Causative and Contributive Factors to Asthma Severity and Patterns of Medication Use in Patients Seeking Specialized Asthma Care*

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Study objectives: (1) To assess the prevalence of specific factors considered causative or contributive to asthma in a population of patients seen in a specialized asthma clinic, and to determine whether any of these factors were associated with more severe disease; and (2) to assess the utilization of inhaled steroids by asthma severity in this population and compare it with published guidelines of the National Heart, Lung, and Blood Institute (NHLBI).

Design, setting, and patient population: We conducted a retrospective chart review of new patients seen in a specialized asthma treatment center over a 2.5-year period and recorded the prevalence of 14 causative or contributive factors, the severity of asthma, and the intensity of treatment with inhaled corticosteroids in each patient. Patients were grouped as mild asthma vs moderate/severe asthma and compared by χ² analysis and stepwise logistic regression to determine whether certain factors were associated with more severe asthma.

Measurements and results: The average number of factors recorded was 2.9 ± 1.8 in the mild group (± SD) and 3.5 ± 1.6 in the moderate/severe asthma group. This difference was statistically significant (p = 0.014). Increasing age, male gender, symptomatic gastroesophageal reflux disease (GERD), and chronic sinusitis were independently associated with more severe asthma. Suboptimal use of inhaled corticosteroids was more common in patients with mild persistent asthma, but suboptimal dosing of inhaled corticosteroids was equally common in mild and moderate/severe asthma. No relationship was found between allergen sensitization combined with exposure to cats, dogs, dust mite, or molds and more severe asthma.

Conclusions: This study confirms earlier studies showing that symptomatic GERD and chronic sinusitis are important comorbid conditions in patients with asthma, both being associated with greater asthma severity. This study further shows that the doses of inhaled corticosteroids used for treatment of asthma fall short of NHLBI guidelines in the majority of patients regardless of asthma severity.

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Key words: asthma; inhaled steroids; medication use; severity

Abbreviations: ASA/NSAID = aspirin or nonsteroidal anti-inflammatory drug; GERD = gastroesophageal reflux disease; NHLBI = National Heart, Lung, and Blood Institute; OR = odds ratio; PFT = pulmonary function test; VCD = vocal cord dysfunction

The incidence of asthma has risen alarmingly in the past few decades.¹ With this, the number of patients seeking specialized asthma care has also increased. As the health-care impact of asthma continues to increase, it becomes important to identify factors that could impact on asthma severity. The main objective of our study was to characterize in a population of asthma patients, the presence of specific factors identified to be causative or contributive to asthma, hypothesizing that certain factors or a greater number of factors may be associated with more severe disease.

As a second objective, we wished to characterize the patterns of medication use in our patients and...

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determine whether the doses of inhaled steroids used were in line with National Heart, Lung, and Blood Institute (NHLBI) recommendations. Our hypothesis was that suboptimal treatment, particularly suboptimal treatment with inhaled corticosteroids, might be another factor associated with more severe asthma.

**Materials and Methods**

**Patient Selection**

The study population included all new adult patients initially seen in a regional university-based referral center, The Asthma Center, between the dates of January 1, 1997, and June 18, 1999. Each patient was confirmed to have asthma as defined by the American Thoracic Society, which required demonstration of reversible obstructive airway disease with a ≥ 15% decrement in predicted FEV₁ as well as improvement in expiratory flow rates to ≥ 15% of predicted after inhalation of a β₂-selective bronchodilator or other previous treatment such as corticosteroids. The period of the study was chosen to coincide with publication of the most recent NHLBI guidelines in 1997. Patients were excluded if they were < 18 years of age or had one or more of the following comorbidities: congestive heart failure, other lung disease (including but not limited to COPD, cystic fibrosis, and interstitial lung disease), or other medical conditions, such as severe anemia or malignancy, that could have rendered categorization of asthma severity difficult.

**Data Collection**

This study was approved by the Institutional Review Board of our institution. Records of four faculty physicians were reviewed. Information was obtained from a comprehensive questionnaire completed by all new patients. The questionnaires contained information regarding personal habits (i.e., cigarette smoking and smoke exposure), occupational exposure, indoor allergen or irritant exposures, symptoms of gastroesophageal reflux disease (GERD), chronic sinusitis, rhinitis, and aspirin sensitivity. When available, prior physicians' notes, pulmonary function test (PFT) results, allergy skin test results, sinus radiographs, psychosocial evaluations, and results of rhinolaryngoscopy were also utilized. The physician's printed note from the initial evaluation was also utilized to confirm and clarify the history and laboratory data.

