Global Strategy for Asthma Management and Prevention (2016 update)

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Disclosures
Over the past 20 years, the Global Initiative for Asthma (GINA) has regularly published and annually updated a global strategy for asthma management and prevention that has formed the basis for many national guidelines. However, uptake of existing guidelines is poor. A major revision of the GINA report was published in 2014, and updated in 2015.
Asthma is a serious global health problem affecting all age groups, with global prevalence ranging from 1% to 21% in adults, and with up to 20% of children aged 6–7 years experiencing severe wheezing episodes within a year.
Although some countries have seen a decline in asthma-related hospitalizations and deaths, the global burden for patients from exacerbations and day-to-day symptoms has increased by almost 30% in the past 20 years.
Since the last major revision of the GINA report in there has been a transition in understanding of asthma and chronic obstructive pulmonary disease (COPD) as heterogeneous and sometimes overlapping conditions, awareness of the contribution of common problems such as adherence, inhaler technique and health literacy to poorly controlled asthma.
The aim of this presentation is to summarise the key changes in the GINA strategy report.
Providing a summary of evidence about asthma care is not sufficient to change outcomes; there is now a strong evidence base about effective (and ineffective) methods for implementing clinical guidelines. And achieving behavior change by health professionals and patients.
Definition, description and diagnosis

Key changes

• A new definition of asthma

• Practical tools - Clinical flow-chart for diagnosis of asthma and table of diagnostic criteria.

■ Advice about confirming asthma diagnosis in patients already on treatment, and in special populations, including pregnant women and the elderly.
Rationale for change

Improving the diagnosis of asthma is the first step to improving outcomes. At a global level asthma is both under- and over-diagnosed.
The new definition of asthma

“Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.”
The rationale is that, although chronic airway inflammation is characteristic of most currently known asthma phenotypes, the absence of inflammatory markers should not preclude the diagnosis of asthma being made in patients with variable expiratory airflow limitation and variable respiratory symptoms.
Many phenotypes have been identified

**Allergic asthma**: this is the most easily recognized asthma phenotype, which often commences in childhood and is associated with a past and/or family history of allergic disease such as eczema, allergic rhinitis, or food or drug allergy. Examination of the induced sputum of these patients before treatment often reveals eosinophilic airway inflammation. Patients with this asthma phenotype usually respond well to inhaled corticosteroid (ICS) treatment.

**Non-allergic asthma**: some adults have asthma that is not associated with allergy. The cellular profile of the sputum of these patients may be neutrophilic, eosinophilic or contain only a few inflammatory cells (paucigranulocytic). Patients with non-allergic asthma often respond less well to ICS.

**Late-onset asthma**: some adults, particularly women, present with asthma for the first time in adult life. These patients tend to be non-allergic, and often require higher doses of ICS or are relatively refractory to corticosteroid treatment.

**Asthma with fixed airflow limitation**: some patients with long-standing asthma develop fixed airflow limitation that is thought to be due to airway wall remodeling.

**Asthma with obesity**: some obese patients with asthma have prominent respiratory symptoms and little eosinophilic airway inflammation.
This should **not** be taken to suggest a lesser emphasis on anti-inflammatory treatment; on the contrary, indications for inhaled corticosteroid (ICS) treatment have been expanded.
Practical tools for diagnosis of asthma.

The key changes in this section are consequent upon the new definition of asthma, and are aimed at reducing both under- and over-diagnosis. There is an emphasis on making a diagnosis in patients presenting with respiratory symptoms, preferably before commencing treatment, and on documenting the basis of the diagnosis in the patient’s medical records.
Diagnostic flow-chart for asthma in clinics

- Patient with respiratory symptoms
  - Are the symptoms typical of asthma?
    - YES
    - Detailed history/examination for asthma
      - History/examination supports asthma diagnosis?
        - NO
        - Further history and tests for alternative diagnoses
          - Alternative diagnosis confirmed?
            - NO
            - Empiric treatment with ICS and prn SABA
              - Review response
              - Diagnostic testing within 1-3 months
                - NO
                - Repeat on another occasion or arrange other tests
                  - Confirms asthma diagnosis?
                    - NO
                    - Consider trial of treatment for most likely diagnosis, or refer for further investigations
                      - YES
                      - Treat for ASTHMA
                        - YES
                        - Treat for alternative diagnosis

Confirming the diagnosis of asthma in patients already on treatment.

Evidence to support a diagnosis of asthma is often not documented in case notes, and over-diagnosis is common (25–35%) in developed Countries.
### Box 1.2. Diagnostic criteria for asthma in adults, adolescents, and children 6–11 years

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation.

