

# Asthma Quality of Care: Looking Beyond Cost of Drug Therapy

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## Summary

Asthma is a chronic and serious disease state that has a severe economic burden. Patients with difficult-to-treat asthma are responsible for a disproportionately large share of health resource utilization and costs. It is important to include direct medical costs and indirect costs, including absenteeism and lost productivity at work and home, when considering this disease. Despite the use of recommended drug therapies, the disease is poorly controlled in many patients. This results in emergency department (ED) visits, hospitalizations, absenteeism, and lost productivity. Newer drug therapies exhibiting increased efficacy offer the possibility of improved outcomes, particularly reductions of disease exacerbations and improvements in patient quality of life (QOL).

To lessen the burden of the disease and contain costs, asthma should be aggressively and effectively treated to establish and maintain disease control. Drug costs should not be the only consideration when developing a therapeutic regimen to treat asthma. Disease management (DM) programs enable health plans to assess asthma therapy from a quality-of-care standpoint, evaluating patient outcomes as well as cost measures. This comprehensive treatment approach, coupled with a full range of therapeutic options, may serve to improve patient QOL and outcomes and benefit both the health plan and plan member.

## Key Points

- Asthma is a chronic disease that carries a severe economic burden.
- Asthma should be aggressively treated to establish and maintain control of the disease and to lessen its associated direct and indirect costs.
- A comprehensive approach, including DM programs and the use of biologic therapies, may improve patient QOL and outcomes, and benefit the health plan and plan member.

AT A COST TO THE U.S. HEALTH CARE system of more than \$12 billion per year, asthma is a chronic and potentially serious disease state that carries with it a severe economic burden.<sup>1</sup> The prevalence of asthma and the costs associated with the disease have increased over the past several years, amounting to more than nine million physician office visits, 500,000 hospitalizations, and 5,000 deaths annually.<sup>2</sup>

While some patients with uncontrolled asthma could be adequately controlled with improved diagnosis, more appropriate management using

standard therapies, or improved adherence to a treatment plan, other patients have asthma that is difficult to control because of the intrinsic severity of the disease and poor responsiveness to standard therapies. Patients with asthma that is difficult to treat have frequent or severe exacerbations and often need multiple drug therapies or complex medication regimens. They are responsible for a disproportionately large share of health resource utilization and costs.<sup>3</sup> Cross-sectional survey data from a 2003 analysis revealed that the total per-person costs were

\$2,646, \$4,530, and \$12,813 for patients' self-reported mild, moderate, and severe asthma, respectively ( $P < 0.0001$ ).<sup>4</sup> The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study, a large, three-year, multi-center, observational cohort trial, demonstrated that severe and difficult-to-treat asthma is associated with substantially larger health resource utilization and morbidity than mild or moderate disease.<sup>5</sup> Because of the high cost associated with difficult-to-treat asthma, fewer than 20 percent of asthmatics account for approximately 80 percent of direct asthma care expenditures.<sup>6</sup>

Traditional therapies appear to have adequate efficacy for mild to moderate asthma (about 30 percent of the time in moderate disease) but limited efficacy for severe and uncontrolled asthma, further contributing to the economic burden of the disease in this specific demographic.<sup>2,3,7</sup> Newer therapies with higher acquisition costs present an option in treating patients with severe asthma. Their efficacy in reducing costly exacerbations (e.g., hospitalizations, emergency department [ED] visits) and improving patient quality of life (QOL), with a reduction in indirect costs,<sup>3</sup> may serve to offset some the drug-acquisition costs. They may also improve adherence and result in improved monitoring because of their administration profile, which can reduce both direct and indirect costs.<sup>9</sup> Disease-management programs employing guidelines such as those established by the National Heart, Lung, and Blood Institute (NHLBI) also may lead to improved outcomes and allow for more adequate assessment of the effectiveness of newer pharmacotherapeutic agents.<sup>10</sup>

### Cost of Asthma

The total economic burden of asthma is the result of expenditures for the treatment of the disease (i.e., direct costs), as well as costs associated with the effect of the disease on patients' QOL and ability to function in the workplace (i.e., indirect costs). Although the direct costs associated with asthma are more apparent and tangible, the indirect costs often have a greater and more long-lasting effect on the health care system and U.S. economy alike.