**Severity of Asthma**

Patients were classified according to the severity of asthma as mild intermittent, mild persistent, moderate persistent, or severe persistent asthma based on NHLBI criteria. If the severity level based on symptoms corresponded to a different severity level than that which the PFT values indicated, patients were classified in the more severe category.

**Demographics and Contributive Factors**

Each patient’s age, sex, and race was recorded. Patient records were reviewed for the presence or absence of 14 factors thought to be causative or contributive to asthma. A diagnosis of rhinitis was based on symptoms of nasal congestion, itching, and rhinorrhea, either on a seasonal or perennial basis. Allergic rhinitis was defined as rhinitis symptoms associated with sensitization to allergens demonstrated on skin-prick testing. Nonallergic rhinitis was defined as rhinitis occurring without a seasonal pattern and with entirely negative skin-prick test results. Chronic sinusitis was defined as having two or more major factors (facial pain, pressure, or headache; nasal obstruction; nasal purulence or discharge; hyposmia or anosmia) or one major factor and two minor factors (fever, halitosis, dental pain, cough) present for > 12 weeks. The diagnosis of nasal polyps was based on a past history or current presence of nasal polyps. The diagnosis of vocal cord dysfunction (VCD) was established based on strong clinical suspicion, including examination of past and present PFT results (showing truncation of the inspiratory flow loop). In most cases, the diagnosis was confirmed by demonstration of paradoxical vocal cord closure on fiberoptic rhinolaryngoscopic examination. A patient was considered to have symptomatic GERD if he/she exhibited chronic symptoms of acid regurgitation or heartburn or reported current use of a proton-pump inhibitor for these symptoms. In most cases, confirmatory tests, such as esophagogastroduodenoscopy or pH probe testing were not performed. Aspirin or nonsteroidal anti-inflammatory drug (ASA/NSAID) sensitivity was defined clinically as a definite worsening of asthma symptoms after ingestion of an ASA/NSAID. Occupational history was reviewed for exposure to allergens or other sensitizers, including smoke, chemical fumes, and particulates. Occupational exposure was considered positive when the faculty specialist identified it as a contributive factor.

**Smoking History, Indoor Cigarette Smoke Exposure, and Fireplace Smoke Exposure** The number of years and quantity of tobacco smoked as well as the presence or absence of current smoking were recorded. Each patient’s history was also reviewed for regular second-hand exposure to indoor cigarette smoke or indoor exposure to a wood-burning fireplace more frequently than once per week.

**Environmental Allergen Exposure and Allergen Sensitization** Indoor exposure to cats or dogs was noted. The use of indoor dust mite control measures, including encasings on mattresses, pillows, and box springs, was noted. Patients recording a musty smell in the home, visible mold growth on walls, or water seepage problems in the basements were considered to have indoor mold exposure. Sensitivity to environmental allergens was determined by reviewing the results of skin-prick testing which were available for 123 patients. In a few cases, skin-prick tests were only available from a previous evaluation. Skin-prick test results were unavailable for 26 patients. The latter patients were not considered in the analyses of environmental factors.

**Psychosocial Factors** Each patient’s history and questionnaire were reviewed for psychosocial factors (e.g., anxiety disorder) thought to be contributive to asthma severity. A specialist in psychosocial evaluations contributed to the evaluation of these patients.

**Other Contributive Factors** The questionnaires were also reviewed for sensitivity to foods, food additives (e.g., metabolites), allergic bronchopulmonary aspergillosis, latex sensitivity, the use of a beta-blocker, or a history of pregnancy-induced or premenstrual asthma.

