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ORIGINAL ARTICLE

The Impact of Uncontrolled Asthma on Absenteeism and Health-Related Quality of Life

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Objective. To evaluate the impact of uncontrolled asthma on the absenteeism and health-related quality of life (HRQOL) of adults and children with asthma and the caregivers of pediatric patients. **Patients and methods.** Patient information was obtained from datasets maintained by National Jewish Health for this cross-sectional study. Participants in the study were 12 years of age or older. Participants younger than 18 years had their information provided by caregivers. Caregivers also provided 6 months of absenteeism and QOL data. Participants were classified as having uncontrolled asthma based on a treatment and symptom guideline-based algorithm. Absenteeism was assessed from the self-reported number of work or school days missed due to asthma during the previous 6 months. HRQOL among adults was measured using the validated Marks Asthma Quality of Life Questionnaire (Marks-AQLQ) and among caregivers using the validated Pediatric Asthma Caregivers Quality of Life Questionnaire (PACQLQ). To account for the positive skew in absenteeism data, a zero-inflated Poisson regression model was used to compare group differences. HRQOL was analyzed for adults and caregivers using the Wilcoxon-Mann-Whitney test. **Results.** A total of 15,149 patients met the inclusion criteria for the study and were included in the analysis. Adults with uncontrolled asthma and caregivers of children with uncontrolled asthma reported significantly higher absenteeism than their controlled counterparts: 43% vs 24% adults reported missing days of work, with a median 6 days vs 3 days missed; 31% vs 16% of caregivers reported missing days of work, with 4 days vs 2 days missed; and caregivers reported that more than 70% vs 45% pediatric patients missed school, with a median of 6 days vs 4 days missed (uncontrolled vs controlled asthma, respectively). Adult uncontrolled asthmatics and caregivers of uncontrolled pediatric patients had significantly lower HRQOL as indicated by the Marks-AQLQ (scores 1.5 points higher, $p < 0.001$) and PACQLQ (scores < 0.5 points lower, $p < 0.001$), respectively. **Conclusions.** Uncontrolled asthma has far-reaching impact on the productivity and quality of life of asthma patients and their caregivers. Proper assessment, treatment, and disease management to improve asthma control may reduce the impact of uncontrolled asthma on asthmatic adults, children, and the caretakers of pediatric asthmatic patients.

Keywords asthma; uncontrolled asthma; pediatric asthma; caregiver; HRQOL; QOL; quality of life; absenteeism

INTRODUCTION

In 2005 there were more than 22 million people, including approximately 6 million children, with a diagnosis of asthma in the United States (1). The number of visits to physicians and to emergency rooms (ERs) for asthma-related causes as well as overnight stays in the hospital with asthma as a primary diagnosis (10.6 million (2), 1.8 million (1), and 444,000 (3), respectively) indicate both the prevalence and problematic nature of the disease, as well as its associated burden on health care utilization and cost in the US (1, 4–6).

In an effort to standardize asthma diagnosis and treatment and improve the outcomes of asthma patients, in 2002 the National Heart, Lung and Blood Institute commissioned an expert panel to update the National Asthma Education and Prevention Program Committee (NAEPP) guidelines, focusing on a stepwise diagnosis of asthma severity and treatment to improve patient health. This newest iteration of the national guidelines emphasized for the first time that asthma is essentially a fluid disease and that the overall goal of management interventions should be to keep patients with asthma

in a state of “control” for as much of the time as possible. The NHLBI Guidelines were quite clear that there are many factors that can be associated with loss of control; efforts are essential to assess levels of control and re-establish control of the symptoms.

Studies have demonstrated wide variation in health care provider classification of asthma severity, adherence to NAEPP guidelines, and associated treatment patterns. Most of those studies used previous classifications of asthma severity and did not directly address levels of control (7–9). While Bateman et al. demonstrated that a guideline-defined approach to asthma treatment can lead to long-term asthma control irrespective of severity classification (10, 11), uncontrolled asthma remains a problem. In fact, the most recent NAEPP guidelines (2007 update) distinguish between disease severity and control of symptoms and make the assessment and management of control the highest priorities (12). This is clearly the result of a better appreciation of the burden placed by uncontrolled asthma on patients and their families.

