

---

# The relationship of sex to asthma prevalence, health care utilization, and medications in a large managed care organization

Michael Schatz, MD, MS,\* and Carlos A. Camargo, Jr, MD, DrPH†

---

**Background:** Age-related sex differences in asthma hospitalizations and emergency department (ED) visits have been reported, but relationships of these differences to disease prevalence and outpatient management have not been defined.

**Objective:** To define the relationships of sex to asthma-related health care utilization and medications, accounting for age-related differences in asthma prevalence.

**Methods:** Computerized data from Southern California Kaiser-Permanente were used to identify asthmatic patients, aged 2 to 64 years, enrolled continuously during 1999 and 2000. Age-specific asthma prevalence in 1999 was calculated to identify ages of male or female predominance. Males and females were compared with regard to asthma-related health care utilization outcomes (outpatient clinic visits, ED visits, and hospitalizations) and medication use ( $\beta$ -agonists, inhaled steroids, and oral steroids). Hospitalizations, ED visits, and oral steroid use were considered markers of disease severity.

**Results:** Of the 60,694 subjects, the female-male prevalence ratio was approximately 35:65 at each age between 2 and 13 years, it was inverse (65:35) between the ages of 23 and 64 years, and prevalences were relatively similar at the ages of 14 to 22 years. In patients aged 2 to 13 years, most utilization and medication variables were significantly greater in males ( $P < .01$ ). Females aged 14 to 22 years had more outpatient and ED visits and used more oral steroids than males. In patients aged 23 to 64 years, all utilization variables were significantly greater in females, except  $\beta$ -agonist use and mean inhaled steroid dispensings.

**Conclusions:** Asthma utilization and severity appear greater in males aged 2 to 13 years, somewhat greater in females aged 14 to 22 years, and definitely greater in females aged 23 to 64 years. The mechanisms for these striking sex differences merit further investigation.

*Ann Allergy Asthma Immunol.* 2003;91:553–558.

## INTRODUCTION

In the United States, asthma affects at least 15 million to 20 million persons and accounts for 2 million emergency department (ED) visits and more than 470,000 hospitalizations annually.<sup>1</sup> Several prior studies suggest that the burden of asthma is not borne equally by males and females. For example, among patients who are hospitalized with asthma, up to twice as many younger than 15 years are males,<sup>2–10</sup> but up to 3 times as many patients older than 15 years are females.<sup>5,7–9,11–19</sup> However, since many of these data do not take into account sex differences in the *prevalence* of asthma at various ages,<sup>2,3,5–10,14–16,18</sup> they cannot evaluate the role of sex as a specific risk factor for more severe asthma exacerbations. Indeed, the incidence of asthma has been reported to

be higher in males younger than 9 years but higher in females older than 15 years.<sup>20–22</sup>

The main purpose of this retrospective cohort study was to determine sex differences in health care utilization for asthma, accounting for age-related differences in asthma prevalence. The cohort was composed of more than 60,000 individuals with asthma aged 2 to 64 years who were enrolled in a large managed care organization. Sex differences in other potentially related factors, such as socioeconomic status and asthma medications, also were evaluated.

## METHODS

This study was approved by the Southern California Kaiser-Permanente Institutional Review Board. Data were derived from the Southern California Kaiser-Permanente Asthma Case Identification Database (ACID), based on linkage of computer data from a membership database, a hospital discharge database, a diagnosis and procedures database, and a prescription database. Patients were identified as having asthma if they met one or more of the following criteria during 1999:

1. Any discharge diagnosis (principal or other diagnosis) of asthma in the hospitalization database (*International Classification of Diseases, Ninth Edition* [ICD-9] code 493.xx).

2. Asthma-related ED or regular clinic visit in the diagnosis and procedures database.

---

\* Department of Allergy, Kaiser-Permanente Medical Care Program, San Diego, California.

† Department of Emergency Medicine, Massachusetts General Hospital, and Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.

This study was partially funded by the Southern California Permanente Medical Group. Dr. Camargo is supported by grant AI52338 from the National Institutes of Health (Bethesda, MD) and the Emergency Medicine Foundation Center of Excellence Award (Dallas, TX).

Received for publication July 9, 2003.

Accepted for publication in revised form August 6, 2003.