### Direct Costs

The direct costs associated with asthma are most apparent in health care resource utilization resulting from treatment of the disease. From the perspective of costs to society, Cisternas et al reported that the annual per-person cost of asthma averaged \$4,912, with direct costs accounting for

\$3,180 (65 percent), based on 1998 and 1999 equivalents.<sup>4</sup> The largest components within direct costs were pharmacotherapy (\$1,605; 50 percent), hospital admissions (\$463; 15 percent), and non-ED ambulatory visits (\$342; 11 percent).

### Indirect Costs

Although less apparent and often overlooked, the indirect costs associated with asthma are significant and burdensome as well. These costs are realized in lost workdays and reduced productivity at work and at home. Asthma accounts for more than 10 million missed school days and 3 million missed work days annually.<sup>11</sup> Estimated costs resulting from lost work days due to asthma in adults are more than \$800 million per year. An additional \$900 million per year is lost because of work days missed by parents caring for children with asthma.<sup>11</sup> In the analysis by Cisternas et al, the per-person indirect costs associated with asthma accounted for 35 percent of the total economic burden of the disease, at \$1,732 annually.<sup>4</sup> Within these per-person indirect costs, total cessation of work accounted for \$1,062 (61 percent) and the loss of entire work days among those remaining employed accounted for another \$486 (28 percent).<sup>4</sup> Typically, the more severe the asthma, the greater the indirect costs. Additionally, the indirect cost estimates are likely to be low, as it is difficult to measure decreased productivity when the activity-able asthmatic patient goes to work.

The reduced QOL associated with asthma is perhaps the most startling indirect cost. Patients with asthma are affected by their disease daily, which has a profoundly negative impact on their general level of health. In a cross-sectional study by Ford et al, participants with self-reported current asthma reported significantly more age-adjusted physically unhealthy days (6.5 days versus 2.9 days;  $P < 0.001$ ), mentally unhealthy days (5.2 days versus 3.0 days;  $P < 0.001$ ), days with activity limitation (3.7 days versus 1.6 days;  $P < 0.001$ ), and unhealthy physical or mental days (10.0 days versus 5.4 days;  $P < 0.001$ ) in the past 30 days than participants who never had asthma.<sup>12</sup> This translated to 147 million unhealthy functioning days per year among the study population with self-reported asthma. Among persons with asthma compared with those who never had asthma, the odds ratios (ORs) were 2.41 (95 percent confidence interval [CI], 2.21 to 2.63) for reporting poor or fair self-rated health, 2.26 (95 percent CI, 2.06 to 2.49) for reporting  $\geq 14$  days of impaired physical health during the previous 30 days, 1.55 (95 percent CI, 1.40 to 1.72) for reporting  $\geq 14$  days of

poor mental health during the previous 30 days, 1.96 (95 percent CI, 1.73 to 2.21) for reporting  $\geq 14$  activity limitation days, and 1.99 (95 percent CI, 1.84 to 2.15) for reporting  $\geq 14$  days of physically or mentally unhealthy days during the previous 30 days. Participants who previously had, but did not currently have, asthma reported having more unhealthy days with all four measures than those who never had asthma, but fewer than participants who currently had asthma.<sup>12</sup>

