A New Era in Asthma Management: Assessment of Asthma Control

Kevin R. Murphy, MD; Joel Solis, MD

BURDEN OF DISEASE

Asthma is recognized as a chronic, heterogenous disease characterized by airway inflammation and a history of respiratory symptoms (eg, wheeze, shortness of breath, chest tightness, or cough) that vary over time and in intensity.[1] Variations are often triggered by factors such as exercise, allergen or irritant exposure, change in weather, or viral respiratory tract infections. Asthma symptoms and airflow limitation may resolve spontaneously or in response to treatment. Symptoms may be absent for weeks or months, yet airway hyperresponsiveness related to chronic airway inflammation usually persists.[1]

Asthma is a common disease in children, adolescents, and adults that results in substantial morbidity and utilization of health care resources.[2] In 2018, there were an estimated 5.5 million children and 19.2 million adults in the United States with asthma, of whom 45% had ≥1 asthma attack.[2] In 2016, there were nearly 10 million office visits with asthma as a primary diagnosis.[2] One-third (33.1%) of adults with asthma report their health as fair or poor.[3] Anxiety, depression, and asthma control are independent predictors of diminished health-related quality of life in people with asthma.[4]

Kevin R. Murphy, MD, Director, Clinical Research, Allergy, Asthma and Pediatric Pulmonology, Boys Town National Research Hospital, Boys Town, NE.

Joel Solis, MD, Valley Medical Arts Clinic, The University of Texas Rio Grande Valley, McAllen, TX.

DISCLOSURES

Dr. Murphy discloses that he serves on the advisory board and/or speakers' bureau for AstraZeneca, Genentech, Glaxo Smith Kline, Novartis, and Sanofi Regeneron. Dr. Solis and Dr. Scott have no disclosures to report.

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The economic burden of asthma, including costs incurred by absenteeism and mortality, was estimated at $82 billion in 2013.[5] By comparison, the total economic burden – including lost productivity – has been estimated at $330 billion for heart disease and stroke and $327 billion for diabetes.[6] The 20-year estimated burden of direct and indirect costs associated with asthma is $964 billion, with a loss of 15.5 million quality-adjusted life-years in adolescents and adults.[7]

A key factor contributing to the burden of disease associated with asthma is poor adherence to treatment by patients.[8-10] A variety of additional factors contribute, including limited understanding among patients about asthma and its treatment, as well as poor patient-clinician communication.[11-13] Discordance regarding asthma control is common between patients and clinicians.[14] Patients often overestimate their asthma control[15] or may tolerate symptoms indicative of poor control based on the belief that the symptoms are part of living with asthma.[16] Collectively, these factors contribute to suboptimal asthma control.

ASSESSING ASTHMA CONTROL

Asthma control means the extent to which the effects of asthma either can be seen in the patient or have been reduced or resolved by treatment. Asthma control has 2 domains: symptom control and risk factors for future poor outcomes, particularly flare-ups (exacerbations). It is important to assess the patient's future risk for exacerbations, even when symptom control is good. Risk factors for exacerbations that are independent of symptom control include a history of ≥1 exacerbation in the previous year, socioeconomic disadvantages, poor treatment adherence, incorrect inhaler technique, low lung function, smoking, and blood eosinophilia.[1]

Many tools are available to assess asthma control and are listed in the **TABLE**.[17-26] Of those tools, the Asthma Impairment and Risk Questionnaire (AIRQ) and Asthma Control Test (ACT) are validated for patients age ≥12 years and have numerically scored questions providing total scores and cut points for varying levels of asthma control. The ACT (**FIGURE 1**) is limited to assessing symptom control with no direct measure of future risk.[19,20,23]

TABLE. **Tools for assessing asthma control**

Tool	Focus		Target patient age (y)	Administered by	No. of items	Recall time
	Symptoms	Risk				
Asthma APGAR[17,18]	✓	✓	5-45	Self	6	2 wk (symptoms and risk)
Asthma Control Questionnaire[19]	✓		≥11	Self	7	1 wk
	✓		6-10	HCP	7	1 wk
Asthma Control Test[20]	✓		≥12	Self	5	4 wk
Asthma Control and Communication Instrument[21]	✓	✓	≥12	Self	12	Since last visit (symptoms and risk)
Asthma Impairment and Risk Questionnaire[22]	✓	✓	≥12	Self/HCP	10	2 wk (symptoms); 1 year (risk)
Childhood Asthma Control Test[23]	✓		4-11	Self/parent	7	4 wk (symptoms); 1 year (risk)
Composite Asthma Severity Index[24]	✓	✓	6-17	HCP	8	2 wk (symptoms); 2 mo (risk)
Pediatric Asthma Control and Communication Instrument[25]	✓	✓	≤21	Self/parent	12	2 wk (symptoms); since last visit/2 mo (risk)
Test for Respiratory and Asthma Control in Kids[26]	✓	✓	<5	Parent	5	4 wk (symptoms); 12 mo (risk)