**Medications**

Each patient’s asthma medications were reviewed for use of short-acting β-agonists, salmeterol, ipratropium, inhaled corticosteroids, Cromolyn or nedocromil, theophylline or aminophylline, leukotriene antagonist agents, nebulized albuterol and/or ipratropium, and other drugs (e.g., cytotoxic drugs such as methotrexate). They were also reviewed for current or past use of oral corticosteroids. The dosage of inhaled corticosteroids was compared to the dose range recommended by the NHLBI for each severity.
category, and use of suboptimal dosing was defined as a dose below the lower limit recommended for the asthma severity category.2

Data Analysis

For purposes of testing whether certain contributive factors were more strongly associated with moderate/severe asthma, patients were first classified as having either mild intermittent or persistent asthma (mild group) or moderate-to-severe, persistent asthma (moderate/severe group). The prevalence of factors potentially contributing to disease severity were compared using χ² tests. Student t test was used to compare continuous variables across study groups; p < 0.05 was regarded as statistically significant. Stepwise logistic regression was used to determine a best set of independent predictors using all factors that were significant by univariate analysis as potential predictors in the model.

RESULTS

Between January 1, 1997, and June 18, 1999, a total of 176 patients met the inclusion criteria for the study (initial visit, presenting for asthma, and meeting criteria for diagnosis of asthma). Of these, 27 patients were excluded (17 patients had lung disease other than asthma, 3 patients had congestive heart failure, and 7 patients had other comorbidities). The study population therefore consisted of 149 patients. Of these, 97 patients (65.1%) were female, 135 patients (90.6%) were white, 13 patients (8.7%) were African American, and 1 patient (0.7%) was Asian.

Asthma Severity

The relative distribution of patients in each severity category was examined. Of 149 patients, 26 had mild intermittent asthma (17%), 37 had mild persistent asthma (25%), 50 had moderate persistent asthma (34%), and 36 had severe persistent asthma (24%).

Contributive Factors

Total Patient Population: The prevalences of the 14 contributive factors in the 149 patients are shown in Figure 1. Rhinitis was present in 102 patients (69.9%); 95 of these patients had allergic rhinitis (65.1% of total), and 7 patients had nonallergic rhinitis (4.8% of total). Chronic sinusitis was present in 63 patients (42.3%). Nasal polyps were present in 27 patients (18.1%). Eleven patients (7.4%) were sensitive to ASA/NSAIDs.

Exposure to indoor mold was reported by 38 patients (22.5%). Of these, 16 patients tested positive for sensitization to mold (12.7% sensitized and exposed). Of 123 patients tested, 55 patients (44.7%) tested positive for sensitivity to dust mites; of these, 7 patients (5.7%) reported that they were using dust mite-proof encasings, and 48 patients reported that they were not (39.0% sensitized and exposed). Eighty-seven patients (58.4%) reported indoor animal exposure. Of these, 41 patients owned cats (27.5%), and 61 patients owned dogs (40.9%). Twenty-five patients who owned cats tested positive for sensitivity to cat allergens (20.3% sensitized and exposed), and 25 patients who owned dogs tested positive for sensitivity to dog allergens (20.3% sensitized and exposed).

Fifty-five patients reported a history of smoking

![Figure 1. Prevalence of contributive factors in the total patient population (n = 149).](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/22000/)
(36.9%). Nine patients (6.1%) reported they were still smoking. Ongoing second-hand exposure to indoor cigarette smoke was reported by 24 patients (16.7%). Frequent fireplace use was reported by nine patients (6.1%).

Symptomatic GERD was present in 42 patients (28.2%). Of these, 18 patients (12.1%) were being treated with a proton-pump inhibitor and 24 patients were not (16.1%). Vocal cord dysfunction was identified in 11 patients (7.4%). Nine patients (6.0%) had psychosocial factors believed to be contributive to asthma. Three patients (2.0%) had asthma that was influenced by pregnancy, and three patients had asthma influenced by menstrual cycle. Two patients had metabisulfite allergy (1.3%), and one patient each (0.7%) had latex hypersensitivity, allergic bronchopulmonary aspergillosis, and use of a beta-blocker. Exposure to various allergens and sensitizers at work (including smoke, chemical fumes, and other particulates) was reported by 26 patients (17.5%).

Comparison of Mild vs Moderate/Severe Asthma:
The average number of causative or contributive factors was 2.9 ± 1.8 (± SD) in the mild asthma group and 3.5 ± 1.6 in the moderate/severe asthma group. This difference was statistically significant (p = 0.014). The mean age of patients with moderate/severe asthma was greater than that of patients with mild asthma (47.6 ± 2.5 years vs 41.1 ± 2.9 years, p = 0.006). Also, by \( \chi^2 \) analysis, male gender was overrepresented in the moderate/severe asthma group (p = 0.015).

