National trends in asthma visits and asthma pharmacotherapy, 1978-2002

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Background: Research is limited on physicians' compliance with recent clinical guidelines for asthma treatment.
Objective: Our purpose was to investigate the relationships among clinical guidelines, asthma pharmacotherapy, and office-based visits through use of nationally representative data.
Methods: Nationally representative data on prescribing patterns by office-based US physicians were extracted from the National Disease and Therapeutic Index. We tracked 1978-2002 trends in the frequency of asthma visits and patterns of asthma pharmacotherapy, focusing on the use of controller and reliever medications.
Results: The estimated annual number of asthma visits in the United States increased continuously from 1978 through 1990 (18 million visits); since 1990, it has remained relatively stable. Controller medication use increased 8-fold between 1978 and 2002, inhaled corticosteroids manifesting the biggest increases. The use of reliever medications, particularly short-acting oral β_2-agonists, decreased modestly over this period. The aggregate use of controllers (83% of visits) superseded that of relievers (80%) for the first time in 2001. Improved appropriateness of asthma pharmacotherapy was also suggested by an increase in the controller-to-reliever ratio, which reached 92% in 2002. Xanthines, which once dominated asthma therapy (63% of visits in 1978), were used in only 2% of visits in 2002. More recent drug entrants have been adopted rapidly, single-entity long-acting inhaled β_2-agonists being used in 9% of visits and leukotriene modifiers in 24% of visits in 2002.
Conclusion: Asthma pharmacotherapy has changed extensively in the past 25 years. Practices over the last decade are increasingly consistent with evidence-based guidelines. These changes in medication use might have contributed to the lack of a recent increase in asthma visits. (J Allergy Clin Immunol 2003;111:729-35.)

Key words: *Asthma visits, asthma pharmacotherapy, inhaled corticosteroids, bronchodilators, controller-to-reliever ratio, evidence-based guidelines*

Asthma is a serious global health problem that is broadly distributed by age, sex, race/ethnicity, and geographic location. From 1980 to 1999, asthma prevalence in the United States, measured as self-reported asthma episodes during the preceding 12 months, increased by 63% among children aged 0 to 14 years (1.9 vs 3.1 million) and by 45% among those aged 15 years and older (5.1 vs 7.1 million).[1] Other national and international statistics indicate that asthma prevalence, morbidity, and mortality have increased significantly since the early 1970s.[2] Whereas some studies indicate continued increases through the mid 1990s,[2-4] others show recent downward trends, especially in asthma hospitalizations and mortality.[1-4] Among possible contributors to the observed trends are patterns of drug therapy.[5-10]

Patient outcomes in asthma depend strongly on appropriate medication use.[11,12] Traditionally, symptomatic relief of bronchospasm with short-acting β_2 agonists was the mainstay of therapy. Numerous studies, however, suggest that this therapy alone is ineffective and that regular use of β_2 agonists might actually increase the risk of morbidity and mortality.[7,13-16] Not until the early 1990s was inflammation widely recognized as the predominant cause of reversible airway obstruction and airway hyperreactivity.[17] As a result, treatment has shifted to the early and regular use of anti-inflammatory "controller" medications (especially inhaled corticosteroids) for *control* of airway inflammation.[17] Short-acting β_2 agonists and other "reliever" medications are now recommended for as-needed use for *relief* of acute bronchoconstriction.[11,12,18]

Appropriate use of inhaled corticosteroids is associated with improved patient outcomes.[5,7,8,13,14,18-20] Many studies in the last decade, however, suggested underprescription and underutilization of inhaled corticosteroids.[5,7,8,10,21]

Although evidence-based asthma guidelines have been developed to improve quality of care and patient outcomes, guideline publication might not by itself lead to improved clinical practice.[5,10] Limited research is currently available on trends in asthma pharmacotherapy to identify current gaps between guidelines and practice.[13,22-26]

Using 1978-2002 data from the National Disease and Therapeutic Index (NDTI), this study documents 25-year

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Abbreviations used

C:B ratio: Ratio of the use of inhaled corticosteroids to the use of short-acting inhaled β_2-agonists
ICD-9: International Classification of Diseases, Ninth Revision
NDTI: National Disease and Therapeutic Index

trends in asthma office visits and pharmacotherapy, with a focus on the use of controller and reliever medications.

METHODS

Data were extracted from the NDTI, a continuing physician survey conducted by IMS HEALTH (Plymouth Meeting, Pa). The NDTI provides nationally representative diagnostic and prescribing information on patients treated by office-based physicians in the continental United States. A random sample of office-based physicians stratified by specialty and geographic region is selected from the master lists of the American Medical Association (Chicago, Ill) and the American Osteopathic Association (Chicago, Ill). Approximately 3500 physicians participate in each calendar quarter; each physician is randomly assigned 2 consecutive workdays per quarter for data collection.

