Guideline Summary

Guideline Title

Global strategy for asthma management and prevention.

Bibliographic Source(s)

Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. Vancouver (WA): Global Initiative for Asthma (GINA); 2012. 110 p. [445 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. Vancouver (WA): Global Initiative for Asthma (GINA); 2011. 106 p.

In an effort to keep the GINA Workshop report as up to date as possible, a GINA Science Committee has been established to review published research on asthma management and prevention, and to post yearly updates on the GINA Web site. See the GINA Web site for archived versions of the GINA guidelines.

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Scope

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Disease/Condition(s)

Asthma

Guideline Category

Counseling
Diagnosis
Evaluation
Management
Prevention
Treatment

Clinical Specialty

Allergy and Immunology
Emergency Medicine
Family Practice
Internal Medicine

Pediatrics
Preventive Medicine
Pulmonary Medicine

Intended Users

Advanced Practice Nurses
Allied Health Personnel
Emergency Medical Technicians/Paramedics
Health Care Providers
Health Plans
Managed Care Organizations
Nurses
Pharmacists
Physician Assistants
Physicians
Public Health Departments
Respiratory Care Practitioners

Guideline Objective(s)

To produce recommendations for the management of asthma based on the best scientific information available

Target Population

Adults, adolescents, and children (primarily those over 5 years of age) with asthma in countries throughout the world

Note: In 2008, a number of pediatric experts developed a report which focused on asthma care in children 5 years and younger. See the National Guideline Clearinghouse (NGC) summary of the Global Initiative for Asthma (GINA) titled Global strategy for the diagnosis and management of asthma in children 5 years and younger.

Interventions and Practices Considered

Diagnosis/Classification

1. Clinical diagnosis
   - Medical history and physical examination
   - Consideration of signs and symptoms
   - Measurements of lung function via spirometry or peak expiratory flow
   - Measurement of airway responsiveness
   - Measurements of allergic status
2. Consideration of diagnostic challenges and differential diagnosis, including children 5 years and younger, the elderly, as well as occupational asthma
3. Classification of asthma based on level of control (clinical control, frequency of symptoms, limitations, need for reliever treatment)

Management/Prevention/Treatment

1. Development of patient-doctor relationship
   - Patient education, including self-management
   - Personal asthma action plan
2. Identification and reduction of risk factors, including air pollutants and occupational exposures
3. Assessment of asthma control
4. Treatment steps for achieving control:
   - Step 1: As-needed reliever medication
   - Step 2: Reliever medication plus a single controller
   - Step 3: Reliever medication plus one or two controllers
   - Step 4: Reliever medication plus two or more controllers
   - Step 5: Reliever medication plus additional controller options
5. Monitoring to maintain control
   - Stepping down treatment when asthma is controlled
   - Stepping up treatment in response to loss of control
   - Management of difficult-to-treat asthma
   - Thermoplasty
6. Management of asthma exacerbations
   - Assessment of severity
   - Management in community settings with bronchodilators and glucocorticosteroids
   - Management in acute care settings with oxygen, rapid-acting inhaled β_2-agonists, epinephrine, and additional bronchodilators
   - Consideration of discharge versus hospitalization
7. Consideration of special circumstances, including pregnancy; obesity; surgery; rhinitis, sinusitis, and nasal polyps;

occupational asthma; respiratory infections; gastroesophageal reflux; aspirin-induced asthma; and anaphylaxis

Major Outcomes Considered

- Frequency and severity of asthma symptoms, including nocturnal
- Requirement for rescue medications
- Changes in lung function: peak expiratory flow (PEF) or forced expiratory volume in 1 second (FEV_1)
- Frequency of emergency department visits and hospitalization
- Morbidity, including quality of life, due to exacerbations and chronic symptoms
- Mortality
- Socioeconomic burden

Methodology

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Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

To produce the updated documents a PubMed search was done using search fields established by the Committee: 1) asthma, All Fields, All ages, only items with abstracts, Clinical Trial, Human, sorted by Authors; and 2) asthma AND systematic, All fields, ALL ages, only items with abstracts, Human, sorted by author. The first search included publications for July 1–December 30 for review by the Committee during the American Thoracic Society (ATS) meeting. The second search included publications for January 1–June 30 for review by the Committee during the European Respiratory Society (ERS) meeting. (Publications that appeared after June 30 were considered in the first phase of the following year.) To ensure publications in peer review journals not captured by this search methodology were not missed, the respiratory community was invited to submit papers to the Chair, Global Initiative for Asthma (GINA) Science Committee providing an abstract and the full paper were submitted in (or translated into) English.

Number of Source Documents

For the 2012 update, between July 1, 2011 and June 30, 2012, 386 articles met the search criteria. Of the 386, 19 papers were identified to have an impact on the Global Initiative for Asthma (GINA) report.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)
Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Description of Levels of Evidence		
Evidence Category	**Sources of Evidence**	**Definition**
A	Randomized controlled trials (RCTs). Rich body of data.	Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B	RCTs. Limited body of data.	Evidence is from endpoints of intervention studies that include only a limited number of patients, posthoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C	Nonrandomized trials. Observational studies.	Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D	Panel consensus judgment	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses
Systematic Review

Description of the Methods Used to Analyze the Evidence

All members of the Committee receive a summary of citations and all abstracts. Each abstract is assigned to at least two Committee members, although all members are offered the opportunity to provide an opinion on all abstracts. Members evaluate the abstract or, up to her/his judgment, the full publication, and answer four specific written questions from a short questionnaire, and to indicate if the scientific data presented impacts on recommendations in the Global Initiative for Asthma (GINA) report. If so, the member is asked to specifically identify modifications that should be made.

Levels of evidence (see the "Rating Scheme for the Strength of the Evidence" field) are assigned to management recommendations where appropriate in Chapter 4, the Five Components of Asthma Management. Evidence levels are indicated in boldface type enclosed in parentheses after the relevant statement—e.g., (**Evidence A**).

The GINA Science Committee used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to examine use of anti-IgE, omalizumab, intravenous magnesium sulphate, and thermoplasty.

Methods Used to Formulate the Recommendations

Expert Consensus (Consensus Development Conference)

Description of Methods Used to Formulate the Recommendations

The entire Global Initiative for Asthma (GINA) Science Committee meets twice yearly to discuss each publication that was considered by at least 1 member of the Committee to potentially have an impact on the management of asthma. The full Committee then reaches a consensus on whether to include it in the report, either as a reference supporting current recommendations, or to change the report. In the absence of consensus, disagreements are decided by an open vote of the full Committee. Recommendations by the Committee for use of any medication are based on the best evidence available from the literature and not on labeling directives from government regulators. The Committee does not make recommendations for therapies that have not been approved by at least one regulatory agency.

For the 2012 update, between July 1, 2011 and June 30, 2012, 386 articles met the search criteria. Of the 386, 19 papers were identified to have an impact on the Global Initiative for Asthma (GINA) report. The changes prompted by these publications were posted on the website in December 2012. These were either: A) modifying, that is, changing the text or introducing a concept requiring a new recommendation to the report; or B) confirming, that is, adding to or replacing an existing reference.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Cost is recognized as an important barrier to the delivery of optimal evidence-based health care in almost every country, although its impact on patients' access to treatments varies widely both between and within countries. At the country or local level, health authorities make resource availability and allocation decisions affecting populations of asthma patients by considering the balance and tradeoffs between costs and clinical outcomes (benefits and harms), often in relation to competing public health and medical needs. Treatment costs must also be explicitly considered at each consultation between health care provider and patient to assure that cost does not present a barrier to achieving asthma control. Thus, those involved in the adaptation and implementation of asthma guidelines require an understanding of the cost and cost effectiveness of various management recommendations in asthma care. To this end, a short discussion of cost-effectiveness evaluation for asthma care, including utilization and cost of health care resources and determining the economic value of interventions in asthma, can be found in the original guideline document.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Not stated

Recommendations

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Major Recommendations

Levels of evidence (**A-D**) are defined at the end of the "Major Recommendations" field.

Definition and Overview

Key Points

- Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with

widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.
- Clinical manifestations of asthma can be controlled with appropriate treatment. When asthma is controlled, there should be no more than occasional flare-ups and severe exacerbations should be rare.
- Asthma is a problem worldwide, with an estimated 300 million affected individuals.
- Although from the perspective of both the patient and society the cost to control asthma seems high, the cost of not treating asthma correctly is even higher.
- A number of factors that influence a person's risk of developing asthma have been identified. These can be divided into host factors (primarily genetic) and environmental factors.
- The clinical spectrum of asthma is highly variable, and different cellular patterns have been observed, but the presence of airway inflammation remains a consistent feature.

Factors Influencing the Development and Expression of Asthma

Figure: Factors Influencing the Development and Expression of Asthma

Host Factors

- Genetic, e.g.,
  - Genes pre-disposing to atopy
  - Genes pre-disposing to airway hyperresponsiveness
- Obesity
- Sex

Environmental Factors

- Allergens
  - Indoor: Domestic mites, furred animals (dogs, cats, mice), cockroach allergen, fungi, molds, yeasts
  - Outdoor: Pollens, fungi, molds, yeasts
- Infections (predominantly viral)
- Occupational sensitizers*
- Tobacco smoke
  - Passive smoking
  - Active smoking
- Outdoor/indoor air pollution
- Diet

*See Figure 1-3 in the original guideline document for examples of agents causing asthma in selected occupations.

Diagnosis and Classification

Key Points

- A clinical diagnosis of asthma is often prompted by symptoms such as episodic breathlessness, wheezing, cough, and chest tightness.
- Measurements of lung function (spirometry or peak expiratory flow) provide an assessment of the severity of airflow limitation, its reversibility, and its variability, and provide confirmation of the diagnosis of asthma.
- Measurements of allergic status can help to identify risk factors that cause asthma symptoms in individual patients.
- Extra measures may be required to diagnose asthma in children 5 years and younger and in the elderly, and occupational asthma.
- For patients with symptoms consistent with asthma, but normal lung function, measurement of airway responsiveness may help establish the diagnosis.
- Asthma has been classified by severity in previous reports. However, asthma severity may change over time, and depends not only on the severity of the underlying disease but also its responsiveness to treatment.
- To aid in clinical management, a classification of asthma by level of control is recommended (see Figure 2-4 in the original guideline document).
- Clinical control of asthma is defined as:
  - No (twice or less/week) daytime symptoms
  - No limitations of daily activities, including exercise
  - No nocturnal symptoms or awakening because of asthma
  - No (twice or less/week) need for reliever treatment
  - Normal or near-normal lung function
  - No exacerbations

Refer to the original guideline document for more details about the diagnosis and classification of asthma.