<table>
<thead>
<tr>
<th>DIAGNOSTIC FEATURE</th>
<th>CRITERIA FOR MAKING THE DIAGNOSIS OF ASTHMA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. History of variable respiratory symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Wheeze, shortness of breath, chest tightness and cough</td>
<td>Generally more than one type of respiratory symptom (in adults, isolated cough is seldom due to asthma)</td>
</tr>
<tr>
<td>Descriptions may vary between cultures and by age; e.g. children may be described as having heavy breathing</td>
<td>Symptoms occur variably over time and vary in intensity</td>
</tr>
<tr>
<td></td>
<td>Symptoms are often worse at night (wk bkgd)</td>
</tr>
<tr>
<td></td>
<td>Symptoms are often triggered by exercise, laughter, allergens, cold air</td>
</tr>
<tr>
<td></td>
<td>Symptoms often appear or worsen with viral infections</td>
</tr>
</tbody>
</table>

| **2.Confirmed variable expiratory airflow limitation** |  |
| Documented excessive variability in lung function* (one or more of the tests below) AND documented airflow limitation* | The greater the variations, the more confident the diagnosis |
| Positive bronchodilator (BD) reversibility test* (more likely to be positive if BD medication is withheld before test: SABA 24 hours, LABA ≥15 hours) | Adults: increase in FEV1 of ≥12% and ≥200 mL from baseline, 10—15 minutes after 200—400 mcg albuterol or equivalent (greater confidence if increase is ≥15% and ≥400 mL). Children: increase in FEV1 of ≥12% predicted |
| Excessive variability in twice-daily PEF over 2 weeks** | Adults: average daily diurnal PEF variability >10%** |
| | Children: average daily diurnal PEF variability >15%** |
| Significant increase in lung function after 4 weeks of anti-inflammatory treatment | Adults: increase in FEV1 by ≥12% and ≥200 mL (or PEFR by ≥200 mL) from baseline after 4 weeks of treatment, outside respiratory infections |
| Positive exercise challenge test* (usually only performed in adults) | Adults: fall in FEV1 of ≥10% and ≥200 mL from baseline |
| | Children fall in FEV1 of ≥15% predicted, or PEFR >15% |
| Positive bronchial challenge test (usually only performed in adults) | Fall in FEV1, from baseline of ≥20% with standard doses of methacholine or histamine, or ≥15% with standardized hypercapnia, hypertonic saline or marmite challenge |
| Excessive variation in lung function between visits* (less reliable) | Adults: variation in FEV1 of ≥12% and ≥200 mL between visits, outside of respiratory infections |
| | Children: variation in FEV1 of ≥12% in FEV1 or ≥15% in PEFR between visits (may include respiratory infections) |

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BD: bronchodilator (short-acting SABA or rapid-acting LABA); FEV1: forced expiratory volume in 1 second; LABA: long-acting beta agonist; PEFR: peak expiratory flow; wk bkgrd: week before/after; SABA: short-acting beta agonist. See Notes 1–4 for diagnosis in patients already taking controller treatment.

*These tests can be repeated during symptoms or in the early morning. **Daily diurnal PEF variability is calculated from twice daily PEF as (day’s highest minus lowest)/ (mean of day’s highest and lowest) and averaged over one week. Test PEF use the same meter each time, as PEF may vary by as little as 20% between different meters. BD reversibility may be lost during severe exacerbations or viral infections. If bronchodilator reversibility is not present at initial presentation, the next step depends on the availability of other tests and the urgency of the need for treatment. In a situation of clinical urgency, asthma treatment may be commenced and diagnostic testing arranged within the next two weeks (see Notes 1–4, p. 11), but other conditions that mimic asthma (Box 1.3) should be considered, and the diagnosis of asthma confirmed as soon as possible.
History of variable respiratory symptoms

**DIAGNOSTIC FEATURE**

- Wheeze, shortness of breath, chest tightness and cough
- Descriptors may vary between cultures and by age, e.g. children may be described as having heavy breathing

**CRITERIA FOR MAKING THE DIAGNOSIS OF ASTHMA**

- Generally more than one type of respiratory symptom (in adults, isolated cough is seldom due to asthma)
- Symptoms occur variably over time and vary in intensity
- Symptoms are often worse at night or on waking
- Symptoms are often triggered by exercise, laughter, allergens, cold air
- Symptoms often appear or worsen with viral infections
Documented excessive variability in lung function (one or more of the tests below)

The greater the variations, or the more occasions excess variation is seen, the more confident the diagnosis.

AND documented airflow limitation
At least once during diagnostic process when FEV1 is low, confirm that FEV1/FVC is reduced (normally >0.75–0.80 in adults, >0.90 in children)
Positive bronchodilator (BD) reversibility test

(more likely to be positive if BD medication is withheld before test: SABA ≥4 hours, LABA ≥15 hours)

*Adults*: increase in FEV1 of >12% and >200 mL from baseline, 10–15 minutes after 200–400 mcg albuterol or equivalent (greater confidence if increase is >15% and >400 mL).

*Children*: increase in FEV1 of >12% predicted
Excessive variability in twice-daily PEF over 2 weeks

*Adults*: average daily diurnal PEF variability $>10\%$

*Children*: average daily diurnal PEF variability $>13\%$
Significant increase in lung function after 4 weeks of anti-inflammatory treatment

*Adults*: increase in FEV1 by >12% and >200 mL (or PEF† by >20%) from baseline after 4 weeks of treatment, outside respiratory infections
Positive exercise challenge test

*Adults*: fall in FEV1 of >10% and >200 mL from baseline

*Children*: fall in FEV1 of >12% predicted, or PEF >15%
Positive bronchial challenge test (usually only performed in adults)

Fall in FEV1 from baseline of ≥20% with standard doses of methacholine or histamine, or ≥15% with standardized hyperventilation, hypertonic saline or mannitol challenge.
Excessive variation in lung function between visits (less reliable)

*Adults:* variation in FEV1 of >12% and >200 mL between visits, outside of respiratory infections.