Physicians provide information on each patient encounter during their data collection periods. Most of these asthma visits occur in outpatient settings. In 2002, 89% were office visits, 6% were hospital visits, 4% were telephone calls, and 1% were nursing home visits. Each reported patient diagnosis generates a separate diagnosis record on which the physician records information on medication therapies provided for the condition. A single patient contact might generate multiple diagnosis records, each of which might list multiple medications. Diagnosis records might also list no medications if none were being used for the specific condition. Medication reporting reflects the physician's best knowledge of new or continuing prescription and nonprescription medications. The NDTI does not capture information on patient adherence or unreported self-medication.

Using NDTI diagnosis reports from 1978 through the second quarter of 2002, this study tracked annual numbers of asthma encounters and the annual percentage use of major asthma drug classes. Data from the first 2 quarters in 2002 were annualized. From 1978 through 1986, asthma visits were aggregated under one general diagnosis of asthma; beginning in 1987, visits were reported separately for extrinsic asthma (International Classification of Diseases, Ninth Revision [ICD-9]: 493.0) and asthma unspecified (ICD-9: 493.9). Of these 2 diagnostic codes, the latter accounts for the vast majority of visits reported (90% in 2002). Intrinsic asthma (493.1) and chronic obstructive asthma (493.2) represent infrequent diagnoses and were not included.

Annual sample sizes of asthma visits in the NDTI increased from 1793 in 1978 to 7638 in 2001 and 3730 in the first 2 quarters of 2002.

This study reports national estimates that were extrapolated from these sample data. Data extrapolation accounts for the 2-stage stratified cluster sampling method used in the NDTI, whereby office-based physicians are sampled by specialty and geographic area and workdays are then sampled for participating physicians. Annual data are presented as the aggregate of the quarterly surveys conducted within each year. For the sample sizes available for asthma visits, the 95% CIs around our estimates of annual medication usage rates and patient visits are less than ±1% in recent years.

We examined annual prescribing data to assess the proportion of asthma visits in which individual medications or medication classes were reported as specific treatments for asthma. The percentage of visits for which each drug class was prescribed was calculated by dividing the total number of times that the drug class was reported in a calendar year by the estimated number of national visits for asthma for that year. All reported brand and generic names for a specific medication were combined into a single generic name. In conformance with consensus guidelines,[12] we categorized medication classes as controllers (ie, inhaled corticosteroids, cromones [cromolyn sodium and nedocromil], long-acting β_2-agonists, and leukotriene modifiers) and relievers (ie, short-acting inhaled and oral β_2-agonists, anticholinergics, and systemic corticosteroids). Although xanthines share characteristics with control medications,[12] they also are bronchodilators with bronchoprotective effects and can be used as alternative relievers.[11] Given their mixed status, we present xanthines as a category separate from controllers and relievers. Medication use in these classes is not mutually exclusive, because many patients are treated with multiple medications. The ratio of inhaled corticosteroids—recommended *control* medications—to short-acting inhaled β_2-agonists—preferred for quick *relief*—*was* computed as an accepted indicator of the appropriateness of therapy[27,28] and referred to as the *C:B ratio*. Limited information was available on the characteristics of asthma visits, but we also have tracked changes in physician specialty, age, sex, and visit status (new vs return).

RESULTS

Asthma visits

There was a doubling in the estimated national number of annual visits by patients diagnosed with asthma between 1978 (8.5 million visits) and 1990 (17.7 million visits; Fig 1). The number of asthma visits then stabilized at a mean of 16 million between 1991 and 2002. In relation to US population estimates, the number of asthma visits increased from 4 to 7 per 100 people between 1980 and 1990; it has remained at 6 ever since.

The distribution of asthma visits by sex and age has not changed (Table I). From 0 to 19 years of age, more male asthma visits than female asthma visits are noted, but a reversed relationship is evident after the age of 20 years. Across the study period, allergists, general/family practitioners, internists, and pediatricians represent the 4 specialties that primarily treat patients with asthma. The percentage of visits to allergists decreased by more than half—from 28% in 1978 to 12% in 2002—whereas the percentage of visits to general/family practitioners declined from 30% to 25%. Over time, asthma treatment has shifted to internists and pediatricians; the percentage of visits increased from 24% to 30% for internists and from 14% to 27% for pediatricians. More detailed specialty information available after 1990 illustrates that a stable proportion of care has been provided by all primary care physicians (including general internists [43% in 2002]), whereas pulmonologists have consistently provided a modest share of visits (11% in 2002). Between 1978 and 2002, the proportion of first visits increased by more than 10%, accounting for 1 in 4 asthma visits in 2002.

