Intranasal steroids and the risk of emergency department visits for asthma

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Background: In patients with asthma, treatment for associated conditions, such as rhinitis, is recommended. It is unknown whether this treatment can reduce the risk for emergency department (ED) visits for asthma.

Objectives: We sought to determine whether treatment with intranasal steroids or prescription antihistamines in persons with asthma is associated with a reduced risk for ED visits caused by asthma.

Methods: We performed a retrospective cohort study of members of a managed care organization aged greater than 5 years who were identified during the period of October 1991 to September 1994 as having a diagnosis of asthma by using a computerized medical record system. The main outcome measure was an ED visit for asthma.

Results: Of the 13,844 eligible persons, 1031 (7.4%) had an ED visit for asthma. The overall relative risk (RR) for an ED visit among those who received intranasal corticosteroids, adjusted for age, sex, frequency of orally inhaled corticosteroid and β-agonist dispensing, amount and type of ambulatory care for asthma, and diagnosis of an upper airways condition (rhinitis, sinusitis, or otitis media), was 0.7 (95% confidence interval [CI], 0.59-0.94). For those receiving prescription antihistamines, the risk was indeterminate (RR, 0.9; 95% CI, 0.78-1.11). When different rates of dispensing for intranasal steroids were examined, a reduced risk was seen in ED visits in those with greater than 0 to 1 (RR, 0.7; 95% CI, 0.57-0.99) and greater than 3 (RR, 0.5; 95% CI, 0.23-1.05) dispensed prescriptions per year.

Conclusions: Treatment of nasal conditions, particularly with intranasal steroids, confers significant protection against exacerbations of asthma leading to ED visits for asthma. These results support the use of intranasal steroids by individuals with asthma and upper airways conditions. (J Allergy Clin Immunol 2002;109:636-42.)

Key words: *Asthma, rhinitis, therapeutics, outcome assessment*

Abbreviations used
CI: Confidence interval
ED: Emergency department
MCO: Managed care organization
RR: Relative risk

Upper airways conditions, such as rhinitis, sinusitis, and otitis media, have been closely linked pathophysiologically, epidemiologically, and therapeutically to asthma.[1] Between 50% and 80% of adults with asthma can be affected by allergic rhinitis,[2-4] and the concurrence of asthma and rhinitis appears to be increasing.[5] Perennial rhinitis is also strongly associated with asthma in nonatopic individuals with normal IgE levels.[6] Extensive sinus disease, allergy, and asthma are strongly associated.[7,8] Airway responsiveness in sinusitis is correlated with extrathoracic airway hyperresponsiveness and reverses after treatment with antibiotics and nasal steroids.[9] The link of otitis media with allergic rhinitis[10-12] and asthma[13] is also strong. The prevalence of nasal allergy in children older than 3 years with otitis media ranges from 35% to 50%, a 3- to 4-fold greater expression of allergic rhinitis among children with otitis media than among the general pediatric population.[14] Nasal provocation testing with histamine results in eustachian tube dysfunction in persons with allergic rhinitis.[15] In recognition that these conditions can be conceptualized as part of a disease continuum, some authors have suggested they be renamed as "rhinoconjunctivosinopharyngootobronchitis"[16] or "allergic rhinobronchitis."[17]

The coexistence of allergic rhinitis in patients with asthma increases medical care costs compared with those in patients with asthma alone. Yawn et al[18] reported that total medical care and respiratory-only charges for patients with asthma and allergic rhinitis were significantly higher than for patients with asthma alone. For young men in particular, these findings reflected higher emergency department (ED) and hospital charges.[18]

These conditions are intertwined therapeutically. The appropriate use of nasal steroids has been shown to improve seasonal asthma symptoms, exercise-induced bronchoconstriction,[19-21] airway responsiveness,[21,22] and peak expiratory flow measurements in patients with rhinitis and asthma.[23] Oral antihistamines, with or without decongestants, have elicited at least short-term improvements in lung function, as well as in symptoms, when compared with the effects of placebo.[24,25] However,

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some experts remain unconvinced that treating the nose will improve lung function.[26] Critics cite the variation across studies in which there are improvements in some, but not all, asthma outcome measures and that lung function has not been consistently shown to improve with treatment of nasal conditions.

