]
Certainty of evidence is specified in the various key questions' recommendations.

**Section 35. Recommendations for athletes with asthma[1]**

Athletes, particularly those competing at a high level, have a higher prevalence of asthma, EIB, allergic or non-allergic rhinitis, chronic cough, inducible laryngeal obstruction, and recurrent respiratory infections compared to non-athletes. In elite athletes, asthma is commonly characterized by less correlation between symptoms and pulmonary function; higher lung volumes and expiratory flows; less eosinophilic airway inflammation; more difficulty in controlling symptoms; and some improvement in airway dysfunction after cessation of training. We hereby present recommendations for athletes with asthma:

**Recommendation 9b**

9b.1 Athletic children and adolescents with asthma should, as much as possible, avoid training in environments with extreme cold or extreme heat, or with air pollutants and allergens.

Strong consensus-based recommendation adopted from GINA 2021[1]

9b.2 Athletic children and adolescents with asthma should be maintained on adequate anti-inflammatory controller therapy like ICS to reduce overreliance on beta-2 agonists (SABA) to avoid the development of tolerance. The same treatment steps and principles provided in KQ 3 and KQ 4 apply to athletes.

Strong evidence-based recommendation adopted from GINA 2021.[1]
Certainty of evidence is provided in KQ 3 and KQ 4.

**Section 36. Children and adolescents with asthma undergoing surgery**

In Key Question 5, it was emphasized that asthma control in children and adolescents involves two domains: (1) symptom control and (2) future risk of adverse outcomes or exacerbations.[1] Asthma, characterized by chronic airway inflammatory condition associated with hyperresponsiveness and variable expiratory airflow limitation,[1,8] renders a patient at risk for difficult airway access during surgery. Uncontrolled asthma is considered a risk factor for asthma-related death and increases the risk for future exacerbations.

As such, asthma without exacerbation is classified as American Society of Anesthesiology or ASA II (mild systemic disease) while asthma with exacerbation is classified as ASA III (severe systemic disease) in the 2020 ASA Physical Status perioperative risk stratification tool.[9] The ASA-PS for pediatric use has been shown to have moderate interrater reliability overall.[10] The ASA-PS classification was also adopted in the PAPP Position Statement on Preoperative Evaluation.

We present a set of guidelines for children and adolescents with asthma undergoing surgery, adopted from GINA 2021[1] and the PAPP Position Statement Preoperative Evaluation 2021:[11]

**Recommendation 9c**

9c.1 For elective surgeries, good asthma control should be achieved before the surgery. This especially applies for patients with severe asthma, uncontrolled symptoms, recent exacerbations, or persistent airflow limitations. The same recommendations given in KQ 3 for acute exacerbations and KQ 4 for long-term management apply to pediatric patients preparing for surgery.

Strong evidence-based recommendation, adopted from GINA 2021.[1]
Certainty of evidence for treatment recommendations are given in KQ3 and KQ4.

9c.2 Elective surgeries may be performed 4 to 6 weeks after the last asthma exacerbation, in accordance with Recommendation 9c.1 and the PAPP Position Statement on Preoperative Evaluation (as of June 2021)[11]

Conditional consensus-based recommendation adopted from the PAPP Position Statement

9c.3 For emergency surgeries, the risks of proceeding without first achieving good asthma control should be weighed against the need for immediate surgery.

Conditional consensus-based recommendation adopted from GINA 2021[1]

9c.4 Regular controller therapy should be maintained throughout the perioperative period. The same treatment recommendations from KQ 4 apply.

Strong evidence-based recommendation adopted from GINA 2021[1]
Certainty of evidence is based on KQ4

9c.5 Patients taking long-term high dose ICS or who have received OCS for more than 2 weeks during the previous 6 months should receive hydrocortisone perioperatively as they are at risk of adrenal crisis in the context of surgery.

This is a strong consensus-based recommendation adopted from PAPP statement; corroborated by expert opinion, non-systematic reviews, and GINA.[12, 13, 14]

9c.6 In accordance with the PAPP Position Statement on Preoperative Evaluation (as of June 2021), we suggest the following risk reduction strategies for pediatric patients with asthma undergoing surgery:[11]

9c.6.1 For well controlled asthma, use of inhaled beta-2 agonist (SABA) 1-2 hours before surgery.

9c.6.2 For partly controlled asthma, use inhaled corticosteroids with inhaled beta-2 agonist (LABA or SABA) one week before surgery, and inhaled SABA 1-2 hours before surgery

9c.6.3 For poorly controlled asthma, use of systemic corticosteroids for 3 to 5 days prior to surgery, and inhaled beta-2 agonist (SABA) 1-2 hours before surgery.

Consensus-based recommendations adopted from the PAPP statement
Conditional recommendation

Important:
This is considered a conditional recommendation because preoperative risk reduction strategies should be individualized according to the previous maintenance medications, and aligned with the recommendations given in KQ4.

In general, (i) step up current maintenance medications for partly controlled or uncontrolled asthma, and (ii) do not step down medications even if the asthma is controlled.

Recall that GINA 2021 veers away from frequent SABA use and emphasizes inhaled corticosteroids as the primary maintenance medication in long term asthma maintenance.

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# APPENDIX I.

## Appendix 1A. Symptom based written asthma action plan (Tagalog version)

**This is a proposed Filipino version of the WAAP. It is only a sample WAAP and we encourage readers to culturally adapt it to your own setting and dialect. Research and publication on the local validation and implementation of WAAP will be welcome for the succeeding update of this guideline.**

**AKSYON PARA SA HIKA**

**Pangalan _____**

**Telepono _____**

**Petsa ng Pinakabagong Aksyon Para sa Hika: Buwan_____/Araw_____/Taon_____**

**Dalhin ang kopyang ito tuwing pagbisita/ konsulta sa iyong doktor/nars.**

| | IYONG DOKTOR | SA BIGLANG PANGANGAILANGAN, MAARING TUMAWAG SA: | TAONG MAAARING TAWAGAN SA PANAHON NG BIGLAANG PANGANGAILANGAN |
|---|---|---|---|
| PANGALAN | | | |
| TELEPONO | | | |