*Children:* variation in FEV1 of >12% in FEV1 or >15% in PEF between visits (may include respiratory infections)
Sub-types

Diagnosis of asthma in special populations (e.g. pregnancy, occupational asthma, older patients, smokers and athletes). These sections are consistent with the emphasis in GINA on tailoring asthma management for different populations.
Patients presenting with cough as the only respiratory symptom

- Diagnoses to be considered are cough variant asthma, cough induced by angiotensin converting enzyme (ACE) inhibitors, gastroesophageal reflux, chronic upper airway cough syndrome (often called ‘postnasal drip’), chronic sinusitis, and vocal cord dysfunction.

- It is more common in children and often more problematic at night; lung function may be normal.

- For these patients, documentation of variability in lung function is important.

- Cough-variant asthma must be distinguished from eosinophilic bronchitis in which patients have cough and sputum eosinophils but normal spirometry and airway responsiveness.
Occupational asthma and work-aggravated asthma Asthma acquired in the workplace is frequently missed.

Asthma may be induced or (more commonly) aggravated by exposure to allergens or other sensitizing agents at work, or sometimes from a single, massive exposure.

Occupational rhinitis may precede asthma by up to a year and early diagnosis is essential, as persistent exposure is associated with worse outcomes.
Athletes

The diagnosis of asthma in athletes should be confirmed by lung function tests, usually with bronchial provocation testing.

Conditions that may either mimic or be associated with asthma, such as rhinitis, laryngeal disorders (e.g. vocal cord dysfunction), dysfunctional breathing, cardiac conditions and over-training, must be excluded.
Pregnant women

Pregnant women and women planning a pregnancy should be asked whether they have asthma so that appropriate advice about asthma management and medications can be given.

If objective confirmation of the diagnosis is needed, it would not be advisable to carry out a bronchial provocation test or to step down controller treatment until after delivery.
The elderly

Asthma is frequently undiagnosed in the elderly, due to poor perception of airflow limitation; acceptance of dyspnea as being ‘normal’ in old age; lack of fitness; and reduced activity. The presence of comorbid diseases also complicates the diagnosis.

In older people with a history of smoking or biomass fuel exposure, COPD and asthma–COPD overlap syndrome (ACOS) should be considered.
Smokers and ex-smokers

Asthma and COPD may be difficult to distinguish in clinical practice, particularly in older patients and smokers and ex-smokers, and these conditions may overlap (asthma-COPD overlap syndrome, or ACOS).
- Nasal polyposis and reaction to NSAIDS (ASA Exacerbated)

- Chronic sputum production (ABPA)
Assessment and Control of Asthma
Asthma control is assessed from two domains: symptom control and risk factors.

Lung function is no longer included among symptom control measures, but after diagnosis it is used primarily for initial and ongoing risk assessment.

Asthma severity is a retrospective label, assessed from treatment needed to control asthma.

Practical tools
Template for assessing asthma control, including key risk factors
Clinical algorithm for distinguishing between uncontrolled and severe refractory asthma
A clinical algorithm for distinguishing between uncontrolled asthma and severe refractory asthma. Protocols for identifying severe refractory asthma often start with confirmation of the diagnosis of asthma.

The GINA report takes a more pragmatic approach, with the algorithm starting with the most common causes of uncontrolled asthma, namely incorrect inhaler technique (up to 80% of patients) and poor adherence (at least 50% of patients).
Asthma severity is a retrospective label, assessed after a patient has been on treatment for at least several months.
Treating to control symptoms and minimize future risk
control-based asthma management cycle (assess – adjust treatment – review response), to prompt a comprehensive but clinically feasible approach.

An explicit framework for tailoring treatment to individual patients.

New indications for initial controller treatment, including in mild asthma.

A strong emphasis on checking diagnosis, inhaler technique and adherence before considering any treatment step-up.

Advice about tailoring treatment for special populations and clinical contexts.
Practical tools

Strategies to reduce the impact of impaired health literacy.
A new stepwise treatment figure, visually emphasizing key concepts.
Current options for stepping down treatment
Treatment of modifiable risk factors.
Non-pharmacological interventions.
Indications for referral for expert advice.
Strategies to ensure effective use of inhaler devices.
How to ask patients about their adherence.
Summary of investigations and management for severe asthma.
**Good communication is essential** – establish a partnership with the patient
- Consider health literacy, personal goals and fears, and cultural issues

**Treatment choices**
- * Population-level decisions: efficacy, effectiveness, safety, cost, regulations
- * Patient-level decisions for tailoring treatment: also discuss patient characteristics (phenotype) that predict response or risk; patient preference; practical issues inhaler technique, adherence, and cost; treat modifiable risk factors; use non-pharmacological strategies where appropriate

**Stepwise medication adjustment**
- * Consider stepping up if uncontrolled symptoms, exacerbations or risks, but check diagnosis, inhaler technique, adherence and modifiable risk factors first
- * Consider stepping down if symptoms controlled for 3 months and low risk for exacerbations. For adults, ceasing ICS is not advised.
Asthma control is assessed from two domains: symptom control and risk factors.
### GINA assessment of symptom control