In contrast to the improvements seen in other disease parameters in asthma, it is unknown whether medication used to treat upper airways diseases can also reduce acute health care use, such as ED visits caused by asthma. Because these events are relatively unusual, it will be logistically difficult and extremely costly to conduct a randomized controlled trial of sufficient power to examine this question. An observational study design allows us to assess the effectiveness of medications under conditions of actual use in the real-world setting of clinical practice.[27,28] This article describes a population-based cohort of members of a managed care organization (MCO). A previous study from this population demonstrated a protective effect of orally inhaled corticosteroids on asthma hospitalizations but did not consider the effect of intranasal corticosteroids or prescription antihistamines.[29] In this study we assess the effect of medication for treatment of chronic upper airways conditions on the occurrence of ED visits for asthma.

METHODS

All subjects were members of Harvard Pilgrim Health Care and received care at any one of 14 staff-model centers (now Harvard Vanguard Medical Associates) located in eastern Massachusetts. The MCO maintains computerized information systems that capture basic demographic data, medical records that include coded diagnoses, tests and procedures from each ambulatory encounter, and claims files for all hospitalizations and ED visits. Automated pharmacy records maintained by or available at all sites contain detailed information on all prescriptions dispensed at all outpatient pharmacies. Approximately 90% of members receive prescription drug coverage that provides up to a month's supply of medicine for a nominal payment. There are pharmacies in each of the clinical centers.

The study population consisted of all individuals aged greater than 5 years cared for at one of the 14 health centers who had a primary diagnosis of asthma (International Classification of Diseases, Ninth Revision, Clinical Modification codes 493.00-493.99) listed for at least 1 ambulatory encounter, a hospitalization, or an ED visit during the study period from October 1991 to September 1994. Only persons continuously enrolled for at least 1 year during the study observation period and who had complete prepaid prescription drug coverage were included as eligible subjects for analysis. The MCO at this time did not reimburse payment for drugs obtained at pharmacies outside its system.

In addition, within the group who satisfied the eligibility criteria for asthma, we identified those with an additional upper airways disease diagnosis of rhinitis, sinusitis, otitis media, or a combination thereof. Rhinitis is difficult to define because the boundary between health and disease is ill defined.[30] In addition, allergic rhinitis is very common but is difficult to differentiate from nonallergic and infectious forms of rhinitis.[30] For these reasons, we used a very broad definition for upper airways diseases. These included the following diagnoses. For *rhinitis*, diagnoses included allergic, perennial, vasomotor, nonallergic, viral and infectious rhinitis, seasonal allergy, rhinorrhea, respiratory allergy, nasal polyps, rhinitis, and hay fever. The *otitis* category included otitis media, adhesive, subacute, acute, serous, suppurative, and chronic otitis. The *sinusitis* diagnoses were sinusitis and sinobronchitis. Approval was obtained from the MCO's institutional review board.

Person-time was defined for an individual as the beginning of the study period or at enrollment in the MCO. The end of person-time was defined as the first ED visit for asthma, disenrollment, or the end of the study period. For the analysis, person-time or events occurring after the first ED visit were censored. Dispensing rates for each type of drug were calculated for each individual by summing the number of canisters or containers of drug dispensed and dividing by the person-time. Asthma controller medications included inhaled corticosteroids (referred to as *inhaled steroids*) and inhaled cromolyn (referred to as *cromolyn*). β-*Agonists* included inhaled or pediatric oral preparations (and also included anticholinergics but excluded long-acting β-agonists such as salmeterol). Nasal steroids included all corticosteroids identified as delivered nasally. Prescription antihistamines included all medications covered by the AHFS code of 040000. Nonprescription antihistamines were not able to be included in the analysis.

The main outcome of interest was ED visits for asthma. No independent or objective marker of disease severity was available. The rate of β-agonist dispensing served as a surrogate for clinical asthma control. This technique has been successfully used in previous studies to stratify individual risk for asthma morbidity, such as hospitalization or near-fatal episodes.[29,31] Recently, a pharmacy-derived severity categorization of asthma demonstrated a monotonic relationship with inpatient resource use for asthma.[32] The main variables for stratification in the analysis were the rates of dispensing of nasal steroids or prescription antihistamines. Potential covariates included age, sex, frequency of routine ambulatory visits, frequency of urgent care visits, and rates of dispensing of orally inhaled corticosteroids and β-agonists for asthma. In the previous study in this population examining the effect of (oral) inhaled steroids, these variables were shown to be independently associated with asthma hospitalizations.[29] In that study no effect was seen on the results when persons with less than 30, 60, or 120 days of follow-up were excluded.[29] Information on race was unavailable for a substantial proportion of the population and was therefore not considered in this analysis. Pharmacy data included any initial dispensed medications and refills of all prescription medications.