Patients with uncontrolled asthma use more healthcare resources, which include doctor visits, emergency room (ER) care, and unexpected hospitalizations (13, 14). The monetary costs of such utilization are considerable (6, 15, 16). More indirect costs related to asthma have also been quantified: Uncontrolled asthma also leads to reduced school performance,

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elevated absenteeism, and lowered health-related quality of life (HRQOL).

With the recent publication of the new guidelines in 2007, few studies have focused on the direct impact of levels of control and their burden on asthmatics and their families. This study was conducted retrospectively, using the newest classifications of asthma control, to evaluate the impact of uncontrolled asthma upon the absenteeism and HRQOL of adults with asthma, children with asthma and the caregivers of pediatric patients. We hypothesized that (1) adult patients, caregivers of pediatric patients, and pediatric asthmatic patients would experience an increase in absenteeism as a result of uncontrolled asthma as seen in work days missed by adults and adult caretakers, and school days missed by children; and (2) both uncontrolled adults and caregivers of children with uncontrolled asthma would report a decreased quality of life compared to adult asthmatics and caretakers of children with controlled asthma.

METHODS

Study Design and Data Source

Patient information was obtained from datasets maintained by National Jewish Health for this cross-sectional study. The National Jewish Health's disease management database contains data on more than 44,000 patients across the US enrolled in the center's respiratory disease management programs between 1996 and 2006. Patients who would benefit from additional disease management are identified for inclusion in the National Jewish program either by health plan selection or through referrals by physicians participating in the National Jewish Network. On program entry, patients provided self-reported data for the previous 6-month period. It is on the basis of these initial self-reported data that this study was conducted. Data included demographics, asthma-related utilization, medication use, missed school and work within the past 6 months, and HRQOL. Participants in the study included patients who were 12 years of age or older. Participants younger than 18 years had their health and utilization information provided by caregivers. Caregivers also provided 6 months of data, including questionnaires reporting their own missed work and QOL assessment.

Six months of self-reported utilization and symptom data in the National Jewish Health database were required for a participant to be included in the study. Patients who were missing data on utilization or symptoms during the previous 6 months were excluded from the study.

Study Measures

Symptom control was determined by participant response to key components of asthma control delineated by the 2002 guidelines from the NAEPP. The NAEPP categorizes Severe Persistent Asthma as the highest level of severity for the diagnosis of chronic asthma. This stratum is defined as continuous symptoms, frequent nighttime symptoms, and a reduced level of pulmonary function before treatment (12). For the purpose of this investigation, uncontrolled asthma does not imply severity but rather the lack of response to adequate pharmacologic therapy. This added step recognizes that individuals of any level of disease severity have the potential to be "in control" if adequately treated. This is consistent

with the 2007 NAEPP Guidelines. To identify patients with uncontrolled asthma, a pre-specified algorithm was used that was based on the 2007 NAEPP guidelines for severity and medication use; it also incorporated information about response to pharmacologic therapy.

Based on this algorithm, participants were classified as having uncontrolled asthma if they met the following criteria: they were on guideline-recommended controller medications, which included inhaled corticosteroids, leukotriene receptor antagonists, cromolyn, methylxanthines, Advair, Combivent, and Xolair; and they reported any of the following three criteria: (1) they had experienced a hospitalization (including intensive care unit admission) or an emergency room visit within the past 6 months; (2) they complained of nighttime symptoms; or (3) they complained of daily or continual asthma symptoms. All other participants who met the study inclusion criteria were classified as having controlled asthma.

Absenteeism

Absenteeism was assessed from the self-reported number of work or school days missed due to asthma during the previous 6 months. Adults with asthma reported the number of workdays missed due to asthma. Caregivers of children with asthma reported the number of workdays missed due to the child's asthma. Caregivers also reported the number of school days missed by their child due to asthma.