QOL measures are not only indicative of patients' general well being, they also are significant drivers of indirect cost. In fact, available data demonstrate that asthma-specific, health-related quality of life (HRQOL) is associated with future asthma-related health utilization and cost. In a prospective cohort study, Eisner et al observed that better baseline asthma-specific HRQOL was associated with a decreased risk of asthma-related ED visits or hospitalization during longitudinal follow-up (OR per 10-point HRQOL score increment, 0.84; 95 percent CI, 0.74 to 0.95), controlling for demographic and clinical factors.<sup>13</sup> Better baseline generic physical HRQOL was associated with a decreased risk of future all-cause hospitalization (OR, 0.68; 95 percent CI, 0.60 to 0.77). More favorable asthma-specific HRQOL scores also were related to decreased asthma-related health care costs during the ensuing year ( $-0.086$  log-dollars per 10-point score increment; 95 percent CI,  $-0.11$  to  $-0.06$ ). Better generic physical HRQOL scores were associated with lower total costs ( $-0.24$  log-dollars; 95 percent CI,  $-0.32$  to  $-0.17$ ). Looking at health care expenditures in relation to HRQOL, Eisner et al reported a difference of more than \$100 in average cost per person per year between patients with an "excellent" HRQOL score and those with a "poor" HRQOL score (\$208.06 versus \$314.71, respectively).<sup>13</sup>

### **The Cost of Illness Versus the Cost of Wellness**

As is apparent from the available data, asthma, particularly difficult-to-treat asthma, remains a costly disease for the health care system. In addition to the direct costs associated with treatment, underlying costs contribute to the overall economic burden when treatment is inadequate and the disease remains uncontrolled. Despite this, however, a significant number of patients ( $\approx 40$  percent) remain symptomatic, with suboptimally controlled asthma symptoms.<sup>14,15</sup> In a study by Bateman et al, patients with moderate asthma achieved complete control only one third of the time when treated with the widely accepted therapy of inhaled corticosteroids plus a long-acting beta-agonist.<sup>7</sup> In another study by

Bateman et al of patients with uncontrolled asthma who received increasing doses of inhaled corticosteroids plus a long acting beta-agonist based on their symptoms, just 41 percent of the patients were able to achieve complete control of their disease.<sup>8</sup> As patients remain symptomatic despite guideline-recommended therapy, health care costs rise as a result of hospitalizations, physician visits, and ED visits.

To lessen this burden and contain costs, asthma should be aggressively and effectively treated to establish and maintain control of the disease.<sup>4,16</sup> In doing so, treatment failures, repeat hospital and physician visits, and absenteeism all can be significantly reduced, thereby reducing both the direct and indirect costs associated with asthma.<sup>16</sup> But treatment is a joint effort between the health care system and the patient. A variety of factors can lead to failure of therapy. Patients need adequate training, access to effective drugs, an understanding of and ability to utilize avoidance of triggers, and a high level of compliance to those drugs that control the primary and secondary processes leading to the symptoms of asthma. If any of these is absent, failure of control can manifest itself in higher ED visit rates or admissions to the hospital. Effective asthma management programs must address all of these issues. In other words, effective asthma care requires a system of care that is now termed disease management.

Aggressive asthma therapy involves additional expenditures, primarily on pharmacotherapeutic agents, and contributes to direct health care costs; however, both non-drug direct and indirect costs will be subsequently reduced if asthma control is established.<sup>16</sup> Even a shift as small as 5 percent in the proportion of patients categorized as having severe to moderate asthma status is estimated to save \$1.4 billion annually.<sup>4</sup> An analysis of the TENOR study data revealed that the mean cost for patients who remained controlled through the two-year study period was \$6,452, compared with \$14,212 for patients who remained uncontrolled.<sup>2</sup> Attaining the goal of asthma control is imperative to ultimately addressing the overall economic and human burden of the disease, even if additional pharmacotherapy expenditures are required.<sup>3</sup>

### **Drug Acquisition Costs Versus Total Disease Costs**

For a disease state as costly as asthma, pharmacoeconomic analyses can be beneficial for evaluating the cost-effectiveness of potential drug therapies. In performing these analyses, it is imperative to consider both drug acquisition costs *and* total

health care costs to allow for a comprehensive and accurate assessment of a drug's potential economic impact. A newer agent may carry a high acquisition cost, but this cost may be at least partially offset because its improved efficacy over existing therapies may result in lower health care expenditures in other areas.

When evaluating the cost-effectiveness of pharmacotherapeutic options for the treatment of asthma, two preventable and costly components are hospitalizations and ED visits.<sup>17</sup> These components are markers for asthma exacerbations. Because these two components make up 37 percent of health care expenditures for asthma, reducing their frequency through improved asthma control would significantly lessen the economic burden of the disease.<sup>17,18</sup> Agents such as omalizumab, that carry a higher acquisition cost but reduce hospitalizations and ED visits, present an attractive option in decreasing the economic burden of asthma despite their apparent costliness, especially when other less costly alternative have failed to effect disease control.

