

Asthma - Getting to the Guidelines

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Summary

Asthma is a significant illness in terms of costs, morbidity, and mortality. Although clinical practice guidelines have been around for several years, numerous studies have shown that adoption of these guidelines is not optimal. An update of the National Asthma Education and Prevention Program (NAEPP) Guidelines for the Diagnosis and Management of Asthma was published in the summer of 2007. The major changes to the guidelines include breaking down recommendations into more age groups (0-4, 5-11, 12 and older), redefining how to assess disease control, and recommending allergy and specialist evaluation for many patients. Some changes to the medication recommendations were also made. Programs to help practitioners adopt the asthma management guidelines should help managed care save significant health care expenses.

Key Points

- The United States has the fourth highest prevalence of asthma in the world.
- Costs depend on the severity of disease, extent of exacerbations, and degree of disease control.
- There are approximately 5,000 possibly preventable deaths in the U.S. each year from asthma.
- Adoption of the asthma management guidelines has not been optimal.
- Achieving disease control is a major focus of the updated asthma management guidelines.
- Disease control is defined differently for each level of disease severity.
- For patients with moderate persistent asthma or worse, increasing the dose of inhaled corticosteroids is considered equivalent to adding a long acting beta agonist inhaler to the patient's regimen.
- Specialist care and allergy testing are recommended for patients with moderate persistent asthma or worse.
- Wider implementation of the asthma management guidelines should help control the costs of asthma management by reducing the morbidity associated with uncontrolled disease.

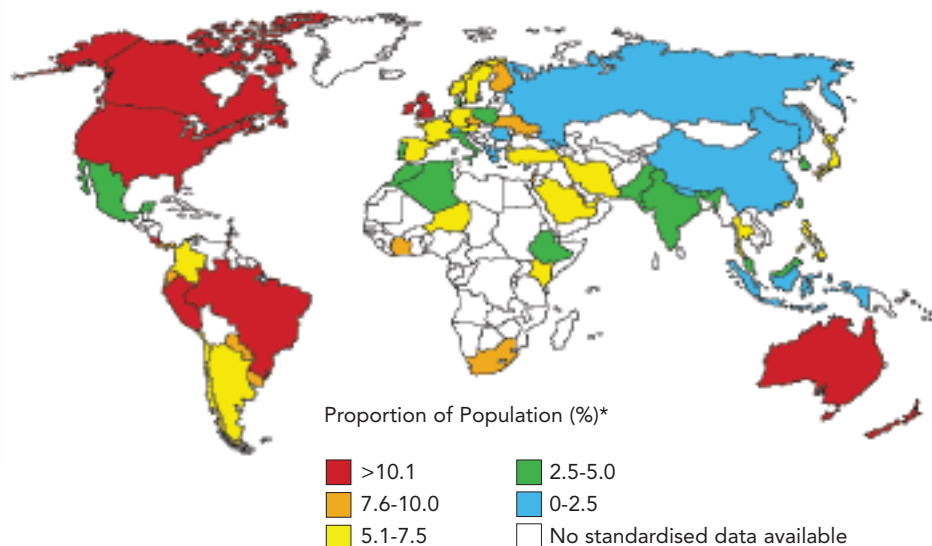
ASTHMA INVOLVES PEOPLE OF ALL AGES and in all countries. Since the '80s, there has been a doubling in the incidence of asthma in the general population. This has occurred specifically in developed countries, but even to a certain extent in underdeveloped countries. Asthma is a significant burden, not only in terms of health care costs but also of lost productivity (work and school) and reduced participation in family life.

The worldwide prevalence of asthma is more than 300 million cases. The affected population varies from 1 to 18 percent in different countries (Exhibit

1).¹ Countries with the highest prevalence include Scotland (18.4 percent), New Zealand (15.1 percent), Canada (14.1 percent) and the United States (10.9 percent). The international patterns of asthma prevalence are not explained by the current knowledge of the causation of asthma. Research into the causation of asthma, and the efficacy of primary and secondary intervention strategies, represents key priority areas in the field of asthma research.