Health-Related Quality of Life

HRQOL was measured using the validated Marks Asthma Quality of Life Questionnaire (AQLQ) (17, 18) and was assessed among adults only. The Marks AQLQ consists of 20 items scored on a Likert response scale from 0 = "not at all" to 4 = "very severely" and contains 4 subscales (breathlessness, mood disturbance, social disruption, and concern for health). The total Marks AQLQ score was calculated as the mean of all 20-item scores, multiplied by 2.5 to produce a total AQLQ score ranging from 0 to 10. Marks AQLQ subscales were similarly calculated.

While no HRQOL assessment was made for pediatric patients, their caregiver HRQOL was assessed using the validated Pediatric Asthma Caregivers Quality of Life Questionnaire (PACQLQ). This instrument consists of 13 questions assessing 2 domains: activity limitation and emotional function. Each question was assessed on a 7-point scale from 1 = "all the time" to 7 = "none of the time" for 9 of the questions and from 1 = "very, very worried/concerned" to 7 = "not worried/concerned" for the remaining 4 questions. Each domain is the mean score of the items in that domain (19). Scores range from 1 to 7, with lower scores indicating greater limitations or lower functioning. Changes in scores of 0.5 units are considered a minimally important difference in quality of life (20).

Data Analysis

Patients were categorized on the basis of their asthma being uncontrolled or controlled according to the described algorithm. Differences in proportions across sociodemographic variables were evaluated using chi square tests, and differences in means were assessed using the *t* test procedure. Absenteeism was analyzed as workdays missed for adults

and caregivers and school days missed for children. Work and school absenteeism data had positively skewed distributions, with many patients responding to questionnaires with “zero.” To account for this, a zero-inflated Poisson regression model was used to compare group differences. HRQOL was analyzed for adults and caregivers. When the data distribution suggested that the *t* test was inappropriate, the Wilcoxon-Mann-Whitney test was used to compare median values.

RESULTS

Participant Characteristics

Of 40,617 patients 12 years of age or older enrolled in the National Jewish Asthma Disease Management program between 1996 and 2006, 15,149 met the inclusion criteria for the study and were included in the analysis (Figure 1). Approximately 90% of these asthma patients reported using a short-acting beta-agonist to control acute symptoms. Nearly 50% of the patients received inhaled corticosteroids, 36% received long-acting beta-agonists, and 28% received leukotriene modifiers; and nearly 19% were taking Advair (Glaxo-SmithKline Philadelphia, PA), Combivent (Boehringer Ingelheim Corporation, Ridgefield, CT), or Xolair (Novartis Pharmaceuticals Corporation, East Hanover, NJ). Nearly 75% of the patients used a controller medication; 37% experienced an inpatient hospitalization or ER visit during the 6 months preceding the study; 28% complained of nighttime symptoms; and 36% reported daily or continual symptoms of asthma.