**BERDENG SONA (Tuloy): Hika ay kontrolado.**

| | |
|---|---|
| ○ Hindi nagigising sa gabi dahil sa ubo/hika<br>○ Nagagawa ang karaniwang aktibidad/kilos<br>○ Walang sintomas ng atake/pagsiklab ng hika<br>○ Maayos at regular sa paggamit ng mga gamot sa hika | ● Bilang ng komportableng paghinga (*Resting RR; Normal for age)*<br>1-12 buwan = ≤ 50 kada minuto<br>1- 5 taong gulang = ≤ 40 kada minuto<br>6-10 taong gulang = ≤ 30 kada minuto<br>11-18 taong gulang = ≤20 kada minuto<br>● Kung mayroon nito: *Peak flow* sa pagitan ng ____ at ____L/minuto |

**AKSYON**

- **Ipagpatuloy ang pang araw-araw na mga gamot sa hika at subaybayan ang mga sintomas.**

  **1. _____ 2. _____ 3. _____**

- **Bumalik sa iyong doktor sa takdang petsa.**

**DILAW NA SONA (Mag-ingat): Atake ay Banayad – Katamtaman *(Mild-Moderate)*. Hika ay lumalala.**

| | |
|---|---|
| ○ Nagigising sa gabi dahil sa ubo/hika<br>○ Hindi nagagawa ang karaniwang aktibidad/ kilos<br>○ Tumitindi ang sintomas ng hika (paninikip ng dibdib, kakulangan sa paghinga, pag uubo, may paghuni sa paghinga *(audible wheeze)*<br>○ Kinailangan ng gamot na "reliever" ng mas madalas kaysa karaniwan | ● Bilang ng Komportableng Paghinga (*Resting RR*): ____ hinga kada minuto<br>*(depende sa edad ng pasyente, hinggil sa doktor)<br><br>● Kung mayroon nito: *Peak flow* sa pagitan ng ____ at ____L/minuto |

**AKSYON**

- **Ipagpatuloy ang pang araw-araw na mga gamot sa hika at subaybayan ang mga sintomas. IDAGDAG ANG GAMOT NA PANGSAGIP (*RESCUE MEDICATIONS).***

- **GAMOT NA PANGSAGIP (instruksyon/direksyon)**

**Hakbang 1:**

- **_____ higop *(puffs)* ng SABA MDI *(+/- spacer)* kung kinakailangan.**
- **0 pausok ng SABA (kung mayroong nebulizer), 1 nebula ng SABA gamit ang *face mask/ mouthpiece*.**
- **0 para sa 12 taong gulang at mahigit: dagdagan ang dosis ng ICS/formoterol (pinakamataas: 72mcg formoterol sa loob ng isang araw)**

**Hakbang 2: Bilangin ang bilis ng paghinga habang kalmado ang bata makalipas ang 10 minuto matapos bigyan ng gamot na pangsagip.**

**Hakbang 3: Ulitin ang SABA kung kinakailangan na may pagitan na 20 minuto. Maaaring ulitin hanggang 3 beses. Suriin ang epekto at sundin ang mga sumusunod na instruksyon na nakasulat sa ibaba.**

- **Ipagbigay alam sa iyong doktor para sa karagdagang instruksyon.**

| | |
|---|---|
| **EPEKTO AY MAAYOS (Good Response) kung:**<br><br>**Bilang ng paghinga habang kalmado ang bata (*Resting RR*): ≤ ___ hinga kada minuto**<br><br>**Lumuwag ang paghinga**<br><br>**Ang epekto ng SABA ay tumagal ng hindi bababa sa 4 na oras (walang pakiramdam na kinakailangang dagdagan ang higop (o puff) o pausok dahil sa hirap sa paghinga** | **Ipagpatuloy:**<br><br>**1. Pausok ng SABA o higop ng MDI *(puffs)* sa pamamagitan ng *spacer* ___ higop kada 4 na oras sa loob ng _____ araw.**<br><br>**2. Para sa 12 taong gulang at mahigit: Dagdagan ang dosis ng ICS/formoterol (pinakamataas: 72mcg formoterol sa loob ng isang araw)**<br><br>**3. Kung may gamot na pang araw-araw (*maintenance medication)*, dagdagan ang ICS ng _____ higop *(puffs)* beses kada araw sa loob ng ___ araw.** |
| **EPEKTO AY HINDI MAAYOS (Poor Response) kung:**<br><br>**Bilang ng paghinga (*Resting RR)*:**<br>**> _____ hinga kada minuto**<br>**Matinding sintomas ng hika sa kabila ng paggamit ng gamot na pangsagip** | **Basahin ang Pulang Sona para sa patuloy na gamutan.** |

**PULANG SONA (Mapanganib): Matinding Atake ng Hika. Sintomas ng hika ay matindi.**

| | |
|---|---|
| ○ Malimit ang gising sa gabi dahil sa ubo/hika<br>○ Matinding limitasyon ng karaniwang aktibidad/ kilos<br>○ Matinding kakulangan sa paghinga<br>○ Dama ang sintomas ng higit sa 24 oras<br>○ Kinailangan ng gamot na "reliever" nang mas malimit kaysa kada 3-4 oras | ● Bilang ng komportableng paghinga (*Resting RR*): ____ hinga kada minuto<br>* (depende sa edad ng pasyente, hinggil sa doktor)<br><br>● Hindi bumuti ang sintomas mula sa DILAW NA SONA. |

**AKSYON**

- **Ipagpatuloy ang pang araw-araw na mga gamot sa hika at subaybayan IDAGDAG ANG GAMOT NA PANGSAGIP *(RESCUE MEDICATIONS).***

- **GAMOT NA PANGSAGIP (Instruksyon)**

**Hakbang 1:**
- **_____ bilang ng higop *(puffs)* SABA MDI (+/- spacer) kada oras.**
- **0 pausok ng SABA (kung mayroong nebulizer), 1 nebula ng SABA gamit ang *face mask/ mouthpiece*.**
- **0 para sa 12 taong gulang at mahigit: Dagdagan ang dosis ng ICS/formoterol (pinakamataas: 72mcg formoterol sa loob ng isang araw)**

**Hakbang 2: Bilangin ang bilis ng paghinga habang kalmado ang bata makalipas ang 5 - 10 minuto matapos bigyan ng gamot na pangsagip.**