Omalizumab, an injectable antibody targeting IgE, has significantly lowered rates of asthma-related hospitalizations compared with placebo<sup>19</sup> and has demonstrated efficacy in reducing exacerbations at a rate of approximately 17 additional patients for every 100 treated.<sup>20</sup> Holgate et al reported that 50 percent of exacerbations were prevented with omalizumab treatment, and that 5.7 patients needed to be treated with omalizumab to maintain one patient as exacerbation-free.<sup>20</sup>

As discussed, an unusually high proportion of asthma-related health care expenditures are accounted for by patients with poorly controlled or difficult-to-treat asthma.<sup>18</sup> In treating this cost-inflating demographic, highly effective and more costly agents, such as omalizumab, may be of further value.<sup>21,22</sup> Difficult-to-treat asthmatic patients account for an even greater proportion of costly hospitalizations and ED visits, and a reduction in the incidence of these events would represent a cost saving that could partially offset the higher acquisition cost of newer agents such as omalizumab.

The cost to society needs to be considered in the cost equation as well. As cited previously, loss of work time and days is noteworthy for patients with mild, moderate, and severe asthma and may occur in the absence of hospitalizations or ED visits. Therapies that decrease absenteeism and improve productivity must include these benefits in their cost-effectiveness evaluation. To evaluate cost-effectiveness on the basis of direct costs only will result in ignoring

improvement in QOL and savings in absenteeism and presenteeism costs.

## Disease Management

Disease Management was introduced more than a decade ago as a viable strategy for the comprehensive treatment of chronic diseases such as asthma. This system of coordinated health care interventions and communications for populations with conditions in which patient self-care efforts are significant<sup>23</sup>:

- Supports the physician or practitioner/patient relationship and plan of care,
- Emphasizes prevention of exacerbations and complications utilizing evidence-based practice guidelines and patient-empowerment strategies, and
- Evaluates clinical, humanistic, and economic outcomes on an ongoing basis with the goal of improving overall health.

The components of DM include:

- Population identification processes,
- Evidence-based practice guidelines,
- Collaborative practice models to include physician and support-service providers,
- Patient self-management education,
- Process and outcomes measurement, evaluation, and management, and
- A routine reporting/feedback loop.

The DM perspective allows health plans to look at asthma therapy from a quality-of-care standpoint, evaluating patient outcomes as well as cost measures. In this manner, the value of seemingly excessively costly therapies, such as the recently introduced biologics, is more aptly assessed. Although these therapies typically carry a higher drug acquisition cost, added value can be found in their improved efficacy in controlling symptoms and managing severe or difficult-to-treat asthma over standard therapies.<sup>20-2</sup>

A strong DM approach using nationally acceptable guidelines and specialty expert advice is likely to ensure that a stepped care approach is followed before more advanced and sometimes more expensive agents are utilized. Such an approach is advocated by the National Asthma Education and Prevention Program (NAEPP), established by the NHLBI, in the recently released *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma*, which can be found at [www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm](http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm). The primary function of a DM program is to ensure patients are adequately trained on their disease process, preventive measures, and control medications, and that the control medications are being used in the appropriate dose, frequency, and manner. DM organizations routinely measure adherence and compliance and persistency

(collectively referred to as compliance) via both direct inquiries to the patient as well as via pharmacy data analysis. They then actively intervene if less than adequate compliance is discovered. They also ensure proper technique for inhaled products, and they measure outcomes using tools such as the Asthma Control Test (ACT) to evaluate whether the prescribed therapy is having the desired effect. Another common function of an effective DM program is to measure and intervene if patients are not receiving high-quality advice and treatment from their provider, and to recommend specialty consultation where indicated.

All of these activities are likely to reassure a health plan that all basic therapies are being adequately attempted. With a strong DM approach, virtually all failures of therapy should meet prior authorization criteria for the more expensive therapies, such as omalizumab.