Asthma Treatments

Key Points

- Medications to treat asthma can be classified as controllers or relievers. Controllers are medications taken daily on a long-term basis to keep asthma under clinical control chiefly through their anti-inflammatory effects. Relievers are medications used on an as-needed basis that act quickly to reverse bronchoconstriction and relieve its symptoms.
- Asthma treatment can be administered in different ways—inhaled, orally, or by injection. The major advantage of inhaled therapy is that drugs are delivered directly into the airways, producing higher local concentrations with significantly less risk

of systemic side effects.
- Inhaled glucocorticosteroids are the most effective controller medications currently available.
- Rapid-acting inhaled β_2-agonists are the medications of choice for relief of bronchoconstriction and for the pretreatment of exercise-induced bronchoconstriction, in both adults and children of all ages.
- Increased use, especially daily use, of reliever medication is a warning of deterioration of asthma control and indicates the need to reassess treatment.

Refer to the original guideline document for more information about specific controller and reliever medications, including information about asthma treatment in children.

Asthma Management and Prevention

Introduction

Asthma has a significant impact on individuals, their families, and society. Although there is no cure for asthma, appropriate management that includes a partnership between the physician and the patient/family most often results in the achievement of control.

The goals for successful management of asthma are to:

- Achieve and maintain control of symptoms
- Maintain normal activity levels, including exercise
- Maintain pulmonary function as close to normal as possible
- Prevent asthma exacerbations
- Avoid adverse effects from asthma medications
- Prevent asthma mortality

These goals for therapy reflect an understanding of asthma as a chronic inflammatory disorder of the airways characterized by recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. Clinical studies have shown that asthma can be effectively controlled by intervening to suppress and reverse the inflammation as well as treating the bronchoconstriction and related symptoms. Furthermore, early intervention to stop exposure to the risk factors that sensitized the airway may help improve the control of asthma and reduce medication needs. Experience in occupational asthma indicates that long-standing exposure to sensitizing agents may lead to irreversible airflow limitation.

The management of asthma can be approached in different ways, depending on the availability of the various forms of asthma treatment and taking into account cultural preferences and differing health care systems. The recommendations in this section reflect the current scientific understanding of asthma. They are based as far as possible on controlled clinical studies, and the text references many of these studies. For those aspects of the clinical management of asthma that have not been the subject of specific clinical studies, recommendations are based on literature review, clinical experience, and expert opinion of project members.

The recommendations for asthma management are laid out in five interrelated components of therapy:

1. Develop Patient/Doctor Partnership
2. Identify and Reduce Exposure to Risk Factors
3. Assess, Treat, and Monitor Asthma
4. Manage Asthma Exacerbations
5. Special Considerations

Component 1: Develop Patient/Doctor Relationship

Key Points

- The effective management of asthma requires the development of a partnership between the person with asthma and his or her health care professional(s) (and parents/caregivers, in the case of children with asthma).
- The aim of this partnership is guided self-management— that is, to give people with asthma the ability to control their own condition with guidance from health care professionals.
- The partnership is formed and strengthened as patients and their health care professionals discuss and agree on the goals of treatment, develop a personalized, written asthma action plan including self-monitoring, and periodically review the patient's treatment and level of asthma control.
- Education should be an integral part of all interactions between health care professionals and patients, and is relevant to asthma patients of all ages.
- Personal written asthma action plans help individuals with asthma make changes to their treatment in response to changes in their level of asthma control, as indicated by symptoms and/or peak expiratory flow, in accordance with written predetermined guidelines.

See "Essential Features of the Doctor-Patient Partnership to Achieve Guided Self-Management in Asthma" below.

This approach is called guided self-management and has been shown to reduce asthma morbidity in both adults (**Evidence A**) and children (**Evidence A**).

Figure: Essential Features of the Doctor-Patient Partnership to Achieve Guided Self-Management in Asthma

- Education
- Joint setting of goals
- Self-monitoring. The person with asthma is taught to combine assessment of asthma control with educated interpretation of key symptoms.
- Regular review of asthma control, treatment, and skills by a health care professional

- Written action plan. The person with asthma is taught which medications to use regularly and which to use as needed, and how to adjust treatment in response to worsening asthma control.
- Self-monitoring is integrated with written guidelines for both the long-term treatment of asthma and the treatment of asthma exacerbations.

Asthma Education

Education should be an integral part of all interactions between health care professionals and patients, and is relevant to asthma patients of all ages. Although the focus of education for small children will be on the parents and caregivers, children as young as 3 years of age can be taught simple asthma management skills. Adolescents may have some unique difficulties regarding adherence that may be helped through peer support group education in addition to education provided by the health care professional but regional issues and the developmental stage of the children may affect the outcomes of such programs.

The figure below outlines the key features and components of an asthma education program. The information and skills training required by each person may vary, and their ability or willingness to take responsibility similarly differs. Thus all individuals require certain core information and skills, but most education must be personalized and given to the person in a number of steps. Social and psychological support may also be required to maintain positive behavioral change.

Figure: Education and the Patient/Doctor Partnership

Goal: To provide the person with asthma, their family, and other caregivers with suitable information and training so that they can keep well and adjust treatment according to a medication plan developed with the health care professional.

Key components:

- Focus on the development of the partnership
- Acceptance that this is a continuing process
- A sharing of information
- Full discussion of expectations
- Expression of fears and concerns

Provide specific information, training, and advice about:

- Diagnosis
- Difference between "relievers" and "controllers"
- Potential side effects of medications
- Use of inhaler devices
- Prevention of symptoms and attacks
- Signs that suggest asthma is worsening and actions to take
- Monitoring control of asthma
- How and when to seek medical attention

The person then requires:

- A written asthma action plan
- Regular supervision, revision, reward, and reinforcement

Good communication is essential as the basis for subsequent good compliance/adherence (**Evidence B**). Key factors that facilitate good communication are:

- A congenial demeanor (friendliness, humor, and attentiveness)
- Engaging in interactive dialogue
- Giving encouragement and praise
- Empathy, reassurance, and prompt handling of any concerns
- Giving of appropriate (personalized) information
- Eliciting shared goals
- Feedback and review

Teaching health care professionals to improve their communication skills can result in measurably better outcomes–including increased patient satisfaction, better health, and reduced use of health care–and these benefits may be achieved without any increase in consultation times. Lay educators can be recruited and trained to deliver a discrete area of respiratory care (for example, asthma self-management education) with comparable outcomes to those achieved by primary care based practice nurses (**Evidence B**). See the original guideline document for more information about developing the patient/doctor relationship.

Personal Written Asthma Action Plans

Personal written asthma action plans help individuals with asthma make changes to their treatment in response to changes in their level of asthma control, as indicated by symptoms and/or peak expiratory flow, in accordance with written predetermined guidelines.

The effects were greatest where the intervention involved each of the following elements: education, self-monitoring, regular review, and patient-directed self-management using a written asthma action plan (**Evidence A**). Within these studies, the effects were also greater when the action plans themselves both stepped up inhaled glucocorticosteroids and added oral glucocorticosteroids, and for peak flow-based plans, when they were based on personal best rather than percent predicted peak flow. Patients experience a one-third to two-thirds reduction in hospitalizations, emergency room visits, unscheduled visits to the doctor for asthma, missed days of work, and nocturnal wakening. It has been estimated that the implementation of a self-management program in 20 patients prevents one hospitalization, and successful completion of such a program by eight patients prevents one emergency department visit. Less intensive interventions that involve self-management education but not a written plan are less effective. The efficacy is similar regardless of whether patients self-adjust their medications according to an individual written plan or adjustments of

medication are made by a doctor (**Evidence B**).

The Education of Others

Specific advice about asthma and its management should be offered to school teachers and physical education instructors, and several organizations produce materials for this purpose. Schools may need advice on improving the environment and air quality for children with asthma. It is also helpful for employers to have access to clear advice about asthma. Most occupations are as suitable for those with asthma as for those without, but there may be some circumstances where caution is needed. See the original guideline document for more information.

Component 2: Identify and Reduce Exposure to Risk Factors

Key Points

- Pharmacologic intervention to treat established asthma is highly effective in controlling symptoms and improving quality of life. However, measures to prevent the development of asthma, asthma symptoms, and asthma exacerbations by avoiding or reducing exposure to risk factors should be implemented wherever possible.
- At this time, few measures can be recommended for prevention of asthma because the development of the disease is complex and incompletely understood.
- Asthma exacerbations may be caused by a variety of risk factors, sometimes referred to as "triggers," including allergens, viral infections, pollutants, and drugs.
- Reducing a patient's exposure to some categories of risk factors improves the control of asthma and reduces medication needs.
- The early identification of occupational sensitizers and the removal of sensitized patients from any further exposure are important aspects of the management of occupational asthma.

Introduction

Although pharmacologic intervention to treat established asthma is highly effective in controlling symptoms and improving quality of life, measures to prevent the development of asthma and asthma symptoms by avoiding or reducing exposure to risk factors should be implemented wherever possible. At this time, few measures can be recommended for prevention of asthma because the development of the disease is complex and incompletely understood. This area is a focus of intensive research, but until such measures are developed prevention efforts must primarily focus on prevention of asthma symptoms and attacks.

Asthma Prevention

Measures to prevent asthma may be aimed at the prevention of allergic sensitization (i.e., the development of atopy, likely to be most relevant prenatally and perinatally), or the prevention of asthma development in sensitized people. Other than preventing tobacco exposure both *in utero* and after birth, there are no proven and widely accepted interventions that can prevent the development of asthma.

