

Age dependent sex disproportion in US asthma hospitalization rates, 2000–2010

Robert Yao-wen Lin, MD ^{*,†}; Rong Ji, MD ^{*}; and William Liao ^{*}

^{*} Department of Medicine, New York Downtown Hospital, New York, New York

[†] Department of Medicine, Weill Cornell Medical College, New York, New York

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ABSTRACT

Background: Age-stratified sex differences in asthma hospitalizations rates have been reported to be most marked between the ages of 40 and 54 years in New York. It is not known whether age-dependent sex differences in asthma hospitalization rates also exist for the entire United States.

Objectives: To compare sex-specific hospitalization rates for asthma in adults in the United States and to describe the adjusted associations between female sex and age in the fifth to sixth decades of life.

Methods: The National Inpatient Sample databases for 2000–2010 were queried for a principal diagnosis of asthma to calculate the ratio of female to male hospitalization rates for different decades of adult life. Logistic regression modeling was used to determine whether age in the fifth to sixth decades of life had associations with female sex that remained significant after adjusting for comorbidities and demographic features.

Results: For all years of the study, there was a distinct peaking in female to male ratio most manifested in the fifth to sixth decades of life. This age grouping was significantly associated with female sex. Models revealed that female sex was significantly associated with this age grouping, even after adjustment for obesity, chronic obstructive pulmonary disease, race, insurance status, discharge year, and smoking. Excluding identifiable repeat admissions also did not abrogate the age grouping association.

Conclusion: There is a striking propensity of women in their fifth to sixth decades of life to be admitted for asthma, which appears to be independent of many known comorbidities.

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Introduction

Asthma is more prevalent in women, and asthma hospitalization and death rates, adjusted for asthma prevalence, are also higher in women.^{1,2} Interestingly in children, asthma is more prevalent in males.¹ Female predominance in asthma prevalence begins around the time of puberty.¹ This observation is one of several that is consistent with the hypothesis that estrogen plays an active role in asthma, possibly through signaling pathways directly related to organ function or by influencing T_H2 phenotypic responses.³ Previously examined sex-specific hospitalization rates in New York State from 1990 to 2006⁴ indicated that the ratio of female to male hospitalization rates was greatest between the ages of 40 and 54 years. This age range is of particular interest with respect to the assertions by some investigators that menopausal asthma may have a distinct biological phenotype.⁴

Hospitalization patterns vary considerably in different geographic regions within the United States.⁵ The Northeast region of the United States, for example, has a higher prevalence of current asthma compared with the Southern region.⁶ Given this variation,

it is of interest to ascertain whether the age-dependent sex differences in asthma hospitalization are reflected in the entire United States. Thus, this study sought to examine the pattern of hospitalization rates in women compared with men for different age intervals, including a focus on patients in the middle decades of adult life in the United States during the new millennium years. The influence of comorbid conditions on age and sex associations was also of interest because smoking and obesity are known contributing factors in airway disease severity. Understanding the epidemiology of asthma hospitalizations may help to identify subgroups with high hospitalization rates, which in turn can provide a rationale for better health care and preventive measures targeting this group(s).

Methods

Data Sources

The National Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project (HCUP), is funded by the US government's Agency for Healthcare Research and Quality (AHRQ) and contains annual hospital discharge data from a stratified, random sample of hospitals across the United States.⁷ The NIS includes public and private hospitals, teaching and nonteaching hospitals, urban and rural hospitals, and small, medium, and large bed-sized hospitals.

Reprints: Robert Y. Lin, MD, Department of Medicine, New York Presbyterian Lower Manhattan Hospital, 170 William Street, Ste 722, New York, NY 10038; E-mail: rol3002@med.cornell.edu.