As mentioned previously, the prevention of exacerbations and complications via adherence to evidence-based practice guidelines is integral to the concept of DM in the treatment of asthma. The treatment guidelines of the NAEPP are generally the most widely accepted guidelines in the United States for the treatment of asthma.<sup>10</sup> The NAEPP recommendations for the treatment of asthma were organized around four components of effective asthma management: the use of objective measures of lung function, oral corticosteroid use, medical care utilization, and symptoms to assess the severity of asthma and monitor the course of therapy; environmental control measures to avoid or eliminate factors that precipitate asthma symptoms or exacerbation; comprehensive short- and long-term pharmacotherapy to manage asthma exacerbations and reverse and prevent the characteristic airway inflammation; and patient education that fosters a partnership among the patient, the patient's family, and the health care professional.

The NAEPP goals of therapy for asthma control are to prevent chronic and troublesome symptoms, maintain (near) normal pulmonary function and normal activity levels (including exercise and other physical activity), prevent recurrent exacerbations of asthma, minimize the need for ED visits or hospitalizations, provide optimal pharmacotherapy with the least amount of adverse effects, and meet patient and family expectations for, and satisfaction with, asthma care. To determine whether the goals of therapy are being met, the following parameters should be assessed<sup>10</sup>:

1. Asthma signs and symptoms—at each health care visit, thorough physical examination and appropriate questions.

2. Pulmonary function—through spirometry and self-monitoring of peak expiratory flow (PEF). Spirometry is recommended at the time of the initial assessment, after treatment is initiated and symptoms and PEF have stabilized, and at least every one to two years.

3. QOL/functional status—has asthma caused missed work days or school days, a reduction in usual activities, or disturbances in sleep?

4. History of asthma exacerbations—during periodic assessments, physicians should question patients and evaluate any records of self-monitoring to detect exacerbations, both self-treated and treated by other healthcare providers.

5. Pharmacotherapy—monitor patient adherence to the regimen, inhaler technique, level drug usage, and adverse effects of medications, as well as the use of rescue medication.

6. Patient-provider communication—assess routinely.

7. Patient satisfaction—specifically, monitor asthma control and quality of care. Physicians and patients should perform an asthma assessment. Patients with mild intermittent or mild persistent asthma that has been under control for at least three months should be seen by a physician approximately every 6 months, whereas those with uncontrolled and/or severe persistent asthma should be seen more often. Patients should perform self-assessments by keeping a daily diary and/or completing a self-assessment form at office visits.

A program employing a DM intervention based on the 1997 NAEPP guidelines (EPR-2) was evaluated in a study by Buchner et al.<sup>24</sup> In the program's second year, asthmatic plan members received fewer inpatient services and the proportion of asthmatic plan members prescribed oral inhaled corticosteroids increased 30 percent. Likewise, HRQOL, satisfaction with quality of care, exposure to patient education, knowledge of the disease, and members' confidence in their ability to manage their disease demonstrated statistically significant improvements during the follow-up year (i.e., the second year) of the program for both adult and child asthmatic members. In a similar study, Patel et al evaluated the impact of a multidisciplinary asthma management program on processes of care and health care utilization for adults and children with asthma in a large urban medical group practice.<sup>25</sup> Chart review and administrative claims analyses showed that the program had beneficial results in several areas from baseline. Primarily, medical record documentation improved for asthma diagnosis (83.3 percent vs. 98.6 percent,  $P<0.001$ ) and patient education (15.7 percent vs. 26.1 percent,  $P<0.001$ ). Asthma-related ED visits decreased from 148 per

1000 to 88 per 1000 ( $P < 0.001$ ) and asthma-related hospitalizations decreased from 81 per 1000 to 37 per 1000 ( $P < 0.001$ ).<sup>25</sup> But, it is important to note that even with a well developed and implemented DM program, inadequate control of asthma as measured by admissions and ED visits occurs. This points to the need for the acceptance of more advanced therapies.