Exposure to tobacco smoke both prenatally and postnatally is associated with measurable harmful effects, including effects on lung development and a greater risk of developing wheezing illnesses in childhood. Although there is little evidence that maternal smoking during pregnancy has an effect on allergic sensitization, passive smoking increases the risk of allergic sensitization in children. Both prenatal and postnatal maternal smoking is problematic. Pregnant women and parents of young children should be advised not to smoke (**Evidence B**).

See the original guideline document for a discussion of other topics related to asthma prevention.

Prevention of Asthma Symptoms and Exacerbations

Asthma exacerbations may be caused by a variety of factors, sometimes referred to as "triggers," including allergens, viral infections, pollutants, and drugs. Reducing a patient's exposure to some of these categories of risk factors (e.g., smoking cessation, reducing exposure to secondhand smoke, reducing or eliminating exposure to occupational agents known to cause symptoms, and avoiding foods/additives/drugs known to cause symptoms) improves the control of asthma and reduces medication needs. In the case of other factors (e.g., allergens, viral infections and pollutants), measures where possible should be taken to avoid these. Because many asthma patients react to multiple factors that are ubiquitous in the environment, avoiding these factors completely is usually impractical and very limiting to the patient. Thus, medications to maintain asthma control have an important role because patients are often less sensitive to these risk factors when their asthma is under good control. Patients with well-controlled asthma are less likely to experience exacerbations than those whose asthma is not well-controlled.

Indoor Allergens

Domestic Mites

No single measure is likely to reduce exposure to mite allergens, and single chemical and physical methods aimed at reducing mite allergens are not effective in reducing asthma symptoms in adults (**Evidence A**). One study showed some efficacy of mattress encasing at reducing airway hyperresponsiveness in children (**Evidence B**). An integrated approach including barrier methods, dust removal and reduction of microhabitats favorable to mites has been suggested, although its efficacy at reducing symptoms has only been confirmed in deprived populations with a specific environmental exposure (**Evidence B**) and a recommendation for its widespread use cannot be made.

Cockroaches

Avoidance measures for cockroaches include eliminating suitable environments (restricting havens by caulking and sealing cracks in the plasterwork and flooring, controlling dampness, and reducing the availability of food), restricting access (sealing entry sources such as around paperwork and doors), chemical control, and traps. However, these measures are only partially effective in removing residual allergens (**Evidence C**).

Indoor Air Pollutants

The most important measure in controlling indoor air pollutants is to avoid passive and active smoking. Secondhand smoke increases the frequency and severity of symptoms in children with asthma. Parents/caregivers of children with asthma should be advised not to smoke and not to allow smoking in rooms their children use. In addition to increasing asthma symptoms and causing long-term impairments in lung function, active cigarette smoking reduces the efficacy of inhaled and systemic glucocorticosteroids (**Evidence B**). Asthma patients who smoke, and are not treated with inhaled glucocorticosteroids, have a greater decline in lung function than asthmatic patients who do not smoke. Smoking cessation needs to be vigorously encouraged for all patients with asthma who smoke.

Outdoor Air Pollutants

Avoidance of unfavorable environmental conditions is usually unnecessary for patients whose asthma is controlled. For patients with asthma that is difficult to control, practical steps to take during unfavorable environmental conditions include avoiding strenuous physical activity in cold weather, low humidity, or high air pollution; avoiding smoking and smoke-filled rooms; and staying indoors in a climate-controlled environment.

Occupational Exposures

The early identification of occupational sensitizers and the removal of sensitized patients from any further exposure are important aspects of the management of occupational asthma (**Evidence B**). Once a patient has become sensitized to an occupational allergen, the level of exposure necessary to induce symptoms may be extremely low, and resulting exacerbations become increasingly severe. Attempts to reduce occupational exposure have been successful especially in industrial settings, and some potent sensitizers, such as soy castor bean, have been replaced by less allergenic substances (**Evidence B**). Prevention of latex sensitization has been made possible by the production of hypoallergenic gloves, which are powder free and have a lower allergen content (**Evidence C**). Although more expensive than untreated gloves, they are cost effective.

Food and Food Additives

When food allergy is demonstrated, food allergen avoidance can reduce asthma exacerbations (**Evidence D**).

Drugs

Some medications can exacerbate asthma. Aspirin and other nonsteroidal anti-inflammatory drugs can cause severe exacerbations and should be avoided in patients with a history of reacting to these agents. There is some evidence that exposure to acetaminophen increases the risk of asthma and wheezing in both children and adults but further studies are needed.

β-blocker drugs administered orally or intraocularly may exacerbate bronchospasm (**Evidence A**) and close medical supervision is essential when these are used by patients with asthma. β-blockers have a proven benefit in the management of patients with acute coronary syndromes and for secondary prevention of coronary events. Data suggest that patients with asthma who receive newer more cardio-selective β-blockers within 24 hours of hospital admission for an acute coronary event have lower in-hospital mortality rates.

Obesity

Increases in body mass index (BMI) have been associated with increased prevalence of asthma. Weight reduction in obese patients with asthma, including by bariatric surgery, has been has been demonstrated to improve lung function, symptoms, morbidity, and health status (**Evidence B**).

See the original guideline document for a more detailed discussion of risk factors, including indoor and outdoor allergens, indoor and outdoor air pollutants, occupational exposures, food and food additives, drugs, influenza vaccination, obesity, emotional stress, and other factors that may exacerbate asthma.

Component 3: Assess, Treat, and Monitor Asthma

Key Points

- The goal of asthma treatment, to achieve and maintain clinical control, can be reached in a majority of patients with a pharmacologic intervention strategy developed in partnership between the patient/family and the doctor.
- Treatment should be adjusted in a continuous cycle driven by the patient's asthma control status. If asthma is not controlled on the current treatment regimen, treatment should be stepped up until control is achieved. When control is maintained for at least three months, treatment can be stepped down.
- In treatment-naïve patients with persistent asthma, treatment should be started at *Step 2*, or, if very symptomatic (uncontrolled), at *Step 3*. For *Steps 2* through *5*, a variety of controller medications are available.
- At each treatment step, reliever medication should be provided for quick relief of symptoms as needed.
- Ongoing monitoring is essential to maintain control and to establish the lowest step and dose of treatment to minimize cost and maximize safety.

Introduction

The goal of asthma treatment, to achieve and maintain clinical control, can be reached in the majority of patients with a pharmacologic intervention strategy developed in partnership between the patient/family and the doctor. Each patient is assigned to one of five "treatment steps" depending on their current level of control and treatment is adjusted in a continuous cycle driven by changes in their asthma control status. This cycle involves:

- Assessing Asthma Control
- Treating to Achieve Control
- Monitoring to Maintain Control

In this Component, this cycle is described for long-term treatment of asthma. Treatment for exacerbations is detailed in Component 4.

Assessing Asthma Control

Each patient should be assessed to establish his or her current treatment regimen, adherence to the current regimen, and level of asthma control. A simplified scheme for recognizing controlled, partly controlled, and uncontrolled asthma in a given week is provided in the figure below. This is a working scheme based on current opinion and has not been validated. Several composite control measures (e.g., Asthma Control Test, Asthma Control Questionnaire, Asthma Therapy Assessment Questionnaire, Asthma Control Scoring System) have been developed and are being validated for various applications, including use by health care providers to assess the state of control of their patients' asthma and by patients for self-assessments as part of a written personal asthma action plan. Uncontrolled asthma may progress to the point of an exacerbation, and immediate steps, described in Component 4, should be taken to regain control.

Figure: Levels of Asthma Control

A. Assessment of Current Clinical Control (preferably over 4 weeks)

Characteristic	Controlled (all of the following)	Partly Controlled (any measure present)	Uncontrolled
Daytime symptoms	None (twice or less/week)	More than twice/week	Three or more features of partly controlled asthma*†
Limitations of activities	None	Any	
Nocturnal symptoms/awakening	None	Any	
Need for reliever/rescue treatment	None (twice or less/week)	More than twice/week	
Lung function (PEF or FEV_1)‡	Normal	<80% predicted or personal best (if known)	

B. Assessment of Future Risk (risk of exacerbations, instability, rapid decline in lung function, side-effects)

Features that are associated with increased risk of adverse events in the future include:
Poor clinical control, frequent exacerbations in past year*, ever admission to critical care for asthma, low FEV_1, exposure to cigarette smoke, high dose medications.

FEV_1, forced expiratory volume in 1 second; PEF, peak expiratory flow

*Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.

†By definition, an exacerbation in any week makes that an uncontrolled asthma week.

‡Without administration of bronchodilator. Lung function is not a reliable test for children 5 years and younger.

Treating to Achieve Control

The patient's current level of asthma control and current treatment determine the selection of pharmacologic treatment. For example, if asthma is not controlled on the current treatment regimen, treatment should be stepped up until control is achieved. If control has been maintained for at least three months, treatment can be stepped down with the aim of establishing the lowest step and dose of treatment that maintains control (see "Monitoring to Maintain Control," below.) If asthma is partly controlled, an increase in treatment should be considered, subject to whether more effective options are available (e.g., increased dose or an additional treatment), safety and cost of possible treatment options, and the patient's satisfaction with the level of control achieved. The scheme presented in Figure 4.3-2 in the original guideline document is based upon these principles, but the range and sequence of medications used in each clinical setting will vary depending on local availability (for cost or other reasons), acceptability, and preference.

Treatment Steps for Achieving Control

Step 1: As-Needed Reliever Medication

Step 1 treatment with an as-needed reliever medication is reserved for untreated patients with occasional daytime symptoms (cough, wheeze, dyspnea occurring twice or less per week, or less frequently if nocturnal) of short duration (lasting only a few hours) comparable with controlled asthma (see figure above). Between episodes, the patient is asymptomatic with normal lung function and there is no nocturnal awakening. When symptoms are more frequent, and/or worsen periodically, patients require regular controller treatment (see *Steps 2* or higher) in addition to as-needed reliever medication (**Evidence B**).

For the majority of patients in *Step 1*, a rapid-acting inhaled β_2-agonist is the recommended reliever treatment (**Evidence A**). An inhaled anticholinergic, short-acting oral β_2-agonist, or short-acting theophylline may be considered as alternatives, although they have a slower onset of action and higher risk of side effects (**Evidence A**).