3. Two or more asthma-related medication dispensings (excluding oral steroids, inhaled ipratropium, and inhaled combination albuterol-ipratropium) in the prescription database, including  $\beta$ -agonists (excluding oral terbutaline), inhaled steroids, other inhaled anti-inflammatory drugs, and oral leukotriene modifiers.

This algorithm is based on the evidence that identifying “physician-diagnosed asthma” is a valid way to identify asthmatic patients in epidemiologic studies.<sup>23</sup> Physician-diagnosed asthma is captured explicitly with criteria 1 and 2 and implicitly with criterion 3.

Patients in the present cohort were aged 2 to 64 years, included in ACID, and continuously enrolled during 1999 and 2000. Sex differences in prevalence were evaluated by determining the proportion of males vs females in the cohort at each age (based on 1999 age). Sex differences in hospital utilization were determined by comparing the proportion of male vs female patients who required an ED visit or hospitalization with a primary diagnosis of asthma (ICD-9 code 493.xx) at a Kaiser Foundation Hospital or at an outside hospital during the 2 years of follow-up in the various age groups. Mean length of hospital stay (in hours) also was compared in males vs females. During the 2-year period, the following parameters also were compared between males and females in the various age groups: (1) proportion with subsidized insurance (Medicare or Medicaid), a marker of lower socioeconomic status; (2) mean number of asthma-related, non-ED outpatient visits; (3) mean number of dispensings of short-acting, inhaled  $\beta$ -agonists; (4) any dispensing of inhaled steroids; (5) mean number of inhaled steroid dispensings (in patients receiving inhaled steroids); (6) any dispensing of oral steroids; and (7) mean number of oral steroid dispensings (in patients receiving oral steroids).

To determine the relationship of sex to major outcomes, while controlling for demographic factors (age, socioeconomic status), disease severity (hospital and oral steroid utilization), and therapy (short-acting  $\beta$ -agonists, inhaled steroids), multivariate logistic regression was performed. The analyses were stratified by age groups based on the asthma prevalence results: ages of male predominance, transition years, and ages of female predominance. Outcomes were (1) any year 2000 ED visit with a diagnosis of asthma (ICD-9 code 493.xx) and (2) any year 2000 hospitalization with a primary diagnosis of asthma (ICD-9 code 493.xx). Potential predictors for the analyses included sex, 1999 age, 1999 asthma hospitalization or ED visit (as defined herein), number of 1999 short-acting, inhaled  $\beta$ -agonist dispensings, number of 1999 inhaled steroid dispensings, and number of 1999 oral steroid dispensings.

The ratio of female to male patients by age was plotted using Microsoft Excel (Microsoft, Redmond, WA) with a smoothed curve fitted using a fourth-degree polynomial function. All analyses were conducted using SAS statistical software version 8.0 for Windows (SAS Institute Inc, Cary, NC). Hypothesis testing for continuous predictors in univariate analyses was conducted using the *t* test. Hypothesis testing for bi-

nary predictors was conducted using the  $\chi^2$  test. A 2-sided  $P < .05$  was considered statistically significant. Odds ratios (ORs) are presented with 95% confidence intervals (CIs).

## RESULTS

The total number of members of the Southern California Kaiser-Permanente Medical Care Program who were aged 2 to 64 years in 1999 and who were continuously enrolled during 1999 and 2000 was 1,850,478 (957,978 females and 892,500 males). This population is demographically similar to the general Southern California working population (D. Pettiti, unpublished data, 2003). The asthma cohort included 60,694 subjects, of whom 54% were female and 46% male. The total prevalence of active asthma in this cohort was thus 3.3% (3.9% female, 3.1% male).

Comparing the proportion of males vs females in the cohort at each age in 1999 (Fig 1) revealed that the female-male prevalence ratio was approximately 35:65 at each age between 2 and 13 years, whereas it was inverse (65:35) between the ages of 23 and 64 years; at ages 14 to 22 years, the sex prevalences were relatively similar. These 3 age groups were thus evaluated separately in subsequent analyses.

Females were significantly more likely than males to have subsidized (Medicare or Medicaid) vs commercial insurance at all ages (Table 1). Table 1 also compares the prevalence, utilization, and medication outcomes in males vs females in the 3 age groups. Males in the ages 2 to 13 years cohort made a larger number of outpatient visits than females. In addition, the proportion of males in this age group with ED visits was higher than the proportion of females, whereas hospitalization rates and mean length of stay were comparable between groups. Males in this age group used more  $\beta$ -agonists, inhaled steroids, and oral steroids than females.