**Hakbang 3: Ulitin ang SABA kung kinakailangan, na may pagitan na 20 minuto. Maaaring ulitin hanggang 3 beses.**

**Hakbang 4: Simulan ang Prednisone/ Prednisolone (__mg/ml); magbigay ng ___ml**

- **Suriin ang epekto at sundin ang mga sumusunod na instruksyon:**

| EPEKTO HINDI MAAYOS (Poor Response) kung: | Ipagpatuloy: |
|---|---|
| Bilang ng komportableng paghinga (*Resting RR*): > ___ hinga kada minuto | 1. Pausok ng SABA o MDI ___ bilang ng higop *(puffs)* kada 20 minuto kada _____ oras |
| Matinding sintomas ng hika sa kabila ng gamot na pangsagip. | 2. Para sa 12 taong gulang at mahigit: Dagdagan ang dosis ng ICS/formoterol bilang gamot na pangsagip (pinakamataas: 72mcg formoterol). |

**KAAGAD tawagan ang iyong Doktor/ *Emergency Room*. Kung walang matawagan, dalhin agad ang pasyente sa pinakamalapit na ospital.**

**Matapos ang sariling pag-gamot ng atake ng hika, pinapayuhang ipagpaalam ito sa inyong doktor. Bumalik sa inyong doktor sa loob ng isang linggo para sa pagsusuri ng kontrol ng sintomas, pagtuklas ng sanhi ng atake, at pagbabago ng AKSYON PARA SA HIKA. Subalit, kung nananatiling may sintomas ng atake ng hika o pagtindi nito, tumawag at makipagkita kaagad sa inyong doktor.**

## Appendix 1B. Dosages of inhaled corticosteroids per age group

**Children below 6 years**
Before stepping up, review inhaler technique and adherence, treat modifiable risk factors and check for alternative diagnosis.

| Inhaled Corticosteroid | Low total daily dose (mcg) |
|---|---|
| BDP (pMDI standard particle) | 100 (ages 5 years and older) |
| BDP (pMDI extrafine particle) | 50 (ages 5 years and older) |
| Budesonide nebulized | 500 (ages 1 year and older) |
| Fluticasone propionate (pMDI, standard) | 50 (ages 4 years and older) |
| Mometasone furoate (pMDI, standard) | 100 (ages 5 years and older |
| Fluticasone furoate (DPI) | Not sufficiently studied in children 5 years and younger |

**Children 6 -11 years old**

- Before stepping up, review inhaler technique and adherence, treat modifiable risk factors and check for alternative diagnosis.
- Total daily ICS dose (mcg)

| | LOW DOSE | MEDIUM DOSE | HIGH DOSE |
|---|---|---|---|
| Beclometasone dipropionate (pMDI, standard particle) | 100 - 200 | >200 - 400 | > 400 |
| Beclometasone dipropionate (pMDI, extrafine) | 50 - 100 | >100 - 200 | > 200 |
| Budesonide DPI | 100 – 200 | > 200 - 400 | > 400 |
| Budesonide (nebules) | 250 – 500 | >500 - 1000 | > 1000 |
| Fluticasone furoate DPI | 50 | | n.a. |
| Fluticasone propionate DPI | 50 - 100 | > 100 – 200 | > 200 |
| Fluticasone propionate (pMDI, standard particle) | 50 - 100 | > 100 – 200 | > 200 |
| Mometasone furoate (pMDI, standard particle) | 100 | | 200 |

**Adults and adolescents (12 years and older)**

- Before stepping up, review inhaler technique and adherence, treat modifiable risk factors and check for alternative diagnosis.
- Total daily ICS dose (mcg)

| | LOW DOSE | MEDIUM DOSE | HIGH DOSE |
|---|---|---|---|
| Beclometasone dipropionate (pMDI, standard particle) | 200 - 500 | >500 - 1000 | > 1000 |
| Beclometasone dipropionate (pMDI, extrafine) | 100 - 200 | >200 - 400 | > 400 |
| Budesonide DPI or pMDI | 200 – 400 | > 400 - 800 | > 800 |
| Fluticasone furoate DPI | 250 – 500 | >500 - 1000 | > 1000 |
| Fluticasone propionate (DPI) | 100 | | 200 |
| Fluticasone propionate (pMDI, standard particle) | 100 - 250 | > 250 - 500 | > 500 |
| Mometasone furoate (DPI) | 100 - 250 | > 250 - 500 | > 500 |
| Mometasone furoate (pMDI, standard particle) | 200 - 400 | | > 400 |

## Appendix 1C. Basic parameters and reference values for pulmonary function tests

Specific tests and basic parameters that are measured and reported:

1. Spirometry
    a. $FEV_1$/FVC
    b. $FEV_1$
    c. FVC
    d. $FEF_{25-75\%}$
2. Spirometry with bronchodilator challenge test
    a. $FEV_1$ and percent change pre - and post bronchodilator
    b. FVC and percent change pre - and post - bronchodilator
    c. $FEF_{25-75\%}$ and percent change pre- and post - bronchodilator
3. Spirometry with exercise challenge test
    a. $FEV_1$ and percent change pre - and post – bronchodilator

- Additional parameters that may be measured and reported: $FEF_{25\%}$, $FEF_{75\%}$, MVV

BASIS FOR REFERENCE VALUES:

This CPG was published ahead of the updated PAPP PFT Proceedings 2021. This updated proceedings is scheduled to be released in mid-2022. The Asthma Committee received approval from the PFT Task Force to provide this short summary.

Pulmonary Function differs with age, standing height, sex, and ethnicity. The Global Lung Initiative (GLI) 2012 Task Force was formed with the European Respiratory Society, ERS sponsorship and in cooperation with the ATS PFT Committee to merge all the available data and develop reference equations that may be applicable worldwide.

The GLI 2012 was able to establish reference values for four groups: whites, African Americans, North East Asians, and South East Asians.[1]

| | **NORMAL** |
|---|---|
| **FEV1/FVC** | ≥80% of predicted |
| **FVC** | ≥80% of predicted |
| **FEV1** | ≥80% of predicted |
| **FEF 25-75%** | ≥65% of predicted (optional parameter) |

We adapted from the 2014 First PAPP Proceedings on Pediatric Pulmonary Function Testing the use of 80 percent predicted as the cut-off point between abnormal and normal values for FEV1/FVC, FVC, and FEV1.