Exercise-induced bronchoconstriction. Physical activity is an important cause of asthma symptoms for most asthma patients, and for some it is the only cause. However, exercise-induced bronchoconstriction often indicates that the patient's asthma is not well controlled, and stepping up controller therapy generally results in the reduction of exercise-related symptoms. For those patients who still experience exercise-induced bronchoconstriction despite otherwise well-controlled asthma, and for those in whom exercise-induced bronchoconstriction is the only manifestation of asthma, a rapid-acting inhaled β_2-agonist (short- or long-acting), taken prior to exercise or to relieve symptoms that develop after exercise, is recommended. A leukotriene modifier or cromone are alternatives (**Evidence A**). Training and sufficient warm-up also reduce the incidence and severity of exercise-induced

bronchoconstriction (**Evidence B**). Information on treatment of exercise-induced asthma in athletes can be found in a Joint Task Force Report prepared by the European Respiratory Society, the European Academy of Allergy and Clinical Immunology, and GA(2)LEN and the World Anti-Doping Agency website (http://www.wada-ama.org).

Step 2: Reliever Medication Plus a Single Controller

Treatment *Steps 2* through *5* combine an as-needed reliever treatment with regular controller treatment. At *Step 2*, a low-dose inhaled glucocorticosteroid is recommended as the initial controller treatment for asthma patients of all ages (**Evidence A**). Equivalent doses of inhaled glucocorticosteroids, some of which may be given as a single daily dose, are provided in Figure 3-1 in the original guideline document for adults and in Figure 3-4 in the original guideline document for children older than 5 years.

Alternative controller medications include leukotriene modifiers (**Evidence A**), appropriate particularly for patients who are unable or unwilling to use inhaled glucocorticosteroids, or who experience intolerable side effects such as persistent hoarseness from inhaled glucocorticosteroid treatment and those with concomitant allergic rhinitis (**Evidence C**).

Other options are available but not recommended for routine use as initial or first-line controllers in *Step 2*. Sustained-release theophylline has only weak anti-inflammatory and controller efficacy (**Evidence B**) and is commonly associated with side effects that range from trivial to intolerable. Cromones (nedocromil sodium and sodium cromoglycate) have comparatively low efficacy, though a favorable safety profile (**Evidence A**).

Step 3: Reliever Medication Plus One or Two Controllers

At *Step 3*, the recommended option for children, adolescents and adults is to combine a low-dose of inhaled glucocorticosteroid with an inhaled long-acting β_2-agonist, either in a combination inhaler device or as separate components (**Evidence A**). Because of the additive effect of this combination, the low-dose of glucocorticosteroid is usually sufficient, and need only be increased if control is not achieved within 3 or 4 months with this regimen (**Evidence A**). The long-acting β_2-agonist formoterol, which has a rapid onset of action whether given alone or in combination inhaler with budesonide, has been shown to be as effective as short-acting β_2-agonist in acute asthma exacerbation. However its use as monotherapy as a reliever medication is strongly discouraged since it must always be used in association with an inhaled glucocorticosteroid.

For all children but particularly those 5 years and younger, combination therapy has been less well studied and the addition of a long-acting β_2-agonist may not be as effective as increasing the dose of inhaled glucocorticosteroids in reducing exacerbations.

If a combination inhaler containing formoterol and budesonide is selected, it may be used for both rescue and maintenance. This approach has been shown to result in reductions in exacerbations and improvements in asthma control in adults and adolescents at relatively low doses of treatment (**Evidence A**). Whether this approach can be employed with other combinations of controller and reliever requires further study.

Another option for both adults and children, but the one recommended for children, is to increase to a medium-dose of inhaled glucocorticosteroids (**Evidence A**). For patients of all ages on medium- or high-dose of inhaled glucocorticosteroid delivered by a pressurized metered-dose inhaler (MDI), use of a spacer device is recommended to improve delivery to the airways, reduce oropharyngeal side effects, and reduce systemic absorption (**Evidence A**).

Another option at *Step 3* is to combine a low-dose inhaled glucocorticosteroid with leukotriene modifiers (**Evidence A**). Alternatively, the use of sustained-release theophylline given at low-dose may be considered (**Evidence B**). These options have not been fully studied in children 5 years and younger.

Step 4: Reliever Medication Plus Two or More Controllers

The selection of treatment at *Step 4* depends on prior selections at *Steps 2* and *3*. However, the order in which additional medications should be added is based, as far as possible, upon evidence of their relative efficacy in clinical trials. Where possible, patients who are not controlled on *Step 3* treatments should be referred to a health professional with expertise in the management of asthma for investigation of alternative diagnoses and/or causes of difficult-to-treat asthma.

The preferred treatment at *Step 4* is to combine a medium- or high-dose of inhaled glucocorticosteroid with a long-acting inhaled β_2-agonist. However, in most patients, the increase from a medium- to a high-dose of inhaled glucocorticosteroid provides relatively little additional benefit (**Evidence A**), and the high-dose is recommended only on a trial basis for 3 to 6 months when control cannot be achieved with medium-dose inhaled glucocorticosteroid combined with a long-acting β_2-agonist and/or a third controller (e.g., leukotriene modifiers or sustained-release theophylline) (**Evidence B**). Prolonged use of high-dose inhaled glucocorticosteroids is also associated with increased potential for adverse effects. At medium- and high-doses, twice-daily dosing is necessary for most but not all inhaled glucocorticosteroids (**Evidence A**). With budesonide, efficacy may be improved with more frequent dosing (four times daily) (**Evidence B**). (Refer to Figure 3-1 in the original guideline document for adults and Figure 3-4 in the original guideline document for children older than 5 years for recommendations on dosing and frequency for different inhaled glucocorticosteroids.)

Leukotriene modifiers as add-on treatment to medium-to high-dose inhaled glucocorticosteroids have been shown to provide benefit (**Evidence A**), but usually less than that achieved with the addition of a long-acting β_2-agonist (**Evidence A**). The addition of a low-dose of sustained-release theophylline to medium- or high-dose inhaled glucocorticosteroid and long-acting β_2-agonist may also provide benefit (**Evidence B**).

Step 5: Reliever Medication Plus Additional Controller Options

Addition of oral glucocorticosteroids to other controller medications may be effective (**Evidence D**) but is associated with severe side effects (**Evidence A**) and should only be considered if the patient's asthma remains severely uncontrolled on *Step 4* medications with daily limitation of activities and frequent exacerbations. Patients should be counseled about potential side effects and all other alternative treatments must be considered.

Addition of anti-immunoglobulin E (anti-IgE) treatment to other controller medications has been shown to improve control of allergic

asthma when control has not been achieved on combinations of other controllers including high-doses of inhaled or oral glucocorticosteroids (**Evidence B**).

Monitoring to Maintain Control

When asthma control has been achieved, ongoing monitoring is essential to maintain control and to establish the lowest step and dose of treatment necessary, which minimizes the cost and maximizes the safety of treatment. On the other hand, asthma is a variable disease, and treatment has to be adjusted periodically in response to loss of control as indicated by worsening symptoms or the development of an exacerbation.

Asthma control should be monitored by the health care professional and preferably also by the patient at regular intervals, using either a simplified scheme as presented in the "Levels of Asthma Control" figure, above, or a validated composite measure of control. The frequency of health care visits and assessments depends upon the patient's initial clinical severity, and the patient's training and confidence in playing a role in the on-going control of his or her asthma. Typically, patients are seen one to three months after the initial visit, and every three months thereafter. After an exacerbation, follow-up should be offered within two weeks to one month (**Evidence D**). General practitioners should be encouraged to assess asthma control at every visit, not just when the patient presents because of their asthma.

Duration and Adjustments to Treatment

For most classes of controller medications, improvement begins within days of initiating treatment, but the full benefit may only be evident after 3 or 4 months. In severe and chronically undertreated disease, this can take even longer.

The reduced need for medication once control is achieved is not fully understood, but may reflect the reversal of some of the consequences of long-term inflammation of the airways. Higher doses of anti-inflammatory medication may be required to achieve this benefit than to maintain it. Alternatively, the reduced need for medication might simply represent spontaneous improvement as part of the cyclical natural history of asthma. Rarely, asthma may go into remission particularly in children aged 5 years and younger and during puberty. Whatever the explanation, in all patients the minimum controlling dose of treatment must be sought through a process of regular follow-up and staged dose reductions.

At other times treatment may need to be increased either in response to loss of control or threat of loss of control (return of symptoms) or an acute exacerbation, which is defined as a more acute and severe loss of control that requires urgent treatment. (An approach to exacerbations is provided in Component 4 below.)

Stepping Down Treatment When Asthma Is Controlled

There is little experimental data on the optimal timing, sequence, and magnitude of treatment reductions in asthma, and the approach will differ from patient to patient depending on the combination of medications and the doses that were needed to achieve control. These changes should ideally be made by agreement between patient and health care professional, with full discussion of potential consequences including reappearance of symptoms and increased risk of exacerbations. Although further research on stepping down asthma treatment is needed, some recommendations can be made based on the current evidence:

- When inhaled glucocorticosteroids alone in medium-to-high-doses are being used, a 50% reduction in dose should be attempted at 3 month intervals (**Evidence B**).
- Where control is achieved at a low-dose of inhaled glucocorticosteroids alone, in most patient's treatment may be switched to once-daily dosing (**Evidence A**).
- When asthma is controlled with a combination of inhaled glucocorticosteroid and long-acting β_2-agonist, the preferred approach is to begin by reducing the dose of inhaled glucocorticosteroid by approximately 50% while continuing the long-acting β_2-agonist (**Evidence B**). If control is maintained, further reductions in the glucocorticosteroid should be attempted until a low-dose is reached, when the long-acting β_2-agonist may be stopped (**Evidence D**). An alternative is to switch the combination treatment to once-daily dosing. A second alternative is to discontinue the long-acting β_2-agonist at an earlier stage and substitute the combination treatment with inhaled glucocorticosteroid monotherapy at the same dose contained in the combination inhaler. However, this is more likely to lead to loss of asthma control (**Evidence B**).
- When asthma is controlled with inhaled glucocorticosteroids in combination with controllers other than long-acting β_2-agonists, the dose of inhaled glucocorticosteroid should be reduced by 50% until a low-dose of inhaled glucocorticosteroid is reached, then the combination treatment stopped as described above (**Evidence D**).
- Controller treatment may be stopped if the patient's asthma remains controlled on the lowest dose of controller and no recurrence of symptoms occurs for one year (**Evidence D**).