Abbreviations: HCP, health care professional.

ASTHMA IMPAIRMENT AND RISK QUESTIONNAIRE

To address the gaps in commonly used tools for assessing asthma control, the Asthma Impairment and Risk Questionnaire (AIRQ) was recently developed.[22] The AIRQ was devised using a modified Delphi process by a network of 190 US scientific experts and primary and specialty care clinicians with diverse practice experiences in geographic areas representing a high burden of disease. The AIRQ was validated using patients (N=442) from geographically diverse US allergy/immunology and pulmonology clinics. The symptom control domain of the AIRQ was validated against the ACT, whereas the future risk domain was validated against the patient's prior-year exacerbations as documented in their medical record. From the initial 15 questions that assessed symptom control and risk, the final questionnaire includes 10 dichotomous (yes or no) questions, 7 focusing on symptom control and 3 on future risk (**FIGURE 2**).[49] The 10 questions evaluate symptoms, social and physical activities, exacerbations, related health care resource utilization, perception of asthma control, and use of rescue medications. The AIRQ score ranges from 0 to 10. A score of 0 or 1 indicates asthma is well-controlled, whereas a score of 2 to 4 indicates asthma is not well-controlled. A score of 5 to 10 indicates asthma is very poorly controlled.

The AIRQ performed exceptionally well, including a superior comparison to the ACT.[20,22] Importantly, as shown in the AIRQ validation study, 31% of patients classified as well-controlled by ACT score (≥20) had suffered ≥1 exacerbation in the previous year, suggesting limitations in using ACT as a sole measure of asthma control.[22] Inclusion of the wide array of items in AIRQ to assess both symptom control and future risk identified many patients with exercise limitations and exacerbations that were characterized by acute treatment with oral corticosteroids or emergency department/unplanned office visits, events that are not assessed by the ACT or many other asthma control tools for patients age ≥12 years.