Differences in the proportion of children hospitalized in each stratum were assessed for significance by using χ^2 tests and Mantel-Haenszel methods. β-Agonist and orally inhaled steroid-dispensing rates were collapsed into 4 categories (0, >0-1, >1-8, and >8 dispensed prescriptions). Age was also divided into 3 groups (6-17, 18-34, and ≥35 years). All dispensed prescriptions of asthma-controller medication were weighted equally in these analyses because fluticasone propionate and budesonide were not in use during this time period. Multiple logistic regression was used to model asthma-related ED visits. We have used the term *relative risk* for the odds ratios produced to enhance readability and because the 2 closely approximate each other if the probability of the event is uncommon.[33] Effect modification was evaluated by means of stratified analysis and inclusion of interaction terms in the logistic model.

RESULTS

During the 3-year study period, 13,844 persons satisfied the eligibility criteria for asthma. The overall observation time was 40,402 person-years. The median duration of observation time was 3 years, and 75% of the study population were members of the MCO for at least 2.3 years. The mean age of the population was 26 years (SD, 17 years). The majority were adults, with 3888 aged

TABLE I. Frequency of upper airways disease diagnoses among persons with asthma in different age groups

Age in years (n)	Rhinitis (%)	Sinusitis (%)	Otitis media (%)	Total UAD (%)*
6-17 (3888)	1174 (30)	903 (23)	1344 (35)	2307 (59)
18-34 (5134)	1752 (34)	1095 (21)	685 (13)	2609 (51)
>35 (4822)	1405 (29)	1117 (23)	569 (12)	2254 (47)
Total (13,844)	4331 (31)	3115 (23)	2598 (19)	7170 (52)

UAD, Upper airways disease.
*Persons given a diagnosis of one or more of the following during the study period: rhinitis, sinusitis, or otitis media.

TABLE II. Frequency of patients within different categories of rates of dispensing for nasal steroids and prescription antihistamines according to upper airways disease diagnosis

		Rate of medication dispensing			
	n	>0-1 (%)	>1-3 (%)	>3 (%)	Total (%)
Nasal steroids					
Rhinitis	4331	1038 (24)	413 (10)	186 (4)	1637 (38)
UAD*	7170	1301 (18)	468 (7)	211 (3)	1980 (28)
No UAD	6674	210 (3)	55 (1)	31 (0.5)	296 (4)
Total	13,844	1511 (11)	523 (4)	242 (2)	2276 (16)
Antihistamines					
Rhinitis	4331	887 (20)	582 (13)	347 (8)	1816 (42)
UAD	7170	1353 (19)	754 (11)	418 (6)	2525 (35)
No UAD	6674	869 (13)	241 (4)	83 (1)	1193 (18)
Total	13,844	2222 (16)	995 (7)	501 (4)	3718 (27)

UAD, Upper airway disease.
*Persons given a diagnosis of one or more of the following: rhinitis, sinusitis, otitis.

between 6 and 17 years, 5134 aged between 18 and 34 years, and 4822 aged 35 years and older. Female patients comprised 56% of the overall population, although male patients predominated in the child population (58%), whereas female patients were the majority in the adult population (65%). Table I shows the proportion of the population given a diagnosis of rhinitis, sinusitis, otitis media, or a combination thereof during the study period. Otitis media was far more common among children than adults, whereas rhinitis and sinusitis were more evenly spread across age groups.

Asthma pharmacotherapy was dispensed to 12,183 (88%) members of the population during the study period. A single prescription was dispensed to 2354 (17%) persons. Nearly all (98%) of those dispensed any asthma drug received 1 or more dispensed prescriptions of a β-agonist. Orally inhaled steroids were dispensed on at least one occasion to 40% of the study population. In children 11% were dispensed (oral) inhaled steroids, rising to 28% in those over 45 years old. Cromolyn was dispensed to 16% of children and 3% of adults. Table II shows the proportions of persons dispensed nasal steroids and prescription antihistamines. Both types of medications were dispensed more commonly to those with an upper airways disease diagnosis, particularly rhinitis. Thirty-five percent of patients with an upper airways disease diagnosis were dispensed prescription antihistamines and 28% received nasal steroids compared with 18% and 4%, respectively, in those without an upper airways disease diagnosis. Most persons dispensed either nasal steroids or prescription antihistamines had infrequent dispensed prescriptions. Among those with an upper airways disease, only 3% received greater than 3 dispensed prescriptions of nasal steroids per person-year, whereas just 6% received prescription antihistamines at this rate. We also examined whether there were differences in the frequency of nasal steroid or prescription antihistamine dispensing within different categories of rate of β-agonist dispensing. Among those with upper airways diseases, in each β-agonist dispensing-rate category approximately 10% were dispensed nasal steroids, 13% to 17% were dispensed prescription antihistamines, and 22% to 25% were dispensed either of these medications.

