

The Burden of Asthma and Improving Patient Outcomes

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Prevalence and Epidemiology of Asthma

In an era of scientific research and breakthroughs, asthma still exacts a significant national burden owing to patient morbidity and mortality, rising healthcare costs, and employee absenteeism. This burden is due to both the sheer number of people with asthma and a small subset of patients with refractory or difficult to control asthma who require much urgent care and hospitalization for asthma. The American Lung Association estimates that approximately 38.4 million Americans, or 12.8% of the population, have been diagnosed with asthma at some point in their lifetime.¹ Currently, asthma affects an estimated 23.3 million Americans (7.8% of the population), including 6.9 million children.¹ Asthma affects all races, sexes, and ages, in all regions (Figure 1).¹

All patients with asthma benefit from medical care. In 2006, asthma was responsible for 10.6 million physician office visits, 1.2 million hospital outpatient department visits, and 1.7 million emergency department visits.¹ Estimated medical costs for asthma in 2010 were \$5.5 billion for hospital care, \$5.9 billion for prescription care, and \$4.2 billion for physicians' services, totaling \$15.6 billion in direct medical expenses.¹

As the number of clinicians involved in direct or indirect management of asthma continues to grow, it becomes increasingly important for physicians to be aware of the guidelines for asthma management and use them appropriately.

Asthma Treatment Guidelines

To improve diagnosis and treatment of asthma, the National Heart, Lung, and Blood Institute established the National Asthma Education and Prevention Program (NAEPP) guidelines in 1991.² As our knowledge about asthma advanced, these guidelines were updated twice,^{3,4} and the latest version was published in 2007.⁵ The current version stresses 4 central components for the management of asthma: (1) measures of assessment and monitoring (obtained by patient history and patient reports; physical examinations and objective tests to confirm, diagnose, and assess severity of asthma initially, and to monitor asthma control subsequently); (2) education for a partnership in asthma care; (3) a focus on control of environmental factors and comorbid conditions that affect asthma; and (4) evidence-based decision making about pharmacologic therapy.

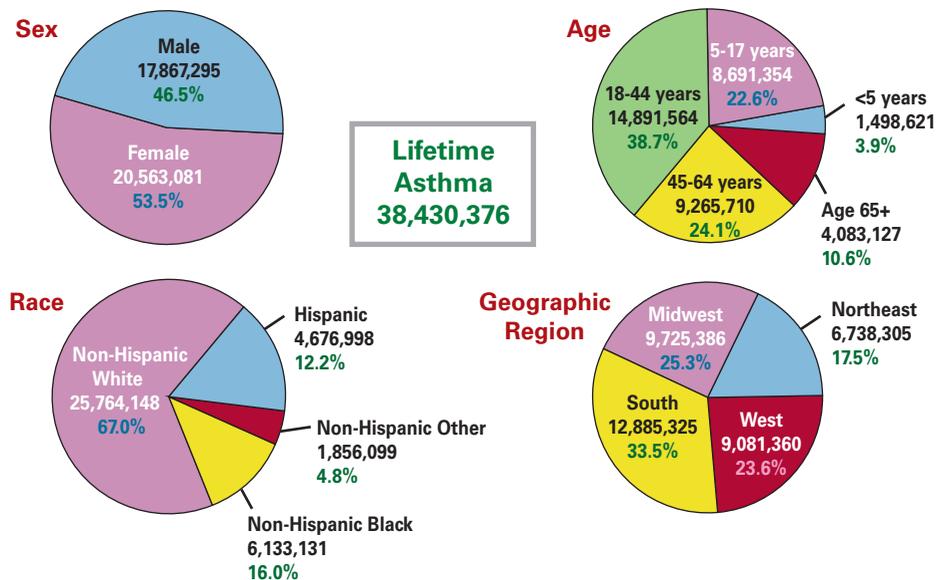
Abstract

Asthma is a significant national burden owing to patient morbidity and mortality, rising healthcare costs, and employee absenteeism. The National Asthma Education and Prevention Program (NAEPP) guidelines were created to improve the diagnosis and treatment of asthma, and stress 4 central components for the management of asthma: (1) measures of assessment and monitoring (obtained by patient history and patient reports; physical examinations and objective tests to confirm, diagnose, and assess severity of asthma initially, and to monitor asthma control subsequently); (2) education for a partnership in asthma care; (3) a focus on control of environmental factors and comorbid conditions that affect asthma; and (4) evidence-based decision making about pharmacologic therapy. The NAEPP guidelines recommend step-up and step-down programs for pharmacologic therapy. There are several barriers to effective asthma control. Treatment adherence in patients with asthma is suboptimal. Moreover, clinicians may not completely adhere to treatment guidelines. Finally, insurance companies may indirectly contribute to poor guideline adherence by failing to adequately recognize the time required to educate patients on asthma and develop a partnership for success, as requested by the guidelines. Successful asthma management requires effort by all parties involved, with the ultimate goal of improved outcomes, including reduced medical complications and costs.