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Table 1
Yearly and overall characteristics of the adult asthma hospitalizations

Characteristic	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	All years
No. of patients	238,586	243,839	258,795	301,622	268,055	288,944	284,276	274,549	296,929	314,319	293,133	3,063,045
Age, mean, y	51.0	52.5	53.0	53.5	54.6	55.6	55.2	55.2	56.2	55.3	55.9	54.5
African American, %	24.1	24.0	25.5	24.8	26.8	20.3	25.5	26.3	23.5	24.7	29.1	25.0
Matching cases,* %	29.1	29.5	30.3	33.2	31.1	31.6	32.0	30.6	32.2	33.5	33.0	31.6
Medicaid or self-pay, %	28.3	28.6	27.8	29.0	28.6	26.5	28.6	28.1	26.7	30.9	30.8	28.6
Tobacco use disorder, %	4.1	4.8	6.3	6.8	8.0	9.5	9.9	10.7	12.1	12.1	13.4	9.1
COPD, %	2.0	1.9	1.9	1.7	1.8	2.1	2.1	2.4	3.0	2.8	4.8	2.5
Obesity, %	9.9	11.0	11.6	12.6	13.8	15.4	15.9	17.4	18.0	20.2	21.1	15.4
Fifth or sixth decade, %	39.3	38.9	39.8	39.5	40.2	40.4	41.5	41.9	40.6	41.9	42.0	40.6
Female, %	74.0	73.9	73.1	72.6	72.8	73.0	72.3	71.9	72.1	72.1	72.0	72.7

Abbreviation: COPD, chronic obstructive pulmonary disease.

Each NIS patient record includes data fields that consist of demographic, clinical, and financial information. These fields include primary and secondary diagnostic fields, procedure codes, age, sex, race, total charges, and length of stay and disposition status. Weights are provided for calculation of national estimates. The database for each year accessed contains hospital discharges accounting for 36,417,575 (2000) to 39,008,298 discharges per year (2010).

Case Selection and Classification and Data Elements

The NIS databases for 2000 to 2010 were queried for *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code relating to asthma (ICD-9-CM code 493.*) present in the principal diagnosis. Patients older than 18 years were studied as an adult cohort. For the asthma cohort, hospitalizations were examined for conditions of known relationship to airway disease: tobacco use (ICD-9-CM code 305.*), obesity (ICD-9-CM code 278.*), and chronic and obstructive pulmonary disease (COPD) (ICD-9-CM codes 491.*, 492.*, and 496.*). Also some common disorders were characterized: hypertension (ICD-9-CM code 401.*), ischemic heart disease (ICD-9-CM codes 410.*–414.*), chronic renal disease (ICD-9-CM code 585.*), congestive heart failure (ICD-9-CM code 428.*), pneumonia or influenza (ICD-9-CM code 48.*), acute respiratory infections (ICD-9-CM code 46.*), and diabetes mellitus (ICD-9-CM code 250.*). For some analyses, categorization of white race was performed. The study was approved by the New York Downtown Hospital Institutional Review Board as exempt from informed consent requirements.

Statistical Analysis

Hospitalizations between the third to eighth decades of life were used to calculate decade-specific hospital rates for female and male using the national resident population estimates⁸ between 2000 and 2010. The ratio of the female to male hospitalization rates (based on US Census population rates) was graphed for the third through eighth decades of life in summary and yearly representations.

In addition to the population rate–based hospitalization rate described above, the hospitalization rate of asthma based on the number of persons with asthma was also calculated. The number of persons with current asthma for the third through eighth decades of life was calculated for each year by using the reported asthma prevalence.¹ The US Census estimates of the population for each year of age⁸ was multiplied by the estimated current asthma prevalence (aggregate for 2001–2009) for the corresponding year of age to calculate the number of males and females with current asthma (L. J. Akinbami, MD, personal e-mail communication, January 13, 2013).¹ The number of males and females with current asthma for the study period was summed for the 10 years of each yearly age for each decade examined (third through eighth decades) to calculate the number of males and females with current

asthma for each decade, using the mean for the study period (2000–2010). The sex-specific hospitalizations per estimated persons with current asthma, thus calculated, was depicted for the third through eighth decades of life for the entire study period, as was the female to male rate ratios for these age groups.