During the study period, 1610 (11.6%) persons had 2245 ED visits for asthma. Treatment directed at the upper airways had a significant effect on asthma-related ED visits (Table III). The rates of asthma-related ED visits were reduced in those dispensed either nasal steroids or prescription antihistamines. This relationship held across all age groups and for different upper airways diseases. Although the frequency of ED visits declined with age, the benefit of treatment directed at the nose remained similar for adults and children. The absolute reduction in events was greater for nasal steroids than prescription antihistamines in almost all categories. There were no significant differences seen between the individual diagnoses (rhinitis, sinusitis, and otitis), with nasal steroids or antihistamines being equally effective for each condition in reducing ED visits.

Among persons who were dispensed (oral) inhaled

TABLE III. Frequency (rate per 100 person-years) of asthma-related ED visits within different age groups according to upper airways treatment

	Treatment category			
Age, y (n)	Nasal steroid (+) (n = 2276)	Nasal steroid (–) (n = 11,568)	Antihistamine (+) (n = 3718)	Antihistamine (–) (n = 10,126)
6-17 (3888)	35 (6.9)	336 (9.9)*	43 (7.1)	328 (10.0)*
18-34 (5314)	36 (4.1)	342 (8.1)‡	99 (5.8)	279 (8.2)*
≥35 (4822)	27 (3.1)	255 (6.5)†	57 (4.1)	225 (6.6)†
All (13,844)	98 (4.3)	933 (8.1)‡	199 (5.4)	832 (8.2)‡

*$P < .03$.
†$P = .0001$.
‡$P < .0001$.

TABLE IV. Frequency (rate per 100 person-years) and unadjusted odds ratios of an asthma-related ED visit according to upper airways treatment stratified by whether individuals were dispensed or were not dispensed oral inhaled corticosteroids for asthma.

	Upper airways treatment					
Asthma treatment	Nasal steroid (+)	Nasal steroid (–)	OR	Antihistamine (+)	Antihistamine (–)	OR
(+) ICS (n = 6110)	47 (6.8)	558 (10.3)	0.66*	103 (7.6)	505 (10.6)	0.72†
(–) ICS (n = 7734)	51 (3.2)	375 (6.1)	0.52‡	97 (4.1)	327 (6.1)	0.67†

ICS, Orally inhaled corticosteroids; *(+)*, received medication; *(–)*, did not receive medication.
*$P = .01$.
†$P = .001$.
‡$P < .0001$.

steroids for asthma, use of either nasal steroids or prescription antihistamines was associated with reductions in asthma-related ED visits (Table IV). A similar reduction for both medications was also seen among those not using (oral) inhaled steroids for asthma (Table IV).

In multiple logistic regression analysis a significant protective effect was found for any dispensing of nasal steroids on ED visits for asthma. In persons with asthma, after simultaneously controlling for rate of (oral) inhaled corticosteroid dispensing, rate of β-agonist dispensing, age, sex, frequency of urgent care visits, frequency of routine ambulatory visits, and upper airways disease diagnoses, the adjusted relative risk (RR) for an asthma-related ED visit for those dispensed any nasal steroids was 0.7 (95% confidence interval [CI], 0.59-0.94; $P = .01$) but was indeterminate for those receiving prescription antihistamines (RR, 0.9; 95% CI, 0.78-1.11; $P = .4$). Consistent with our previous findings for asthma hospitalizations, in the multivariate model oral inhaled corticosteroids were associated with a reduced risk for asthma-related ED visits after adjusting for severity, as measured by means of β-agonist use. Increasing use of β-agonists was associated with an increased risk for ED visits. The inclusion of oral corticosteroids into the model did not affect the results.

Regression models were developed with nasal steroids and prescription antihistamines categorized by rate of dispensing into groups of 0, greater than 0 to 1, greater than 1 to 3, and greater than 3 (Table V). For nasal steroids, a reduced risk was seen in ED visits in those with greater than 0 to 1 and also greater than 3 dispensed prescriptions per year, although in the latter case this just failed to reach statistical significance (RR, 0.5; 95% CI, 0.23-1.05; $P = .07$). With prescription antihistamines, reductions were seen in the risk of ED visits in the greater than 1 to 3 and greater than 3 categories, although the CIs for both crossed unity.