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■ **Figure 1.** Percentage Distribution of Lifetime Asthma by Sex, Age, Ethnic Origin, and Geographic Region, 2008^{a,1}



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^aLifetime prevalence is defined as answering yes to “Have you EVER been told by a doctor or other health professional that you had asthma?”

The preferred method to utilize pharmacologic agents in asthma that is recommended by the NAEPP is a step-up and step-down program (Figure 2).⁵ Although the program emphasizes the pharmacologic options that are available for each level of asthma severity, it is recognized that pharmacologic therapy is only 1 of the 4 central components of asthma management, and that each component is important to long-term asthma control.

Assessment and Monitoring

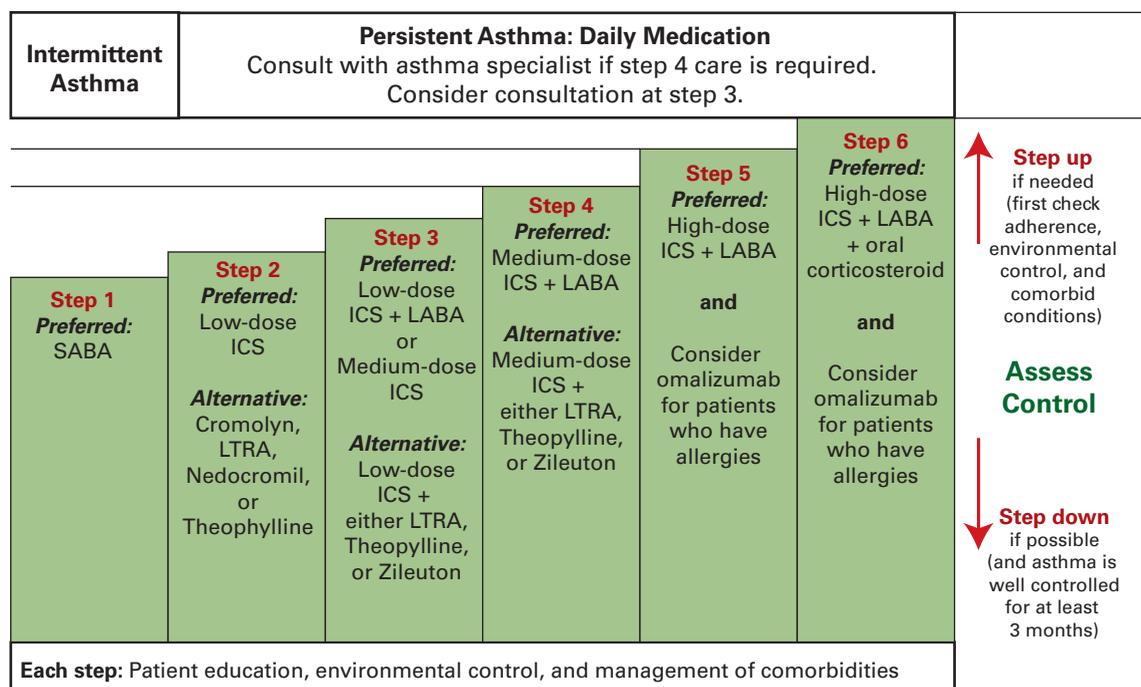
Assessment and monitoring tools are used longitudinally in the management of asthma. They are utilized initially to determine patients’ asthma severity at the time of initial diagnosis and then subsequent control of asthma and responsiveness to treatment.⁵ Severity is best determined if the patient has not begun long-term treatment; otherwise, it can be inferred from the least amount of treatment required to maintain control. Asthma severity and asthma control are determined clinically through assessment of impairment (ie, symptom severity and functional limitations), lung function, and future risk of exacerbations or decline in lung function. Attention is also paid to medication side effects. For assessment of asthma control, patient-centric questionnaires such as the Asthma Control Test,⁶ the Childhood Asthma Control Test,⁷ the Asthma Control Questionnaire,⁸ and the Asthma Therapy

Assessment Questionnaire control index⁹ can be used by patients to guide themselves and clinicians.