With the 2021 edition of the PAPP Proceedings, for the $FEF_{25-75\%}$, the value of <65% of predicted may be considered abnormal.[2] Simon et.al. in 2010 validated this proposed cut off with their additional findings that $FEF_{25-75\%}$ at 65% of predicted value had a 90% sensitivity and a 67% specificity for detecting a 20% increase in $FEV_1$ after albuterol inhalation.[3]

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## Appendix 1D. Bronchoprovocation Testing

Bronchoprovocation tests are examinations performed to assess the susceptibility of an individual to develop airflow obstruction when airways are challenged with stimuli: direct by using methacholine , or indirectly via physical exertion or pharmacological agents.[1] These stimuli, when applied, trigger decrease in airway caliber due to the activation of inflammatory or neuronal cells present in the respiratory system.[1,2] In the case of a direct stimulation such as the methacholine test, the agent act directly on the airway smooth muscle receptors.[3] This airway hyperresponsiveness or AHR is important in the detection of presence of asthma and in the evaluation of the patient's response to treatment. According to Liem et al in 2008, BPT, usually equated to the methacholine test, was quite safe for children.[2]

Indications:

BPT are usually performed among patients who underwent spirometry to confirm clinical diagnosis of asthma, as evidence by history, presence of wheezing when in exacerbation and with appropriate response to therapy, but the test results were inconclusive especially if patients have normal or near normal lung function values.[4] It can be also be utilized to screen individuals with atypical results after spirometry or response to therapy.[4]

Contraindications:

BPT is contraindicated to the following patients:[4]

1. Low FEV1 – FEV1 <60% predicted, FEV1 <75% if one is to perform indirect test using exercise as stimulus
2. Spirometry quality – quality of BPT results is highly dependent on the ability of the patient to perform acceptable maneuvers used in spirometry
3. With cardiovascular problems
4. Underwent recent eye surgery – BPT can increase intraocular pressure
5. Current use of cholinesterase inhibitor medications – relative contraindication

Patient preparation: *(Adopted from: Coates AL, Wanger J, Cockcroft DW, Culver BH, Carlsen KH, Diamant Z, et al. ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests. Eur Respir j. 2017 May 1; 49(5):1601526. DOI: 10.1183/13993003.01526-2016.)*

1. Give the parents/guardians a list of medications to avoid prior to testing upon scheduling of the test. Advise them to better consult with an attending pediatrician if any of the child's medication is listed. May continue other medications other than bronchodilators if the purpose of the test is to monitor the child's response to his present asthma therapy. Influenza vaccination does not significantly affect airway responsiveness. Antihistamines have no effect on methacholine response.
2. Administer the pre-test evaluation to the parent or guardian to be filled up on behalf of the child to be tested. The pre-test will screen for (a) presence of contraindications, (b) conditions or exposures which could temporarily increase airway hyperresponsiveness that might lead to false -positive result, (c) presence of medications that may alter the airway response.
3. Explain the test to the patient and his parents/guardian including the symptoms that they might experience during the test such as coughing or chest tightness.
4. Ask the patient if they could urinate first before starting the test since forced expiration can precipitate stress incontinence.
5. Obtain informed consent.
6. Perform a pre-test examination of the chest and lungs.
7. During the test, explain each step clearly so that the patient can perform reliable spirometry maneuvers necessary for the test.
8. Make the patient seat comfortably during the duration of the test on a stable chair with elbows elbow rest and no wheels.

Procedure: *(Adopted from: Coates AL, Wanger J, Cockcroft DW, Culver BH, Carlsen KH, Diamant Z, et al. ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests. Eur Respir j. 2017 May 1; 49(5):1601526. DOI: 10.1183/13993003.01526-2016.)*

1. Prepare the pre-determined methacholine concentrations in sterile vials. Keep refrigerated until the test is performed. Make sure that the spirometer is working properly and calibrated.
2. Remove the prepared vials from the refrigerator 30 minutes before the actual test. Instill appropriate volume of diluent into the nebulizer.
3. Check if the patient is in the correct position before administering the test. Perform baseline spirometry to check if the patient can correctly perform the maneuvers. This can also help you determine and confirm if the patient is fit to do the test.
4. Start aerosolizing the diluent using the pre-calibrated nebulizer that will be used for the methacholine challenge proper. This step is necessary especially if this is the initial BPT testing of the patient. This will also ensure that there is no excessive AHR. Apply the nose clip and ask the patient to relax and breathe quietly for an appropriate time for a specific nebulizer. The nebulizer can be held by the patient or placed on a holder stand.
5. Observe the patient to make sure that he is breathing comfortably and not tipping the nebulizer. After nebulization with the diluent, turn off the flowmeter and remove the apparatus.
6. Perform post-diluent spirometry at 30 and 90 s after the completion of nebulization. Acceptable quality FEV1 and FVC must be obtained. This may need repeated attempts. Calculate target FEV1 that indicates 20% decrease in FEV1 using the post diluent data.
    - Target FEV1 = baseline FEV1 x 0.8
    - Diluent nebulization should not cause significant change from pre-challenge testing spirometry.
        i. + <10% increase or decrease in FEV1: proceed with first dose of methacholine following steps 4 and 5 of diluent nebulization.
        ii. + 10-20% increase or decrease in FEV1: repeat step 4
        iii. Change in FEV1 is too significant: the patient is unstable to proceed with the challenge and the test must be rescheduled. If $\geq$ 20% decrease in FEV1 after diluent nebulization, the challenge should be canceled.
7. After repeating step 4 and 5 for methacholine, perform post-methacholine spirometry at 30 and 90s after nebulization completion. Obtain acceptable FEV1 at each timepoint. Perform a maximum of 4 maneuvers, maximum of 3 min each, after each dose. To attain a constant cumulative effect of methacholine, the interval between initiation of two serial concentrations should be kept consistent at 5 min.
8. Report the highest FEV1 from acceptable maneuvers after each dose.
    - If FEV1 <20% from post diluent FEV1: empty nebulizer then add appropriate volume of the next highest concentration and repeat step 7
    - If FEV1 >20% from the post diluent FEV1 or after highest dose step given:
        i. Halt giving methacholine
        ii. Note of signs and symptoms
        iii. Administer rapid acting inhaled bronchodilator
        iv. Wait for 5-10 min then repeat spirometry
        * suspected of vocal cord dysfunction as evident in the symptoms of patient, perform full inspiratory and expiratory flow-volume loops prior to giving the bronchodilator

Result reporting:[3]

- Methacholine doses expressed as PD20
- PD20: the dose of methacholine causes 20% fall in the FEV1. Calculated as same as PC20 (for formula, please see Appendix E supplementary material of:
- If FEV1:
    - Does not fall by at least 20% following the highest dose, report PD20 as greater than the final dose given.
    - Does fall by >20% following inhalation by diluent, do not report PD20. Just state that "there is a significant decrease in lung function following inhalation of the diluent with methacholine not given".