The relative prevalence of each causative or contributive factor in the two groups is illustrated in Figure 2 and analyzed in Table 1. Of the 14 factors, the only factor that was statistically more prevalent in the moderate/severe group by univariate analysis was symptomatic GERD (p = 0.013; odds ratio [OR], 2.7). Chronic sinusitis was also more prevalent in the moderate/severe group, but this difference did not quite reach statistical significance (p = 0.058; OR, 1.9). VCD and indoor smoke exposure also had ORs > 2 (OR, 3.6 and 2.0, respectively). There was no association between severity group and rhinitis (OR, 1.2), history of smoking (OR, 1.5), indoor animal sensitized and exposed (OR, 1.3), nasal polyps (OR, 1.3), occupational exposure (OR, 0.83), indoor mold sensitized and exposed (OR, 1.2), ASA/NSAID sensitivity (OR, 0.87), psychosocial factors (OR, 1.5), frequent fireplace use (OR, 0.57), or suboptimal treatment with inhaled steroids (OR, 0.75). The factor of dust mite sensitivity with exposure (without intervention) had a decreased OR of 0.52 (p = 0.08). Although the number of patients with nonallergic rhinitis was small (n = 7), it was interesting that six of these patients were in the moderate/severe asthma group. When the “indoor animal sensitized and exposed” patients were classified by exposure to

![Figure 2](http://publications.chestnet.org/pdflaccess.ashx?url=/data/journals/chest/22000/)

**Figure 2.** Prevalence of contributive factors in patients with mild asthma (n = 63) vs moderate/severe asthma (n = 86). *Statistically significant, p = 0.013 by univariate analysis. Patients with mild intermittent asthma were excluded from this analysis.
either cats or dogs, no relationship with asthma severity was found for either animal.

Stepwise logistic regression was used to select the significant independent predictors of asthma severity from the variables that were identified in the univariate analysis: age, gender, symptomatic GERD, chronic sinusitis, VCD, and dust mite sensitivity/exposure. The analysis confirmed that age was independently associated with moderate/severe asthma (OR, 1.031 per decade with confidence bounds of 1.006 to 1.057; p = 0.007). Also, male gender was independently associated with moderate/severe asthma (OR, 2.22 with confidence bounds of 1.04 to 4.76; p = 0.036). The analysis also confirmed that GERD was independently associated with moderate/severe asthma (OR, 2.77 with confidence bounds of 1.20 to 6.40; p = 0.015). Chronic sinusitis was also found to be independently associated with moderate/severe asthma (OR, 2.22 with confidence bounds of 1.08 to 4.60; p = 0.032). Applying a logistic model to the data using only the factors of GERD and chronic sinusitis gave a sensitivity of 58.8% and a specificity of 76.5% for prediction of moderate/severe asthma. Neither VCD nor dust mite sensitivity/exposure were significant in the logistic regression analysis.

**Patterns of Medication Use**

All information regarding medication use was obtained by self-report of the patients. Furthermore, because the NHLBI guidelines recommend that treatment for mild intermittent asthma consist only of as-needed use of short-acting β-agonists, medication use patterns were only analyzed in subjects with mild, moderate, or severe persistent asthma (n = 123).

![Table 1—Comparison of Factor Prevalence, Mild Persistent vs Moderate/Severe Asthma (n = 123)](data:image/png;base64,iVBORw0KGgoAAAANSUhEUgAAA...)

![Table 2—Comparison of Medication Use, Mild Persistent vs Moderate/Severe*](data:image/png;base64,iVBORw0KGgoAAAANSUhEUgAAA...)

The patterns of medication use in mild vs moderate/severe asthma are summarized in Table 2 and Figure 3. Patients with moderate/severe asthma were 4.2 times more likely to be using crom lyn or nedocromil (p = 0.14), 8.9 times more likely to be using theophylline or aminophylline (p = 0.014), 4.3 times more likely to be using a leukotriene receptor antagonist (p = 0.043), 4.6 times more likely to be using an oral steroid (p = 0.01), and 2.6 times more likely to be using salmeterol (p = 0.035). None of the patients with mild asthma used ipratropium or more than four asthma medications daily.