Although asthma was somewhat more common in males than females in patients aged 14 to 22 years, females in this age group made more outpatient and ED visits than males. The hospitalization rate was equal in this age group, and there was no significant difference between groups in mean length of stay. Males used more  $\beta$ -agonists, but females were more likely to use inhaled steroids and used more oral steroids than males in this age group. However, among patients prescribed inhaled steroids, males used more inhaled steroids than females.

In patients aged 23 to 64 years, asthma was more common in women, but, even accounting for this difference, women were significantly more likely than men ( $P < .001$ ) to have an outpatient visit, require an ED visit, or be hospitalized for asthma. As in the other age groups, mean length of hospital stay in patients aged 23 to 64 years was similar between sexes, and men used more  $\beta$ -agonists than their female counterparts. Women were more likely to use an inhaled steroid, although men in this age group on average received more dispensings of inhaled steroids. Finally, women in this age group were more likely to require oral steroids, although the mean number of dispensings of oral steroids in patients who required them did not differ between men and women.

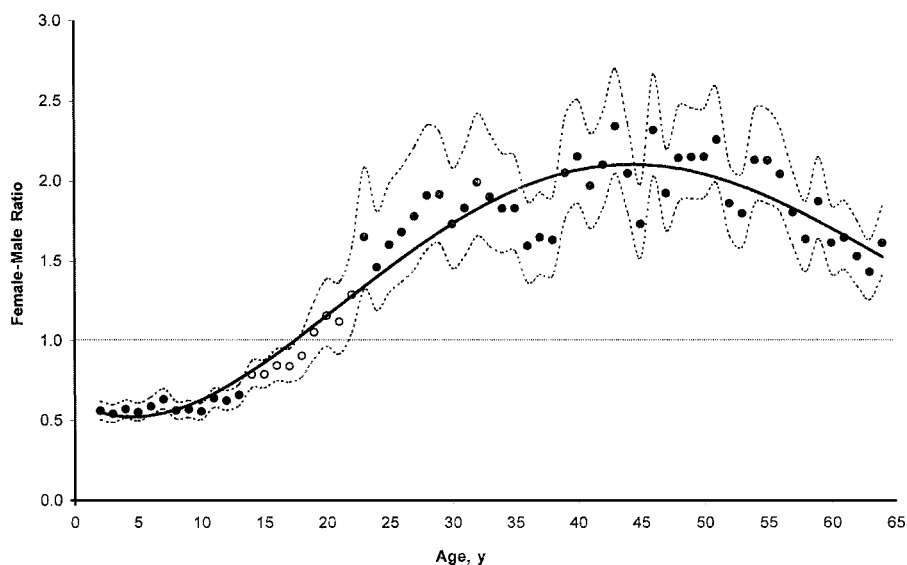


Figure 1. Ratio of female to male asthma patients, ages 2 to 64 years. Ratios are presented with 95% confidence intervals (dashed lines) and a smoothed curve of the relation between age and female-male ratio. The empty circles denote sex ratios at ages 14 to 22 years.

Table 1. Asthma Prevalence, Health Care Utilization, and Medication Use among Male and Female Subjects, Stratified by Age Groups (Combined 1999 and 2000 Results)

| Parameters                               | Age 2–13 y<br>(n = 20,559) |        | Age 14–22 y<br>(n = 7,158) |        | Age 23–64 y<br>(n = 32,977) |        |
|------------------------------------------|----------------------------|--------|----------------------------|--------|-----------------------------|--------|
|                                          | Male                       | Female | Male                       | Female | Male                        | Female |
| Prevalence, %                            | 63                         | 37     | 53                         | 47     | 35                          | 65     |
| Subsidized insurance, %                  | 7.9†                       | 9.2    | 4.3§                       | 5.5    | 1.4‡                        | 3.6    |
| Mean no. of outpatient visits            | 2.8†                       | 2.7    | 1.7‡                       | 1.9    | 1.4‡                        | 1.8    |
| Any emergency department visit, %        | 15.2‡                      | 13.3   | 14.9§                      | 16.8   | 10.7‡                       | 12.2   |
| Any hospitalization, %                   | 4.0                        | 3.6    | 2.6                        | 2.6    | 1.7‡                        | 2.8    |
| Mean length of stay, h                   | 41.4                       | 43.2   | 38.4                       | 39.3   | 46.3                        | 49.8   |
| Mean no. of $\beta$ -agonist dispensings | 5.0‡                       | 4.5    | 7.9‡                       | 6.2    | 7.7‡                        | 6.0    |
| Any inhaled steroid dispensing, %        | 49‡                        | 46     | 59†                        | 63     | 72‡                         | 75     |
| Mean no. of inhaled steroid dispensings* | 3.1‡                       | 2.9    | 2.8†                       | 2.6    | 4.5‡                        | 4.0    |
| Any oral steroid dispensing, %           | 58‡                        | 53     | 41                         | 43     | 45‡                         | 53     |
| Mean no. of oral steroid dispensings*    | 2.2‡                       | 2.1    | 1.8†                       | 1.9    | 2.7                         | 2.7    |