**Interpretation:**

| **Categories of response to direct BPT** | | |
|---|---|---|
| PD20 umol(ug) | PC20 $mg.ml^{-1}$ | **Interpretation** |
| >2(>400) | >16 | **Normal** |
| 0.5-2.0 (100-400) | 4-16 | **Borderline AHR** |
| 0.13-0.5 (25-100) | 1-4 | **Mild AHR** |
| 0.03-0.13 (6-25) | 0.25-1 | **Moderate AHR** |
| <0.03 (<6) | <0.25 | **Marked AHR** |
| [+]PD20: provocative dose causing a 20% fall in FEV1; PC20: provocative concentration causing 20% fall inFEV1; AHR: airway hyperresponsiveness | | |

Adapted from: Coates AL, Wanger J, Cockcroft DW, Culver BH, Carlsen KH, Diamant Z, et al. ERS technical standard on bronchial challenge testing: general considerations and performance of methacholine challenge tests. Eur Respir j. 2017 May 1; 49(5):1601526. DOI: 10.1183/13993003.01526-2016.

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## Appendix 1E. Volcanic Eruptions (abridged from PAPP advisory on respiratory health effects of volcanic eruption)

Volcanic eruptions pose respiratory health threats resulting from ash falls, pyroclastic flows, volcanic gasses and volatile substances. Ash fall can affect the greatest number of people because of wide areas that can be covered by a fall out and its tendency to be remobilized by wind or human activities; hence, the health risk from exposure is not limited to the time frame of eruption but may continue long after volcanic activity has ceased.

Signs and symptoms include the following:

- Nose and throat discomfort
- Cough, sputum production
- Exacerbations of pre-existing lung diseases like asthma and chronic lung disease - Airway irritation, chest tightness, wheezing

Recommendations:

- Stay indoors as much as possible. Keep windows and doors closed.
- Turn off all fans and air conditioning systems.
- Eliminate other sources of indoor pollution like tobacco smoke, mold, and dust.
- Children should be advised against strenuous activities when ash is in the air since exertion leads to heavier breathing drawing small particles more deeply into the lungs. They should be prevented from playing in areas where ash is deep on the ground or piled up.
- Adhere to personalized asthma treatment plan – compliance with maintenance medications and availability of rescue medication.
- If symptoms are persistent, seek medical attention.
- Use respiratory protection materials (i.e., well-fitting, industry certified face masks when available; or simple healthcare masks and cloth materials) outdoors during ashfall or afterwards.
- Masks should not be put on for children under two years old as they will not fit properly and will interfere with breathing.
- Listen for emergency information and alerts.

## Appendix 1F. Asthma and the COVID-19 Pandemic

### Section 1. Asthma Management during the COVID-19 pandemic

**Adapted from the PAPP Interim Guidelines on Pulmonary Care in Pediatric COVID-19 as of May 8, 2021**

Patients with asthma have not been shown to have increased risk of COVID-19 infection and death. However, an increased risk of COVID-19 death was found to be associated with those recently given oral corticosteroids for acute attacks. Therefore, it is crucial to continue good asthma management with strategies to maintain good symptom control and reduce risk of severe exacerbations as well as minimize the need for oral corticosteroids.

1. Patients on controller medications are advised to continue treatment as prescribed.
2. Regular follow up and monitoring of asthma symptom control is important to identify patients that may require adjustment of medications.
3. An asthma action plan will guide patients and their family to recognize worsening asthma, how to increase their controller and reliever medications and when to seek medical help.
4. Use of nebulizers is discouraged and mainly restricted to management of (a) severe life threatening respiratory distress (b) patients with compromised ventilation (c) uncooperative patients and (d) history of poor response to pMDI. In these situations, nebulization should be done under strict infection control measures.
5. A pressurized metered dose inhaler (MDI) and spacer, with a mouthpiece or tightly fitting face mask, may be used to deliver short acting beta2 agonist or ICS.
6. Single patient device use must be observed at all times.
7. Routine spirometry testing is not advisable to decrease the risk of viral transmission. However, if urgently needed for clinical management, strict infection control and airborne precautions must be instituted.

### Section 2. Asthma and vaccines during the COVID-19 pandemic

Annual influenza vaccination is recommended for asthmatic patients, more so during this pandemic. The COVID-19 vaccination for children is also now available and recommended by the Department of Health and the Philippine Pediatric Society following guidelines from the WHO, with those who are 12 years and older receiving the FDA-approved COVID-19 mRNA vaccine at a 2-dose primary series same as in adults at 28 days apart.

Likewise, among asthmatic patients, COVID-19 vaccines are recommended to be given as the benefits outweigh possible risks. Currently, the local government requires for children with comorbidity, including bronchial asthma, to have a medical certificate provided for by their physician prior to vaccination.

Note: As of writing, COVID-19 vaccination has been expanded to include children 5 to 11 years old, with the vaccine dose given at one-third of the adult dose. The readers are encouraged to stay updated with the living recommendations for COVID-19.

## Appendix 1G. Questions raised during the initial presentation to the PAPP plenary (January 26, 2022)

**1. Can I use oral corticosteroids as maintenance medication instead of inhaled corticosteroids (ICS) because it is not available in some settings?**
The use of oral corticosteroids instead of inhaled corticosteroids is not among the current recommendations. Local physicians must coordinate with their public health and LGU systems to provide recommended medications and devices, especially with the advent of universal healthcare. Furthermore, the safety and effectiveness of oral corticosteroids for long term use in asthma must be considered.

**2. Can we use impulse oscillometry (IOS) in the diagnosis of asthma?**
We recognize that the evidence for impulse oscillometry is growing. We anticipate this to be among future issues to be included in succeeding updates of the guideline.

**3. Can we use homemade or makeshift asthma spacer devices?**
We are aware that makeshift inhaler or spacer devices are occasionally used in low resource settings. These are innovations that require both formal engineering and real-world evidence to determine whether it is non-inferior over FDA approved devices. Medical devices also require FDA approval.

**4. Can we use lagundi for asthma?**
One of the claimed benefits of lagundi is its bronchodilation effects. Evidence of its use and efficacy in pediatric asthma is still lacking. Studies on Vitex negundo for asthma symptoms will be welcomed by the Asthma CPG Committee.