Developed nations have more problems with asthma than some of the undeveloped nations. The rate of asthma increases as communities adopt Western

Exhibit 1: World Map of the Prevalence of Clinical Asthma



lifestyles and become urbanized. Part of this is explained by the theories of hygiene, obesity, and pollution playing a role in the development of asthma. With the projected increase in the proportion of the world's population that is urban — from 45 percent to 59 percent by 2025 — there is likely to be a marked increase in the number of asthmatics worldwide during the next two decades. It is estimated that an additional 100 million to 150 million persons are likely to have asthma by 2025.¹

Asthma-related fatality rates range from 0 to almost 40 fatalities per 100,000 asthmatics. Despite having an asthma prevalence at the lower end of the scale, countries such as China, Russia, and Mexico have fatality rates at the high end of the scale (36.7, 28.6, and 14.5 fatalities per 100,000 asthmatics, respectively).¹ The countries where controller therapies are not available have the highest asthma mortality rates.

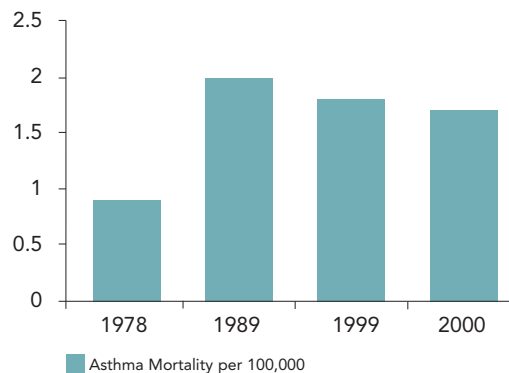
It is estimated that asthma accounts for about 1 in every 250 deaths worldwide. Approximately 5,000 people die from asthma annually in the U.S. The U.S. overall asthma-related death rate (Exhibit 2) has flattened out since the early 1980s.² Despite this flattening, asthma deaths have increased in the past 20 years in poor minority groups with limited access to health care. The asthma related deaths are related to suboptimal long-term medical care and delay in obtaining help during the final attack and are thus preventable. There is significant room for improvement in the area of asthma related deaths as well as the day-to-day care of asthmatic patients.

Costs depend on the severity of disease, extent of exacerbations, and degree of disease control. Patients with uncontrolled asthma use a disproportionate share

of resources.³ They are going to have the most exacerbations, hospitalizations, and need for medication. This is a group of patients who need the closest monitoring.

The annual cost of asthma in the U.S. is over \$15 billion.⁴ Fifty percent of this is patient borne in the form of copays and loss from work, and 50 percent is for medical care. Of the medical costs, half are for rescue or emergency treatment and a third are for medications and regular treatments. During 2000, there were 1.8 million emergency room visits for asthma and nearly 500,000 hospitalizations.⁵ The aging of our population is having an impact on hospital admission rates for asthma.⁶ Older patients are likely to have some chronic obstructive pulmonary disease (COPD) component to their asthma, which may not be adequately treated. Reducing the number of emergency room visits and hospitalizations is an area for greatest improvements in care and reduction in costs.

Exhibit 2: Annual Rate of Deaths: 1978-2000



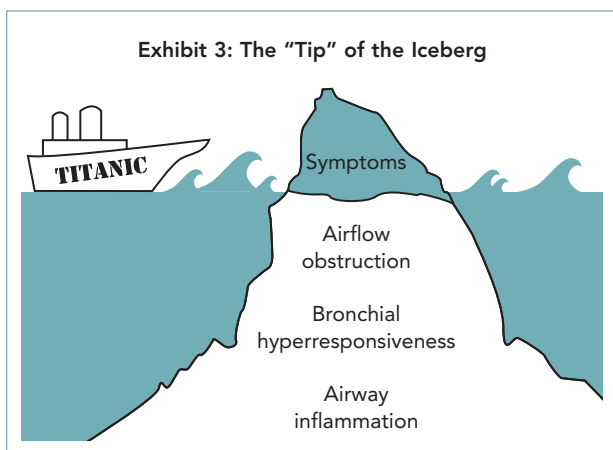


Exhibit 3 illustrates one of the biggest problems in current management of asthma by non-specialists. This is the dependence on patient symptoms to determine medical care.