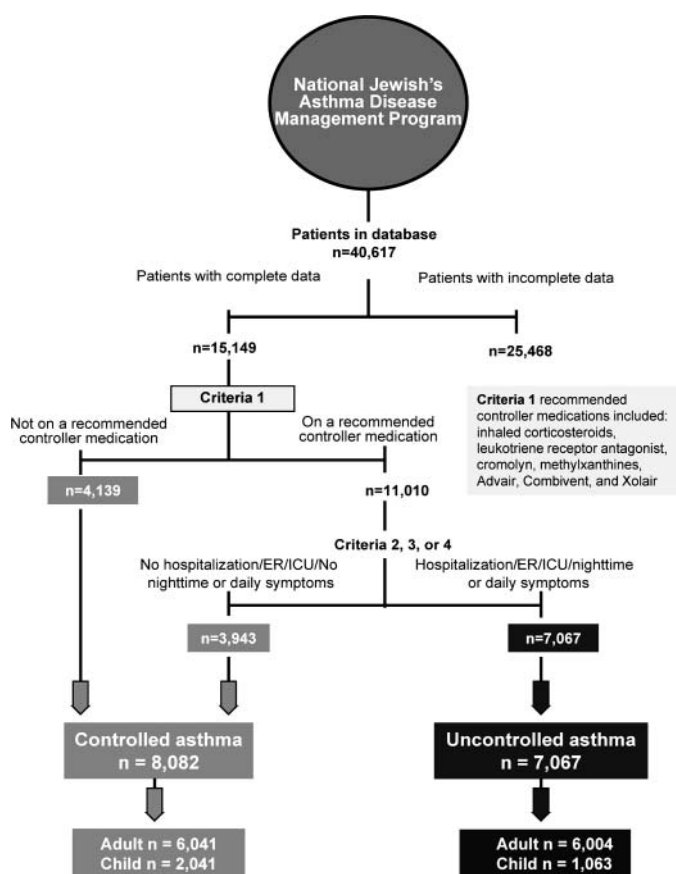


FIGURE 1.—Study Recruitment Flowchart.

TABLE 1.—Patient characteristics.

	Uncontrolled	Controlled	<i>p</i> Value
Gender, n (%) [*]			
Male	1,672 (23.8)	2,429 (30.2)	<0.001
Female	5,356 (76.2)	5,625 (69.8)	
Age by category, n (%)	n = 7,067	n = 8,082	
12–17	1,063 (15.0)	2,041 (25.3)	<0.001
18–39	2,275 (32.2)	2,630 (32.5)	
40–64	3,438 (48.7)	3,101 (38.4)	
65+	291 (4.1)	310 (3.8)	
Mean age, years (SD)	39.3 (16.0)	35.4 (17.1)	<0.001

^{*}Gender missing in 67 patients.

Based on the algorithm developed for this study, 7,067 (46.7%) patients were categorized as having uncontrolled asthma. Patients were compared on demographic variables. Uncontrolled asthma patients were more likely to be female (76.2% vs. 69.8%) and older (mean age 39 vs. 35 years) compared with controlled asthma patients ($p < 0.001$) (Table 1).

Absenteeism

Absenteeism data (Table 2) were available for 10,470 adults, 2,535 caregivers, and 3,028 children. In general, the proportion of participants and caregivers reporting days missed from school or work due to uncontrolled asthma was nearly twice that of controlled asthma. Approximately 43% of uncontrolled adult asthma patients reported missing work due to asthma, with a median of 6 days missed in the previous 6 months. Among controlled adult asthmatics, 24% reported missing work due to asthma, with a median of 3 missed workdays during the previous 6 months ($p < 0.001$).

Absenteeism among caregivers of pediatric patients was directly related to their child's symptom control. Slightly more than 31% of caregivers reported missing workdays due to their child's asthma, compared with 16% of caregivers of controlled patients. Caregivers of pediatric patients with uncontrolled asthma reported missing a median of 4 work days during the previous 6 months due to their child's asthma, compared with 2 days for caregivers of patients with controlled asthma ($p < 0.001$).

Caregiver reports also show that slightly more than 70% of uncontrolled pediatric patients missed school due to asthma, with a median of 6 school days missed during the previous 6 months; 45% of controlled pediatric asthma patients missed school due to asthma, with a median of 4 school days missed ($p < 0.001$).

Statistical significance did not change after adjustment for age and gender.

Health-Related Quality of Life

Total AQLQ scores were available from 7,861 adults. HRQOL was significantly lower for uncontrolled asthmatic adults compared to controlled adults, with average total Marks AQLQ scores 1.5 points higher among uncontrolled asthma patients, indicating lower HRQOL ($p < 0.001$) (Tables 3 and 4). Among the four sub-domains evaluating adult HRQOL, median scores for each of the domains were between 1.4 and 2.0 points higher among uncontrolled compared to controlled adults ($p < 0.001$ for each domain).

TABLE 2.—Asthma-related missed work or school days during the previous 6 months for respondents with uncontrolled and controlled asthma.

	Uncontrolled				Controlled				P Value	
	n	Mean	% non-zero	Median (range)	n	Mean	% non-zero	Median (range)	Zero-inflation	Count
Adults with asthma										
Work days missed due to asthma	5,084	4.65	43.3	6 (1–180)	5,386	1.51	24.1	3 (1–150)	<0.001	<0.001
Caretakers of children with asthma										
Work days missed due to child's asthma	846	1.93	31.1	4 (1–56)	1,689	0.67	16.0	2 (1–30)	<0.001	<0.001
Children with asthma										
School days missed due to asthma	1,038	6.39	70.5	6 (1–70)	1,990	2.60	44.9	4 (1–60)	<0.001	<0.001

Statistical significance did not change after adjustment for age and gender.

