REVIEW

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Getting Control of Uncontrolled Asthma

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ABSTRACT

Despite various treatment modalities, a large proportion of patients have asthma that remains uncontrolled. These patients remain at an increased risk of developing severe exacerbations, have a poor quality of life, and pose a high economic healthcare burden, with an estimated mean annual cost more than double that of patients with good symptom control. It is therefore important to accurately diagnose asthma and continually assess asthma control. Several validated tools are available to do this, including questionnaires, biomarker analysis, and bronchoscopy. Current guidelines advise physicians to establish a self-management program for the patient to assess and monitor asthma control. A further recommendation is the establishment of an educational action plan to increase treatment adherence and to improve asthma control. National and international guidelines provide long-term management strategies for these patients and recommend a stepwise approach for achieving and maintaining asthma control. Despite availability of a wide range of controller and reliever therapies, uncontrolled asthma remains a challenge and reflects the need for new therapeutic options. This review discusses current global guidelines for the assessment and management of asthma control and summarizes the broad spectrum of novel therapeutic agents currently under development for the treatment of asthma, including anticholinergics, chemoattractant receptor-homologous molecules expressed on T-helper 2 lymphocyte antagonists, and anti-interleukin (IL)-5, anti-IL-13, and anti-IL-4 agents.

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Asthma affects approximately 300 million people worldwide across ages and ethnic groups, with an additional 100 million patients estimated to be affected by 2025.[1] The increase in this global burden likely reflects a true increase in the incidence of the disease.[1]

Despite available treatment modalities and decreased associated death rates over the last decade,[2] a large proportion of patients still have uncontrolled asthma.[3] In the United States, the Asthma Control Characteristics and Prevalence Survey Studies observed uncontrolled asthma in 58.8% and 49.7% of adult and pediatric patients, respectively,[4] similar to the prevalence reported by the European National Health and Wellness Surveys (53.5%).[5] However, a higher incidence (85.7%) was reported in the US Comprehensive Survey of Healthcare Professionals and Asthma Patients Offering Insight on Current Treatment Gaps and Emerging Device Options.[6]

This review summarizes current guidelines for asthma diagnosis and management, examines risk factors and healthcare burden associated with uncontrolled asthma, and reviews tools to assess asthma control. Currently available medications and emerging therapeutic options are discussed.

WHAT IS LACK OF CONTROL?

Definitions of Asthma Control

The Global Initiative for Asthma Guidelines, a Global Strategy for Asthma Management and Prevention, define uncontrolled asthma as patients who are symptomatic and experience rescue medication administration >2 times/week; nocturnal symptoms; activity limitations; lung

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function obstruction (<80% predicted identified using spirometry); or daytime symptoms >2 times/week.[1]

National Asthma Education and Prevention Program guidelines define asthma severity as intrinsic disease intensity, whereas control is the degree to which asthma manifestations are reduced, and therapy goals are achieved.[7] Patients are classified as having "well-controlled," "not well-controlled," and "very poorly controlled" asthma, according to impairment criteria (nocturnal awakenings, normal activity limitations, rescue medication use, lung function abnormalities assessed by spirometry) and risk criteria (exacerbations, decreased lung growth, drug-related adverse events).[7]

Differing Perceptions Between Patients and Physicians

Asthma control perceptions can differ greatly between patients and physicians, both underestimating severity and control. Some patients may not recognize symptom severity and tolerate what would be considered "unacceptable" to physicians.[7,8] Patients also may have low expectations of therapeutic benefit and accept less control than is achievable with effective disease management.[9] Furthermore, patients may overestimate asthma control, consequently underusing controller therapies or allowing medication reductions by their physician.[10]

Patients may lack knowledge about available treatments or asthma causes,[11] leading to medication underuse, especially of inhaled corticosteroids.[12] Because inhaled corticosteroids generally have no immediate effect, patients may dismiss them as ineffective.

Physicians may underestimate disease severity or overestimate disease control, resulting in medication underprescription.[13] Because symptoms and pathophysiology vary over time, accurate assessment of disease severity, asthma control, and prescription of the most effective medication may be difficult. A self-management program focused on the individual patient's needs may aid in effective asthma control management.[1,7]

IS LACK OF ASTHMA CONTROL A MAJOR PROBLEM?

Patients with uncontrolled asthma pose higher economic burdens than those with well-controlled asthma because of direct costs (medications, asthma-related hospitalization, visits to the emergency department) and indirect costs (low work productivity, absenteeism, loss of future earnings).[14-19] The US annual total economic burden of asthma-related costs has been estimated at $56 billion/year.[14] In an observational study of patients aged ≥13 years, annual mean costs attributed to uncontrolled asthma were more than double that for controlled asthma ($5964 and $2422, respectively) (Figure 1).[18] Likewise, an observational European study calculated that average healthcare costs over 3 months attributed to uncontrolled asthma were considerably higher than for controlled asthma.[20]

CLINICAL SIGNIFICANCE

- Large proportions of patients have asthma that remains uncontrolled despite available treatment.
- These patients have higher economic burdens than those with well-controlled asthma because of increased medication need, asthma-related hospitalizations/emergency department visits, and work absenteeism/loss of future earnings.
- Some risk factors for uncontrolled asthma can be modified with self-management and educational action plans.
- Novel therapies are emerging that will help address the needs of patients with uncontrolled asthma.

HOW IS ASTHMA CONTROL MEASURED?

Although physicians generally diagnose asthma on the basis of characteristic symptoms, validated tools are available that provide standardized methods for confirming diagnosis and assessing asthma control.

Symptoms

Cough, wheeze, dyspnea, nocturnal awakenings, seasonal variation, and irritant triggering are commonly reported with symptomatic asthma. Symptoms may be intermittent and overlooked or misdiagnosed. Combination symptom and exacerbation frequency may be an important marker of lack of control.

Lung Function Tests

Spirometry helps establish an asthma diagnosis. Low forced expiratory volume in 1 second (FEV_1) (<80% of predicted normal) indicates lung function impairment and increased risk of exacerbations and developing uncontrolled asthma. Airflow limitation is assessed using FEV_1 to forced vital

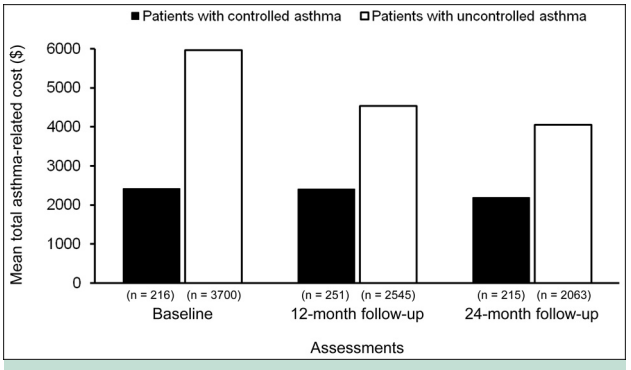

Figure 1 Annual asthma-related costs, including variables relating to productivity loss, healthcare use, and medication use, by control status at baseline and at 12- and 24-month follow-up (based on Sullivan et al,[18] 2007).