Possible repeat admissions within the same calendar year were defined on the basis of matching on discharge year, age at the time of admission, sex, hospital identification number, race, and payment source. Self-pay and Medicaid payment sources were identified as a marker of lower socioeconomic status.

Summary data generation and all data analysis were performed using SPSS statistical software for Windows, version 13 (SPSS Inc, Chicago, Illinois). Logistic regression was performed to examine whether the age association (in particular the ages in the fifth and sixth decades) with female sex was affected by other demographic and clinical parameters. These parameters included demographic variables (age, race, and year of study), Medicaid or self-pay status, tobacco use, obesity status, COPD diagnosis, and other common comorbidities as noted above. The age decades of the fifth and sixth decades were of key interest, and this was used as the key predictor variable in univariate and multivariate analyses. Stepwise forward selection was used for multivariate regression. Logistic regression was also performed with possible repeat admissions in the same year excluded. Linear regression analysis was used to characterize the variability (sum of squares between groups divided by the sum of squares total) in the ratio of female to male hospitalizations rates explained by year and decade of age. A polynomial (third order) function of decade of age was used.

Results

The yearly and overall characteristics of the adult asthma hospitalizations are listed in Table 1. The total number of asthma hospitalizations for the study period was 3,063,045. A total of 2,233,849 hospitalizations were in females. The mean age was 54.5 years. Tobacco dependence increased from 4.1% in 2000 to 13.4% in 2010. Obesity increased from 9.9% in 2000 to 21.1% in 2010. COPD also increased from 2.0% in 2000 to 4.8% in 2010.

A distinct peaking in female-male hospitalization rate ratio (greatest for the fifth to sixth decades of life) was observed for all years (Fig 1A). The female-male ratio of asthma hospitalization rate ranged from 1.80 to 2.35 in the third decade of life and 1.89 to 2.01 in the eighth decade of life. In comparison, the rate ratio ranged from 2.62 to 3.07 in fifth decade of life and 2.57 to 3.12 in sixth decade of life, respectively (Fig 1A). A similar pattern with somewhat lower female-male hospitalization rate ratios were noted if possible repeat admissions (within the same calendar year) were excluded (Fig 1B). Multivariate analysis with linear regression, using age decade (third-order polynomial transformed) and study year (negative coefficient), explained 89% of the variation in the female-male ratio for patients 20 to 89 years old.