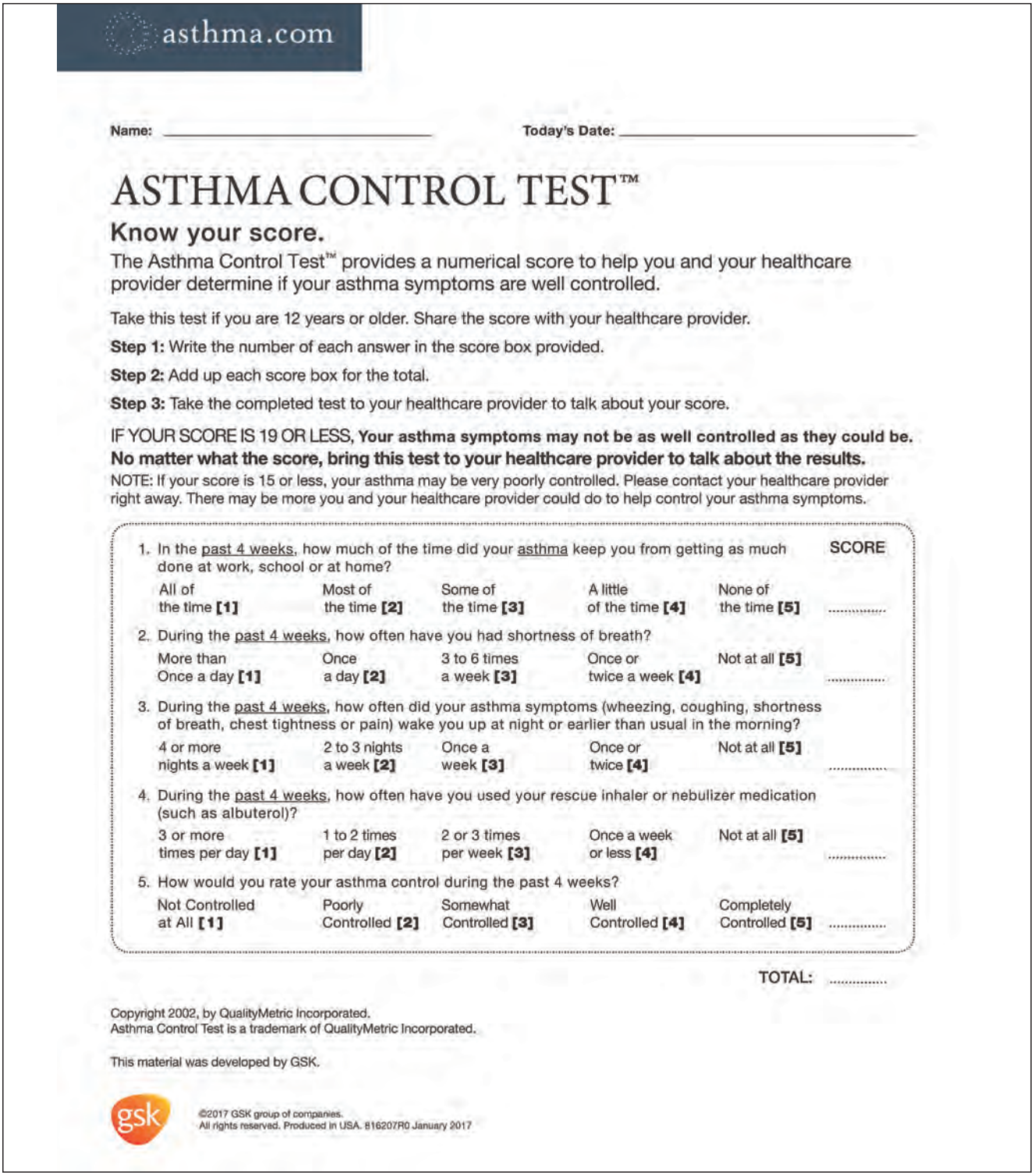
MANAGEMENT OF PATIENTS WITH UNCONTROLLED ASTHMA

The most up-to-date recommendations for managing patients with uncontrolled asthma (discussed below) were released by Global Initiative for Asthma (GINA) in 2020.[1] Updated recommendations by the National Asthma Education and Prevention Program (NAEPP) Expert Panel Report-4 (EPR-4) have been circulated in draft form and are currently being finalized.

Patients found to have uncontrolled asthma should continue to receive care that meets their clinical and personal needs and capabilities. A key step in managing a patient with uncontrolled asthma is to confirm the asthma diagnosis. If not done as part of assessing asthma control, lung function should be measured. In addition, reevaluation of asthma control is appropriate to ensure that the treatment plan is consistent with recommended evidence-based therapy.

Attention should be paid to verify that all modifiable

FIGURE 1. **Asthma Control Test**[48]



asthma.com

Name: _____ Today's Date: _____

ASTHMA CONTROL TEST™

Know your score.

The Asthma Control Test™ provides a numerical score to help you and your healthcare provider determine if your asthma symptoms are well controlled.

Take this test if you are 12 years or older. Share the score with your healthcare provider.

Step 1: Write the number of each answer in the score box provided.

Step 2: Add up each score box for the total.

Step 3: Take the completed test to your healthcare provider to talk about your score.

IF YOUR SCORE IS 19 OR LESS, **Your asthma symptoms may not be as well controlled as they could be. No matter what the score, bring this test to your healthcare provider to talk about the results.**

NOTE: If your score is 15 or less, your asthma may be very poorly controlled. Please contact your healthcare provider right away. There may be more you and your healthcare provider could do to help control your asthma symptoms.

					SCORE
1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?	All of the time **[1]**	Most of the time **[2]**	Some of the time **[3]**	A little of the time **[4]**	None of the time **[5]**	.....
2. During the past 4 weeks, how often have you had shortness of breath?	More than Once a day **[1]**	Once a day **[2]**	3 to 6 times a week **[3]**	Once or twice a week **[4]**	Not at all **[5]**	.....
3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?	4 or more nights a week **[1]**	2 to 3 nights a week **[2]**	Once a week **[3]**	Once or twice **[4]**	Not at all **[5]**	.....
4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?	3 or more times per day **[1]**	1 to 2 times per day **[2]**	2 or 3 times per week **[3]**	Once a week or less **[4]**	Not at all **[5]**	.....
5. How would you rate your asthma control during the past 4 weeks?	Not Controlled at All **[1]**	Poorly Controlled **[2]**	Somewhat Controlled **[3]**	Well Controlled **[4]**	Completely Controlled **[5]**	.....