Controllers versus relievers

Substantial changes have occurred in asthma pharmacotherapy over the past 25 years. The aggregate prescription rate for long-term controllers increased continuously between 1978 and 2002. In 2001, controllers were reported in 83% of visits—higher, for the first time, than the rate for relievers (80%; Fig 2). This differential between controller use and reliever use widened in 2002

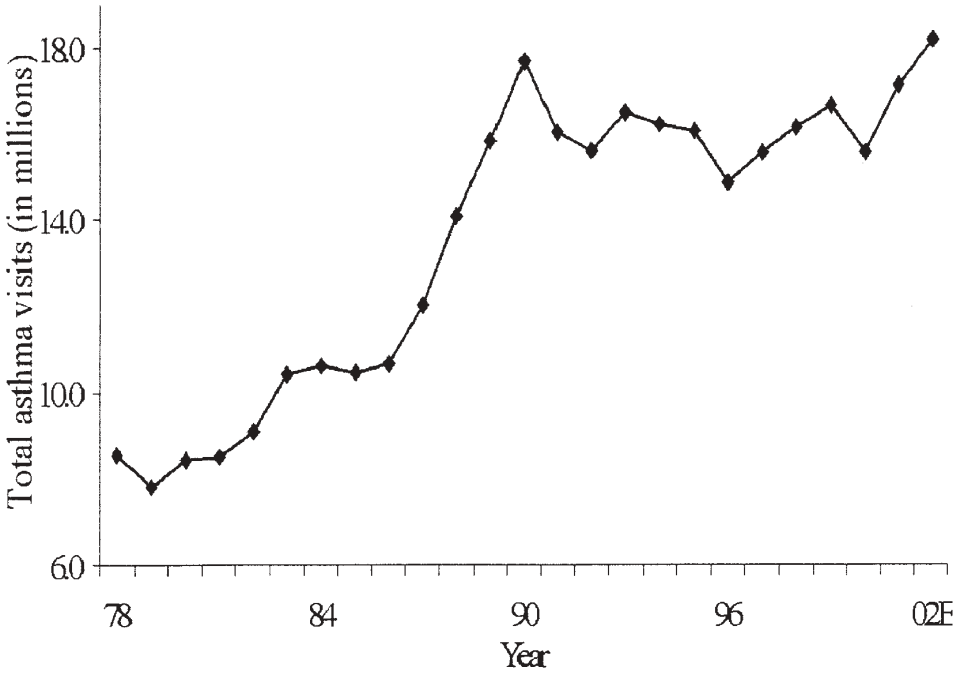


FIG 1. National trends in the number of office-based visits by patients with asthma, according to IMS HEALTH's NDTI for January 1978 through June 2002. Numbers for 2002 are estimates *(E)* based on data for January through June 2002.

(81% vs 72%). Increases in the prescription rates of controllers reflect a rise in the use of inhaled corticosteroids, long-acting β_2-agonists, and, more recently, leukotriene modifiers. Aggregate prescription rates for relievers increased from 1978 (58%) through 1993 (102%), reflecting multiple relievers per patient, but have since declined. The decline between 1994 and 2002 in reliever medication use resulted from decreased short-acting oral β_2-agonist and systemic corticosteroid use and from stabilized use of short-acting inhaled β_2-agonists.

In 1978, inhaled corticosteroids and short-acting inhaled β_2-agonists were both prescribed in 8% of visits, resulting in a 100% C:B ratio. This ratio quickly dropped to 30% by 1983 and remained below 30% for the following 6 years, primarily because of markedly increased prescription rates of short-acting inhaled β_2-agonists. Beginning in 1989, the C:B ratio consistently increased, reaching 92% in 2002.

Before 1990, xanthines dominated the treatment of asthma. However, after a sizable increase from 40% in 1978 to 63% in 1984, xanthine use dropped to just 2% in 2002.

From 1978 to 1989, the average number of medications per patient increased from 1.7 to 2.0. Since 1989, this figure has been stable at 2.0 medications per patient, despite the increasing number of medications and classes available for treatment.

TABLE I. General characteristics of physician-patient visits for asthma by year

	Year					
	1978	**1983**	**1988**	**1993**	**1998**	**2002**
Sex						
Male	44%	41%	38%	39%	40%	41%
Female	52%	49%	51%	51%	52%	51%
Age (y)						
0-2	4%	5%	6%	5%	4%	5%
3-19	30%	30%	27%	28%	31%	32%
20-64	49%	42%	45%	42%	43%	41%
65+	15%	18%	20%	15%	14%	13%
Specialty						
Allergy	28%	17%	10%	14%	14%	12%
Primary care*	30%	24%	29%	27%	26%	25%
Internal medicine†	24%	32%	34%	33%	30%	30%
Pediatrics	14%	20%	21%	19%	24%	27%
Other	4%	7%	6%	7%	6%	6%
Visit stage						
First	14%	16%	20%	27%	26%	25%
Referral‡	25%	23%	18%	18%	21%	20%
Subsequent	80%	76%	71%	68%	69%	69%

Percentages were calculated relative to the total annual number of asthma visits; missing data were present where percentages do not add up to 100%.
*Includes general practice, family practice, and osteopathic medicine.
†Includes internal medicine, nonspecialty and internal medicine, and pulmonary disease.
‡Percent of first visits that were referred to the physician.