\* Among patients with any dispensings.

†  $P < .01$ .

‡  $P < .001$ .

§  $P < .05$ .

Multivariable analyses explored the relationship between sex and asthma-related ED visits or hospitalizations, independent of other demographic, severity (prior hospital, ED, and oral steroid utilization), and treatment parameters. After controlling for these factors, the relationship between sex and ED visits was of borderline statistical significance in each age group: for age 2 to 13 years, the female OR was 0.91 (95% CI, 0.82–1.02); for age 14 to 22 years, the female OR was 1.18 (95% CI, 0.99–1.39); and for age 23 to 64 years, the female OR was 1.09 (95% CI, 0.99–1.20). Although sex was not an independent predictor of asthma hospitalization in patients aged 2 to 13 years (female OR, 0.95; 95% CI, 0.77–1.18) or aged 14 to 22 years (female OR, 0.92; 95% CI, 0.58–1.46), female sex was independently associated with

subsequent asthma hospitalizations in patients aged 23 to 64 years (OR, 1.70; 95% CI, 1.35–2.14), after adjusting for the other parameters (Table 2).

## DISCUSSION

Previous studies have reported age-related sex differences in asthma prevalence or hospital utilization, but few studies have addressed both prevalence and hospital utilization concurrently. The current study confirms that asthma is almost twice as prevalent in males younger than 14 years and in females older than 22 years. Furthermore, it shows that, even accounting for these prevalence differences, asthma is more severe (based on hospital utilization and oral steroid use) in males younger than 14 years and in females 14 years or older.

Table 2. Multivariate Logistic Regression Analysis of Year 1999 Predictors of Year 2000 Asthma Hospitalizations in 60,694 Individuals Aged 23 to 64 years

| 1999 Predictor                 | OR (95% CI)      | P value |
|--------------------------------|------------------|---------|
| Female                         | 1.70 (1.35–2.14) | <.001   |
| Age                            | 1.02 (1.01–1.03) | <.001   |
| Has subsidized insurance       | 2.56 (1.75–3.74) | <.001   |
| ED visit or hospitalization    | 4.29 (3.37–5.45) | <.001   |
| Short-acting $\beta$ -agonists | 1.02 (0.99–1.04) | .18     |
| Inhaled steroids               | 0.86 (0.81–0.91) | <.001   |
| Oral steroids                  | 1.16 (1.10–1.22) | <.001   |

Abbreviations: CI, confidence interval; ED, emergency department; OR, odds ratio.

Unique aspects of this study include the large number of asthmatic patients managed by a single integrated health care system, the ability to account for prevalence in evaluating sex differences in health care utilization, and the evaluation of medication use as an additional measure of severity (oral steroids) or management (inhaled steroids).