Stepping Up Treatment in Response to Loss of Control

Treatment has to be adjusted periodically in response to worsening control, which may be recognized by the minor recurrence or worsening of symptoms. Treatment options are as follows:

- Rapid-onset, short-acting or long-acting β_2-agonist bronchodilators. Repeated dosing with bronchodilators in this class provides temporary relief until the cause of the worsening symptoms passes. The need for repeated doses over more than one or two days signals the need for review and possible increase of controller therapy.
- In the context of asthma self-management studies, action plans in which the dose of inhaled glucocorticosteroids was at least doubled were associated with improved asthma outcomes and reduced health care utilisation. In placebo-controlled trials, temporarily doubling the dose of inhaled glucocorticosteroids was not effective (**Evidence A**), but an average interval of 5-7 days between the onset of worsening symptoms and increase of the inhaled glucocorticosteroid dose may have been a factor. There is emerging evidence that higher doses of inhaled glucocorticosteroid might be effective for preventing progression to severe exacerbation. Patients who quadrupled their dose of inhaled glucocorticosteroid after their peak flow fell were significantly less likely to require oral glucocorticosteroids. In adult patients with an acute deterioration, high-dose inhaled glucocorticosteroids have been demonstrated to be equivalent to a short course of oral glucocorticosteroids

(**Evidence A**). In these studies, the higher dose was maintained for seven to fourteen days. More research is needed in both adults and children to standardize the approach.

- Combination of inhaled glucocorticosteroids and rapid and long-acting β_2-agonist bronchodilator (e.g., formoterol) for combined relief and control. The use of the combination of a rapid and long-acting β_2-agonist (formoterol) and an inhaled glucocorticosteroid (budesonide) in a single inhaler both as a controller and reliever is effective in maintaining a high level of asthma control and reduces exacerbations requiring systemic glucocorticosteroids and hospitalization (**Evidence A**). The benefit in preventing exacerbations appears to be the consequence of early intervention at a very early stage of a threatened exacerbation since studies involving doubling or quadrupling doses of combination treatment once deterioration is established (for 2 or more days) show some benefit but results are inconsistent. Because there are no studies using this approach with other combinations of controller and relievers, other than budesonide/formoterol, the alternative approaches described in this section should be used for patients on other controller therapies.

For children (6 to 17 years) who have uncontrolled asthma despite the use of low-dose inhaled glucocorticosteroids, step-up therapy with long-acting β_2-agonist bronchodilator was significantly more likely to provide the best response than either step-up therapy with inhaled glucocorticosteroids or leukotriene receptor antagonist. However, many children had a best response to inhaled glucocorticosteroids or leukotriene receptor antagonist step-up therapy, highlighting the need to regularly monitor and appropriately adjust each child's asthma therapy.

Combination therapy with budesonide and formoterol used both as maintenance and rescue has been shown to reduce asthma exacerbations in children ages 4 years and older with moderate to severe asthma.

The usual treatment for an acute exacerbation is a high-dose of β_2-agonist and a burst of systemic glucocorticosteroids administered orally or intravenously. (Refer to Component 4 below for more information.)

Following treatment for an exacerbation of asthma, maintenance treatment can generally be resumed at previous levels unless the exacerbation was associated with a gradual loss of control suggesting chronic undertreatment. In this case, provided inhaler technique has been checked, a step-wise increase in treatment (either in dose or number of controllers) is indicated.

Difficult-to-Treat Asthma

Although the majority of asthma patients can obtain the targeted level of control, some patients will not do so even with the best therapy. Patients who do not reach an acceptable level of control at *Step 4* (reliever medication plus two or more controllers) can be considered to have difficult-to-treat asthma. These patients may have an element of poor glucocorticosteroid responsiveness, and require higher doses of inhaled glucocorticosteroids than are routinely used in patients whose asthma is easy to control. However, there is currently no evidence to support continuing these high doses of inhaled glucocorticosteroids beyond 6 months in the hope of achieving better control. Instead, dose optimization should be pursued by stepping down to a dose that maintains the maximal level of control achieved on the higher dose.

Because very few patients are completely resistant to glucocorticosteroids, these medications remain a mainstay of therapy for difficult-to-treat asthma, while additional diagnostic and generalized therapeutic options can and should also be considered:

- Confirm the diagnosis of asthma. In particular, the presence of chronic obstructive pulmonary disease (COPD) must be excluded. Vocal cord dysfunction must be considered.
- Investigate and confirm adherence with treatment. Incorrect or inadequate use of medications and inhalers remains the most common reason for failure to achieve good control. In patients with difficult-to-treat asthma, improved adherence and improved health outcomes can be achieved with a comprehensive concordance intervention.
- Consider smoking, current or past, and encourage complete cessation. A history of past tobacco smoking is associated with a reduced likelihood of complete asthma control, and this is only partly attributable to the presence of fixed airflow obstruction. In addition, current smoking reduces the effectiveness of inhaled and oral glucocorticosteroids. Counseling and smoking cessation programs should be offered to all asthma patients who smoke.
- Investigate the presence of comorbidities that may aggravate asthma. Chronic sinusitis, gastroesophageal reflux, and obesity/obstructive sleep apnea have been reported in higher percentages in patients with difficult-to-treat asthma. Psychological and psychiatric disorders should also be considered. If found, these comorbidities should be addressed and treated as appropriate, although the ability to improve asthma control by doing so remains unconfirmed.

When these reasons for lack of treatment response have been considered and addressed, a compromise level of control may need to be accepted and discussed with the patient to avoid futile over-treatment (with its attendant cost and potential for adverse effects). The objective is then to minimize exacerbations and need for emergency medical interventions while achieving as high a level of clinical control with as little disruption of activities and as few daily symptoms as possible. For these difficult-to-treat patients, frequent use of rescue medication is accepted, as is a degree of chronic lung function impairment.

Although lower levels of control are generally associated with an increased risk of exacerbations, not all patients with chronically impaired lung function, reduced activity levels, and daily symptoms have frequent exacerbations. In such patients, the lowest level of treatment that retains the benefits achieved at the higher doses of treatment should be employed. Reductions should be made cautiously and slowly at intervals not more frequent than 3 to 6 months, as carryover of the effects of the higher dose may last for several months and make it difficult to assess the impact of the dose reduction (**Evidence D**). Referral to a physician with an interest in and/or special focus on asthma may be helpful and patients may benefit from phenotyping into categories such as allergic, aspirin-sensitive, and/or eosinophilic asthma. Patients categorized as allergic might benefit from anti-IgE therapy, and leukotriene modifiers can be helpful for patients determined to be aspirin sensitive (who are often eosinophilic as well).

Thermoplasty

Grading of Recommendations Assessment, Development and Evaluation (GRADE) evidence technology was used to evaluate research on thermoplasty.

Question: "In adult patient whose asthma is uncontrolled despite recommended therapeutic regimens, does thermoplasty, compared

to placebo improve patient outcomes?"

The consensus recommendation:

For adult patients whose asthma remains uncontrolled despite application of this therapeutic paradigm, and referral to an asthma specialty center, bronchial thermoplasty is now a possible option in some countries. In this bronchoscopic treatment, airways are treated on three occasions with a localized radiofrequency pulse. The treatment, which itself is associated with asthma exacerbations in the months post bronchoscopy, results in a subsequent decrease in exacerbations. There are no significant effects on lung function or asthma symptoms. Extended follow-up on a small number of patients has provided some additional support for long-term safety of bronchial thermoplasty. However, longer-term follow-up of larger number of control and active patients is needed to assess effectiveness and caution should be used in selecting patients for this procedure.

Component 4: Manage Asthma Exacerbations

Key Points

- Exacerbations of asthma (asthma attacks or acute asthma) are episodes of progressive increase in shortness of breath, cough, wheezing, or chest tightness, or some combination of these symptoms.
- Exacerbations are characterized by decreases in expiratory airflow that can be quantified and monitored by measurement of lung function (peak expiratory flow rate [PEF] or forced expiratory volume in one second [FEV_1]).
- The primary therapies for exacerbations include the repetitive administration of rapid-acting inhaled bronchodilators, the early introduction of systemic glucocorticosteroids, and oxygen supplementation.
- The aims of treatment are to relieve airflow obstruction and hypoxemia as quickly as possible, and to plan the prevention of future relapses.
- Severe exacerbations are potentially life threatening, and their treatment requires close supervision. Most patients with severe asthma exacerbations should be treated in an acute care facility. Patients at high risk of asthma-related death also require closer attention.
- Milder exacerbations, defined by a reduction in peak flow of less than 20%, nocturnal awakening, and increased use of short acting β_2-agonists can usually be treated in a community setting.

Introduction

Exacerbations of asthma (asthma attacks or acute asthma) are episodes of progressive increase in shortness of breath, cough, wheezing, or chest tightness, or some combination of these symptoms. Exacerbations usually have a progressive onset but a subset of patients (mostly adults) present more acutely. Respiratory distress is common. Exacerbations are characterized by decreases in expiratory airflow that can be quantified by measurement of lung function (PEF or FEV_1). These measurements are more reliable indicators of the severity of airflow limitation than is the degree of symptoms. The degree of symptoms may, however, be a more sensitive measure of the onset of an exacerbation because the increase in symptoms usually precedes the deterioration in peak flow rate. Still, a minority of patients perceive symptoms poorly, and may have a significant decline in lung function without a significant change in symptoms. This situation especially affects patients with a history of near-fatal asthma and also appears to be more likely in males. A clinically useful tool to assess the likelihood of asthma-related hospitalizations or emergency department visits in adults with severe or difficult to treat asthma has been described.