Prescription rates of long-term control medications

The proportion of annual total asthma visits for which an inhaled corticosteroid is prescribed remained constant (approximately 8%) from 1978 to 1988 and then began rising; it reached 48% in 2002 (Fig 3). Beclomethasone is the inhaled corticosteroid that has been on the market

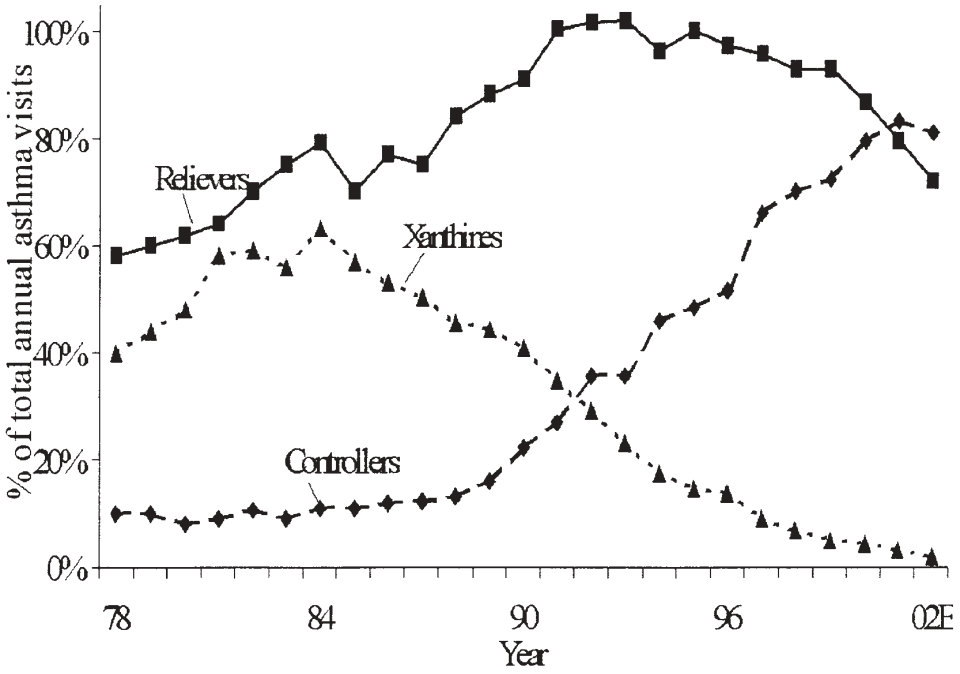


FIG 2. National trends in the aggregate prescription rates of long-term controllers, quick relievers, and xanthines for asthma treatment, according to IMS HEALTH's NDTI for January 1978 through June 2002. Numbers for 2002 are estimates *(E)* based on data for January through June 2002.