#### A. Symptom control

<table>
<thead>
<tr>
<th>In the past 4 weeks, has the patient had:</th>
<th>Level of asthma symptom control</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Daytime asthma symptoms more than twice a week?</td>
<td>Well-controlled</td>
</tr>
<tr>
<td>• Any night waking due to asthma?</td>
<td>Partly controlled</td>
</tr>
<tr>
<td>• Reliever needed for symptoms*</td>
<td>Uncontrolled</td>
</tr>
<tr>
<td>• Any activity limitation due to asthma?</td>
<td></td>
</tr>
</tbody>
</table>

- **Yes** □ **No** □
- **None of these**
- **1-2 of these**
- **3-4 of these**

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

- Assess risk factors at diagnosis and periodically
- Measure FEV₁ at start of treatment, after 3 to 6 months of treatment to record the patient’s personal best, then periodically for ongoing risk assessment

**ASSESS PATIENT’S RISKS FOR:**
- Exacerbations
- Fixed airflow limitation
- Medication side-effects
Asthma Control Questionnaire (ACQ)

Scores range from 0–6 (higher is worse). A score of 0.0–0.75 is classified as well-controlled asthma;

0.75–1.5 as a ‘grey zone’;

>1.5 as poorly controlled asthma.

The ACQ score is calculated as the average of 5, 6 or 7 items: all versions of the ACQ include five symptom questions.
Asthma Control Test (ACT)

Scores range from 5–25 (higher is better).

Scores of 20–25 are classified as well-controlled asthma;
16–20 as not well-controlled;
5–15 as very poorly controlled asthma.

The ACT includes four symptom/reliever questions plus a patient self-assessed level of control. The minimum clinically important difference is 3 points.
1. In the past **4 weeks**, how much of the time did your **asthma** keep you from getting as much done at work, school or at home?
   - All of the time
   - Most of the time
   - Some of the time
   - A little of the time
   - None of the time

2. During the past **4 weeks**, how often have you had shortness of breath?
   - More than once a day
   - Once a day
   - 3 to 6 times a week
   - Once or twice a week
   - Not at all

3. During the past **4 weeks**, how often did your **asthma** symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?
   - 4 or more nights a week
   - 2 or 3 nights a week
   - Once a week
   - Once or twice
   - Not at all

4. During the past **4 weeks**, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?
   - 3 or more times per day
   - 1 or 2 times per day
   - 2 or 3 times per week
   - Once a week or less
   - Not at all

5. How would you rate your **asthma** control during the **past 4 weeks**?
   - Not controlled at all
   - Poorly controlled
   - Somewhat controlled
   - Well controlled
   - Completely controlled
How to distinguish between uncontrolled and severe asthma

1. Watch patient using their inhaler. Discuss adherence and barriers to use.
   - Compare inhaler technique with a device-specific checklist, and correct errors. Recheck frequently. Have an empathic discussion about barriers to adherence.

2. Confirm the diagnosis of asthma.
   - If lung function normal during symptoms, consider halving ICS dose and repeating lung function after 2–3 weeks.

   - Check for risk factors or inducers such as smoking, beta-blockers, NSAIDs, allergen exposure. Check for comorbidities such as rhinitis, obesity, GERD, depression/anxiety.

   - Consider step up to next treatment level. Use shared decision-making, and balance potential benefits and risks.

5. Refer to a specialist or severe asthma clinic.
   - If asthma still uncontrolled after 3–6 months on Step 4 treatment, refer for expert advice. Refer earlier if asthma symptoms severe.
How often should Asthma be reviewed?

1 to 3 months after initial treatment started, then every 3-12 months.

During pregnancy, every 4 – 6 weeks.

After an exacerbation, within 1 week.
Treatment

Pharmacotherapy
<table>
<thead>
<tr>
<th>Step</th>
<th>Preferred:</th>
<th>Alternative:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1</td>
<td>Low-dose ICS + LABA OR Medium-dose ICS, Cromolyn, LTRA, Nederland, or Theophylline</td>
<td>Low-dose ICS + either LTRA, Theophylline, or Zileuton</td>
</tr>
<tr>
<td>Step 2</td>
<td>High-dose ICS + LABA AND Consider Omalizumab for patients who have allergies</td>
<td>High-dose ICS + LABA + oral corticosteroid AND Consider Omalizumab for patients who have allergies</td>
</tr>
<tr>
<td>Step 3</td>
<td>Medium-dose ICS + LABA</td>
<td>Consider Omalizumab for patients who have allergies</td>
</tr>
<tr>
<td>Step 4</td>
<td>High-dose ICS + LABA AND Consider Omalizumab for patients who have allergies</td>
<td>Assess control</td>
</tr>
<tr>
<td>Step 5</td>
<td>High-dose ICS + LABA + oral corticosteroid AND Consider Omalizumab for patients who have allergies</td>
<td>Step down if possible (and asthma is well controlled at least 3 months)</td>
</tr>
<tr>
<td>Step 6</td>
<td>Assess control</td>
<td>Step down if possible (and asthma is well controlled at least 3 months)</td>
</tr>
</tbody>
</table>

Each step: Patient education, environmental control, and management of comorbidities.

Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

Quick-relief medication for all patients

- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates need for step-up.
Stepwise approach to asthma treatment

- **Symptoms**
- **Exacerbations**
- **Side-effects**
- **Patient satisfaction**
- **Lung function**

**REVIEW RESPONSE**

**ASSSS**

**ADJUST TREATMENT**

**DIAGNOSIS**
- Symptom control & risk factors (including lung function)
- Inhaler technique & adherence
- Patient preference

**ASMA medications**
- Non-pharmacological strategies
- Treat modifiable risk factors

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**STEP 1**
- **PREFERRED CONTROLLER CHOICE**
- Low dose ICS
- Other controller options

**RELIEVER**
- As-needed short-acting beta₂-agonist (SABA)

**REMEMBER TO...**
- Provide guided self-management education (self-monitoring + written action plan + regular review)
- Treat modifiable risk factors and comorbidities, e.g. smoking, obesity, anxiety
- Advise about non-pharmacological therapies and strategies, e.g. physical activity, weight loss, avoidance of sensitizers where appropriate
- Consider stepping up if... uncontrolled symptoms, exacerbations or risks, but check diagnosis, inhaler technique and adherence first
- Consider stepping down if... symptoms controlled for 3 months + low risk for exacerbations. Ceasing ICS is not advised.

**STEP 2**
- Consider low dose ICS
- Leukotriene receptor antagonists (LTRA)
- Low dose theophylline**

**STEP 3**
- Med/high dose ICS/LABA**
- Add LTRA
- Add theophylline**

**STEP 4**
- Refer for add-on treatment e.g. anti-IgE
- Add ICS + LTRA (or theophylline)

**STEP 5**
- Add ICS + LTRA (or theophylline)
Medication categories for asthma treatment

**Controller**
- Inhaled corticosteroid (ICS)
- ICS/LABA (long-acting beta-2-agonist) combination
- Leukotriene receptor agonists (LTRA)
- Long-acting anticholinergics (LAMA)
- Methylxanthines (theophylline)
- Chromones (practically no longer in use)

**Reliever**
- Short-acting beta-2-agonists (SABA)
- Short-acting anticholinergics (LAMA)

**Add-on therapy**
- Anti-IgE therapy – severe allergic asthma
- Systemic/oral corticosteroids (OCS)
- Anti-IL5 therapy – eosinophilic asthma
- Special (phenotype-specific) treatments and interventions by specialized centers
dd-on Tiotropium by soft-mist inhaler as an “other controller”
Tiotropium

Based on two -Phase III clinical trials

Patients not controlled on ICS or ICS/LABA treatment

Results:

- Improved lung function
- Increased time to first exacerbation
Monoclonal Antibody Therapy

Humanized IgG1 kappa monoclonal antibody specific for interleukin 5 (IL-5).

Mepolizumab

- This is a humanized murine IgG antibody against the Fc component of the IgE antibody

- Omalizumab
NON-PHARMACOLOGICAL INTERVENTIONS
NON-PHARMACOLOGICAL INTERVENTIONS

- cessation of smoking
- physical activity
- avoidance of occupational exposures
- avoidance of medications that may make asthma worse
- avoidance of indoor allergens
Bronchial thermoplasty

For highly-selected adult patients with uncontrolled asthma despite use of recommended therapeutic regimens and referral to an asthma specialty center, bronchial thermoplasty is a potential treatment option in some countries.

Caution should be used in selecting patients for this procedure, as the number of studies is small, and people with chronic sinus disease, frequent chest infections or EV1 <60% predicted were excluded.
Allergen immunotherapy

Compared to pharmacological and avoidance options, potential benefits of allergen immunotherapy (SCIT or SLIT) must be weighed against the risk of adverse effects and the inconvenience and cost of the prolonged course of therapy, including for SCIT the minimum half-hour wait required after each injection.
Management of worsening asthma and exacerbations
continuum of care for worsening asthma (action plans, primary care, acute care, follow-up).

The term “flare-up” is recommended for communication with patients.

Patients at increased risk of asthma-related death should be flagged.

Early rapid increase in ICS is recommended for action plans.

Severity of acute asthma is simplified into mild/moderate, severe, and life-threatening.

Updated recommendations for oxygen therapy, including an upper target for saturation.

Regular ICS-containing controller should be instituted or restarted after any severe exacerbation.
Practical tools

Action plan options for different controller regimens.

Flow-chart for managing asthma exacerbations in primary care.

Flow chart for managing asthma exacerbations in acute care facilities.

Discharge management.
he term “flare-up” is now recommended for communication with patients.

though the term “exacerbations” is standard in medical literature, it is far from patient-friendly.

Attacks” is commonly used, but with such different meanings that it may cause misunderstandings.

or patients, the term “flare-up” was recommended, as it conveys the concept of inflammation, and signals that asthma is present even when symptoms are absent.
Patients at increased risk of asthma-related death should be flagged in medical notes for frequent monitoring.
asthma-related death risks:

- History of near-fatal asthma requiring intubation and mechanical ventilation
- Hospitalization or emergency care visit for asthma in the past year
- Currently using or having recently stopped using oral corticosteroids (a marker of event severity)
- Currently using inhaled corticosteroids
- Over-use of SABAs, especially use of more than one canister monthly
- History of psychiatric disease or psychosocial problems
- Poor adherence with asthma medications and/or poor adherence with (or lack of) a written asthma action plan
- Food allergy in a patient with asthma
An early rapid increase in ICS now recommended for many action plans.