**5. Do we deworm children presenting with asthma-like symptoms prior to initiation of controller asthma medication?**
The PPS Preventive Handbook (2018) recommends deworming for all children regardless of asthma comorbidities. The WHO and DOH both recommend the use of either albendazole or mebendazole starting 12 months of age. Also, the DOH has a National Filariasis Elimination Program implemented in municipalities endemic to filariasis. Mass treatment with Diethylcarbamazine Citrate and Albendazole includes children from 2 years old and above.

Deworming prior to ICS use for long term asthma maintenance is suggested if the child presents with documented parasitism, clinically presents with symptoms suggestive of parasitism and if the local epidemiology shows a high prevalence for parasitism.

**6. Should the child be screened for TB before starting ICS?**
Tuberculosis is a common differential for asthma in the Philippines. If the child presents with signs and symptoms of TB, or has TB exposure, or lives in an area with high prevalence of TB, the physician must provide the standard of care for tuberculosis diagnosis and treatment. Universal screening for TB prior to starting ICS should undergo a formal and full health technology assessment before any recommendation can be made.

# Appendix II for the Methods Section

## Appendix 2A. Guideline Development Groups and Declarations of Conflicts of Interest

### PAPP Asthma CPG Steering Committee

| Name | Qualifications | Conflict of Interest |
|---|---|---|
| Dr. Rozaida Villon | Fellow and Chair, Philippine Academy of Pediatric Pulmonologists-Asthma Committee | No Conflict of Interest |
| Dr. Charito De los Santos | Fellow and Vice Chair, Philippine Academy of Pediatric Pulmonologists-Asthma Committee | No Conflict of Interest |
| Dr. Romina Gerolaga | Diplomate and Secretary, Philippine Academy of Pediatric Pulmonologists-Asthma Committee | No Conflict of Interest |

### Technical Working Group Co-Authors and Peer Reviewers

| Name | Qualifications | Conflict of Interest |
|---|---|---|
| Victoria Jalandoni-Cabahug, MD | Fellow, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |
| Consuelo Lu, MD | Fellow, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |
| Gerarda Ember Afable, MD | Diplomate, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |
| Yadnee Estrera, MD | Diplomate, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |
| Maria Corazon Avanceña, MD | Diplomate, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |
| Kristine Aliling, MD | Diplomate, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |
| Grace Malayan, MD | Fellow, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |
| Alfredo Bongo, Jr., MD | Fellow, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |
| Jacqueline Reyes-Rodolfo, MD | Diplomate, Philippine Society of Asthma, Allergy and Immunology | No Conflict of Interest |
| Victoria Chato-Andeza, MD | Fellow, Philippine Society of Asthma, Allergy and Immunology | No Conflict of Interest |

## PAPP Technical Advisory Group

| Name | Qualifications | Conflict of Interest |
|---|---|---|
| Amelia Cunanan, MD | Fellow, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |
| Nepthalie Ordonez, MD | Fellow, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |
| Anna Putulin, MD | Fellow, Philippine Academy of Pediatric Pulmonologists | No Conflict of Interest |

## PSAAI Asthma CPG Contributors

| Name | Qualifications | Conflict of Interest |
|---|---|---|
| Aileen Elorde, MD | Diplomate, Philippine Society of Asthma, Allergy and Immunology | No Conflict of Interest |
| Rommel Crisenio Lobo, MD | Fellow, Philippine Society of Asthma, Allergy and Immunology | No Conflict of Interest |
| Ivy June Minerva, MD | Diplomate, Philippine Society of Asthma, Allergy and Immunology | No Conflict of Interest |
| Cecil Wong-Chuah, MD | Diplomate, Philippine Society of Asthma, Allergy and Immunology | No Conflict of Interest |
| Jennifer Serrano-Flores, MD | Diplomate, Philippine Society of Asthma, Allergy and Immunology | No Conflict of Interest |

## Evidence Review and Technical Editing (101 Health Research)

| Name | Qualifications | Conflict of Interest |
|---|---|---|
| Venus Oliva Cloma-Rosales, MD MPH | Founder and Managing Director, 101 Health Research | Provided research planning for a non-asthma drug observational study of Novo Nordisk |
| | Founding Member, Philippine Society of Public Health Physicians | Advanced GCP lecturer sponsored by a local pharma company New Marketlink Pharma Corporation |
| | Member, Philippine Association of Medical Journal Editors | To mitigate this COI, Dr. Rosales did not participate in the stakeholder mapping |
| Maria Christine Joy Tanteo, MD | Diplomate, Philippine Pediatric Society | No Conflict of Interest |

| | | |
|---|---|---|
| Rubiliza Onofre Telan, MD | Fellow, Philippine Society of Otorhinolaryngology-Head and Neck Surgery | No Conflict of Interest |
| Aileen Rosales, MD | Diplomate, Philippine Board of Anesthesiology | No Conflict of Interest |
| Richelle Carmela Amponin | Social Sciences and Interdisciplinary Studies<br>Qualitative Research Analyst<br>101 Health Research | No Conflict of Interest |
| Riza Banaag | Graphics Designer, 101 Health Research | No Conflict of Interest |
| Frances Angela Depillo | Administrative Officer, 101 Health Research | No Conflict of Interest |

## CPG Management Team (HPPM, Inc.)

| Name | Qualifications | Conflict of Interest |
|---|---|---|
| Teddy Dizon, RN | Registered Nurse and Public Health Practitioner | No Conflict of Interest |
| Joseph Orano, MD | Medical Doctor and Public Health Practitioner | No Conflict of Interest |
| Jennel Pimentel | Public Health Researcher | No Conflict of Interest |

## Consensus Panel

| Name | Qualifications | Conflict of Interest |
|---|---|---|
| Dr. Diego C. Danila | Medical Specialist III, Department of Health-Family Health Office | No Conflict of Interest |
| Dr. Zashka Alexis M. Gomez | Medical Officer III, Department of Health- Disease Prevention and Control Bureau | No Conflict of Interest |
| Dr. Iluminada Camagay-Carag | Founding President, Philippine Society for Pediatric Anesthesia | No Conflict of Interest |
| Dr. Lydia Chang | Member and Fellow, Philippine Academy of Pediatric Pulmonologists | With Secondary Conflict of Interest, allowed to participate in the CPG development |
| Dr. Jacqueline Reyes-Rodolfo | Diplomate, Philippine Society of Asthma, Allergy and Immunology | No Conflict of Interest |
| Dr. Jennifer Serrano-Flores | Diplomate, Philippine Society of Asthma, Allergy and Immunology | No Conflict of Interest |
| Dr. Edna Sarah C. Morada | Fellow, Philippine Pediatric Society | No Conflict of Interest |
| Dr. Daisy M. Medina | Diplomate and Fellow, Philippine Academy of Family Physicians | No Conflict of Interest |

| | | |
|---|---|---|
| Dr. Jeriel De Silos | Member, Philippine Society of Public Health Physicians, Inc. | No Conflict of Interest |
| Dr. April Llaneta | Fellow, Philippine College of Emergency Medicine | No Conflict of Interest |
| Dr. Katerina Abiertas | Vice President, Association of Municipal Health Officers of the Philippines Region 8 | No Conflict of Interest |
| Ms. Maria Fatima Garcia-Lorenzo | President, Philippine Alliance of Patient Organizations | No Conflict of Interest |