DISCUSSION

These data suggest that treatment for upper airways diseases with nasal steroids and oral antihistamines is associated with a reduced frequency of asthma-related ED visits. The effect of treatment for the nose in reducing asthma-related ED visits was seen in persons who were also being treated with orally inhaled corticosteroids for asthma, as well as in those not using inhaled steroids. After controlling for asthma treatment and indicators of asthma care (routine and urgent ambulatory visits), as well as age and sex, nasal steroids demonstrated a significantly protective effect for asthma-related ED visits. Nasal steroids demonstrated a protective benefit with infrequent dispensing and also with more regular use. This effect was not clearly seen with prescription antihistamines after controlling for other factors. The rates of diagnosis of upper airways diseases were well below those that might be expected from the literature, in which rates of rhinitis in asthma of 50% to 80% are usually seen.[2] In addition, at the time of the study (1991-1994), the majority of patients with asthma and an upper airways disease diagnosis were not being dispensed either nasal corticosteroids or prescription antihistamines, and almost none had sufficient dispensed prescriptions to suggest regular use. Although the revised Guidelines for

TABLE V. Adjusted RRs* for asthma-related ED visits among those within different categories of dispensing rates for nasal steroids and prescription antihistamines

	Nasal steroids		Antihistamines	
Dispensing rate	**n**	**RR (95% CI)**	**n**	**RR (95% CI)**
0	11,568	1.0	10,126	1.0
>0-1	1511	0.74 (0.57-0.99)	2222	0.99 (0.81-1.22)
>1-3	523	0.87 (0.57-1.31)	995	0.83 (0.60-1.14)
>3	242	0.50 (0.23-1.05)	501	0.83 (0.54-1.28)

*Adjusted for age, sex, routine ambulatory visits, urgent care visits, upper airways disease diagnoses, rate of dispensing of orally inhaled corticosteroids, and rate of dispensing of β-agonists.

the Diagnosis and Treatment of Asthma[34] recognize that associated conditions contribute to asthma severity, a recent survey of a random sample of primary care providers in the United States found greater than 90% did not mention rhinitis-sinusitis as a nonenvironmental factor that can exacerbate asthma.[35]

It is likely that the therapeutic effect of these agents is restricted to the upper airways and not the result of a direct effect on the lungs.[36,37] Studies have demonstrated minimal deposition of intranasal corticosteroids into the lungs.[20,38] This suggests a key role for nasal inflammation in modulating lower airway responsiveness associated with rhinitis.[36]

Our study has a number of limitations. The use of computerized databases eliminates the risk of recall bias for drug exposure. However, we have relied on medication dispensing as a surrogate for actual medication use. This may have produced some confounding in a number of ways. Dispensed prescriptions would tend to overestimate the actual use of both asthma controller and nasal medication and underestimate their effect. We were unable to identify use of nonprescription antihistamine use obtained over-the-counter by patients. It is therefore possible that a large group of exclusively nonprescription antihistamines users were inadvertently included in the nonuser group, and this could distort the study findings regarding the protective effect of antihistamines. However, because even a single dispensed prescription of antihistamine over 3 years would put a patient into the user group, regardless of whether the rest of their use is over-the-counter, it is unlikely that large numbers of patients will have been incorrectly classified as nonusers. We did not have any objective marker of asthma severity or control, and the frequency of β-agonist dispensing was used as a surrogate measure. Although this method has been successfully used previously,[29,31,32] there is likely to be some residual confounding by severity of asthma (confounding by indication). Furthermore, we have no marker of upper airways disease severity. It may be argued that because patients with more severe upper airways disease who are at risk for adverse events are also more likely to have been given a diagnosis and received treatment, then any residual confounding will be toward underestimating the protective effect of nasal treatment. Children with physician-diagnosed rhinitis have significantly more lower respiratory symptoms, such as wheezing, than children without rhinitis or children with non–physician-diagnosed rhinitis.[39] By using automated databases, there is the potential for misclassification in recording by clinicians of an upper airways disease diagnosis and also between different upper airways disease diagnoses. This could affect the study conclusions regarding the influence of upper airways diagnoses on asthma-related ED visits. It is less likely that this would materially affect the conclusions regarding the protective effect of nasal treatment on asthma-related ED visits in the multivariate model. Length of follow-up may influence the results, with patients with more severe disease having less time before events. However, previous results from this population have shown no effect on the protective effect of asthma therapy when persons with shorter lengths of follow-up were excluded from the analysis.