Strategies for treating exacerbations, though generalizable, are best adapted and implemented at a local level. Severe exacerbations are potentially life threatening, and their treatment requires close supervision. Patients with severe exacerbations should be encouraged to see their physician promptly or, depending on the organization of local health services, to proceed to the nearest clinic or hospital that provides emergency access for patients with acute asthma. Close objective monitoring (PEF) of the response to therapy is essential.

The primary therapies for exacerbations include—in the order in which they are introduced, depending on severity—repetitive administration of rapid-acting inhaled bronchodilators, early introduction of systemic glucocorticosteroids, and oxygen supplementation. The aims of treatment are to relieve airflow obstruction and hypoxemia as quickly as possible, and to plan the prevention of future relapses.

Patients at high risk of asthma-related death require closer attention and should be encouraged to seek urgent care early in the course of their exacerbations. These patients include those:

- With a history of near-fatal asthma requiring intubation and mechanical ventilation
- Who have had a hospitalization or emergency care visit for asthma in the past year
- Who are currently using or have recently stopped using oral glucocorticosteroids
- Who are not currently using inhaled glucocorticosteroids
- Who are overdependent on rapid-acting inhaled β_2-agonists, especially those who use more than one canister of salbutamol (or equivalent) monthly
- With a history of psychiatric disease or psychosocial problems, including the use of sedatives
- With a history of poor adherence with asthma medications and/or a written asthma action plan.

Response to treatment may take time and patients should be closely monitored using clinical as well as objective measurements. The increased treatment should continue until measurements of lung function (PEF or FEV_1) return to their previous best (ideally) or plateau, at which time a decision to admit or discharge can be made based upon these values. Patients who can be safely discharged will have responded within the first two hours, at which time decisions regarding patient disposition can be made.

Assessment of Severity

The severity of the exacerbation (see Figure 4.4-1 in the original guideline document) determines the treatment administered. Indices of severity, particularly PEF (in patients older than 5 years), pulse rate, respiratory rate, and pulse oximetry, should be

monitored during treatment.

Management—Community Settings

Most patients with severe asthma exacerbations should be treated in an acute care facility (such as a hospital emergency department) where monitoring, including objective measurement of airflow obstruction, oxygen saturation, and cardiac function, is possible. Milder exacerbations, defined by a reduction in peak flow of less than 20%, nocturnal awakening, and increased use of short acting β_2-agonists can usually be treated in a community setting. If the patient responds to the increase in inhaled bronchodilator treatment after the first few doses, referral to an acute care facility is not required, but further management under the direction of a primary care physician may include the use of systemic glucocorticosteroids. Patient education and review of maintenance therapy should also be undertaken.

Treatment

Bronchodilators

For mild to moderate exacerbations, repeated administration of rapid-acting inhaled β-agonists (2 to 4 puffs every 20 minutes for the first hour) is usually the best and most cost-effective method of achieving rapid reversal of airflow limitation. After the first hour, the dose of β-agonist required will depend on the severity of the exacerbation. Mild exacerbations respond to 2 to 4 puffs every 3 to 4 hours; moderate exacerbations will require 6 to 10 puffs every 1 or 2 hours. Treatment should also be titrated depending upon the individual patient's response, and if there is a lack of response or other concern about how the patient is responding, the patient should be referred to an acute care facility.

Many patients will be able to monitor their PEF after the initiation of increased bronchodilator therapy. Bronchodilator therapy delivered via an MDI, ideally with a spacer, produces at least an equivalent improvement in lung function as the same dose delivered via nebulizer. At the clinic level, this route of delivery is the most cost effective, provided patients are able to use an MDI. No additional medication is necessary if the rapid-acting inhaled β-agonist produces a complete response (PEF returns to greater than 80% of predicted or personal best) and the response lasts for 3 to 4 hours.

Glucocorticosteroids

Oral glucocorticosteroids (0.5 to 1 mg of prednisolone/kg or equivalent during a 24-hour period) should be used to treat exacerbations, especially if they develop after instituting the other short-term treatment options recommended for loss of control (see "Stepping up treatment in response to loss of control" in Component 3 above and in the original guideline document). If patients fail to respond to bronchodilator therapy, as indicated by persistent airflow obstruction, prompt transfer to an acute care setting is recommended, especially if they are in a high risk group.

Management—Acute Care Settings

Severe exacerbations of asthma are life-threatening medical emergencies, treatment of which is often most safely undertaken in an emergency department. The algorithm in Figure 4.4-2 in the original guideline document illustrates the approach to acute care-based management of exacerbations.

Assessment

A brief history and physical examination pertinent to the exacerbation should be conducted concurrently with the prompt initiation of therapy. The history should include severity and duration of symptoms, including exercise limitation and sleep disturbance; all current medications, including dose (and device) prescribed, dose usually taken, dose taken in response to the deterioration, and the patient's response (or lack thereof) to this therapy; time of onset and cause of the present exacerbation; and risk factors for asthma-related death.

The physical examination should assess exacerbation severity by evaluating the patient's ability to complete a sentence, pulse rate, respiratory rate, use of accessory muscles, and other signs detailed in Figure 4.4-2 in the original guideline document. Any complicating factors should be identified (e.g., pneumonia, atelectasis, pneumothorax, or pneumomediastinum). Functional assessments such as PEF or FEV_1 and arterial oxygen saturation measurements are strongly recommended as physical examination alone may not fully indicate the severity of the exacerbation, particularly the degree of hypoxemia. Without unduly delaying treatment, a baseline PEF or FEV_1 measurement should be made before treatment is initiated, although spirometry may not be possible in children with acute asthma. Subsequent measurements should be made at intervals until a clear response to treatment has occurred.

Oxygen saturation should be closely monitored, preferably by pulse oximetry. This is especially useful in children because objective measurements of lung function may be difficult. Oxygen saturation in children should normally be greater than 95%, and oxygen saturation less than 92% is a good predictor of the need for hospitalization (**Evidence C**).

In adults a chest x-ray is not routinely required, but should be carried out if a complicating cardiopulmonary process is suspected, in patients requiring hospitalization, and in those not responding to treatment where a pneumothorax may be difficult to diagnose clinically. Similarly, in children routine chest x-rays are not recommended unless there are physical signs suggestive of parenchymal disease.

Although arterial blood gas measurements are not routinely required, they should be completed in patients with a PEF of 30% to 50% predicted, those who do not respond to initial treatment, or when there is concern regarding deterioration. The patient should continue on supplemental oxygen while the measurement is made. A partial pressure of oxygen in arterial blood (PaO_2) <60 mm Hg (8 kPa) and a normal or increased partial pressure of carbon dioxide in the arterial blood ($PaCO_2$) (especially >45 mm Hg, 6 kPa) indicates the presence of respiratory failure.

Treatment

The following treatments are usually administered concurrently to achieve the most rapid resolution of the exacerbation:

Oxygen

To achieve arterial oxygen saturation of 90% (95% in children), oxygen should be administered by nasal cannulae, by mask, or rarely by head box in some infants. For severe asthma exacerbations, controlled oxygen therapy using pulse oximetry to maintain oxygen saturation at 90 – 93% is associated with better physiological outcomes, compared to high flow 100% oxygen therapy. Oxygen therapy should be titrated against pulse oximetry to maintain a satisfactory oxygen saturation. However, oxygen should not be withheld if oximetry is not available.

Rapid-Acting Inhaled β_2-Agonists

Rapid-acting inhaled β_2-agonists should be administered at regular intervals (**Evidence A**). The most cost effective and efficient delivery is by meter dose inhaler and a spacer device. Although most rapid-acting β_2-agonists have a short duration of effect, the long-acting bronchodilator formoterol, which has both a rapid onset of action and a long duration of effect, has been shown to be equally effective without increasing side effects, though it is considerably more expensive. The importance of this feature of formoterol is that it provides support and reassurance regarding the use of a combination of formoterol and budesonide early in asthma exacerbations.

A modestly greater bronchodilator effect has been shown with levalbuterol compared to racemic albuterol in both adults and children with an asthma exacerbation. In a large study of acute asthma in children, and in adults not previously treated with glucocorticosteroids, levalbuterol treatment resulted in lower hospitalization rates compared to racemic albuterol treatment, but in children the length of hospital stay was no different.

A reasonable approach to inhaled therapy in exacerbations would be the initial use of continuous therapy, followed by intermittent on-demand therapy for hospitalized patients. There is no evidence to support the routine use of intravenous β_2-agonists in patients with severe asthma exacerbations.

Epinephrine

A subcutaneous or intramuscular injection of epinephrine (adrenaline) may be indicated for acute treatment of anaphylaxis and angioedema, but is not routinely indicated during asthma exacerbations.

Additional Bronchodilators

Ipratropium Bromide

A combination of nebulized β_2-agonist with an anticholinergic (ipratropium bromide) may produce better bronchodilation than either drug alone (**Evidence B**) and should be administered before methylxanthines are considered. Combination β_2-agonist/anticholinergic therapy is associated with lower hospitalization rates (**Evidence A**) and greater improvement in PEF and FEV_1 (**Evidence B**). Similar data have been reported in the pediatric literature (**Evidence A**). However, once children with asthma are hospitalized following intensive emergency department treatment, the addition of nebulized ipratropium bromide to nebulized β_2-agonist and systemic glucocorticosteroids appears to confer no extra benefit.

Theophylline

In view of the effectiveness and relative safety of rapid-acting β_2-agonists, theophylline has a minimal role in the management of acute asthma. Its use is associated with severe and potentially fatal side effects, particularly in those on long-term therapy with sustained-release theophylline, and their bronchodilator effect is less than that of β_2-agonists. The benefit as add-on treatment in adults with severe asthma exacerbations has not been demonstrated. However, in one study of children with near-fatal asthma, intravenous theophylline provided additional benefit to patients also receiving an aggressive regimen of inhaled and intravenous β_2-agonists, inhaled ipratropium bromide, and intravenous systemic glucocorticosteroids.