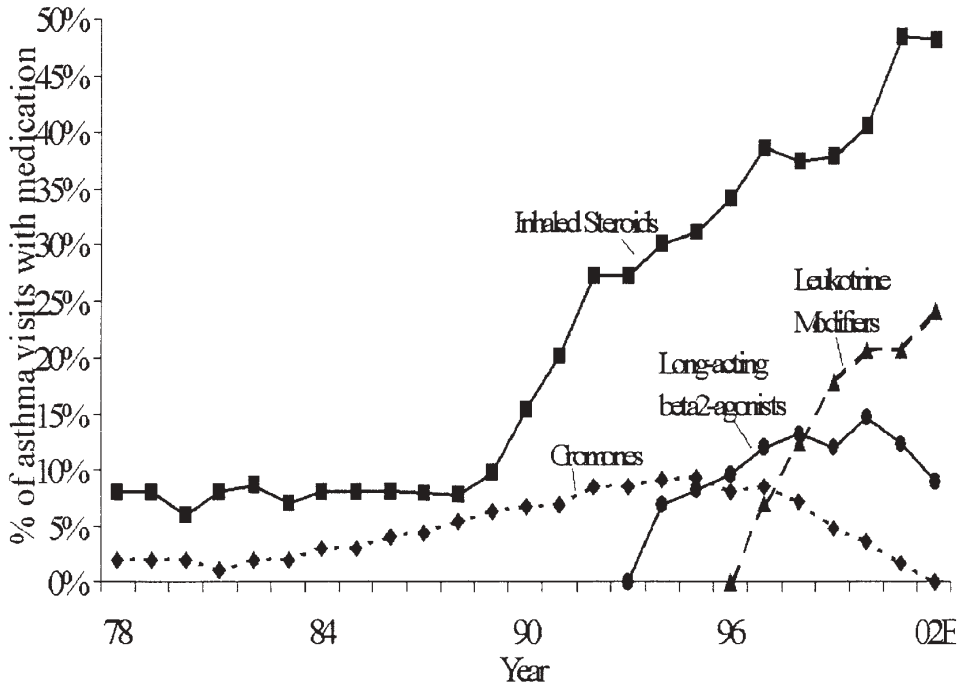


FIG 3. National trends in the use of inhaled corticosteroids, cromones, long-acting β_2-agonists, and leukotriene modifiers for asthma treatment, according to IMS HEALTH's NDTI for January 1978 through June 2002. Numbers for 2002 are estimates *(E)* based on data for January through June 2002.

for the longest time; its prescription rates remained consistent at approximately 10% through 1998, but its use has declined in the last 4 years (1% in 2002) as additional inhaled steroids have become available. Between 1988 and 1997, increasing aggregate use of inhaled steroids reflected small increases in beclomethasone use, the entry of flunisolide, and increasing use of triamcinolone (4% in 1989 to 15% in 1997). Fluticasone, released in

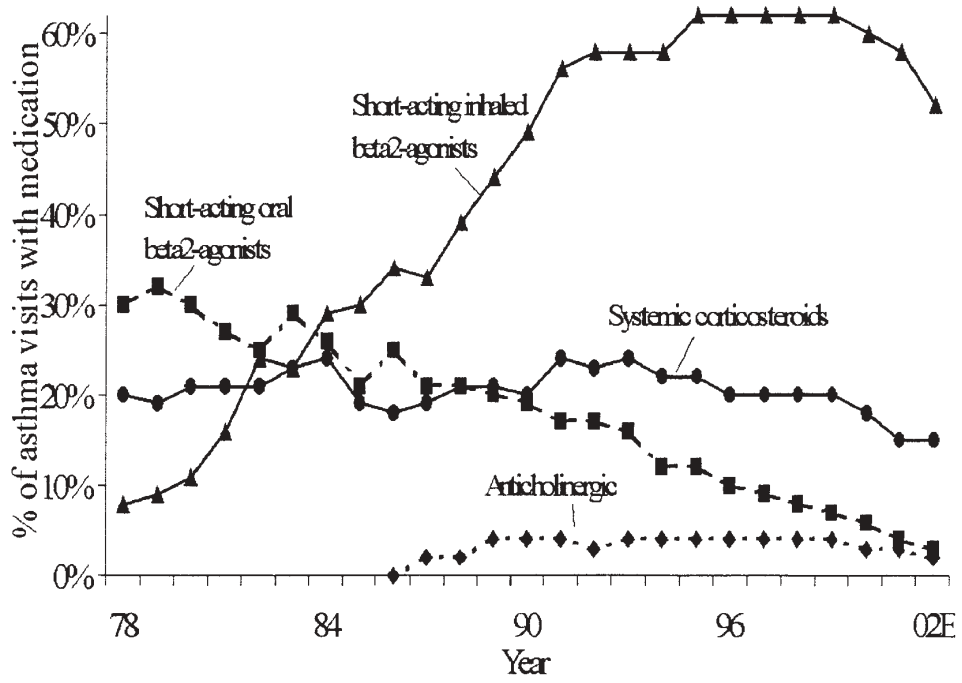


FIG 4. National trends in the use of short-acting β_2-agonists, systemic corticosteroids, and anticholinergics for asthma treatment, according to IMS HEALTH's NDTI for January 1978 through June 2002. Numbers for 2002 are estimates *(E)* based on data for January through June 2002.

1996, has been the most frequently prescribed inhaled corticosteroid since 1998 (20% in 2002). The formulated combination of fluticasone and salmeterol (a long-acting β_2-agonist) was reported in 20% of asthma visits in 2002, its second year on the market. Use of budesonide increased from 2% in 1998, its first year on the market, to 8% in 2002.

Although they are prescribed relatively infrequently, the use of cromones—mostly cromolyn (but rarely nedocromil)—had increased from 2% of visits in 1978 to 9% of visits in 1995; it has since declined to <1% of visits in 2002.