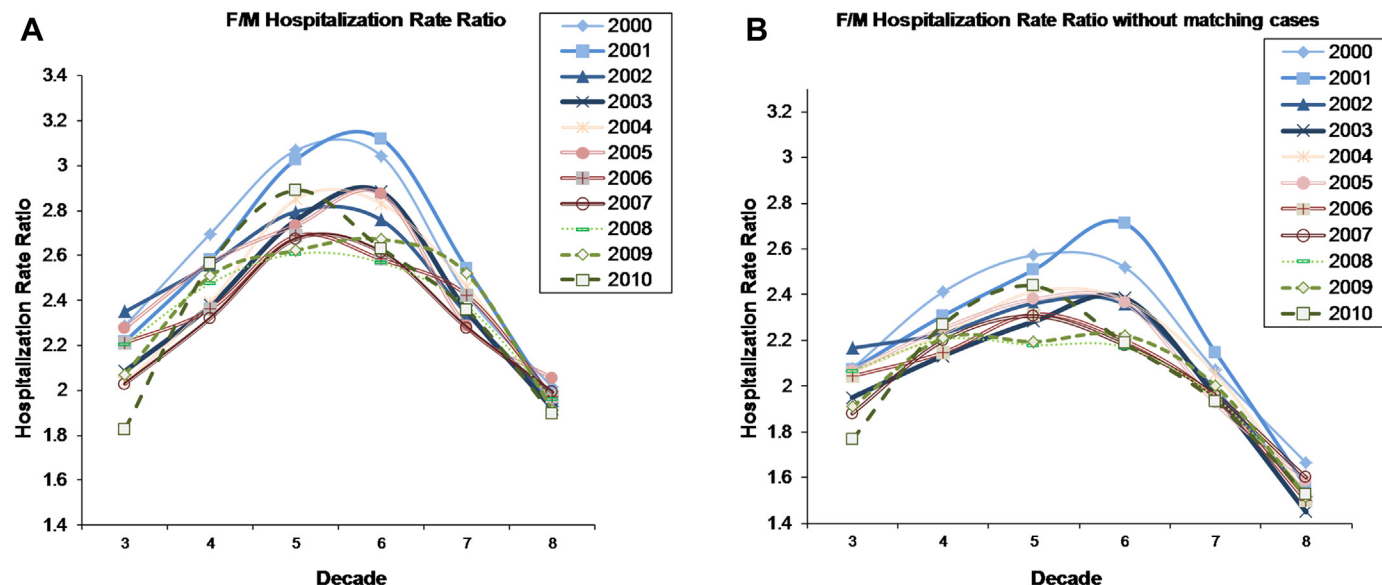


Figure 1. Ratio of the hospitalization rates for women and men in specific decades; (A) all hospitalizations and (B) hospitalizations excluding matching cases.

Univariate logistic regression revealed that being in the fifth and sixth decades of life had a significant association with female sex, with an odds ratio of 1.16 (95% confidence interval [CI], 1.15–1.16) on all hospitalizations and 1.13 (95% CI, 1.12–1.14) in hospitalizations not identified as potential repeats within the same calendar year. Multivariate regression models (Table 2) predicting female sex revealed that being in the fifth to sixth decades of life remained a significant association (adjusted odds ratio, 1.12; 95% CI, 1.11–1.13) even after inclusion of other significant demographic and clinical predictors. Being in the fifth to sixth decade of life and obesity were positive predictors, whereas discharge year, COPD, and smoking were negative predictors. Excluding possible repeat admissions did not abrogate the fifth to sixth decade association (Table 2) (adjusted odds ratio, 1.10; 95% CI, 1.09–1.10).

Graphic examination of the hospitalization rates based on US Census population and the decade-specific hospitalizations in persons with current asthma rate revealed a similar age related pattern for men and women except in women aged in the eighth decade, for whom the hospitalizations per current asthma case diverged downward (Fig 2). When the ratio of the female to male hospitalizations per current asthma cases were compared with the ratios of female to male hospitalization rates (based on population), there was both a diminution in the overall the female to male rate ratio and a dampening of the peak effect (Fig 3).

Discussion

The disparity between female and male asthma hospitalization rates in adults appears to peak in the fifth and sixth decades of life in the United States. This pattern is similar to findings in New York State reported by Lin et al⁵ for a period spanning 1990 through 2006. Chen et al⁹ compared Canadian asthma hospitalization rates between 1994 and 1997 in women and men and found a peak female to male hospitalization rate ratio of 2.7 for individuals 45 to 49 years of age, which decreased with older age. This Canadian peak female to male hospitalization rate ratio is similar to the mean ratio of 2.8 (in the fifth and sixth decades of life) observed in the current study. In the United States, the sex- and age-specific asthma prevalence rates also reveal a peaking in the fifth to sixth decades of life (L. J. Akinbami, personal communication, January 13, 2013).¹ However, the maximum ratio of the female to male asthma prevalence in the United States between 2001 and 2009 (L. J. Akinbami, personal communication, January 13, 2013)¹ is only 1.87 at 47 years of age, which is less than the peak hospitalization sex ratio described herein. In the current study, the association between the female hospitalizations and being in the fifth to sixth decades of life was confirmed by multivariate analysis, which took into account several common comorbid conditions, including tobacco smoking and obesity.¹⁰ Obesity and cigarette smoking have been reported