One of the most interesting and unexplained observations is the sex shift in prevalence and severity that occurs around the age of 13 years. One study has suggested that it is not a selective loss of asthma in males compared with females during puberty that accounts for this shift,<sup>24</sup> and several studies have shown that the incidence of asthma is higher in women than men after the age of 15 years.<sup>20–22,25,26</sup> Potential mechanisms include sex hormones,<sup>27–37</sup> changes in airway size,<sup>38</sup> anxiety-depression,<sup>14,39–42</sup> or obesity.<sup>25,39,43–45</sup> The current study does not shed light on these mechanisms. In addition to a sex shift in asthma prevalence, this study confirms a significant increase in the occurrence of hospitalizations for asthma in women older than 23 years, even after accounting for prevalence, a marker of socioeconomic status, prior health care utilization, and asthma medications. This observation suggests that asthmatic women experience more morbidity from their disease than men, consistent with the results of a prior study in which asthmatic women aged 16 to 77 years reported significantly lower general quality-of-life (Medical Outcomes Study 36-Item Short-Form Health Survey) scores in 7 of 9 domains compared with men.<sup>46</sup> There are 3 potential explanations for these observations: (1) increased inherent disease severity in women, (2) increased perception of or reactivity to asthma physiologic changes in women with increased health-seeking behavior, or (3) less aggressive treatment in women, due to either provider or patient behaviors.

Against the concept of increased inherent severity in asthmatic women vs men is the observation in the current study and a previous study<sup>16</sup> that, once hospitalized for asthma, the length of stay was not significantly different for women compared with men. In addition, in a large study of sex differences in 46,587 admissions to 91 intensive care units, no differences in acute physiology score, APACHE II (Acute Physiology and Chronic Health Evaluation II) score, or percent mortality were seen in 490 women compared with 233

men admitted for asthma.<sup>47</sup> In another study of 103 patients with 2 or more asthma hospitalizations to a single institution, Pco<sub>2</sub> levels were higher in men.<sup>18</sup> Furthermore, if pulmonary function can be considered a marker of inherent asthma severity, the data do not support the hypothesis of inherently greater severity in women vs men.<sup>11,14,48</sup> For example, in a study of patients aged 18 to 54 years presenting to the ED with moderate to severe exacerbations, women were more likely to report “severe” complaints in terms of symptom frequency, intensity, and activity limitation, but men had a lower average percent predicted peak expiratory flow rate.<sup>11</sup> Similarly, in a cohort of patients with physician-diagnosed asthma in a health maintenance organization, women had increased symptoms and decreased quality of life but demonstrated a higher mean forced expiratory volume in 1 second than men.<sup>48</sup>

The pattern seen in several other adult diseases is that women tend to get more care than men for the same type of illness or complaint unless a major diagnostic or therapeutic intervention is involved.<sup>49</sup> This would suggest either increased perception of or increased reactivity to symptoms by women compared with men. These possibilities are supported by the previously discussed observation that women have more symptoms and hospital utilization for a given level of pulmonary function compared with men.<sup>11,14</sup> Our study showed that, at all ages, short-acting, inhaled  $\beta$ -agonist use was greater in males than females and that females older than 13 years made significantly more outpatient asthma visits than males. This would be consistent with the hypothesis that men may perceive symptoms similarly to women but that their approach may be to use rescue inhalers rather than to seek medical attention.

Another general explanation for increased adverse outcomes in asthmatic women compared with men would be sex-based treatment differences. Although females older than 13 years in the current study were more likely than males to be dispensed any inhaled steroids, among those who received inhaled steroids, females received a significantly lower number of dispensings compared with males (Table 1). Similarly, one prior study<sup>12</sup> reported that more women than men in a managed care organization possessed inhaled steroids but that men who had inhaled steroids were more likely than women who had inhaled steroids to use them daily. These data suggest that poorer adherence to preventive medications could contribute to the increased hospital utilization observed in females older than 13 years. However, the increased risk of asthma hospitalization in women persisted in the current study even after accounting for inhaled steroid dispensings (Table 2). In addition, one recent study found increased self-reported adherence to asthma medications in women compared with men.<sup>50</sup>

It would have been useful to be able to adjust our results for cigarette smoking, but this information was not available in the electronic database. One study has reported that asthmatic women from a health maintenance organization population were more likely to be current smokers than asthmatic

men from the same population,<sup>48</sup> and the relationship between asthma prevalence and cigarette smoking in adults in California is stronger in women than in men.<sup>39</sup> However, a large, multicenter study of adult asthmatic patients presenting to the ED did not find a significant sex difference in cigarette smoking.<sup>11</sup> Unfortunately, previous reports of decreased quality of life or increased symptoms in asthmatic women compared with men have also not been specifically adjusted for cigarette smoking.<sup>11,14,46,48</sup>