Systemic Glucocorticosteroids

Systemic glucocorticosteroids speed resolution of exacerbations and should be utilized in the all but the mildest exacerbations (**Evidence A**), especially if:

- The initial rapid-acting inhaled β_2-agonist therapy fails to achieve lasting improvement
- The exacerbation develops even though the patient was already taking oral glucocorticosteroids
- Previous exacerbations required oral glucocorticosteroids

Oral glucocorticosteroids are usually as effective as those administered intravenously and are preferred because this route of delivery is less invasive and less expensive. If vomiting has occurred shortly after administration of oral glucocorticosteroids, then an equivalent dose should be re-administered intravenously. In patients discharged from the emergency department, intramuscular administration may be helpful, especially if there are concerns about compliance with oral therapy. Oral glucocorticosteroids require at least 4 hours to produce clinical improvement. Daily doses of systemic glucocorticosteroids equivalent to 60-80 mg methylprednisolone as a single dose, or 300-400 mg hydrocortisone in divided doses, are adequate for hospitalized patients, and 40 mg methylprednisolone or 200 mg hydrocortisone is probably adequate in most cases (**Evidence B**). An oral glucocorticosteroid dose of 1 mg/kg daily is adequate for treatment of exacerbations in children with mild persistent asthma. A 7-day course in adults has been found to be as effective as a 14-day course, and a 3- to 5-day course in children is usually considered appropriate (**Evidence B**). Two days of oral dexamethasone can also be used to treat asthma exacerbations, but there are concerns about metabolic side-effects if dexamethasone is continued beyond two days. Evidence suggests that there is no benefit to tapering the dose of oral glucocorticosteroids, either in the short-term or over several weeks, as long as the patient is on maintenance inhaled glucocorticosteroids (**Evidence B**).

Inhaled Glucocorticosteroids

Inhaled glucocorticosteroids are effective as part of therapy for asthma exacerbations. In one study, the combination of high-dose inhaled glucocorticosteroids and salbutamol in acute asthma provided greater bronchodilation than salbutamol alone (**Evidence B**), and conferred greater benefit than the addition of systemic glucocorticosteroids across all parameters, including hospitalizations, especially for patients with more severe attacks.

Inhaled glucocorticosteroids can be as effective as oral glucocorticosteroids at preventing relapses. Patients discharged from the emergency department on prednisone and inhaled budesonide have a lower rate of relapse than those on prednisone alone (**Evidence B**). A high dose of inhaled glucocorticosteroid (2.4 mg budesonide daily in four divided doses) achieves a relapse rate similar to 40 mg oral prednisone daily (**Evidence A**). Cost is a significant factor in the use of such high-doses of inhaled glucocorticosteroids, and further studies are required to document their potential benefits, especially cost effectiveness, in acute asthma.

Magnesium

Intravenous magnesium sulphate (usually given as a single 2 g infusion over 20 minutes) is not recommended for routine use in asthma exacerbations, but can help reduce hospital admission rates in certain patients, including adults with FEV_1 25%-30% predicted at presentation, adults and children who fail to respond to initial treatment, and children whose FEV_1 fails to improve above 60% predicted after 1 hour of care (**Evidence A**). Nebulized salbutamol administered in isotonic magnesium sulphate provides greater benefit than if it is delivered in normal saline (**Evidence A**). Intravenous magnesium sulphate has not been studied in young children.

Helium Oxygen Therapy

A systematic survey of studies that have evaluated the effect of a combination of helium and oxygen, compared to helium alone, suggests there is no routine role for this intervention. It might be considered for patients who do not respond to standard therapy.

Leukotriene Modifiers

There are little data to suggest a role for leukotriene modifiers in acute asthma. Small investigations have demonstrated improvement in PEF, but clinical relevance requires more study.

Sedatives

Sedation should be strictly avoided during exacerbations of asthma because of the respiratory depressant effect of anxiolytic and hypnotic drugs. An association between the use of these drugs and avoidable asthma deaths has been demonstrated.

Criteria for Discharge from the Emergency Department vs. Hospitalization

Patients with a pre-treatment FEV_1 or PEF <25% predicted or personal best, or those with a post-treatment FEV_1 or PEF <40% predicted or personal best, usually require hospitalization. Patients with post-treatment lung function of 40%-60% predicted may be discharged, provided that adequate follow-up is available in the community and compliance is assured. Patients with post-treatment lung function ≥60% predicted can be discharged.

Management of acute asthma in the intensive care unit is beyond the scope of this document and readers are referred to recent comprehensive reviews.

For patients discharged from the emergency department:

- At a minimum, a 7-day course of oral glucocorticosteroids for adults and a shorter course (3 to 5 days) for children should be prescribed, along with continuation of bronchodilator therapy.
- The bronchodilator can be used on an as-needed basis, based on both symptomatic and objective improvement, until the patient returns to his or her pre-exacerbation use of rapid-acting inhaled β_2-agonists.
- Ipratropium bromide is unlikely to provide additional benefit beyond the acute phase and may be quickly discontinued.
- Patients should initiate or continue inhaled glucocorticosteroids.
- The patient's inhaler technique and use of peak flow meter to monitor therapy at home should be reviewed. Patients discharged from the emergency department with a peak flow meter and action plan have a better response than patients discharged without these resources.
- The factors that precipitated the exacerbation should be identified and strategies for their future avoidance implemented.
- The patient's response to the exacerbation should be evaluated. The action plan should be reviewed and written guidance provided.
- Use of controller therapy during the exacerbation should be reviewed: whether this therapy was increased promptly, by how much, and, if appropriate, why oral glucocorticosteroids were not added. Consider providing a short course of oral glucocorticosteroids to be on hand for subsequent exacerbations.
- The patient or family should be instructed to contact the primary health care professional or asthma specialist within 24 hours of discharge. A follow-up appointment with the patient's usual primary care professional or asthma specialist should be made within a few days of discharge to assure that treatment is continued until baseline control parameters, including personal best lung function, are reached. Prospective data indicate that patients discharged from the emergency department for follow-up with specialist care do better than patients returned to routine care.

An exacerbation severe enough to require hospitalization may reflect a failure of the patient's asthma management or lack of a written asthma plan. Hospitalized patients may be particularly receptive to information and advice about their illness. Health care providers should take the opportunity to review patient understanding of the causes of asthma exacerbations, avoidance of factors that may cause exacerbations (including, where relevant, smoking cessation), the purposes and correct uses of treatment, and the actions to be taken to respond to worsening symptoms or peak flow values (**Evidence A**).

Referral to an asthma specialist should be considered for hospitalized patients. Following discharge from continuous supervision, the patient should be reviewed by the family health care professional or asthma specialist regularly over the subsequent weeks until

personal best lung function is reached. Use of incentives improves primary care follow up but has shown no effect on long term outcomes. Patients who come to the emergency department with an acute exacerbation should be especially targeted for an asthma education program, if one is available.

Component 5: Special Considerations

Special considerations are required in managing asthma in relation to pregnancy; surgery; rhinitis, sinusitis, and nasal polyps; occupational asthma; respiratory infections; gastroesophageal reflux; aspirin-induced asthma; and anaphylaxis. (For a more detailed discussion of the following special considerations, see the original guideline document.)

Pregnancy

Using medications to obtain optimal control of asthma is justified even when their safety in pregnancy has not been unequivocally proven. For most medications used to treat asthma there is little evidence to suggest an increased risk to the fetus. Appropriately monitored use of theophylline, inhaled glucocorticosteroids, β_2-agonists, and leukotriene modifiers (specifically montelukast) is not associated with an increased incidence of fetal abnormalities. Inhaled glucocorticosteroids have been shown to prevent exacerbations of asthma during pregnancy (**Evidence B**). As in other situations, the focus of asthma treatment must remain on control of symptoms and maintenance of normal lung function. Acute exacerbations should be treated aggressively in order to avoid fetal hypoxia. Treatment should include nebulized rapid-acting β_2-agonists and oxygen and systemic glucocorticosteroids should be instituted when necessary.

While all patients should have adequate opportunity to discuss the safety of their medications, pregnant patients with asthma should be advised that the greater risk to their baby lies with poorly controlled asthma, and the safety of most modern asthma treatments should be stressed. Even with a good patient/health care professional relationship, independent printed material, such as a statement from the US National Asthma Education and Prevention Program on the treatment of asthma during pregnancy, will provide important additional reassurance.

Obesity

Asthma is more difficult to control in the obese patient. This may be due to a different type of airway inflammation (less eosinophilic), obesity-related co-morbidities such as obstructive sleep apnea and gastroesophageal reflux, mechanical factors or other as yet undefined factors. There is not sufficient evidence to suggest that the management of asthma in the obese should be different than in patients with normal weight. However, there seems to be a reduced response to inhaled glucocorticosteroids in the obese patient, and although this seems to be less evident with leukotriene antagonists, inhaled glucocorticosteroids are considered the mainstay of asthma treatment in this population.

Although asthma is not more often over-diagnosed in obese compared to non-obese patients, it is particularly important to confirm the diagnosis by objective measures of variable airway obstruction or bronchial hyperresponsiveness, as respiratory symptoms associated to obesity may mimic asthma. Weight loss in the obese patient improves asthma control, lung function and reduces medication needs and should be included in the treatment plan.

Surgery

Airway hyperresponsiveness, airflow limitation, and mucus hypersecretion predispose patients with asthma to intraoperative and postoperative respiratory complications. The likelihood of these complications depends on the severity of asthma at the time of surgery, the type of surgery (thoracic and upper abdominal surgeries pose the greatest risks), and type of anesthesia (general anesthesia with endotracheal intubation carries the greatest risk). These variables need to be assessed prior to surgery and pulmonary function should be measured. If possible, this evaluation should be undertaken several days before surgery to allow time for additional treatment. In particular, if the patient's FEV_1 is less than 80% of personal best, a brief course of oral glucocorticosteroids should be considered to reduce airflow limitation (**Evidence C**). Furthermore, patients who have received systemic glucocorticosteroids within the past 6 months should have systemic coverage during the surgical period (100 mg hydrocortisone every 8 hours intravenously). This should be rapidly reduced 24 hours following surgery, as prolonged systemic glucocorticosteroid therapy may inhibit wound healing (**Evidence C**).