In the mild asthma group, 16 patients (43.2%) were using inhaled corticosteroids; and in the moderate/severe asthma group, 61 patients (70.9%) were using them. This difference was highly statistically significant (p = 0.0002). The percentages of patients self-reporting use of a dose of inhaled corticosteroids below NHLBI guidelines were 73.0% for mild persistent, and 69.8% for moderate/severe. This difference was not statistically significant. Seven patients (5.7%) reported using a dose of inhaled corticosteroids higher than recommended in the NHLBI guidelines.

**Discussion**

The primary objective of this study was to examine causative and contributive factors to asthma severity in a population of patients referred to a university-based asthma center, with the hypothesis that certain factors or a greater number of factors might be associated with more severe disease. We found that patients with moderate/severe asthma have a significantly greater overall prevalence of causative and contributive factors and were more likely to be male than female. We also confirmed that two factors, namely symptomatic GERD and chronic sinusitis, were independently associated with more severe asthma. Our hypothesis that patients with more severe asthma would be more likely to receive...
Suboptimal doses of inhaled corticosteroids was not confirmed. Instead, we found that the majority of patients in all severity levels of asthma were receiving doses of inhaled corticosteroids below NHLBI recommendations.

In a previous study, Irwin et al. investigated contributive factors in a population of patients whose asthma had been difficult to control. In agreement with our findings, the most common factor identified was GERD. The major differences between our study and that of Irwin et al. are that the latter study did not include a comparison group of mild asthmatics but did utilize esophagoscopy and pH probe testing to establish the diagnosis of GERD. Using only a clinical definition of GERD, we found a statistically significant increased prevalence of symptomatic GERD in patients with moderate/severe asthma. Of note, only 28.2% of our patients had symptomatic GERD, as compared to a group of asthmatics studied by Field et al., in which the symptoms of heartburn, regurgitation, and swallowing difficulties were reported in 77%, 55%, and 24%, respectively. A Veterans Affairs population also noted heartburn in 72% of 189 asthma patients. The lower prevalence of heartburn in our population may reflect a trend toward lesser use of theophylline; however, it is also possible that our questionnaire placed less emphasis on GERD by listing it alongside other questions related to general health rather than asthma.

The overall impact of GERD on asthma may have been even greater if asymptomatic GERD had been taken into account. In the patients with difficult-to-control asthma studied by Irwin et al., the prevalence of asymptomatic GERD was 24%. Using 24-h esophageal pH testing, Harding et al. reported abnormal results in 62% of asthma patients without symptoms of reflux. The importance of GERD in asthma is supported by recent studies such as that of Harding et al., in which dosage titration of omeprazole was used to confirm complete control of acid reflux based on pH probe testing and patients were treated for at least 3 months. In this study, 27% of the patients required treatment with > 20 mg/d of omeprazole, but overall a significant improvement in asthma was achieved. In earlier studies, the benefit of proton-pump inhibitor treatment for asthma was not nearly as convincing; however, the completeness of acid suppression was not determined.

Chronic sinusitis was also found to be independently associated with more severe asthma. The relationship between chronic sinusitis and severe asthma has been previously studied, but the results have been conflicting. For instance, in a study by Ishioka et al., no association was found between chronic sinusitis and severe, steroid-dependent asthma in adult patients. However, Bresciani et al. found that a greater degree of clinical rhinosinusitis severity and sinus CT abnormality in patients with severe compared to mild-to-moderate asthma. The link between chronic sinusitis and asthma has been postulated to be due to aspiration of postnasal drainage, sinonobronchial reflexes, a pharyngobronchial reflex, or due to the fact that a single pathogenetic process may affect the upper and lower airways. The most compelling evidence supports a pharyngobronchial reflex mechanism and a single pathogenetic process. The former is due to irritation...
of sensory nerve fibers in the posterior pharynx by postnasal drainage leading to a constriction of the pharynx and a reduction in inspiratory flow rates. Some degree of actual bronchoconstriction may also occur due to this process. This mechanism may well explain the common clinical observation of increased asthma symptoms at times of exacerbations of sinusitis. The latter mechanism, dubbed “cross-talk” in allergic inflammation, has been confirmed with allergen challenge studies showing that a single exposure of either the lungs or nasal mucosa to allergen elicits an inflammatory response in the unexposed site. This cross-talk may be mediated by systemically active cytokines and circulating inflammatory cells, as rhinitis and sinusitis are so strongly related, these studies support a theory of systemic amplification of inflammatory processes from the lungs to the sinuses and vice versa. Studies have also demonstrated a positive effect of treatment of sinusitis on asthma in both children and adults.