This study has some additional potential limitations. Prevalence was based on electronic capture of physician-diagnosed asthma, which was dependent on resource utilization. However, the observed changing sex prevalence with age is consistent with prior reports and suggests that there was not a significant sex bias in the way patients entered the current asthmatic cohort. It has been previously reported that using "physician-diagnosed asthma" as the definition of asthma is more specific than sensitive regarding detecting asthma in a population.<sup>23</sup> Thus, the patients entered into the current cohort are more likely to have asthma, but some patients with asthma in our population may not have been identified. However, the capture of outpatient and hospital-based health care utilization and all asthma medications in a population with prepaid health care access would be expected to identify most patients with active asthma. This hypothesis can be partly tested by comparing the observed prevalence in the current study to the reported prevalence of asthma in California from the 2001 California Health Interview Survey.<sup>51</sup> In that study, asthma symptom prevalence (symptoms at least once a year) was reported to be 8.8%. Of those patients, approximately 40% (approximately 3.5% of the total population) had symptoms once a month or more, which could be considered active asthma and agrees relatively well with our 3.3% prevalence figure of active asthma requiring medical visits or medication.

Another potential limitation is that medication use in this study was evaluated by computerized pharmacy dispensing records rather than by more direct means. Although medication use for patients who obtain their medications from non-Kaiser-Permanente pharmacies would not have been captured, 95% of asthmatic patients included in ACID have a Kaiser pharmacy prescription benefit (R. Nakahiro, unpublished data, 2003). There is no reason to suspect sex bias in the potential loss of information from patients who do not have such a benefit. Finally, although dispensing of a medication does not ensure that the patient is using the medication, pharmacy records are recommended as a method of assessing patient adherence.<sup>52</sup>

## CONCLUSION

This study shows that asthma is more severe in males younger than 14 years and in females 14 years and older, even accounting for differences in disease prevalence. Although these differences may be due to inherent sex-related differences in severity, possible sex differences in reactivity to airway obstruction or medication adherence may contrib-

ute in postpubertal females. The exact mechanisms for these striking sex differences merit further investigation.

## ACKNOWLEDGMENT

We thank Sharon Hunter for her assistance with ACID.

## REFERENCES

1. Mannino DM, Homa DM, Akinbami LJ, Moorman JE, Gwynn C, Redd SC. Surveillance for asthma—United States, 1980–1999. *MMWR Morb Mortal Wkly Rep.* 2002;51:1–13. Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5101a1.htm>. Accessed October 1, 2002.
2. Kao CC, See LC, Yan DC, Ou LS, Huang JL. Time trends and seasonal variations in hospital admissions for childhood asthma in Taiwan from 1990 to 1998. *Asian Pacific J Allergy Immunol.* 2001;19:63–68.
3. Joseph CL, Havstad SL, Ownby DR, Johnson CC, Tiley BC. Racial differences in emergency department use persist despite allergist visits and prescriptions filled for antiinflammatory medications. *J Allergy Clin Immunol.* 1998;101:484–490.
4. Schaubel D, Johansen H, Mao Y, Dutta M, Manfreda J. Risk of preschool asthma: incidence, hospitalization, recurrence and readmission probability. *J Asthma.* 1996;33:97–103.
5. Skobeloff EM, Spivey WH, St. Clair SS, Schoffstall JM. The influence of age and sex on asthma admissions. *JAMA.* 1992; 268:3437–3440.
6. To T, Dick P, Feldman W, Hernandez R. A cohort study on childhood asthma admissions and readmissions. *Pediatrics.* 1996;98:191–195.
7. Von Behren J, Kreutzer R, Smith D. Asthma hospitalization trends in California 1983–1996. *J Asthma.* 1999;36:675–682.
8. Wilkins K, Mao Y. Trends in rates of admission to hospital and death from asthma among children and young adults in Canada during the 1980s. *Can Med Assoc J.* 1993;148:185–190.
9. Hyndman SJ, Williams DR, Merrill SL, Lipscombe JM, Palmer CR. Rates of admission to hospital for asthma. *BMJ.* 1994;308: 1596–1600.
10. Bloomberg GR, Trinkaus KM, Fisher EB Jr, Musick JR, Strunk RC. Hospital readmissions for childhood asthma: a 10-year metropolitan study. *Am J Respir Crit Care Med.* 2003;167:1068–1076.
11. Cydulka RK, Emerman CL, Clark S, Woodruff PG, Singh AK, Camargo CA Jr. Differences between men and women in reporting of symptoms during an asthma exacerbation. *Ann Emerg Med.* 2001;38:123–128.
12. Krishnan JA, Diette GB, Skinner EA, Clark BD, Steinwachs D, Wu AW. Race and sex differences in consistency with national asthma guidelines in managed care organizations. *Arch Intern Med.* 2001;161:1660–1668.
13. Prescott E, Lange P, Vestbo J. Effect of gender on hospital admissions for asthma and prevalence of self-reported asthma: a prospective study based on a sample of the general population. *Thorax.* 1997;52:287–289.
14. Singh AK, Cydulka RK, Stahmer SA, Woodruff PG, Camargo CA Jr. Sex differences among adults presenting to the emergency department with acute asthma. *Arch Intern Med.* 1999; 159:1237–1243.
15. Awadh N, Chu S, Grunfeld A, Simpson K, FitzGerald JM. Comparison of males and females presenting with acute asthma to the emergency department. *Respir Med.* 1996;90:485–489.
16. Tuuponen TT. Asthma-related hospital use among Finnish asthmatics of working age. *Public Health.* 1993;107:163–170.