## Appendix 2B. Literature Search Strategies and Output

| Search database | Search terms | Publication date | Article type | Language | Text availability | Number of articles |
|---|---|---|---|---|---|---|
| Herdin | ("bronchial asthma" OR "asthma") AND "exacerbation*" AND "control" AND "severity" AND ("pediatric" OR "children" OR "adolescent*") | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 212 |
| Herdin | ("bronchial asthma" OR "asthma") AND "diagnosis" AND "spirometry" AND "lung function test*" AND ("pediatric" OR "children" OR "adolescent*") | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 21 |
| Herdin | asthma AND health education AND pediatrics | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 1 |
| Herdin | asthma AND exercise AND pediatrics | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 3 |
| Herdin | asthma AND control AND pediatrics | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 3 |
| PubMed | ("asthma"[MeSH Terms] OR "asthma"[All Fields] OR "asthmas"[All Fields] OR "asthma s"[All Fields]) AND ("health education"[MeSH Terms] OR ("health"[All Fields] AND "education"[All Fields]) OR "health education"[All Fields]) AND ("filipino"[All Fields] OR "filipinos"[All Fields]) AND ("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields]) | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 0 |
| PubMed | "asthma"[All Fields] AND ("health"[All Fields] AND "promotion"[All Fields]) AND "pediatrics"[All Fields] AND "Philippines"[All Fields] | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| PubMed | ("asthma"[MeSH Terms] OR "asthma"[All Fields] OR "asthmas"[All Fields] OR "asthma s"[All Fields]) AND ("health promotion"[MeSH Terms] OR ("health"[All Fields] AND "promotion"[All Fields]) OR "health promotion"[All Fields]) AND ("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields]) AND ("philippine"[All Fields] OR "philippines"[MeSH Terms] OR "philippines"[All Fields]) | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 0 |
| PubMed | ("asthma"[MeSH Terms] OR "asthma"[All Fields] OR "asthmas"[All Fields] OR "asthma s"[All Fields]) AND ("prevent"[All Fields] OR "preventability"[All Fields] OR "preventable"[All Fields] OR "preventative"[All Fields] OR "preventatively"[All Fields] OR "preventatives"[All Fields] OR "prevented"[All Fields] OR "preventing"[All Fields] OR "prevention and control"[MeSH Subheading] OR ("prevention"[All Fields] AND "control"[All Fields]) OR "prevention and control"[All Fields] OR "prevention"[All Fields] OR "prevention s"[All Fields] OR "preventions"[All Fields] OR "preventive"[All Fields] OR "preventively"[All Fields] OR "preventives"[All Fields] OR "prevents"[All Fields]) AND ("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields]) AND ("philippine"[All Fields] OR "philippines"[MeSH Terms] OR "philippines"[All Fields]) | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 13 |
| PubMed | ("asthma"[MeSH Terms] OR "asthma"[All Fields] OR "asthmas"[All Fields] OR "asthma s"[All Fields]) AND ("vaccin"[Supplementary | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Concept] OR "vaccin"[All Fields] OR "vaccination"[MeSH Terms] OR "vaccination"[All Fields] OR "vaccinable"[All Fields] OR "vaccinal"[All Fields] OR "vaccinate"[All Fields] OR "vaccinated"[All Fields] OR "vaccinates"[All Fields] OR "vaccinating"[All Fields] OR "vaccinations"[All Fields] OR "vaccination s"[All Fields] OR "vaccinator"[All Fields] OR "vaccinators"[All Fields] OR "vaccine s"[All Fields] OR "vaccined"[All Fields] OR "vaccines"[MeSH Terms] OR "vaccines"[All Fields] OR "vaccine"[All Fields] OR "vaccins"[All Fields]) AND ("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields]) AND ("filipino"[All Fields] OR "filipinos"[All Fields]) | | | | | |
| Google Scholar | ("bronchial asthma" OR "asthma") AND "exacerbation*" AND "control" AND "severity" AND ("pediatric" OR "children" OR "adolescent*") AND "Filipino*" | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 276 |
| Google Scholar | ("bronchial asthma" OR "asthma") AND "diagnosis" AND "spirometry" AND "lung function test*" AND ("pediatric" OR "children" OR "adolescent*") AND "Philippines" | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 6 |
| Google Scholar | ("bronchial asthma" OR "asthma") AND "diagnosis" AND "spirometry" AND "lung function test*" AND ("pediatric" OR "children" OR "adolescent*") AND "Philippines | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 34 |
| Google Scholar | asthma AND health education AND filipino AND parents AND caregivers | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 2680 |

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|---|---|---|---|---|---|---|
| EBSCO Host | ("bronchial asthma" OR "asthma") AND "diagnosis" AND "spirometry" AND "lung function test*" AND ("pediatric" OR "children" OR "adolescent*") | Any period | RCT<br>Clinical trials (not randomized)<br>Observational cohort<br>Case-control<br>Case studies | English<br>Filipino | Full text | 186 |