Assessment should evaluate both impairment and risk. Determining impairment is often straightforward. Determining risk of future exacerbations or loss of lung function is more difficult. A medical history may help to infer the patient’s risk. For example, patients without a good asthma action plan, or those with a history of recent exacerbations requiring emergency department visits, hospitalization, or intensive care unit admission, generally are at greater risk of future exacerbations.¹⁰⁻¹² Evaluation of lung function through spirometry is commonly used as part of the assessment of risk of future adverse events. Development of biomarkers, however, would be beneficial and may enable better risk assessment.

Selecting the proper treatment program (including appropriate and directed environmental modification, recognition and management of comorbid conditions, and careful choice of pharmacotherapy) is essential to improve asthma control.¹³ Assessment and monitoring of treatment should include focus on the environment the patient inhabits (Table). Monitoring asthma control in the manner outlined above is important, as it can determine if the patient was prescribed appropriate therapy and if he or she is adhering to the treatment regimen. Evaluation of response to pharmacotherapy is also important, as some patients do not respond well to prescribed therapy. An asthma specialist may be needed to

■ **Figure 2.** NAEPP Stepwise Approach for Managing Asthma in Those at Least 12 Years of Age^{a,5}



ICS indicates inhaled corticosteroid; LABA, long-acting inhaled beta₂-agonist; LTRA, leukotriene receptor antagonist; NAEPP, National Asthma Education and Prevention Program; SABA, inhaled short-acting beta₂-agonist.

^aDeciding which step of care is appropriate for a patient depends on whether long-term control therapy is being initiated for the first time or whether therapy is being adjusted. Care is stepped up to regain control, and it is stepped down for patients who have maintained control for a sufficient length of time to determine the minimal amount of medication required to maintain control and/or reduce the risk of side effects. Adapted from National Heart, Lung, and Blood Institute. National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf>. Accessed March 2, 2011.

determine whether poor response is due to poor adherence to treatment, comorbid conditions, or other factors.

Patient Education

Asthma self-management education is important to achieve asthma control and improve outcomes, as most asthma treatment is self-administered. Patients must be familiar, at some level, with the pathophysiology of asthma, and with how (and when) to correctly use different asthma medications. Asthma self-management education should be provided by trained healthcare professionals and be considered an integral part of effective asthma care for policies and reimbursement.⁵ This education should also be repeated and reinforced often. In addition to in-office education, written materials should be given to the patient, and, at the very least, patients should receive a written action plan that includes: (1) daily management recommendations and (2) how to recognize and handle worsening asthma.⁵ Patient education should also include a detailed understanding of how asthma symptoms are influenced by treatment adherence

and the environment. Clinicians can encourage treatment adherence by recommending a regimen that achieves asthma control, is simple to follow, and addresses the preferences that may be important to the patient and caregiver.

Control of Environmental Factors and Comorbid Conditions

As shown in the Table,⁵ numerous environmental factors can contribute to asthma severity. Asthma is associated with an allergic response. As such, patients need to be adequately evaluated and specifically educated on reducing exposure to identified and relevant allergens. During a medical examination, clinicians need to evaluate the potential role of allergens, particularly indoor inhalant allergens and indoor sources of irritants, including environmental tobacco smoke. A medical history, together with allergy skin tests or in vitro testing for specific immunoglobulin E (IgE), will determine relevant allergens to avoid.

Clinicians should also look for chronic comorbid conditions such as gastroesophageal reflux disease, obesity, obstructive

Table. Suggested Items for Medical History of Patients Known or Thought to Have Asthma^{a,5}

A detailed medical history of the new patient who is known or thought to have asthma should address the following items:

1. Symptoms

- Cough
- Wheezing
- Shortness of breath
- Chest tightness
- Sputum production

2. Pattern of symptoms

- Perennial, seasonal, or both
- Continual, episodic, or both
- Onset, duration, frequency (number of days or nights, per week or month)
- Diurnal variations, especially nocturnal and on awakening in early morning