17. Legorreta AP, Christian-Herman J, O'Connor RD, Hasan MM, Evans R, Leung KM. Compliance with national asthma management guidelines and specialty care. *Arch Intern Med.* 1998;158:457–464.
18. Trawick DR, Holm C, Wirth J. Influence of gender on rates of hospitalization, hospital course, and hypercapnea in high-risk patients admitted for asthma. *Chest.* 2001;119:115–119.
19. Shireman TI, Heaton PC, Gay WE, Cluxton RJ Jr, Moomaw CJ. Relationship between asthma drug therapy patterns and health-care utilization. *Ann Pharmacother.* 2002;36:557–564.
20. Anderson HR, Pottier AC, Strachan DP. Asthma from birth to age 25: incidence and relation to prior and concurrent atopic disease. *Thorax.* 1992;47:537–542.
21. Yunginger JW, Reed CE, O'Connell EJ, Melton LJ III, O'Fallon WM, Silverstein MD. A community-based study of the epidemiology of asthma. *Am Rev Respir Dis.* 1992;146:888–894.
22. DeMarco R, Locatelli F, Sunyer J, Burney P. Differences in incidence of reported asthma related to age in men and women. *Am J Respir Crit Care Med.* 2000;162:68–74.
23. Toren K, Brisman J, Jarvholm B. Asthma and asthma-like symptoms in adults assessed by questionnaires: a literature review. *Chest.* 1993;104:600–608.
24. Nicolai T, Illi S, Tenborg J, Kiess W, Mutius VE. Puberty and prognosis of asthma and bronchial hyper-reactivity. *Pediatr Allergy Immunol.* 2001;12:142–148.
25. Chen Y, Dales R, Tang M, Krewski D. Obesity may increase the incidence of asthma in women but not in men: longitudinal observations from the Canadian National Population Health Surveys. *Am J Epidemiol.* 2002;155:191–197.
26. McWhorter WP, Polis MA, Kaslow RA. Occurrence, predictors, and consequences of adult asthma in NHANES I and follow-up survey. *Am Rev Respir Dis.* 1989;139:721–724.
27. Hamano N, Terada N, Maesako K, Numata T, Konno A. Effect of sex hormones on eosinophilic inflammation in nasal mucosa. *Allergy Asthma Proc.* 1998;19:263–269.
28. Henderson ID. Cyclical changes in female mucous. *J Clin Endocrinol.* 1956;16:905–909.
29. Tan KS, McFarlane LC, Lipworth BJ. Paradoxical down-regulation and desensitization of  $\beta_2$ adrenoceptors by exogenous progesterone in female asthmatics. *Chest.* 1997;111:847–851.
30. Kirsch EA, Yuhanna IS, Chen Z, German Z, Sherman TS, Shaul PW. Estrogen acutely stimulates endothelial nitric oxide synthase in H441 human airway epithelial cells. *Am J Respir Cell Mol Biol.* 1999;20:658–666.
31. Barr RG, Camargo CA Jr. Hormone replacement therapy and obstructive airway diseases. *Am J Respir Crit Care Med.* In press.
32. Agarwal SK, Marshall GD. Premenstrual alterations in type-1/type-2 cytokine balance of normal women. *Ann Allergy Asthma Immunol.* 1999;83:222–228.
33. Skobeloff EM, Spivey WH, Silverman R, Eskin BA, Harchelroad F, Alessi TV. The effect of the menstrual cycle on asthma presentations in the emergency department. *Arch Intern Med.* 1996;156:1837–1850.
34. Zimmerman JL, Woodruff PG, Clark S, Camargo CA Jr. Relation between phase of menstrual cycle and emergency department visits for acute asthma. *Am J Respir Crit Care Med.* 2000;162:512–515.
35. Gibbs CJ, Coutts II, Lock R, Finnegan OC, White RJ. Premenstrual exacerbation of asthma. *Thorax.* 1984;39:833–836.