Total PACQLQ was available for 1,543 caregivers. Uncontrolled asthma was significantly associated with reduced HRQOL among caregivers of pediatric asthma patients; median scores for total PACQLQ and the two sub-domains evaluating emotional function and activity limitation were more than 0.5 points lower for caregivers of patients with uncontrolled asthma compared to controlled ($p < 0.001$).

DISCUSSION

Episodes of uncontrolled asthma affect more than 50% of persons with the disease, and the impact of these episodes goes beyond the period of attack (21, 22). Uncontrolled asthma has been shown to increase absenteeism from work and school: Chen et al. surveyed 2,529 participants enrolled in the TENOR study and demonstrated a direct link between elevated absenteeism and uncontrolled symptoms (23). Similarly, Cisternas et al. showed that total abeyance of work as well as workdays missed due to uncontrolled asthma account for 35% of the total costs associated with asthma (24). Our findings demonstrate that uncontrolled asthma was associated with greater work and school absenteeism among adult and pediatric patients, respectively, as well as with caregivers of pediatric asthma patients.

Stretching beyond what was captured through this dataset is that one of the major manifestations of out-of-control asthma is nocturnal symptoms, particularly in children. While our results capture days missed from work and school, daytime productivity may also be affected by the loss of sleep resulting from nocturnal asthma problems. It is clear that being awake during the night affects many aspects of daytime performance. Most of the time, these effects are difficult to quantify. People may go to work but may not perform optimally or be at greater risk for accidents. Children may be able to attend school, but are not learning at the same rate

as their peers. It is well established that nocturnal asthma is directly correlated with airway inflammation. Therefore, as the inflammatory state worsens, asthma control becomes more difficult to establish. Nocturnal asthma, which closely relates to overall quality of life, is one of the first signs of this lack of control. Questioning the patient about nocturnal symptoms is critical. In children, this means that the child has had to wake the parent or caregiver for them to be aware of the problem. Thus, there may be many episodes of nocturnal asthma in children that never become apparent to parents (25–27).

Uncontrolled asthma is also linked to lowered adult and pediatric HRQOL. Graham et al. showed a direct association between NAEPP asthma severity staging and pediatric and adult asthma patient-reported QOL (28). Researchers have also demonstrated significant associations between poor asthma control and quality of life (13, 29, 30). Uncontrolled asthma affects how children learn and associate with their peer groups and affects the lifestyle of their parents or caregivers (31). Our results corroborate previous findings that uncontrolled asthma is associated with a reduced HRQOL in adult patients and pediatric caregivers. Adults with uncontrolled asthma had significantly lower HRQOL as compared with those with controlled asthma. Similarly, uncontrolled asthma in pediatric patients affected their caretakers, resulting in activity limitation and lowered emotional functioning. These data highlight the extent to which uncontrolled asthma negatively affects not only those affected by the disease but their families.

This study demonstrates the difficulty facing both clinicians and researchers in separating the concepts and measurement of the severity of asthma from its level of control. Almost three quarters of patients enrolled in the disease management program reported being treated with a recommended controller medication. However, 64% of these individuals reported acute care utilizations or ongoing symptoms that

TABLE 3.—AQLQ among respondents at baseline by case status.

	Uncontrolled		Controlled		Difference (uncontrolled – controlled) median	p Value†
	n	median	n	median		
Total AQLQ*	3,723	3.6	4,138	2.1	+1.5	<0.001
Breathlessness		4.5		2.5	+2.0	<0.001
Mood		3.5		2.5	+1.0	<0.001
Social		2.9		1.4	+1.4	<0.001
Concerns		3.2		1.8	+1.4	<0.001

*Higher AQLQ scores indicate lower HRQOL.
†Both median and mean values are provided for comparison; p values are provided for the comparison of median values (see Methods section).