Rhinitis, Sinusitis, and Nasal Polyps

Rhinitis

Treatment of rhinitis may improve asthma symptoms (**Evidence A**). Anti-inflammatory agents including glucocorticosteroids and cromones as well as leukotriene modifiers and anticholinergics can be effective in both conditions. However, some medications are selectively effective against rhinitis (e.g., H_1-antagonists) and others against asthma (e.g., β_2-agonists) (**Evidence A**). Use of intra-nasal glucocorticosteroids for concurrent rhinitis has been found to have a limited benefit in improving asthma and reducing asthma morbidity in some but not all studies. Leukotriene modifiers, allergen-specific immunotherapy, and anti-IgE therapy are effective in both conditions (**Evidence A**).

Sinusitis

Sinusitis is a complication of upper respiratory infections, allergic rhinitis, nasal polyps, and other forms of nasal obstruction. Both acute and chronic sinusitis can worsen asthma. Clinical features of sinusitis lack diagnostic precision, and computed tomography (CT) scan confirmation is recommended when available. In children with suspected rhinosinusitis, antibiotic therapy for 10 days is recommended (**Evidence B**). Treatment should also include medications to reduce nasal congestion, such as topical nasal decongestants or topical nasal or even systemic glucocorticosteroids. These agents remain secondary to primary asthma therapies.

Nasal Polyps

Nasal polyps associated with asthma and rhinitis, and sometimes with aspirin hypersensitivity, are seen primarily in patients over 40 years old. Children with nasal polyps should be assessed for cystic fibrosis and immotile cilia syndrome. Nasal polyps are quite responsive to topical glucocorticosteroids. A limited number of patients with glucocorticosteroid-refractory polyps may benefit from

surgery.

Occupational Asthma

Pharmacologic therapy for occupational asthma is identical to therapy for other forms of asthma, but it is not a substitute for adequate avoidance. Consultation with a specialist in asthma management or occupational medicine is advisable.

Respiratory Infections

Treatment of an infectious exacerbation follows the same principles as treatment of other asthma exacerbations—that is, rapid-acting inhaled β_2-agonists and early introduction of oral glucocorticosteroids or increases in inhaled glucocorticosteroids by at least four-fold are recommended. Because increased asthma symptoms can often persist for weeks after the infection is cleared, anti-inflammatory treatment should be continued for this full period to ensure adequate control.

Gastroesophageal Reflux

There is considerable evidence that gastroesophageal reflux is more common in patients with asthma than in the general population. This has led to research to determine whether treatment of gastroesophageal reflux can improve asthma symptoms or control. Gastroesophageal reflux is undoubtedly a cause of dry cough and some of the confusion in the literature is probably due to patients with dry cough symptoms being attributed to asthma. This relationship may in part relate to the use of medications to manage asthma, such as β2-agonists and theophylline which cause relaxation of the lower oesophageal sphincter.

Despite a high prevalence of asymptomatic gastroesophageal reflux among patients with poorly controlled asthma, treatment with proton-pump inhibitors does not improve asthma control in adults or children. Asymptomatic gastroesophageal reflux is not a likely cause of poorly controlled asthma. Surgery for gastroesophageal reflux is reserved for the severely symptomatic patient with well-documented esophagitis and failure of medical management. In patients with asthma, it should be demonstrated that the reflux causes asthma symptoms before surgery is advised.

Aspirin-Induced Asthma (AIA)

A characteristic history of reaction is considered adequate for initiating avoidance strategies. However, the diagnosis can only be confirmed by aspirin challenge, as there are no suitable in vitro tests for diagnosis. The aspirin challenge test is not recommended for routine practice as it is associated with a high risk of potentially fatal consequences and must only be conducted in a facility with cardiopulmonary resuscitation capabilities. Further safeguards are that patients should only be challenged when their asthma is in remission and their FEV_1 is greater than 70% of predicted or personal best. Bronchial (inhalational) and nasal challenges with lysine aspirin are safer than oral challenges and may be performed in specialized centers. Once aspirin or nonsteroidal anti-inflammatory drug (NSAID) hypersensitivity develops, it is present for life. Patients with AIA should avoid aspirin, products containing it, other analgesics that inhibit cyclooxygenase-1 (COX-1), and often also hydrocortisone hemisuccinate. Avoidance does not prevent progression of the inflammatory disease of the respiratory tract. Where a NSAID is indicated, a cyclooxygenase-2 (COX-2) inhibitor may be considered with appropriate physician supervision and observation for at least one hour after administration (**Evidence B**). Glucocorticosteroids continue to be the mainstay of asthma therapy, but leukotriene modifiers may also be useful for additional control of the underlying disease (**Evidence B**). For NSAID-sensitive patients with asthma who require NSAIDs for other medical conditions, desensitization may be conducted in the hospital under the care of a specialist.

Generally, asthma patients, especially those with adult onset asthma and associated upper airway disease (nasal polyposis), should be counseled to avoid NSAIDs, taking acetaminophen/paracetamol instead.

Anaphylaxis and Asthma

If there is a possibility that anaphylaxis is involved in an asthma attack, epinephrine should be the bronchodilator of choice. Prompt treatment for anaphylaxis is crucial and includes oxygen, intramuscular epinephrine, injectable antihistamine, intravenous hydrocortisone, oropharyngeal airway, and intravenous fluid. Preventing a recurrence of anaphylaxis depends on identifying the cause and instructing the patient on avoidance measures and self-administered emergency treatment with pre-loaded epinephrine syringes.

Definitions:

Description of Levels of Evidence		
Evidence Category	**Sources of Evidence**	**Definition**
A	Randomized controlled trials (RCTs). Rich body of data.	Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B	RCTs. Limited body of data.	Evidence is from endpoints of intervention studies that include only a limited number of patients, posthoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C	Nonrandomized trials. Observational studies.	Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D	Panel consensus judgment	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.

Clinical Algorithm(s)

The following algorithms are provided in the original guideline document:

- Management Approach Based on Control
- Management of Asthma Exacerbations in Acute Care Setting

Evidence Supporting the Recommendations

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Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

The recommendations on asthma management and prevention are based as far as possible on controlled clinical studies. For those aspects of the clinical management of asthma that have not been the subject of specific clinical studies, recommendations are based on literature review, clinical experience, and expert opinion of project members.

Levels of evidence are assigned to management recommendations in the Global Initiative for Asthma documents where appropriate in Chapter 4, "The Five Components of Asthma Management." Evidence levels are indicated in boldface type enclosed in parentheses after the relevant statement—e.g., (**Evidence A**).

Benefits/Harms of Implementing the Guideline Recommendations

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Potential Benefits

- There is now good evidence that the clinical manifestations of asthma—symptoms, sleep disturbances, limitations of daily activity, impairment of lung function, and use of rescue medications—can be controlled with appropriate treatment.
- Although there is no cure for asthma, appropriate management that includes a partnership between the physician and the patient/family most often results in the achievement of control.
- The goals for successful management of asthma are to:
  - Achieve and maintain control of symptoms
  - Maintain normal activity levels, including exercise
  - Maintain pulmonary function as close to normal as possible
  - Prevent asthma exacerbations
  - Avoid adverse effects from asthma medications
  - Prevent asthma mortality

Potential Harms

See Chapter 3, "Asthma Treatments," in the original guideline document for a full discussion of asthma medications for adults and children, including their side effects.

Contraindications

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Contraindications

- Sedation is contraindicated in the treatment of an asthma exacerbation.
- Patients with aspirin-induced asthma (AIA) should avoid aspirin, products containing it, other analgesics that inhibit cyclooxygenase 1 (COX-1), and often also hydrocortisone hemisuccinate.
- Generally, asthma patients, especially those with adult onset asthma and associated upper airway disease (nasal polyposis), should be counseled to avoid nonsteroidal anti-inflammatory drugs (NSAIDs), taking acetaminophen/paracetamol instead.

Qualifying Statements

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Qualifying Statements

A large segment of the world's population lives in areas with inadequate medical facilities and meager financial resources. The Global Initiative for Asthma (GINA) Executive Committee recognizes that "fixed" international guidelines and "rigid" scientific protocols will not work in many locations. Thus, the recommendations found in this Report must be adapted to fit local practices and the availability of health care resources.

Implementation of the Guideline

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Description of Implementation Strategy

A thorough explanation of the Global Initiative for Asthma's guideline implementation strategies is given in Chapter 5 of the original guideline document.

Implementation Tools

Chart Documentation/Checklists/Forms
Clinical Algorithm
Foreign Language Translations
Patient Resources
Pocket Guide/Reference Cards
Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

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IOM Care Need

Getting Better
Living with Illness
Staying Healthy

IOM Domain

Effectiveness
Patient-centeredness

Identifying Information and Availability

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Bibliographic Source(s)

Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. Vancouver (WA): Global Initiative for Asthma (GINA); 2012. 110 p. [445 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

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Guideline Committee

Global Initiative for Asthma Science Committee

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Financial Disclosures/Conflicts of Interest

Disclosures for members of Global Initiative for Asthma (GINA) Executive and Science Committees can be found on the GINA Web site.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. Vancouver (WA): Global Initiative for Asthma (GINA); 2011. 106 p.

In an effort to keep the GINA Workshop report as up to date as possible, a GINA Science Committee has been established to review published research on asthma management and prevention, and to post yearly updates on the GINA Web site. See the GINA Web site for archived versions of the GINA guidelines.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Global Initiative for Asthma (GINA) Web site.

Availability of Companion Documents

The following are available:

- Pocket guide for asthma management and prevention. Vancouver (WA): Global Initiative for Asthma; 2012 Dec. 32 p. Available in a variety of languages.
- Pocket guide for asthma management and prevention in children 5 years and younger. Vancouver (WA): Global Initiative for Asthma; 2009 May. 16 p. Available in English and Spanish.
- At-a-glance asthma management reference. Vancouver (WA): Global Initiative for Asthma; 2012. 4 p.

Electronic copies: Available from the Global Initiative for Asthma (GINA) Web site.

Additional resources, such as instructions for inhaler and spacer use, are also available from the GINA Web site.

Also, an example of the contents of an action plan is available in Chapter 4 of the original guideline document.

Patient Resources

A variety of patient resources, including an interactive introduction to asthma, are available from the Global Initiative for Asthma (GINA) Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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