Symptoms are the peak of the iceberg. Waiting until the patient is physically symptomatic means their disease has been out of control for quite a long period of time. Asthma symptoms can be triggered by many exacerbating factors including allergens, exercise, irritants, viral infections, gastroesophageal reflux, and sinusitis. Many asthmatics will cough long before they will wheeze. This is especially true in pediatric patients, but in adults as well. Patients are already in moderate distress when they present with wheezing, difficulty breathing, and chest tightness. Once symptomatic, they have significant levels of airflow obstruction, bronchial hyper-reactivity, and airway inflammation.

Patients with asthma develop a tolerance for their reduced lung function. They will tolerate 40 percent reductions in lung functions without complaints and will limit their exercise because they know it bothers them. They figure that is the way life will be. Relying on symptoms without associated pulmonary function testing allows patients to leave the physician's office out of control. Any asthma trigger such as a viral infection or air pollution will prompt a major decline in function, and the patient will end up in the emergency room and possibly the hospital.

There is a neurological irritant respiratory link between the upper and lower airway. Patients' asthma will not be controlled until their upper respiratory problems such as sinusitis are controlled. About 80 percent of asthmatic patients have significant upper airway disease, and 20 percent of allergic rhinitis patients have asthma.^{7,8}

For office diagnosis of asthma, many people rely on peak flow. Asthma may be indicated if peak expiratory flow (PEF) increases >20 percent after a short acting bronchodilator. Unfortunately, peak

flow only measures large airway function. It does not measure small airway function and small airway irritability and inflammation, which is a major contributor to asthma. Spirometry is recommended over peak flow meters for diagnostic purposes. Only through pulmonary function testing can a good assessment of the patient's lung function be obtained. One of the premier points of guidelines is normalization of pulmonary functions. Pulmonary function testing needs to be incorporated in the care of asthmatic patients.

The National Asthma Education and Prevention Program (NAEPP) Guidelines for the Diagnosis and Management of Asthma were first released in 1997 and have been updated twice since. The most recent update was published in August of 2007.⁹ The initial asthma management guidelines recognized that most adverse outcomes result from poor diagnosis, inadequate prescribing, and less than optimal adherence to therapy.

Implementation of the asthma management guidelines has been poor, and adherence to guidelines has not achieved the hoped-for results.^{10, 11, 12} Problems with clinicians following the guidelines have occurred. Under-diagnosis has been a significant problem. Patients are treated as having less severe disease than they actually have. That leads to inadequate prescribing with low usage of inhaled corticosteroids, the gold standard for decreasing lung inflammation. Another problem has been inadequately educating the patients so there is poor buy-in from the patient and, therefore, poor adherence to therapy.

One group assessed tertiary care center physicians on their abilities to understand the asthma guidelines.¹⁰ When quizzed about the guidelines, the mean correct total score for all physicians was 60 ± 2 percent (mean \pm SEM). Asthma specialists scored higher in total score and in pharmacology and prevention. However, no group performed well on estimating disease severity. There is some loss of transference of the guidelines into practice. Cabana and colleagues found similar problems with translation of the guidelines by pediatricians.¹¹ Although most of the surveyed pediatricians were aware of the guidelines (88 percent) and reported having access to a copy of the guidelines (81 percent), they had self-reported rates of adherence between 39 percent and 53 percent for the guideline components.

Exhibit 4 shows the major changes in the newest revision of the asthma management guidelines. The guidelines are now broken down into more age groups (0-4, 5-11, 12 and older). Children need a slightly different approach than adults.

Understanding the variability of disease and focusing on control is the approach of the latest edition of the

guidelines. The guidelines use a step-wise approach to the treatment of asthma, which has been modified slightly in the newest edition. For mild persistent, mild intermittent, and even mild moderate persistent, inhaled corticosteroids are recommended. When low dose of inhaled corticosteroid use is not sufficient, it is now considered appropriate to increase the dose of the inhaled corticosteroid before adding a long-acting beta-agonist or some other medication. Once a patient is under good control, medications can be stepped down.