TOTAL: .....

This material was developed by GSK.

[https://www.asthma.com/additional-resources/asthma-control-test.html]

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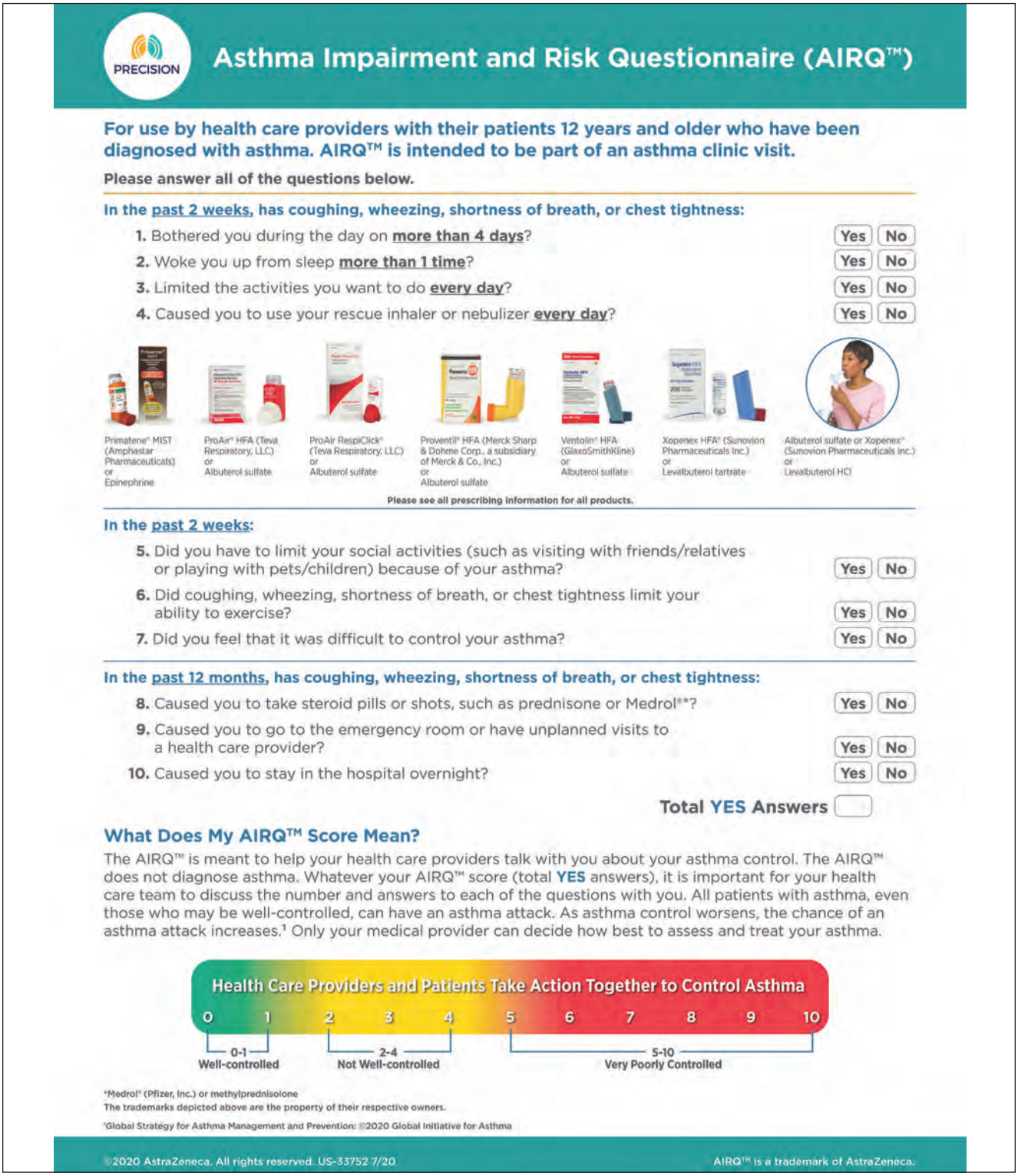
FIGURE 2. **Asthma Impairment and Risk Questionnaire**[49]



PRECISION

Asthma Impairment and Risk Questionnaire (AIRQ™)

For use by health care providers with their patients 12 years and older who have been diagnosed with asthma. AIRQ™ is intended to be part of an asthma clinic visit.