NA now recommends that an early increase in ICS dose should be advised in action plans, either by prescribing the ICS/formoterol maintenance and reliever regimen, or by a short-term increase in the dose of maintenance ICS/formoterol, or by adding an extra ICS inhaler.

The rationale for these recommendations included the following considerations.

Most exacerbations are characterised by increased inflammation; studies with doubling ICS comprise most of the strong evidence base that continues to support recommendations for asthma self-management and written asthma action plans → action plans which include both increased ICS (usually doubling) and oral corticosteroids.
Exacerbation severity classification has been streamlined into mild/moderate, severe, and life-threatening.
Revised recommendations for oxygen therapy, including an upper target for saturation.

The recommendation is now for controlled or titrated oxygen therapy where available, with a target saturation of 93–95% (94–98% for children 6–11 years).
Regular ICS-containing controller should be instituted or restarted after any severe exacerbation.

Considering short-term outcomes when ICS controllers are given in the context of emergency department or hospital presentations, this recommendation is also based on evidence that any severe exacerbation increases the risk of another in the next 12 months, and that risk of another hospitalisation is reduced by almost 40% with regular use of ICS-containing controller.
WRITTEN ASTHMA ACTION PLANS

All patients should be provided with a written asthma action plan appropriate for their level of asthma control and health literacy, so they know how to recognize and respond to worsening asthma.

Box 9. Self-management with a written action plan

The written asthma action plan should include:
- The patient’s usual asthma medications
- When and how to increase medications, and start OCS
- How to access medical care if symptoms fail to respond

The action plan can be based on symptoms and/or (in adults) PEF. Patients who deteriorate quickly should be advised to go to an acute care facility or see their doctor immediately.

Medication changes for written asthma action plans

Increase frequency of inhaled reliever (SABA, or low dose ICS/formoterol if using maintenance and reliever regimen); add spacer for pMDI.

Increase controller: Rapid increase in ICS component up to max. 2000mcg BDP equivalent. Options depend on usual controller medication, as follows:
- ICS: At least double dose, consider increasing to high dose.
- Maintenance ICS/formoterol: Quadruple maintenance ICS/formoterol dose (to maximum formoterol dose of 72 mcg/day).
- Maintenance ICS/salmeterol: Step up at least to higher dose formulation; consider adding separate ICS inhaler to achieve high ICS dose.
- Maintenance and reliever ICS/formoterol: Continue maintenance dose; increase as-needed ICS/formoterol (maximum formoterol 72 mcg/day).

Oral corticosteroids (preferably morning dosing):
- Adults - prednisolone 1mg/kg/day up to 50mg, usually for 5–7 days.
- For children, 1–2 mg/kg/day up to 40mg, usually for 3–5 days.
- Tapering not needed if treatment has been given for less than 2 weeks.
Action plans include:

1. The patient’s usual Asthma medications
2. When/How to increase reliever + controller or start OCS
3. How to access medical care if symptoms fail to respond
flow charts for managing asthma exacerbations in primary care and acute care.

The emphasis in these flow charts is on a rapid triage assessment while bronchodilator treatment is being instituted, with a more detailed history and examination once the patient is stabilized, a review of response at 1 h or earlier, and a summary of discharge considerations.
**Patient assessment: Medical history and physical examination**

**Mild to moderate:**
- Speaks in sentences
- Not agitated
- Pulse 100-120/s
- \( \text{O}_2 \) saturation 90-95%
- PEF >50% of peak value

**Severe:**
- Speaks in words
- Access, resp. muscles
- Agitated
- Resp. rate >30/min
- Pulse >120/s
- \( \text{O}_2 \) saturation <90%
- PEF ≤ 50% of peak value

**Life-threatening:**
- Sleepy
- Confused
- “Silent chest”

**Start treatment:**
- **SABA:** 4-10 puffs (pMDI w/ spacer) every 20 min f. 1
- **Prednisolone:** 1 mg/kg/d, max. 50 mg (adults)
- **Prednisolone:** 1-2 mg/kg/d, max. 40 mg (children)
- **Oxygen** (if available): Target saturation 93-95%
  - Children 94-98%

**Check after 1 h (or earlier):**
- Measure PEF, SaO2 and symptoms
- Continue SABA as needed

**Transfer to hospital or emergency room:**
- Start treatment while waiting

**Discharge:**
- **Reliever:** Continue as needed
- **Controller:** Initial therapy (see Table 4) or step-up

**Follow-up visit:** in 2-7 days
Management of asthma exacerbations in primary care

**PRIMARY CARE**
Patient presents with acute or sub-acute asthma exacerbation

**ASSESS the PATIENT**
- **Is it asthma?**
- Risk factors for asthma-related death? (Box 4-1)
- Severity of exacerbation?