3. Precipitating and/or aggravating factors

- Viral respiratory infections
- Environmental allergens, indoor (eg, mold, house-dust mite, cockroach, animal dander or secretory products) and outdoor (eg, pollen)
- Characteristics of home including age, location, cooling and heating system, wood-burning stove, humidifier, carpeting over concrete, presence of molds or mildew, characteristics of rooms where patient spends time (eg, bedroom and living room with attention to bedding, floor covering, stuffed furniture)
- Smoking (patient and others in home or daycare)
- Exercise
- Occupational chemicals or allergens
- Environmental change (eg, moving to new home; going on vacation; and/or alterations in workplace, work processes, or materials used)
- Irritants (eg, tobacco smoke, strong odors, air pollutants, occupational chemicals, dusts and particulates, vapors, gases, and aerosols)
- Emotions (eg, fear, anger, frustration, hard crying or laughing)
- Stress (eg, fear, anger, frustration)
- Drugs (eg, aspirin, and other nonsteroidal anti-inflammatory drugs, beta-blockers including eye drops, others)
- Food, food additives, and preservatives (eg, sulfites)
- Changes in weather, exposure to cold air
- Endocrine factors (eg, menses, pregnancy, thyroid disease)
- Comorbid conditions (eg, sinusitis, rhinitis, gastroesophageal disease)

4. Development of disease and treatment

- Age of onset and diagnosis
- History of early-life injury to airways (eg, bronchopulmonary dysplasia, pneumonia, parental smoking)
- Progression of disease (better or worse)
- Present management and response, including plans for managing exacerbations
- Frequency of using short-acting beta₂-agonists
- Need for oral corticosteroids and frequency of use

5. Family history

- History of asthma, allergy, sinusitis, rhinitis, eczema, or nasal polyps in close relatives

6. Social history

- Daycare, workplace, and school characteristics that may interfere with adherence
- Social factors that interfere with adherence, such as substance abuse
- Social support/social networks
- Level of education completed
- Employment

(Continued)

tive sleep apnea, rhinitis/sinusitis, and chronic stress or depression, which may influence the efficacy of asthma therapy. Consideration should also be given to allergic bronchopulmonary aspergillosis.

The central goal of optimal asthma care is to control asthma with the least amount of medication necessary. Therefore, medical care and education must focus on the avoidance of environmental triggers and the recognition and management of comorbidities and complications.

Pharmacologic Therapy

Asthma medications are classified into 2 broad groups, long-term controller medications and quick-relief medications. Long-term controllers are typically taken on a daily basis to maintain control of persistent asthma. Long-term controller medication classes include inhaled corticosteroids (ICSs), long-acting beta₂-agonists (LABAs), leukotriene modifiers, sustained-release theophyllines, cromolyn sodium and nedocromil, and anti-IgE agents (taken every 2-4 weeks).⁵

Of these classes, ICSs are the most potent and effective anti-inflammatory medications currently available in the US market. They block late-phase reactions to allergens, reduce airway hyperresponsiveness, and inhibit inflammatory cell migration and activation. Clinical studies have shown that ICSs have numerous benefits in patients with asthma, including reduction in severity of symptoms, improvement in asthma control and quality of life, improvement in peak expiratory flow and spirometry, diminished airway hyperresponsiveness, prevention of exacerbations, and reduction in systemic corticosteroid requirements, emergency department care, hospitalizations, and deaths (due to asthma).⁵

LABAs are often used in combination with ICSs or other anti-inflammatory agents for control of symptoms, especially nighttime symptoms. LABAs act as bronchodilators. They are not recommended as monotherapy, but are often used in combination with an ICS for step 3 or 4 in the step-up treatment regimen recommended by the NAEPP (Figure 2).⁵ Current ICS/LABA combinations include fluticasone and salmeterol,¹⁴ budesonide and formoterol,¹⁵ and mometasone and formoterol.¹⁶

Leukotriene modifiers, which decrease the production or action of leukotrienes (substances that are potent bronchoconstrictors), may be considered as an alternative to low-dose ICSs in patients greater than 12 years old with mild persistent asthma. Leukotriene modifiers may also be used as adjuvant therapy to ICS therapy, but the combination of ICS plus a LABA is preferred.⁵ Two leukotriene receptor blockers (montelukast and zafirlukast) and 1 leukotriene synthesis inhibitor, a 5-lipoxygenase inhibitor (zileuton), are available.