Please answer all of the questions below.

In the past 2 weeks, has coughing, wheezing, shortness of breath, or chest tightness:

1. Bothered you during the day on **more than 4 days**? Yes No
2. Woke you up from sleep **more than 1 time**? Yes No
3. Limited the activities you want to do **every day**? Yes No
4. Caused you to use your rescue inhaler or nebulizer **every day**? Yes No

Primatene® MIST (Amphastar Pharmaceuticals) or Epinephrine

ProAir® HFA (Teva Respiratory, LLC) or Albuterol sulfate

ProAir RespiClick® (Teva Respiratory, LLC) or Albuterol sulfate

Proventil® HFA (Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.) or Albuterol sulfate

Ventolin® HFA (GlaxoSmithKline) or Albuterol sulfate

Xopenex HFA® (Sunovion Pharmaceuticals Inc.) or Levalbuterol tartrate

Albuterol sulfate or Xopenex® (Sunovion Pharmaceuticals Inc.) or Levalbuterol HCl

Please see all prescribing information for all products.

In the past 2 weeks:

5. Did you have to limit your social activities (such as visiting with friends/relatives or playing with pets/children) because of your asthma? Yes No
6. Did coughing, wheezing, shortness of breath, or chest tightness limit your ability to exercise? Yes No
7. Did you feel that it was difficult to control your asthma? Yes No

In the past 12 months, has coughing, wheezing, shortness of breath, or chest tightness:

8. Caused you to take steroid pills or shots, such as prednisone or Medrol®*? Yes No
9. Caused you to go to the emergency room or have unplanned visits to a health care provider? Yes No
10. Caused you to stay in the hospital overnight? Yes No

Total YES Answers ☐

What Does My AIRQ™ Score Mean?

The AIRQ™ is meant to help your health care providers talk with you about your asthma control. The AIRQ™ does not diagnose asthma. Whatever your AIRQ™ score (total **YES** answers), it is important for your health care team to discuss the number and answers to each of the questions with you. All patients with asthma, even those who may be well-controlled, can have an asthma attack. As asthma control worsens, the chance of an asthma attack increases.† Only your medical provider can decide how best to assess and treat your asthma.