Long-acting β_2-agonists (ie, salmeterol and formoterol) and leukotriene modifiers (ie, montelukast, zafirlukast, and zileuton) are relatively new therapeutic options. In their first years on the market, long-acting β_2-agonists (1994) and leukotriene modifiers (1997) were each reported in 7% of asthma visits. The use of these single-entity long-acting β_2-agonists peaked at 15% in 2000 and has since declined to 9% in 2002. This decline during the past 2 years has coincided with the entry and increasing use of the combination formulation of salmeterol and fluticasone, as noted above. Leukotriene modifier use has increased steadily, reaching 24% in 2002. After entering the market in 1998, montelukast (20% of visits in 2002) has been prescribed more frequently than zafirlukast (2%) and zileuton (<1%).

Prescription rates for quick-relief medications

Prescription rates for the 4 medication classes of asthma relievers have been stable or declining, with the exception of short-acting inhaled β_2-agonists, the rates for which increased markedly from 8% in 1978 to 56% in 1991 and then remained constant at 58% to 62% before a recent decline beginning in 1999 (Fig 4). Albuterol dominates prescriptions for short-acting inhaled β_2-agonists. Prescription rates for short-acting oral β_2-agonists have declined continuously from 30% in 1978 to 3% in 2002. The use of systemic corticosteroids has remained relatively constant at about 20%, with some indications of a decline beginning in 1999. Beginning in 1987, anticholinergics (predominantly ipratropium) have been prescribed in only 2% to 4% of asthma visits, with little variation.

DISCUSSION

Using the 1978-2002 NDTI data, this study documents substantial changes in the number of asthma visits and in asthma pharmacotherapy. Our data indicate that the number of annual asthma visits has remained relatively stable since 1991. There has been an increasing trend in the prescription of controller medications, particularly inhaled corticosteroids, and a decreasing trend in reliever medication use, particularly short-acting oral β_2-agonists. These trends are congruent with consensus guidelines.[11,12] The use of controllers surpassed that of relievers in 2001. Improved appropriateness in medication use for asthma also was suggested by increased C:B ratios. Xanthines, once the dominant drug class, are now prescribed infrequently. In addition to guidelines, reasons for changes in asthma pharmacotherapy might include the availability and increased popularity of new drug

therapies. Prescribing patterns might reflect physician knowledge of medications as well as recommendations for their appropriate use.

Annual asthma visits showed a significant increase from 1978 to 1991, the growth accelerating after 1986—a trend noted elsewhere.[2,3] Although there is suggestive evidence of continued increases in asthma prevalence into the mid 1990s, we found that annual asthma visits were relatively stable after 1992. The number of reported patient visits reflects multiple influences, including disease prevalence, physician ascertainment of asthma, and the degree of treatment success. Although NDTI data do not allow possible mechanisms to be distinguished, our results are consistent with improved pharmacotherapy's moderation of other factors that might have led to increasing asthma visits. Recent reports of decreased asthma hospitalizations and mortality have been attributed to improved pharmacotherapy.[1] We also noted a declining trend in the proportion of return visits, possibly another indirect indicator of improved asthma control. Over time, asthma visits have shifted from allergists and general/family practitioners to internists and pediatricians. Allergists have provided a declining share of asthma treatment. In part, this might reflect the marked drop in immunotherapy for the disease.[22]

Several studies document past trends in asthma pharmacotherapy, but only up to the early 1990s.[22,23,25] This study, examining a 25-year period, not only corroborates past findings but also suggests an increasing pace for recent changes. Until 1992, this and previous studies consistently report, there were increasing trends in the prescribing of inhaled corticosteroids and short-acting inhaled β_2-agonists and a dramatic decrease in xanthine use.[22,25]

Federal consensus guidelines on asthma diagnosis and treatment were first published in 1991,[17] were revised in 1997,[12,18] and were recently updated on selected topics.[18] The guidelines emphasize the importance of long-term control of underlying airway inflammation in asthma treatment, a significant shift from traditional relief therapies. Inhaled corticosteroids, either alone or in combination with long-acting inhaled β_2-agonists, were recommended as first-line therapy for persistent asthma, whereas short-acting inhaled β_2-agonists are the preferred choice only for mild intermittent asthma or the prevention of exercise-induced symptoms.[11,12,18] Since 1991, the proportion of asthma visits at which a controller is prescribed has continued to increase, whereas the proportional use of relievers leveled and has appeared to decline beginning in 1995. Similar changes were found in the use of inhaled corticosteroids and short-acting inhaled β_2-agonists. The C:B ratio increased by 11% from 1991 to 1992, and the rising trend has continued since then, the ratio being 92% in 2002. The 1997 guidelines appear to have had little incremental impact. Patterns of asthma pharmacotherapy since 1997 have not departed from previous trends.