### A Specialist's Perspective

Although patients with uncontrolled or difficult-to-treat asthma appear to be the most likely candidates for newer therapies, from a cost-saving perspective, pulmonary specialists and allergists are best equipped to make the decision as to which patients would be best suited for such therapies. In making this determination, clinicians need to consider a variety of factors, including disease severity disease symptom control, including patient QOL, and risk for future exacerbations. Current data imply that newer therapies can be of particular utility in patients with moderate-severe asthma and that patient QOL is significantly improved.<sup>21,22</sup> One such study, by Luskin et al, analyzed pooled data from two randomized, double-blind, placebo-controlled trials studying the efficacy and safety of omalizumab to evaluate the variability in asthma-related quality-of-life (ARQL), determined by categorizing the Asthma Quality of Life Questionnaire (AQLQ) of each of the study arms.<sup>26</sup> The findings showed that a greater proportion of the patients receiving omalizumab demonstrated improvement in ARQL, especially symptom control and daily functioning, than those receiving placebo.

Specialists should personally question patients regarding their asthma control. Specific areas that should be addressed during such discussions include days missed from work/school, symptoms (shortness of breath, nighttime wakefulness), rescue inhaler use, limitations in activity, and the patient's self-rating of asthma control.

Certain patients at high risk for difficult-to-treat or severe asthma, and thereby at high risk for frequent health care resource utilization, should be considered for aggressive treatment with newer pharmacologic agents, including omalizumab, specialty care, and disease management. Factors to consider when determining risk for severe asthma include obesity, prior health care resource utilization, depression, non-adherence to previous therapies, and suboptimal control of asthma symptoms.

When evaluating the effectiveness of a chosen therapy, the use of self-administered tests, such as ACT, should be routinely conducted. Outcome measures such as absenteeism from work and

productivity at work and home should be included, as these markers identify when patients' daily living is altered by their disease.

### Conclusions

Asthma is a serious health care concern that carries with it a significant financial burden for the U.S. health care system. The costs associated with asthma and its treatment can be categorized as either direct or indirect; both of these types of costs are significant in considering the economic implications of asthma, and the two categories are closely related in the way in which they affect both the patient and the health care system.

Patients with difficult-to-treat or severe asthma account for a large proportion of expenditures ( $\approx 80$  percent) for this disease state.<sup>18</sup> Asthma in such patients is often inadequately controlled, and costly hospitalizations and ED visits are frequent. In this cost-inflating demographic, effective therapy is particularly important, not only to control costs but also to improve patients' QOL as they deal with this burdensome disease.

When considering potential therapies for the treatment of asthma, it is imperative that drug-acquisition costs, total health care costs, and indirect costs are considered, to allow for a comprehensive and accurate assessment of a drug's potential economic impact. Newer drugs with potentially improved efficacy over existing therapies may result in lower health care and disease expenditures in other areas. Total disease costs must not be overlooked, since doing so would exclude the costs associated with key factors such as physician and ED visits as well as indirect costs, thereby making cheaper but less effective therapies seem more cost-effective and attractive. Agents that carry a higher acquisition cost (e.g., omalizumab) may be more cost-effective than they initially appear because of their efficacy in reducing exacerbations and the incidence of ED visits and hospitalizations, as well as improving absenteeism and productivity and daily functioning, particularly in the costly and difficult-to-treat uncontrolled asthma patient population.

Although patients with uncontrolled or difficult-to-treat asthma appear to be the most likely candidates for newer therapies from a cost-saving perspective, pulmonary specialists and allergists are best equipped to make the decision as to which patients would be best suited for therapies such as omalizumab. In doing so, clinicians need to consider a variety of factors such as indirect patient and system costs, including the often-overlooked area of patient QOL, which suffers significantly when asthma is left uncontrolled.

DM programs employing guidelines, such as those set forth by the NAEPP, have been shown to lead to improved patient outcomes in asthma. This comprehensive treatment approach, coupled with novel biologic therapies demonstrating improved efficacy in treating patients with severe disease, may serve to improve patient QOL and outcomes, and benefit both the health plan and plan member. **JMCM**

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