Total = **3435**

## Appendix 2C. AGREE Reporting Checklist

| CHECKLIST ITEM AND DESCRIPTION | REPORTING CRITERIA | Page # |
|---|---|---|
| ***DOMAIN 1: SCOPE AND PURPOSE*** | | |
| **1. OBJECTIVES**<br>*Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.* | Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.)<br>Expected benefit(s) or outcome(s)<br>Target(s) (e.g., patient population, society) | |
| **2. QUESTIONS**<br>*Report the health question(s) covered by the guideline, particularly for the key recommendations.* | Target population<br>Intervention(s) or exposure(s)<br>Comparisons (if appropriate)<br>Outcome(s)<br>Health care setting or context | |
| **3. POPULATION**<br>*Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.* | Target population, sex and age<br>Clinical condition (if relevant)<br>Severity/stage of disease (if relevant)<br>Comorbidities (if relevant)<br>Excluded populations (if relevant) | |
| ***DOMAIN 2: STAKEHOLDER INVOLVEMENT*** | | |
| **4. GROUP MEMBERSHIP**<br>*Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations.* | Name of participant<br>Discipline/content expertise (e.g., neurosurgeon, methodologist)<br>Institution (e.g., St. Peter's hospital)<br>Geographical location (e.g., Seattle, WA)<br>A description of the member's role in the guideline development group | |
| **5. TARGET POPULATION PREFERENCES AND VIEWS**<br>*Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.* | Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences)<br>Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups)<br>Outcomes/information gathered on patient/public information<br>How the information gathered was used to inform the guideline development process and/or formation of the recommendations | |

| | | |
|---|---|---|
| **6. TARGET USERS**<br>*Report the target (or intended) users of the guideline.* | The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators)<br>How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care) | |
| ***DOMAIN 3: RIGOUR OF DEVELOPMENT*** | | |
| **7. SEARCH METHODS**<br>*Report details of the strategy used to search for evidence.* | Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL)<br>Time periods searched (e.g., January 1, 2004 to March 31, 2008)<br>Search terms used (e.g., text words, indexing terms, subheadings)<br>Full search strategy included (e.g., possibly located in appendix) | |
| **8. EVIDENCE SELECTION CRITERIA**<br>*Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.* | Target population (patient, public, etc.) characteristics<br>Study design<br>Comparisons (if relevant)<br>Outcomes<br>Language (if relevant)<br>Context (if relevant) | |
| **9. STRENGTHS & LIMITATIONS OF THE EVIDENCE**<br>*Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.* | Study design(s) included in body of evidence<br>Study methodology limitations (sampling, blinding, allocation concealment, analytical methods)<br>Appropriateness/relevance of primary and secondary outcomes considered<br>Consistency of results across studies<br>Direction of results across studies<br>Magnitude of benefit versus magnitude of harm<br>Applicability to practice context | |
| **10. FORMULATION OF RECOMMENDATIONS**<br>*Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.* | Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered)<br>Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures)<br>How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote) | |
| **11. CONSIDERATION OF BENEFITS AND HARMS**<br>*Report the health benefits, side effects, and risks that were considered when formulating the recommendations.* | Supporting data and report of benefits<br>Supporting data and report of harms/side effects/risks<br>Reporting of the balance/trade-off between benefits and harms/side effects/risks<br>Recommendations reflect considerations of both benefits and harms/side effects/risks | |
| **12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE**<br>*Describe the explicit link between the recommendations and the evidence on which they are based.* | How the guideline development group linked and used the evidence to inform recommendations<br>Link between each recommendation and key evidence (text description and/or reference list)<br>Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline | |

| | | |
|---|---|---|
| **13. EXTERNAL REVIEW**<br>*Report the methodology used to conduct the external review.* | Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence)<br>Methods taken to undertake the external review (e.g., rating scale, open-ended questions)<br>Description of the external reviewers (e.g., number, type of reviewers, affiliations)<br>Outcomes/information gathered from the external review (e.g., summary of key findings)<br>How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations) | |
| **14. UPDATING PROCEDURE**<br>*Describe the procedure for updating the guideline.* | A statement that the guideline will be updated<br>Explicit time interval or explicit criteria to guide decisions about when an update will occur<br>Methodology for the updating procedure | |
| ***DOMAIN 4: CLARITY OF PRESENTATION*** | | |
| **15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS**<br>*Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.* | A statement of the recommended action<br>Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects)<br>Relevant population (e.g., patients, public)<br>Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply)<br>If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline | |
| **16. MANAGEMENT OPTIONS**<br>*Describe the different options for managing the condition or health issue.* | Description of management options<br>Population or clinical situation most appropriate to each option | |
| **17. IDENTIFIABLE KEY RECOMMENDATIONS**<br>*Present the key recommendations so that they are easy to identify.* | Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms<br>Specific recommendations grouped together in one section | |
| ***DOMAIN 5: APPLICABILITY*** | | |
| **18. FACILITATORS AND BARRIERS TO APPLICATION**<br>*Describe the facilitators and barriers to the guideline's application.* | Types of facilitators and barriers that were considered<br>Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation)<br>Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography)<br>How the information influenced the guideline development process and/or formation of the recommendations | |

| | | |
|---|---|---|
| **19. IMPLEMENTATION ADVICE/TOOLS**<br>*Provide advice and/or tools on how the recommendations can be applied in practice.* | Additional materials to support the implementation of the guideline in practice.<br>For example:<br><br>● Guideline summary documents<br>● Links to check lists, algorithms<br>● Links to how-to manuals<br>● Solutions linked to barrier analysis (see Item 18)<br>● Tools to capitalize on guideline facilitators (see Item 18)<br>● Outcome of pilot test and lessons learned | |
| **20. RESOURCE IMPLICATIONS**<br>*Describe any potential resource implications of applying the recommendations.* | Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs)<br>Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.)<br>Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course)<br>How the information gathered was used to inform the guideline development process and/or formation of the recommendations | |
| **21. MONITORING/ AUDITING CRITERIA**<br>*Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.* | Criteria to assess guideline implementation or adherence to recommendations<br>Criteria for assessing impact of implementing the recommendations<br>Advice on the frequency and interval of measurement<br>Operational definitions of how the criteria should be measured | |
| ***DOMAIN 6: EDITORIAL INDEPENDENCE*** | | |
| **22. FUNDING BODY**<br>*Report the funding body's influence on the content of the guideline.* | The name of the funding body or source of funding (or explicit statement of no funding)<br>A statement that the funding body did not influence the content of the guideline | |
| **23. COMPETING INTERESTS**<br>*Provide an explicit statement that all group members have declared whether they have any competing interests.* | Types of competing interests considered<br>Methods by which potential competing interests were sought<br>A description of the competing interests<br>How the competing interests influenced the guideline process and development of recommendations | |

From:
Brouwers MC, Kerkvliet K, Spithoff K, on behalf of the AGREE Next Steps Consortium. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. *BMJ* 2016;352:i1152. doi: 10.1136/bmj.i1152.

For more information about the AGREE Reporting Checklist, please visit the AGREE Enterprise website at http://www.agreetrust.org.