Other treatments are available in both the controller and reliever categories and might be used as add-on therapy to first-line medications.[11,12,18] As noted by Terr and Bloch,[22] cromones are prescribed for a limited portion of patients with asthma; their use is likely concentrated in children.[29] Of note, the most recent update on asthma treatment guidelines recommend inhaled corticosteroids as first-line therapy in children with persistent asthma.[18] Long-acting β_2-agonists and leukotriene modifiers, 2 new classes of controllers, were released in the mid 1990s. Despite the addition of these new medication classes, the average number of medications per patient has remained constant at 2.0 for more than a decade, suggesting that these medications have been used as substitutes rather than being added to existing therapy. Long-acting β_2-agonists are recommended for use in conjunction with inhaled corticosteroids for the treatment of moderate and severe persistent asthma.[18] The use of single-entity long-acting β_2-agonists (ie, salmeterol and formoterol) increased consistently until 2000, when the combination product of salmeterol and fluticasone entered the market and quickly came to be used in 20% of asthma visits. In contrast, use of leukotriene modifiers has increased continuously through 2002. The prescription rate of montelukast surpassed that of zafirlukast and has increased continuously during the past 4 years. Montelukast is probably favored over zafirlukast for its administration convenience, better adverse effect profile, and wider age range applicability. Although leukotriene modifiers can be used as an adjunct to inhaled corticosteroids, this combination, because of lack of evidence, is still not the preferred choice.

The use of the NDTI provides nationally representative trends in the number of visits by patients with asthma and in pharmacotherapy reported for those visits. Several limitations of these data must be acknowledged, however. First, the reporting of asthma in the NDTI changed in 1987; there have been fewer asthma ICD-9 codes since that year. This change, however, had minimal impact, in that no discontinuity in increasing asthma visits was evident. Second, the NDTI does not capture visits to emergency departments and hospital outpatient clinics; consequently, the current findings might not reflect trends for some patients with more severe asthma. Third, the published NDTI diagnostic reports do not document disease severity or special causes of asthma (eg, exercise-induced asthma). As a result, the appropriateness of asthma pharmacotherapy cannot be assessed on the basis of severity or cause. For example, whereas inhaled steroids are first-line therapy for persistent asthma, short-acting β_2-agonists alone might be appropriate for mild intermittent and exercise-induced asthma.[12,18] Fourth, the NDTI reports do not allow the analysis of dosage, specific medication combinations, or patient adherence, though each of these issues is important in asthma treatment. Fifth and finally, the estimates of asthma visits are dependent on physicians accurately diagnosing and documenting asthma in NDTI records, with the potential for either underestimates or overestimates of cases.[11] Of note, however, these limitations by no means diminish the validity and importance of our findings.

This study adds to previous evidence demonstrating that asthma pharmacotherapy is evolving to be more consistent with consensus guidelines, even though underutilization of inhaled corticosteroids and some overreliance on short-acting inhaled β_2-agonists might still be present. Although many factors could account for the apparent plateau in the annual number of asthma visits noted in the 1990s and the continuing favorable evolution in asthma pharmacotherapy, published guidelines on asthma management likely have contributed to these patterns.

IMS HEALTH provided the data used in the analysis.