A major focus of the updated guidelines is evaluating control. Patients with intermittent asthma are under good control when they need a short-acting beta-agonist less than twice a week and use fewer than two or three canisters of short acting inhaler a year. Additionally, to be under control they should not be waking up at night with asthma symptoms more than once or twice a month. Hopefully, they're not waking up at night at all. Exhibit 5 illustrates how disease control is defined for various levels of disease in people over 12 years old.⁹ Achieving good control is a matter of being more aggressive on a day-to-day basis. If patients are under control, it takes a lot more to make them symptomatic and cause an emergency episode.

A key addition to the guidelines is the recommendation that a pulmonary or allergist consultation be obtained for patients with moderate or severe asthma. These are the patients who are going to have the most exacerbations, need the most medications, and have the highest costs. They are also the ones who will gain the most benefit from seeing a specialist. If the specialist can find the triggers or causes of their exacerbations, there will be better success in getting the patients under good control.

Allergy evaluation is recommended for patients with moderate persistent and worse disease. An allergy evaluation can have value for children older than 4, even with mild disease. If they have significant allergies, these can be addressed to improve the patients' disease control.

Asthma action plans are recommended by the guidelines for all patients with asthma. These are specific instructions on how patients should use medications, both on a daily basis and when symptoms occur. Because the medication regimens can be complicated, patients may have difficulty remembering what they are to do in a particular situation. The action plans provide specific directions on what to take and when and when, to seek additional medical attention. Although asthma action plans have been recommended for some time, only 39 percent of children in one study had a plan.¹² When patients do not have an action plan, they have the tendency to overuse their short acting inhaler (e.g., albuterol) before they even bother to call their

Exhibit 4: Major Guideline Changes

- Asthma management broken into age groups 0 to 11, and 12 and older.
- Allergic evaluation for moderate persistent asthma up. Maybe all?
- Consultation with board certified specialists (allergypulmonologists) for moderate persistent asthma and up? Mild persistent as well?
- Equal weighting to increasing ICS vs. adding a LABA in more severe asthmatics (moderate persistent and higher)

doctor. By the time they seek medical attention, the exacerbation will have progressed to a point that it is more difficult to treat.

Another study illustrating the problems with asthma care was published by Scarfone and colleagues.¹³ Among 433 children who visited an emergency room for an acute asthma exacerbation, 76 percent had at least one doctor visit in the preceding 12 months, and 75 percent had at least one emergency department visit in the preceding 12 months. Forty three percent had at least one hospitalization for asthma in the preceding 12 months. Overall, 64 percent had persistent asthma by National Heart Lung Blood Institute (NHLBI) criteria, yet an allergist or pulmonologist cared for just 4 percent. For this group of children, 38 percent took daily anti-inflammatory therapy, 18 percent received a daily inhaled corticosteroid, 48 percent did not use a holding chamber with their meter dose inhaler, and 71 percent did not have a written action plan. These patients didn't know what to do when they started to have problems. These authors found that care for children with persistent asthma did not adhere to the guidelines any better than that for mild intermittent disease.

Exhibit 6 lists some of the reasons there is a lack of adherence among patients with asthma. Costs are definitely a reason for nonadherence. Some managed care plans have made combination products a third or fourth tier for medication copay. This approach means the most severe asthmatic patients have the greatest expense, which may impact their ability to be adherent. In this case, saving pharmaceutical costs may result in more medical costs.

A tremendous number of medications have been introduced in the treatment of asthma. Many of these have been groundbreakers. Inhaled corticosteroids are the gold standard. They are the beginning therapy for most patients with persistent disease. About 60 percent of patients will do well on an inhaled corticosteroid daily with a short-acting beta-agonist for acute symptom relief. The other 40 percent will need some combination of daily therapy to achieve disease control. Stopping daily inhaled corticosteroids will result in declines in lung function to levels seen

Exhibit 5: Assessing Asthma Control in Patients Greater Than 12 Years of Age

Components of Control		Classification of Asthma Control (≥ 12 years of age)		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤ 2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤ 2x/month	1-3x/month	≥ 4x/month
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting beta ₂ -agonist use for symptom control (not prevention of EIB)	≤ 2 days/week	>2 days/week	Several times per day
	FEV ₁ or peak flow	>80% predicted/ personal best	60-80% predicted/ personal best	<60% predicted/ personal best
	Validated questionnaires ATAQ ACQ ACT	0 ≤ 0.75* ≥ 20	1-2 ≥ 1.5 16-19	3-4 N/A ≤ 15
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year Consider severity and interval since last exacerbation	≥ 2/year (see note)	
	Progressive loss of lung function	Evaluation requires long-term follow-up care		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		