Sustained-release theophyllines are primarily used as an adjuvant therapy to ICSs for prevention of nighttime symptoms and may have mild anti-inflammatory effects.⁵

Cromolyn sodium and nedocromil are alternative agents for mild asthma, but not the preferred medications. They are often used in children as long-term controllers. They can also be used to combat exercise- or allergen-induced asthma symptoms. These medications stabilize mast cells and interfere with chloride channel function.⁵

The immunomodulator, omalizumab, is a monoclonal antibody (anti-IgE) used as add-on therapy for severe, persistent asthma (ie, step 5 or 6). It has been shown to reduce exacerbations and improve symptoms. Omalizumab inhibits the binding of IgE to the high-affinity receptors on basophils and mast cells, thus decreasing the release of mediators in response to allergen exposure. It is administered as a subcutaneous injection.⁵ A recent review of 8 placebo-controlled clinical trials which assessed the safety and efficacy of an ICS plus omalizumab found that the combination reduced the

■ **Table. Suggested Items for Medical History of Patients Known or Thought to Have Asthma^{a,5} (Continued)**

7. History of exacerbations
Usual prodromal signs and symptoms
Rapidity of onset
Duration
Frequency
Severity (need for urgent care, hospitalization, intensive care unit admission)
Life-threatening exacerbations (eg, intubation, intensive care unit admission)
Number and severity of exacerbations in the past year
Usual patterns and management (what works?)
8. Impact of asthma on patient and family
Episodes of unscheduled care (emergency department visits, urgent care, hospitalization)
Number of days missed from school/work
Limitation of activity, especially sports and strenuous work
History of nocturnal awakening
Effect on growth, development, behavior, school or work performance, and lifestyle
Impact on family routines, activities, or dynamics
Economic impact
9. Assessment of patient's and family's perceptions of disease
Patient's, parents', and spouse's or partner's knowledge of asthma and belief in the chronicity of asthma and in the efficacy of treatment
Patient's perception and beliefs regarding use and long-term effects of medications
Ability of patient and parents, spouse, or partner to cope with disease
Level of family support and patient's and parents', spouse's, or partner's capacity to recognize severity of an exacerbation
Economic resources
Sociocultural beliefs

^aThis list does not represent a standardized assessment or diagnostic instrument. The validity and reliability of this list have not been assessed. Adapted from National Heart, Lung, and Blood Institute. National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf>. Accessed March 2, 2011.

number of exacerbations by almost 50%.¹⁷

Quick-relief medications are ideally taken on a short-term basis to deliver fast-acting relief of bronchoconstriction and reverse acute airflow obstruction. Quick-relief medications consist of short-acting beta₂-agonists (SABAs), anticholinergics, and oral or systemic corticosteroids.

SABAs are the therapy of choice for relief of acute asthma symptoms and prevention of exercise-induced bronchospasm.⁵ Common SABAs, such as albuterol, levalbuterol, and pirbuterol, are bronchodilators that relax smooth muscle.

The anticholinergic agent, ipratropium bromide, provides additive benefit to SABAs in moderate-to-severe asthma exacerbations. It works by inhibiting muscarinic cholinergic receptors and reducing intrinsic vagal tone of the airway.⁵

Oral systemic corticosteroids are used as adjuncts to SABAs for moderate and severe exacerbations, to speed recovery and prevent recurrence of exacerbations.⁵

Reports

The overarching goal of improved asthma care is to decrease the morbidity and mortality associated with asthma. The NAEPP incorporates this philosophy, with a strong focus on asthma control and a recommended stepwise program of treatment based on the patient's preference and asthma severity (Figure 2).⁵

Treatment Compliance

Asthma, like most chronic conditions, requires long-term adherence to treatment. Unfortunately, treatment adherence in patients with asthma is suboptimal. There are numerous reasons for noncompliance. Poor adherence to asthma treatment is not limited to patients forgetting to take their medicine. Patients may forget to take their rescue inhalant when playing outside with their children. They may not be able to remove the carpeting in their house, or avoid outdoor work during high pollen season. It has been speculated that over half of patients with asthma are not compliant with therapy.¹⁸ Barriers to adherence are numerous, and include sex, ethnicity, socioeconomic status, and age.¹⁹ In addition, psychological factors such as depression and fear of the medical community can result in poor treatment adherence. Clinicians, however, can often recognize patients at risk for not adhering to treatment and make appropriate adjustments.²⁰

Clinicians may also not completely adhere to treatment guidelines. A report by Ohar et al noted that some clinicians are reluctant to use aspects of current guidelines for a variety of reasons.²¹ Some clinicians may be skeptical of newer guidelines, while others are reluctant to abandon practice traditions they feel have worked in the past. Furthermore, many patients with asthma are treated by primary care doctors who may not have the time, funding, or equipment necessary to comply fully with guidelines. The guidelines are not prescriptive, but do provide an evidence base for best practice recommendations.

Finally, insurance companies may indirectly contribute to poor guideline adherence by failing to adequately recognize the time required to educate patients on asthma and develop a partnership for success, as requested by the guidelines.