Health Care Providers and Patients Take Action Together to Control Asthma

0 1 2 3 4 5 6 7 8 9 10

0-1 Well-controlled

2-4 Not Well-controlled

5-10 Very Poorly Controlled

*Medrol® (Pfizer, Inc.) or methylprednisolone

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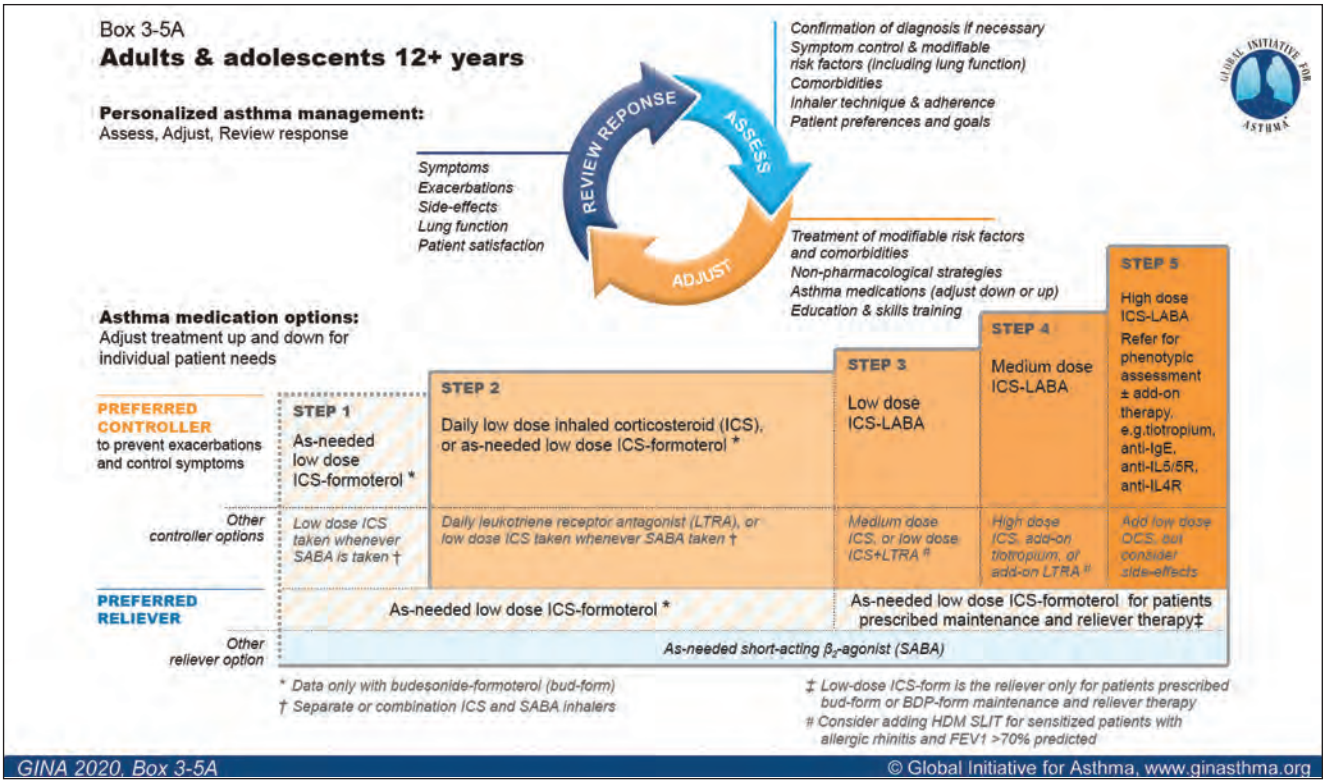
†Global Strategy for Asthma Management and Prevention: ©2020 Global Initiative for Asthma

[http://www.airqscore.com]

FIGURE 3. **Modifying treatment in adults and adolescents with uncontrolled asthma**[1]



Abbreviations: BDP, beclomethasone dipropionate; FEV1, forced expiratory volume in 1 second; HDM SLIT, house dust mite sublingual immunotherapy; ICS, inhaled corticosteroid; IgE, immunoglobulin E; IL5, interleukin-5; IL5R, interleukin-5 receptor; LABA, long-acting beta$_2$-agonist; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroid; SABA, short-acting beta$_2$-agonist.

risk factors have been identified and appropriate treatment instituted. This strategy is particularly important for risk factors that do not require or respond to a step-up in controller treatment. Examples include poor inhaler technique, suboptimal treatment adherence, home and workplace atopic and irritant triggers, tobacco use or exposure, and comorbidities such as gastroesophageal reflux disease, nasal polyposis, obesity, and sleep apnea.

Patient understanding of asthma, treatment goals, and treatment options should be assessed and reinforced with further education. A guide for patients and families is available from the National Heart, Lung, and Blood Institute (https://www.nhlbi.nih.gov/files/docs/public/lung/SoYouHaveAsthma_PRINT-reduced-filesize.pdf). Patients should be educated about the importance of the use of anti-inflammatory medications, because only 39% of adults and 40% of children with asthma use a long-term control medication.[27] In addition, patient education should include the importance of reducing the risk of exposure to allergens or other sensitizing agents.[1]

The patient's familiarity with their written asthma action plan should be assessed routinely, as this is an indicator of the patient's ability to self-manage their asthma. Patients should be invited to share difficulties they may be having with the action plan or any other issues that may affect treatment adherence. If difficulties are identified, focus a collaborative discussion on finding a solution that is acceptable to the patient and that they are able and willing to implement. Sample written action plans are available from the National Heart, Lung, and Blood Institute (https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/asthma-action-plan) and GINA (https://ginasthma.org/wp-content/uploads/2019/01/GINA-Implementation-Toolbox-2019.pdf).

Objective assessment of inhaler technique is especially important because proper technique has a direct impact on patient health outcomes and treatment tolerability.[28] Because administration errors with inhaled medications by patients are common, and clinicians are often unfamiliar with proper administration technique,[29-33] the use of authoritative patient education resources demonstrating proper inhaler technique – such as those by the Centers for

Disease Control and Prevention – is recommended (https://www.cdc.gov/asthma/inhaler_video/default.htm).