EIB, exercise-induced bronchospasm
ATAQ, Asthma Therapy Assessment Questionnaire
ACQ, Asthma Control Questionnaire
ACT, Asthma Control Test

before starting therapy.¹⁴

In many patients, long-acting beta-agonists are added to inhaled corticosteroids when the corticosteroid alone is not sufficient. There are subgroups of patients that are more susceptible to the side effects of long-acting beta-agonists. These long acting agents, such as salmeterol, should never ever be administered as monotherapy. They should always be given with an inhaled corticosteroid. Certain subgroups including African-Americans will get worse with long-acting beta-agonists. This is seen as a deterioration of lung function over time after the long acting beta-agonist is added. Unfortunately, which patients will have this reaction cannot be predicted.

Asthma is a whole lung disease process. Many of the treatments that have been available are large particle inhaler type drugs. They work well, but they only reach the large bronchi. In recent years, development of small particle inhaled corticosteroids that

can reach into the smaller airways has occurred. In one study, the patients who were having difficulty with control had good function of their large airways but not small airways. Not addressing the closure of small airways resulted in these patients having increased costs, emergency room visits, and hospitalizations. Distal airway inflammation is associated with difficult to control asthma.¹⁵

There are many things that are needed to improve asthma care during the next decade. We need better ways to disseminate and get “buy-in” for the NAEPP Guidelines. Patients must be educated on what is “good asthma care.” Physician behavior toward asthma needs to be changed. Pay for performance is one possible way to improve asthma care. We need to develop better asthma disease management programs. These programs need to move from disease control to disease modification to disease prevention (more allergy care, environment controls, etc.). There also

Exhibit 6: Reasons For Nonadherence Among Patients With Asthma

- Lack of knowledge about the severity of asthma
- Lack of expectations from treatment
- Concern of side effects with medications
- Underestimating the severity of symptoms
- Lack of enthusiasm in taking control of their health
- Need for autonomy
- Failure in the system to develop patient self-regulation skills
- Failure to remember the treatment plan
- Cost issues

needs to be a better understanding of the phenotypes of asthma and evaluation of small airways and their impact on disease severity and control.

Conclusion

Asthma is a disease of the entire respiratory tract and must be treated as an inflammatory disease. The key challenges for clinicians who manage patients with asthma include identifying and addressing patient needs; providing appropriate therapy and management for asthma; assessment of associated complications, sinusitis, reflux, small airway disease, smoking, etc; and examination of pulmonary functions. Poorly controlled asthmatics are expensive. Medications are essential for long-term control. But medications alone are not the entire solution to achieving control. Environment, allergies, other diseases, financial situation, asthma education, and many other factors also impact a patient's disease control. Successful disease control requires looking at all aspects of the care of these patients. **JMCM**

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Patient Example:

June is a 16-year-old female seen in a chronic lung disease clinic. She had missed 75 days of school and had 12 hospitalizations and \$250,000 in hospital expenses the previous year. After her evaluation by an asthma and allergy specialist, a public health nurse was sent out to her house to provide education and evaluation of the home environment. During the course of the next year, she was not hospitalized, missed no school days, and had not been seen in an emergency room. She was taking her medications on a regular basis and her lung functions were 100 percent of predicted.

Patient Example:

Alice is a 60-year-old female who had been followed by specialists for asthma for more than 15 years. Because she was debilitated, she saw another asthma specialist for another opinion. Her pulmonary function showed her lung function was 40 percent of predicted. She couldn't climb a flight of steps and couldn't play with her grandchildren. Four years prior, she had been put on a combination of an inhaled corticosteroid and a long-acting beta-agonist. During that time, there had been a consistent deterioration of her asthma. The long-acting beta-agonist was discontinued. Within 60 days, her lung functions were 100 percent of predicted. She was well-controlled on a low dose of inhaled corticosteroid.

Female-Male Ratio in Whites in New York State, 1990-2004.

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