Table 2
Multivariate regression models

Variable	OR (95% CI) for the model with race		OR (95% CI) for the model without race	
	All hospitalizations	Without possible repeat admissions	All hospitalizations	Without possible additional admissions
COPD	0.82 (0.80–0.83)	0.81 (0.79–0.83)	0.82 (0.81–0.84)	0.82 (0.80–0.84)
Fifth or sixth decade of life	1.12 (1.11–1.13)	1.10 (1.09–1.10)	1.12 (1.11–1.12)	1.10 (1.09–1.10)
Acute respiratory infection	1.17 (1.16–1.18)	1.16 (1.14–1.17)	1.18 (1.17–1.19)	1.17 (1.16–1.18)
Obesity	1.91 (1.89–1.92)	1.82 (1.80–1.84)	1.89 (1.87–1.90)	1.8 (1.78–1.82)
Medicaid or self-pay	0.99 (0.98–0.99)	1.08 (1.08–1.09)	0.95 (0.94–0.95)	1.02 (1.02–1.03)
Tobacco disorder	0.69 (0.69–0.70)	0.7 (0.69–0.70)	0.71 (0.71–0.72)	0.71 (0.70–0.72)
Chronic renal disease	0.68 (0.67–0.69)	0.66 (0.64–0.67)	0.68 (0.66–0.69)	0.65 (0.64–0.66)
Congestive heart failure	0.96 (0.95–0.98)	0.93 (0.92–0.94)	0.97 (0.96–0.98)	0.93 (0.92–0.94)
Pneumonia or influenza	0.98 (0.97–0.99)	0.98 (0.97–0.99)	0.98 (0.97–0.99)	0.99 (0.98–1.00)
Year of discharge	0.99 (0.99–0.99)	0.99 (0.99–1.00)	0.99 (0.99–0.99)	0.99 (0.99–0.99)
White race	1.2 (1.19–1.21)	1.32 (1.32–1.34)	Not included	

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio.