**MILD or MODERATE**
- Talks in phrases, prefers sitting to lying, not agitated
- Respiratory rate increased
- Accessory muscles not used
- Pulse rate 100–120 bpm
- $O_2$ saturation (on air) 90–95%
- PEF >50% predicted or best

**SEVERE**
- Talks in words, sits hunched forwards, agitated
- Respiratory rate >30/min
- Accessory muscles in use
- Pulse rate >120 bpm
- $O_2$ saturation (on air) <90%
- PEF ≤50% predicted or best

**LIFE-THREATENING**
- Drowsy, confused or silent chest

**TRANSFER TO ACUTE CARE FACILITY**
- While waiting: give inhaled SABA and ipratropium bromide. $O_2$, systemic corticosteroid

**START TREATMENT**
- **SABA**: 4–10 puffs by pMDI + spacer, repeat every 20 minutes for 1 hour
- Prednisolone: adults 1 mg/kg, max 50 mg, children 1–2 mg/kg, max .40 mg
- Controlled oxygen (if available): target saturation 93–95% (children: 94–98%)

**CONTINUE TREATMENT** with SABA as needed

**ASSESS RESPONSE AT 1 HOUR** (or earlier)

**IMPROVING**
- **ASSESS FOR DISCHARGE**
  - Symptoms improved, not needing SABA
  - PEF improving, and >60-80% of personal best or predicted
  - Oxygen saturation >94% room air
  - Resources at home adequate

**ARRANGE at DISCHARGE**
- **Reliever**: continue as needed
- **Controller**: start (Box 3-4), or step up (Box 4-2)
- Check inhaler technique, adherence
- Prednisolone: continue, usually for 5–7 days
  (3–5 days for children)
- **Follow up**: within 2–7 days

**FOLLOW UP**
- **Reliever**: reduce to as-needed
- **Controller**: continue higher dose for short term (1–2 weeks) or long term (3 months), depending on background to exacerbation
- **Risk factors**: check and correct modifiable risk factors that may have contributed to exacerbation, including inhaler technique and adherence (Box 2-2, Box 3-8)
- **Action plan**: Is it understood? Was it used appropriately? Does it need modification?
A summary of discharge management.

This includes initiating or resuming controller therapy, advice about reducing SABA use, identifying the trigger for the exacerbation, checking self-management skills and written asthma action plan, and arranging a follow-up appointment within 2–7 days.
Diagnosis and initial treatment of asthma–COPD overlap syndrome
new chapter aimed at providing interim practical advice for primary care and non-respiratory specialists, and as a call to regulators that evidence is needed about treatment for patients with features of both asthma and COPD.

A syndromic approach to recognising asthma, COPD and asthma–COPD overlap syndrome (ACOS) in primary care.

Advice about safety considerations for initial treatment.

Practical tool: a stepwise approach to diagnosis and initial treatment of ACOS.

Recommendations for future research about ACOS.
<table>
<thead>
<tr>
<th>Asthma</th>
<th>COPD</th>
<th>ACOS</th>
<th>More compatible with asthma</th>
<th>More compatible with COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usually at childhood, but can present at any age</td>
<td>Usually age ≥40 years</td>
<td>Usually age ≥40 years, but onset of symptoms may have been in childhood or early adulthood</td>
<td>• Onset before age 20 years</td>
<td>• Onset after age 40 years</td>
</tr>
<tr>
<td>May vary from day to day; often triggered by either non-specific stimuli such as exercise and laughter, or exposure to specific inhaled allergens</td>
<td>Chronic usually continuous symptoms, particularly during exercise</td>
<td>Chronic respiratory symptoms including exertional dyspnea are present, but variability of symptoms may be prominent</td>
<td>• Variation in symptoms over minutes, hours, or days</td>
<td>• Persistence of symptoms despite treatment</td>
</tr>
<tr>
<td>Lung function may be normal between symptoms</td>
<td>Persistent airflow obstruction</td>
<td>Persistent airflow obstruction</td>
<td>• Good and bad days but always symptoms and exertional dyspnea</td>
<td>• Slowly improving symptoms</td>
</tr>
<tr>
<td>Current and/or historical variability of airflow obstruction, bronchodilator reversibility, BHR</td>
<td>Airflow obstruction may improve to some extent, but airflow obstruction defined as either post-bronchodilator PEV/FVC &lt;0.7 or LLN persists</td>
<td>Airflow obstruction is not fully reversible, but often with current or historical bronchodilator reversibility, and/or BHR</td>
<td>• Good and bad days but always symptoms and exertional dyspnea</td>
<td>• Slowly improving symptoms</td>
</tr>
<tr>
<td>Often improves with treatment and remains stable over time, but fixed airflow obstruction can develop in a subset of asthmatics</td>
<td>Generally slowly progressive over years despite treatment</td>
<td>Generally slowly progressive decline over years, but to lesser extent than in COPD alone</td>
<td>• Good and bad days but always symptoms and exertional dyspnea</td>
<td>• Slowly improving symptoms</td>
</tr>
<tr>
<td>Many patients have a history of allergy and asthma in childhood and/or a family history of asthma</td>
<td>History of exposure to noxious particles and gases (mainly tobacco smoke and biomass fuels)</td>
<td>Frequently a history of allergy and asthma in childhood and/or a family history of asthma, and/or exposure to noxious particles and gases (mainly tobacco smoke and biomass fuels)</td>
<td>• Good and bad days but always symptoms and exertional dyspnea</td>
<td>• Slowly improving symptoms</td>
</tr>
<tr>
<td>Usually normal</td>
<td>Often shows hyperinflation</td>
<td>Often shows hyperinflation</td>
<td>• Good and bad days but always symptoms and exertional dyspnea</td>
<td>• Slowly improving symptoms</td>
</tr>
<tr>
<td>Exacerbations occur, but can be considerably reduced by treatment</td>
<td>Exacerbations occur and are often related to co-morbidities. Exacerbation frequency can be reduced by treatment</td>
<td>Exacerbations occur more frequently than in asthma or COPD alone, but are reduced by treatment. Co-morbidities can also contribute to exacerbations</td>
<td>• Good and bad days but always symptoms and exertional dyspnea</td>
<td>• Slowly improving symptoms</td>
</tr>
<tr>
<td>Characterized by increased numbers of eosinophils in blood, sputum, and bronchial mucosa</td>
<td>Characterized mainly by neutrophils in sputum lymphocytes in bronchial mucosa</td>
<td>Elevated numbers of eosinophils and/or neutrophils can be present in sputum</td>
<td>• Good and bad days but always symptoms and exertional dyspnea</td>
<td>• Slowly improving symptoms</td>
</tr>
</tbody>
</table>
Diagnosis and management of asthma in children aged 5 years and younger
Recurrent wheezing occurs in a large proportion of children 5 years and younger, typically with viral upper respiratory tract infections.