REFERENCES

1. Centers for Disease Control and Prevention. Surveillance for Asthma—United States, 1980-1999. MMWR Morb Mortal Wkly Rep 2002;51:1-13.
2. Burney PGJ. Epidemiologic trends. In: Barnes PJ, Grunstein MM, Leff AR, Woolcock AJ, editors. Asthma. Philadelphia: Lippincott-Raven Publishers; 1997.
3. Woolcock AJ, Peat JK. Evidence for the increase in asthma worldwide. Ciba Found Symp 1997;206:122-34; discussion 34-9, 57-9.
4. Centers for Disease Control and Prevention. Surveillance for Asthma—United States, 1960-1995. MMWR Morb Mortal Wkly Rep 1998;47:1-28.
5. Laumann JM, Bjornson DC. Treatment of Medicaid patients with asthma: comparison with treatment guidelines using disease-based drug utilization review methodology. Ann Pharmacother 1998;32:1290-4.
6. Bauman A, Cooper C, Bridges-Webb C, Tse M, Miles D, Bhasale A, et al. Asthma management and morbidity in Australian general practice: the relationship between patient and doctor estimates. Respir Med 1995;89:665-72.
7. Jain P, Golish JA. Clinical management of asthma in the 1990s. Current therapy and new directions. Drugs 1996;52 Suppl 6:1-11.
8. Joyce DP, McIvor RA. Use of inhaled medications and urgent care services. Study of Canadian asthma patients. Can Fam Physician 1999;45:1707-13.
9. Bjorksten B. Unmet needs in the treatment of asthmatic children and adolescents: 2. Clin Exp Allergy 2000;30 Suppl 1:73-6.
10. Legorreta AP, Christian-Herman J, O'Connor RD, Hasan MM, Evans R, Leung KM. Compliance with national asthma management guidelines and specialty care: a health maintenance organization experience. Arch Intern Med 1998;158:457-64.
11. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. Bethesda (MD): National Heart, Lung, and Blood Institute; 2002.
12. National Asthma Education Program (NAEP). Expert Panel Report II: guidelines for the diagnosis and management of asthma. Bethesda (MD): National Heart, Lung, and Blood Institute; 1997.
13. Majeed A, Ferguson J, Field J. Prescribing of beta-2 agonists and inhaled steroids in England: trends between 1992 and 1998, and association with material deprivation, chronic illness and asthma mortality rates. J Public Health Med 1999;21:395-400.
14. Nestor A, Calhoun AC, Dickson M, Kalik CA. Cross-sectional analysis of the relationship between national guideline recommended asthma drug therapy and emergency/hospital use within a managed care population. Ann Allergy Asthma Immunol 1998;81:327-30.
15. Boulet LP. Perception of the role and potential side effects of inhaled corticosteroids among asthmatic patients. Chest 1998;113:587-92.
16. Suissa S, Ernst P, Boivin JF, Horwitz RI, Habbick B, Cockroft D, et al. A cohort analysis of excess mortality in asthma and the use of inhaled beta-agonists. Am J Respir Crit Care Med 1994;149:604-10.
17. National Asthma Education Program (NAEP). Expert Panel Report: guidelines for the diagnosis and management of asthma. Bethesda (MD): National Heart, Lung, and Blood Institute; 1991.
18. National Asthma Education Program (NAEP). Executive summary of the NAEPP Expert Panel Report: guidelines for the diagnosis and management of asthma—update on selected topics. Bethesda (MD): National Heart, Lung, and Blood Institute; 2002.
19. Donahue JG, Weiss ST, Livingston JM, Goetsch MA, Greineder DK, Platt R. Inhaled steroids and the risk of hospitalization for asthma. JAMA 1997;277:887-91.
20. Jans MP, Schellevis FG, Le Coq EM, Bezemer PD, van Eijk JT. Health outcomes of asthma and COPD patients: the evaluation of a project to implement guidelines in general practice. Int J Qual Health Care 2001;13:17-25.
21. Reddy P, Kelly ET 3rd, Kophazi ME, Geary EA, Markelon JD, Welter KJ. Medicaid's beta 2-agonist recipients and their treatment by national standards. Ann Pharmacother 2001;35:682-6.
22. Terr AI, Bloch DA. Trends in asthma therapy in the United States: 1965-1992. Ann Allergy Asthma Immunol 1996;76:273-81.
23. Goodman DC, Lozano P, Stukel TA, Chang C, Hecht J. Has asthma medication use in children become more frequent, more appropriate, or both? Pediatrics 1999;104:187-94.
24. Jacobson GA, Peterson GM. Prescribing trends for anti-asthma drugs in Tasmania following the National Asthma Campaign. J Clin Pharm Ther 1996;21:317-24.
25. Kesten S, Rebuck AS, Chapman KR. Trends in asthma and chronic obstructive pulmonary disease therapy in Canada, 1985 to 1990. J Allergy Clin Immunol 1993;92:499-506.
26. Bosco LA, Knapp DE, Gerstman B, Graham CF. Asthma drug therapy trends in the United States, 1972 to 1985. J Allergy Clin Immunol 1987;80:398-402.
27. Frischer M, Heatlie H, Chapman S, Norwood J, Bashford J, Millson D. Should the corticosteroid to bronchodilator ratio be promoted as a quality prescribing marker? Public Health 1999;113:247-50.
28. Shelley M, Croft P, Chapman S, Pantin C. Is the quality of asthma prescribing, as measured by the general practice ratio of corticosteroid to bronchodilator, associated with asthma morbidity? J Clin Epidemiol 2000;53:1217-21.
29. Kemp JP. Comprehensive asthma management: guidelines for clinicians. J Asthma 1998;35:601-20.

Correction

With regard to the January 2003 article entitled "Eighteen-month outcomes of house dust mite avoidance and dietary fatty acid modification in the Childhood Asthma Prevention Study (CAPS)" (Mihrshahi S, Peat JK, Marks GB, Mellis CM, Tovey ER, Webb K, et al. 2003;111:162-8): In Fig 1, showing the CAPS trial profile, the description of one of the four study groups that were established through randomization was incorrect. The actual study groups were as follows:

n = 149 Placebo diet supplements No house dust mite reduction	n = 155 Placebo diet supplements Active house dust mite reduction	n = 159 Active diet supplements No house dust mite reduction	n = 153 Active diet supplements Active house dust mite reduction