Conclusions

Asthma is a complex disease with multiple triggers of exacerbations, and it requires a comprehensive approach to maintain good control. The guidelines developed by the NAEPP provide an excellent starting point to manage patients with asthma. The guidelines are focused on controlling asthma using the minimal amount of medication. Instead of focusing solely on the pharmacologic aspects of asthma control, the guidelines place emphasis on patient education, environ-

mental control, management, recognition and management of comorbidities,¹ and frequent and adequate assessment of asthma control. Asthma management requires constant dialogue between patients and clinicians. Proper knowledge and adherence by all parties involved in the care of asthma can help minimize medical complications and costs.

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REFERENCES

1. **American Lung Association.** Trends in asthma morbidity and mortality: February 2010. Available at: <http://www.lungusa.org/finding-cures/our-research/trend-reports/asthma-trend-report.pdf>. Accessed January 25, 2011.
2. **Expert Panel Report (EPR): Guidelines for the Diagnosis and Management of Asthma (EPR 1991).** NIH Publication No. 91-3642. Bethesda, MD: US Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program, 1991.
3. **Expert Panel Report 2 (EPR-2): Guidelines for the Diagnosis and Management of Asthma (EPR-2 1997).** NIH Publication No. 97-4051. Bethesda, MD: US Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program, 1997.
4. **Expert Panel Report 2 (EPR-2): EPR-Update 2002. Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma. Update on Selected Topics 2002 (EPR-Update 2002).** NIH Publication No. 02-5074. Bethesda, MD: US Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program, June 2003.
5. **National Heart, Lung, and Blood Institute.** National Asthma Education and Prevention Program. *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma.* August 2007. <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf>. Accessed March 2, 2011.
6. **Nathan RA, Sorkness CA, Kosinski M, et al.** Development of the Asthma Control Test: a survey for assessing asthma control. *J Allergy Clin Immunol.* 2004;113(1):59-65.
7. **Liu AH, Zeiger R, Sorkness C, et al.** Development and cross-sectional validation of the Childhood Asthma Control Test. *J Allergy Clin Immunol.* 2007;119(4):817-825.
8. **Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR.** Development and validation of a questionnaire to measure asthma control. *Eur Respir J.* 1999;14(4):902-907.
9. **Vollmer WM, Markson LE, O'Connor E, et al.** Association of asthma control with health care utilization and quality of life. *Am J Respir Crit Care Med.* 1999;160(5, pt 1):1647-1652.
10. **Adams RJ, Smith BJ, Ruffin RE.** Factors associated with hospital admissions and repeat emergency department visits for adults with asthma. *Thorax.* 2000;55(7):566-573.

11. **Eisner MD, Katz PP, Yelin EH, Shiboski SC, Blanc PD.** Risk factors for hospitalization among adults with asthma: the influence of sociodemographic factors and asthma severity. *Respir Res.* 2001;2(1):53-60.
12. **Lieu TA, Quesenberry CP, Sorel ME, Mendoza GR, Leong AB.** Computer-based models to identify high-risk children with asthma. *Am J Respir Crit Care Med.* 1998;157(4, pt 1):1173-1180.
13. **Bateman ED, Boushey HA, Bousquet J, et al.** Can guideline-defined asthma control be achieved? the Gaining Optimal Asthma Control study. *Am J Respir Crit Care Med.* 2004;170(8):836-844.
14. Advair [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; January 2011.
15. Symbicort [prescribing information]. Wilmington, DE: AstraZeneca LP; 2010.
16. Dulera [prescribing information]. Whitehouse Station, NJ: Schering Corporation; 2010.
17. **Rodrigo FJ, Neffen H, Castro-Rodriguez JA.** Efficacy and safety of subcutaneous omalizumab vs placebo as add-on therapy to corticosteroids for children and adults with asthma: a systemic review. *Chest.* 2011;139(1):28-35.
18. **Vanelli M, Adler S, Vermilyea J.** Moving beyond market share. *In Vivo: The Business and Medicine Report.* 2002;20(3):1-6.
19. **Howell G.** Nonadherence to medical therapy in asthma: risk factors, barriers, and strategies for improving. *J Asthma.* 2008;45(9):723-729.
20. **Smith JR, Mildenhall S, Noble M, Mugford M, Shepstone L, Harrison BD.** Clinician-assessed poor compliance identifies adults with severe asthma who are at risk of adverse outcomes. *J Asthma.* 2005;42(6):437-445.
21. **Ohar JA.** Asthma Treatment guidelines: current recommendations, future goals. *Managed Care.* 2005;14(11):23-27.