36. Shames RS, Heilbron DC, Janson SL, Kishiyama JL, Au DS, Adelman DC. Clinical differences among women with and without self-reported perimenstrual asthma. *Ann Allergy Asthma Immunol.* 1998;81:65–72.
37. Lange P, Parner J, Prescott E, Ulrik CS, Vestbo J. Exogenous female sex steroid hormones and risk of asthma and asthma-like symptoms: a cross sectional study of the general population. *Thorax.* 2001;56:613–616.
38. Britton J, Pavord I, Richards K, et al. Factors influencing the occurrence of airway hyper-reactivity in the general population: the importance of atopy and airway calibre. *Eur Respir J.* 1994;7:881–887.
39. Von Behren J, Kreutzer R, Hernandez A. Self-reported asthma prevalence in adults in California. *J Asthma.* 2002;39:429–440.
40. Nadelson CC, Dickstein L. The mental health of women: an overview. *Clin Obstet Gynecol.* 2002;45:1162–1168.
41. Williams K, Kurina LM. The social structure, stress, and women's health. *Clin Obstet Gynecol.* 2002;45:1099–1118.
42. Dahlen I, Janson C. Anxiety and depression are related to the outcome of emergency treatment in patients with obstructive pulmonary disease. *Chest.* 2002;122:1633–1637.
43. Camargo CA Jr, Weiss ST, Zhang S, Willett WC, Speizer FE. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. *Arch Intern Med.* 1999;159:2582–2588.
44. Guerra S, Sherrill DL, Bobadilla A, Martinez FD, Barbee RA. The relation of body mass index to asthma, chronic bronchitis, and emphysema. *Chest.* 2002;122:1256–1263.
45. US Department of Health and Human Services. The Surgeon General Call to Action to Prevent and Decrease Overweight and Obesity 2001. Available at <http://www.surgeongeneral.gov/topics/obesity/calltoaction/CalltoAction.pdf>. Accessed October 1, 2002.
46. Bousquet J, Knani J, Dhivert H, et al. Quality of life in asthma, I: internal consistency and validity of the SF-36 questionnaire. *Am J Respir Crit Care Med.* 1994;149:371–375.
47. Raine R, Goldfrad C, Rowan K, Black N. Influence of patient gender on admission to intensive care. *J Epidemiol Commun Health.* 2002;56:418–423.
48. Osborne ML, Vollmer WM, Linton KL, Buist AS. Characteristics of patients with asthma within a large HMO: a comparison by age and gender. *Am J Respir Crit Care Med.* 1998;157:123–128.
49. Council on Ethical and Judicial Affairs, American Medical Association. Gender disparities in clinical decision making. *JAMA.* 1991;266:559–562.
50. Lindberg M, Ekstrom T, Moller M, Ahlner J. Asthma care and factors affecting medication compliance: the patient's point of view. *Int J Qual Health Care.* 2001;13:375–383.
51. Brown ER, Meng YY, Babey SH, Malcolm E. Asthma in California in 2001. California Health Interview Survey. Policy Brief. Available at: <http://www.healthpolicy.ucla.edu/pubs/files/AsthmaPB05022002.pdf>. Accessed March 3, 2003.
52. Milgrom H, Bender B, Wamboldt F. Assessing adherence with asthma medication: making the counts count. *Ann Allergy Asthma Immunol.* 2002;88:429–431.

Requests for reprints should be addressed to:  
Michael Schatz, MD, MS  
Department of Allergy  
Kaiser-Permanente Medical Care Program  
7060 Clairemont Mesa Blvd  
San Diego, CA 92111  
E-mail: michael.x.schatz@kp.org