We also found that VCD was more prevalent in patients with moderate/severe asthma, although this relationship did not quite reach statistical significance (p = 0.09; OR, 3.6). Only 11 of our total study patients (7.38%) had a diagnosis of VCD. We suspect that a stronger relationship with asthma severity may have obtained had our patient population included more patients with VCD. These patients often have accelerating symptoms of asthma resulting in overuse of medications, increased numbers of acute asthma exacerbations and emergency visits, and an overreliance on use of systemic steroids. It is important to recognize VCD as a contributive factor to asthma severity, since appropriate treatment usually requires the services of a speech pathologist and a psychological specialist.

Regrettably, a high proportion (36.9%) of our asthma patients had a history of smoking. Although neither smoking nor second-hand smoke exposure was associated with more severe asthma, other studies have found a relationship between tobacco smoke exposure and asthma severity. Obviously, smoking and second-hand smoke exposure are contributive factors that should be discussed with patients as part of a comprehensive asthma treatment plan.

Of the 149 asthma patients studied, 87 patients (58.4%) had indoor animal exposure. However, we found no relationship between asthma severity and indoor animal exposure. In a study by Strachan and Carey, an independent association of severe wheeze in adolescents with ownership of furry pets (OR, 1.5) was noted; they estimated that current and past ownership of a furry pet accounted for 40% of severe wheeze in their population by using adjusted relative risk calculation. We analyzed the impact of indoor animals both in terms of sensitization and exposure. This was based on a previous study by Tunnicliffe et al that found that the strongest relationship between allergen exposure and asthma severity occurred in patients who had both sensitivity to the allergens and exposure; their study demonstrated a significantly higher concentration of dog allergen in the homes of dog-sensitized patients with more severe asthma. Though cat allergen concentrations were not significantly different between groups in their study, a review by Liccardi et al noted that cat allergens are present even in indoor environments known to be free of cats. This serves as a reminder that indoor allergen exposure may not correlate with the patient’s history. This limitation applies to any study that relies on history to assess exposure. In a similar manner, we also examined indoor mold and dust mites as contributive factors, namely in terms of both sensitization and exposure to these allergens. There was no statistically significant difference between mild and moderate/severe asthmatics in prevalence of sensitization with exposure to molds or dust mites (p = 0.69 and 0.08, respectively). Once again, it could be argued that without actual measurement of allergens, these results could be misleading. In fact, it appeared somewhat paradoxical that dust mite sensitivity without intervention was more prevalent in patients with mild asthma (OR, 0.52). It is unclear whether this reflected a greater use of indoor dust mite control measures in patients with moderate/severe asthma.

Finally, we found a high prevalence of underutilization of inhaled steroids among patients regardless of the severity level of their asthma. Overall, 65% of the patients were using a dose of inhaled corticosteroid below that recommended in the NHLBI guidelines. In most cases, this suboptimal treatment appeared to represent physicians’ recommendations, as only five patients reported noncompliance with their corticosteroid regimen. However, we acknowledge that patient self-reporting typically understates medication nonadherence, and our study design did not allow us to confirm the dose of inhaled corticosteroids actually prescribed by each patient’s physician. Nonetheless, lack of physician adherence to NHLBI guidelines for dosing of inhaled corticosteroids has been recognized as a key shortcoming in asthma treatment, and several factors may contribute to it. First, both patients and physicians underestimate asthma severity. Second, physicians may underdose inhaled steroids for fear of adverse side effects. Third, physicians may erradicate the value of inhaled corticosteroids due to lack of awareness or disagreement with the NHLBI guidelines. Consistent with previous reports, it appears that physicians in our community are falling short of the NHLBI guide-
lines for use of inhaled steroids. Increasing efforts to reverse this pattern are clearly needed.28

It is our hope that this report will prove useful to community-based physicians and health-care organizations in their quest for better and more cost-effective strategies for managing asthma, including efforts to identify potential modifiable factors and to improve adherence with NHLBI guidelines. We also hope that this study will highlight the importance of GERD and chronic sinusitis as potential factors contributing to the severity of the disease.

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