PHENOTYPES AND BIOMARKERS

The heterogeneous nature of asthma and the many clusters of demographic, clinical, and/or pathophysiologic characteristics point to the importance of recognizing asthma phenotypes and endotypes in patients with uncontrolled asthma.[1,34] Identifying the asthma phenotype is especially important for patients with moderate or severe uncontrolled asthma because some phenotype-specific treatments are available. For example, omalizumab is indicated for allergic asthma, whereas benralizumab, dupilumab, mepolizumab, and reslizumab are indicated for the eosinophilic phenotype.

Two peripheral biomarkers (Immunoglobulin E [IgE] and eosinophils) are particularly helpful in identifying asthma phenotype and guiding treatment. IgE is the predominant biomarker for allergic asthma that is produced early in the allergic cascade.[35] The serum IgE level correlates closely with the presence and severity of asthma in adults, adolescents, and children.[36,37]

Owing to the inflammatory nature of asthma, eosinophils are recruited through the complex interaction of cytokines and other inflammatory mediators.[38,39] The blood eosinophil count is more closely correlated with risk of asthma exacerbations.[40] Symptom severity is increased in eosinophilic asthma, although symptom severity is not identified exclusively with eosinophilia.[35,41-43]

KEY ASTHMA TREATMENT RECOMMENDATIONS

Global Initiative for Asthma

GINA was implemented in 1993 to develop a network of individuals, organizations, and public health officials for the dissemination of information related to the care of patients with asthma.[44] Another key purpose of GINA was to provide a mechanism to incorporate the results of scientific evidence into asthma care, leading to the first GINA report in 1995, developed in collaboration with the National Heart, Lung, and Blood Institute. The report has been updated several times, and recently on a yearly basis, to reflect the totality of the evolving evidence. Consequently, the GINA report provides comprehensive recommendations for the diagnosis and treatment of patients with asthma.[1] Key recent changes include the recommendations that all adults and adolescents should be treated with an inhaled corticosteroid (ICS) to reduce the risk of severe exacerbations. In addition, treatment with only a short-acting beta$_2$-agonist is no longer recommended.

Specific recommendations for step-up therapy are beyond the scope of this article, as recommendations depend on the patient's current therapy and asthma control. Nonetheless, step-up therapy involves either increasing the dose of the current controller therapy or adding another controller medication. For example, a patient aged ≥12 years whose asthma is uncontrolled with the combination of a low-dose ICS plus a long-acting beta$_2$-agonist may benefit from increasing to a medium-dose ICS plus a long-acting beta$_2$-agonist (**FIGURE 3**).[1] Discussions with a patient about step-up therapy should consider affordability, as asthma care in the United States is associated with high rates of cost-related underuse of medications. Although the reason is unclear, suboptimal adherence to asthma medications does not appear to be directly related to income.[45] Any step-up should be regarded as a therapeutic trial, and the response reviewed after 2 to 3 months.[1] In some cases, for example, during viral infection or seasonal allergen exposure, the duration of step-up therapy may be only 1 to 2 weeks.

National Asthma Education and Prevention Program

The NAEPP was initiated in 1989 to address the growing health problem of asthma in the United States.[46] From the beginning, the NAEPP has involved a wide variety of stakeholder groups and organizations with the general goals to raise awareness among all asthma stakeholders about the importance of asthma, as well as to promote effective, evidence-based treatment so as to reduce the disease burden. The first guideline report was published in 1991, with subsequent updates and comprehensive revisions. The last comprehensive revision was the Expert Panel Report-3 in 2007. The EPR-4, which is a limited revision that focuses on 6 topics, is being finalized.[47]

SUMMARY

Asthma is often uncontrolled in patients of all ages and is frequently unrecognized, resulting in a significant burden of disease. Consequently, assessing asthma control at every opportunity is critical. A wide variety of tools to assess asthma control are available; however, many have clinically important limitations to their use. The AIRQ was developed recently to be more widely applicable, by assessing both symptom control and future risk domains. In patients with uncontrolled asthma, step-up therapy is generally required using evidence-based recommendations for treatment provided in the GINA 2020 report and soon-to-be-released NAEPP EPR-4 report. ●

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