TABLE 4.—PACQLQ among caregivers of pediatric asthma patients at baseline by case status.

	Uncontrolled		Controlled		Difference (uncontrolled – controlled) median	p Value†
	n	median	n	median		
Total PACQLQ*	521	5.9	1,022	6.5	–0.6	<0.001
Emotional function		5.8		6.4	–0.6	<0.001
Activity limitation		6.3		7.0	–0.7	<0.001

*Lower PACQLQ scores indicate lower HRQOL.
†Both median and mean values are provided for comparison; p values were provided for the comparison of median values (see Methods section).

suggested uncontrolled asthma; 20% of patients were not on a recommended controller medication and yet reported acute care utilization or continued symptoms. Observational studies that attempt to clearly delineate between levels of severity or control may find that those definitions are not supported by the underlying data.

Our analysis defined uncontrolled asthmatics as patients who were on a recommended controller medication and yet required hospitalization or emergency healthcare services or experienced continued symptoms, especially at night. As easily demonstrated by the plethora of papers relating to different methods of classifications of asthma severity, assessing the severity of the disease state is complex and related to many different factors. The use of medications to classify adequate treatment can be complicated. The underlying assumption is that physicians are treating patients to an adequate level. However, not all physicians treat according to guidelines, and even those who do are often basing their decisions on a single visit every 6 to 12 months with a 5-minute history, a physical examination, and often no objective measurements. Other classification standards also have limitations: The Health Plan Employer Data and Information Set (HEDIS), a commonly used asthma assessment tool, was redesigned in 2008 to more precisely capture uncontrolled asthmatics (32). Classification determined by clinical tests has been shown to yield different results than the more commonly used and more objective parameters for diagnosis (33). Analysis based on administrative and pharmacy data can produce classification results that can vary with the algorithm used (34). In the last few years, there have been several new assessment tools to evaluate control of asthma rather than disease state severity. There is no standard for these new tools, and they vary considerably; some use subjective responses to questions and others use physiologic measurements of airway function. The variety of tools available to analyze asthma severity and control, and the variance in assessment resulting from that variety, highlight the complex nature of asthma assessment and care.

The research presented in this paper has some limitations. Our results are based on a subgroup of patients who reported a complete set of medication and utilization data. Patients who were lacking part of these data were excluded from analysis. Many of those who were in the dataset were referred to the disease management program, presumably because they had previously experienced some difficulty controlling their asthma. All data were self-reported and thus subject to recall bias. (At the initiation of this analysis, the 2007 NAEPP guidelines were not yet published. While the updated guidelines include methods for identifying patient control, the data collected in this study could not be used to easily operationalize those criteria.) Our dataset did not include an assessment of pediatric HRQOL. Few validated instruments are available for measuring pediatric HRQOL through caregiver proxy and none were assessed in this population. Asthma prevalence among children is high, and the disease's possibly large impact on the crucial years of child development is not assessed here (5). Also missing is the link between pediatric and adult HRQOL. Uncontrolled asthma in childhood may affect adult HRQOL differently than does adult-onset asthma; this relationship needs to be assessed further. Finally, we measure productivity in terms of absen-

teeism rather than performance. It is likely that the indirect costs associated with uncontrolled asthma are higher than realized from these data.

In conclusion, uncontrolled asthma has a far-reaching impact on the absenteeism and quality of life of asthma patients and those associated with their care. Proper assessment, treatment, and disease management to improve asthma control may reduce the impact of uncontrolled asthma on the absenteeism and HRQOL of asthmatic adults, children, and the caretakers of pediatric asthmatic patients, while lowering the direct and indirect costs associated with the disease.

DECLARATION OF INTEREST

This study was funded in full by Wyeth Pharmaceuticals. B.B.D., B.M.C., and S.L.K. are employed by Cerner Life-Sciences, which provides consulting services to the pharmaceutical industry. R.K.K. is employed by Wyeth Pharmaceuticals. D.T. has provided consulting services to Wyeth, Novartis, and Amgen.

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