It is possible that our results are confounded by nasal treatment being in some way a marker of better quality of asthma care. We attempted to control for this by including in the multivariate models the frequency of routine ambulatory visits and the frequency of unscheduled urgent care visits as markers of asthma management. However, the question also arises as to what exactly the possible components of better asthma care may be, other than the appropriate use of asthma medication and the appropriate treatment of associated conditions that may exacerbate asthma (eg, rhinitis). Although the nonpharmacologic aspects of asthma-management guidelines are important,[35] there is little evidence to suggest they alone are effective in reducing morbidity in the absence of appropriate medication. Therefore although recognition of upper airways problems requiring treatment may indicate the patient is receiving good quality of care, it is the manifestation of this higher quality of care in the appropriate use of medication that likely plays the major role in reducing morbidity.

A related issue to this is the observation that a protective effect was seen with infrequent use of nasal treatment, and despite the seasonal nature of many patients' nasal symptoms, there may be some scepticism as to whether this frequency of use would be sufficient to have any clinically significant effect. However, a recent study has indicated that nasal steroids are highly effective in improving symptoms, quality of life, and nasal eosinophil levels in patients with seasonal allergies when used on an as-needed, less-than-daily basis during the allergy season.[40] In addition, a similar pattern has been

reported with orally inhaled corticosteroids for asthma, with which infrequent use has been associated with a significantly decreased risk for hospitalizations.[29] Our results are consistent with those of these studies and suggest at least the possibility that infrequent, as-needed use of these medications can produce clinically significant reductions in morbidity in patients with asthma. It should be noted that more frequent dispensing (>3 per year) provided the greatest protective effect, with a halving of the risk for ED visits. The smaller numbers available for analysis in this category are likely to explain the broader CIs seen in this group.

These data, obtained from 1991 to 1994, do not address the effect of nasal steroids and prescription antihistamines on symptoms or quality of life. As a result of when the data were collected, we were unable to compare the relative effects of newer, higher potency nasal steroids, newer nonsedating antihistamines, or oral antileukotriene preparations with the effects of older medications. At present there are little data to indicate with any certainty that nasal steroids differ significantly from one another in their clinical effectiveness, particularly with regard to their effect on asthma.[26] However, it is possible that the higher systemic bioavailability of the older steroid preparations relative to newer nasal steroids[41] may underlie the observed effects in our study. Further work is needed to examine whether the beneficial effects on asthma are also seen with newer medications, such as nasal mometasone furoate, which have apparently lower systemic effects.[41] In comparison trials of different antihistamines for rhinitis, clinical efficacy and patient acceptance appear similar between different medications.[42,43] Nash et al[44] reported an analysis model with symptom reduction as the outcome, showing that nasal fluticasone was more cost-effective than loratadine. Our results suggest potential benefits from nasal steroids and possibly from antihistamines. For cost-conscious payer organizations, the effect of nasal treatment in asthma on reducing direct costs of ED visits is of some importance. Our findings would suggest that removing nasal steroids or antihistamines from drug formularies may not be cost-effective in overall asthma management, and further critical examination of this issue is needed.

Recent evidence indicates that a cumulative dose of oral inhaled corticosteroids used for asthma treatment may reduce bone mineral density in a dose-dependent manner.[45] Nasal corticosteroids may have similar, negative effects on growth and bone density,[46] although the evidence is inconsistent.[41,47,48] Newer nasal steroid preparations appear to have less systemic bioavailability and, consequently, less effect on bone metabolism.[41] However, the safety of adding nasal steroids to conventional regimens of oral inhaled corticosteroids for asthma remains to be established. In the interim, clinicians should consider the level of total corticosteroid exposure and titrate each medication to the lowest effective dose.

One of the key components of current asthma guidelines is the control of associated conditions, such as rhinitis-sinusitis, that may contribute to asthma morbidity. This study has shown that treatment for the nose, particularly with intranasal corticosteroids, is associated with a reduced risk for subsequent asthma-related ED visits. However, most patients with asthma and upper airways disease were not receiving this form of therapy. There is the potential to reduce asthma health care use by means of increased use of intranasal corticosteroids in persons with coexistent asthma and upper airways diseases. Targeted intervention programs using a variety of strategies directed toward this end can successfully be made part of quality-improvement initiatives.[49] Further studies, possibly including large, prospective, randomized controlled trials are needed to confirm our results.

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