Deciding when this is the initial presentation of asthma is difficult.
Previous classifications of wheezing phenotypes (episodic wheeze and multiple-trigger wheeze; or transient wheeze, persistent wheeze and late onset wheeze) do not appear to identify stable phenotypes, and their clinical usefulness is uncertain.
A diagnosis of asthma in young children with a history of wheezing is more likely if they have:

- Wheezing or coughing that occurs with exercise, laughing or crying in the absence of an apparent respiratory infection.

- A history of other allergic disease (eczema or allergic rhinitis) or asthma in first-degree relatives.

- Clinical improvement during 2–3 months of controller treatment, and worsening after cessation.
Probability of asthma diagnosis or response to asthma treatment in children ≤5 years

Viral induced wheezing

Asthma

Symptom Pattern (may change over time)

- Symptoms (cough, wheeze, heavy breathing) for <10 days during upper respiratory tract infections
  - 2–3 episodes per year
  - No symptoms between episodes

- Symptoms (cough, wheeze, heavy breathing) for >10 days during upper respiratory tract infections
  - >3 episodes per year, or severe episodes and/or night worsening
  - Between episodes child may have occasional cough, wheeze or heavy breathing

- Symptoms (cough, wheeze, heavy breathing) for >10 days during upper respiratory tract infections
  - >3 episodes per year, or severe episodes and/or night worsening
  - Between episodes child has cough, wheeze or heavy breathing during play or when laughing
  - Atopy, or family history of asthma
A probability-based approach to diagnosis and treatment for wheezing children replaces previous classifications by wheezing phenotype.

Asthma control assessment includes both symptom control and risk factors.

New indications for a therapeutic trial of controller treatment
- Emphasis on checking diagnosis, inhaler technique and adherence before considering any step-up.
- Caution about risk of long-term side-effects with episodic parent-administered high dose ICS
- Action plans recommended for all children with asthma.
- Upper limits for OCS dosage.
- Revised oxygen saturation criterion for severe exacerbations, and revised saturation target for oxygen therapy.
- Nebulised magnesium sulphate an option for add-on therapy in severe exacerbations

Practical tools
- A template for assessment of symptom control and risk factors.
- A stepwise treatment figure, similar to that for older children and adults.
- A new flow-chart for assessment and management of acute flare-ups or wheezing episodes in young children.
Advice about primary prevention of asthma is now provided separately from advice about secondary prevention.

Specific recommendations aimed at reducing the risk of a child developing asthma:

- No exposure to tobacco smoke during pregnancy or after birth.
- Encourage vaginal delivery where possible.
- Discourage use of broad-spectrum antibiotics in the first year of life.
- Breast-feeding is advised, but for reasons other than prevention of allergy or asthma.
A summary is provided of evidence about potential factors contributing to the development of asthma, such as nutrition (breast-feeding, vitamin D, delayed introduction of solids, probiotics), exposure to allergens and pollutants, and the potential role of microbial effects, medications and psychosocial factors.
Final topics
Exhaled nitric oxide

The fractional concentration of exhaled nitric oxide (FENO) can be measured in some centers. FENO is increased in eosinophilic asthma but also in non-asthma conditions (e.g. eosinophilic bronchitis, atopy and allergic rhinitis), and has not been established as being useful for making a diagnosis of asthma.
FENO is decreased in smokers and during bronchoconstriction, and may be increased or decreased during viral respiratory infections.

In patients (mainly non-smokers) with non-specific respiratory symptoms, a finding of FENO >50 parts per billion (ppb) was associated with a good short-term response to ICS. However, there are no long-term studies examining the safety of withholding ICS in patients with low initial FENO.

Consequently, FENO cannot be recommended at present for deciding whether to treat patients with possible asthma with ICS.
Several cross-sectional studies have shown that low serum levels of Vitamin D are linked to impaired lung function, higher exacerbation frequency and reduced corticosteroid response. However, to date, Vitamin D supplementation has not been associated with improvement in asthma control or reduction in exacerbations.
Additional resources including pocket guides and slide kits are also available on the GINA website

(www.ginasthma.org).