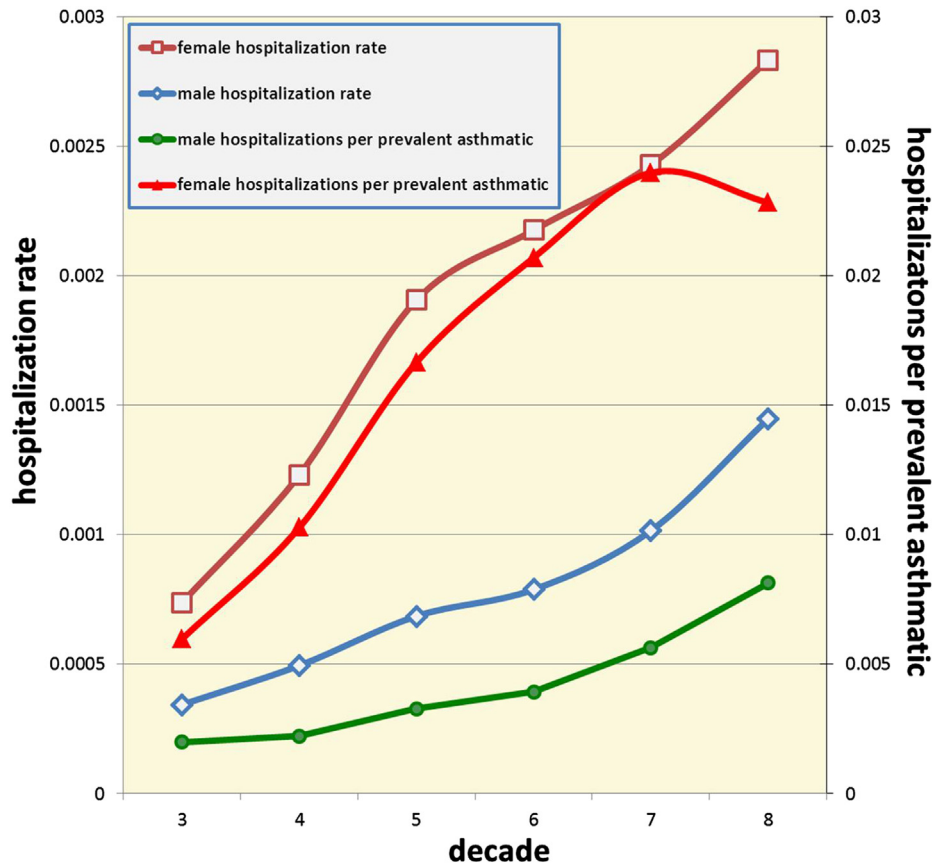


Figure 2. Hospitalization rates for men and women in specific decades.

influence the pattern of inflammation in asthma.^{11,12} The magnitude of the fifth-sixth decade association was not altered by excluding hospitalizations that did not code race or by excluding hospitalizations that may have been repeat admissions during the same calendar year. As might be expected, COPD was associated with male, not female, hospitalizations.

The sex- and decade-specific patterns of asthma hospitalizations revealed similarities when the denominators used were US Census data compared with when estimated current asthmatic patient numbers were used (Fig 2). However, the magnitude of the female to male ratios were markedly less when estimated current asthmatic patient numbers were used as the rate denominators (Fig 3). Moreover, the peaking in the fifth to sixth decades was significantly blunted. A further diminution of the female to male ratios was noted when possible repeat hospitalizations (in the same calendar year) were excluded. Because the matching to identify possible repeat hospitalizations was performed on whole years of age, a significant proportion of possible repeat hospitalizations would be missed. For example, an individual who was hospitalized in September and December of a given year and had a birthday in October would not have these hospitalizations matched as possible repeat hospitalizations (on the same individual) for that year (because the age would not match). These data suggest that repeat hospitalizations in this study are underestimated and that much (but not all) of the sex disparity in adult asthma hospitalizations is accounted for by differences in overall current asthma prevalence, with likely concomitant greater subsequent hospitalization rates for women.

The fifth to sixth decade peak in female to male hospitalization rates did not appear to shift in more recent years except in a reduction of the magnitude of the peak ratio. If the same

hospitalized individuals accounted for the peak over successive years, one would have expected a modal shift to the right in more recent years because of aging. There was no such shift observed.

Although women have a higher hospitalization rate than men, the asthma severity when hospitalized has been found to be similar to men.¹³ One Canadian asthma study suggested that women with equivalent emergency department triage scores and matching age are in fact more likely to be admitted for asthma.¹⁴ In a California study, Schatz and Carmago¹⁵ reported that women with asthma have a higher rate of outpatient clinic visits, emergency department visits, and hospitalizations (ie, higher utilization) compared with men with asthma. There are several findings that may relate to perimenopausal asthma development. Women who develop asthma during their perimenopausal period may have higher levels of 17- β -estradiol compared with controls.¹⁶ Hormone replacement therapy has also been found to increase the risk of asthma in postmenopausal women.¹⁷ However, the current study did not find a marked decrease of the age-related peaking pattern. This finding would have been expected if hormone replacement therapy played a major role in this phenomenon because there has been a 62% decrease in hormone replacement use during the first decade of the second millennium.¹⁸ A multicenter, prospective study of asthma patients during a 2-year period in Spain found that being a woman between the ages of 40 and 60 years was associated with previous hospitalizations and was a risk factor for asthma-related hospitalization.¹⁹ Although the hospitalization rates in the current study indicate that hospitalizations surge in women relative to men during the perimenopausal age range,²⁰ it seems likely that much of the difference relates to prevalence. This finding suggests that asthma severity has similar age and sex distributions in hospitalized asthma patients and asthma patients overall.

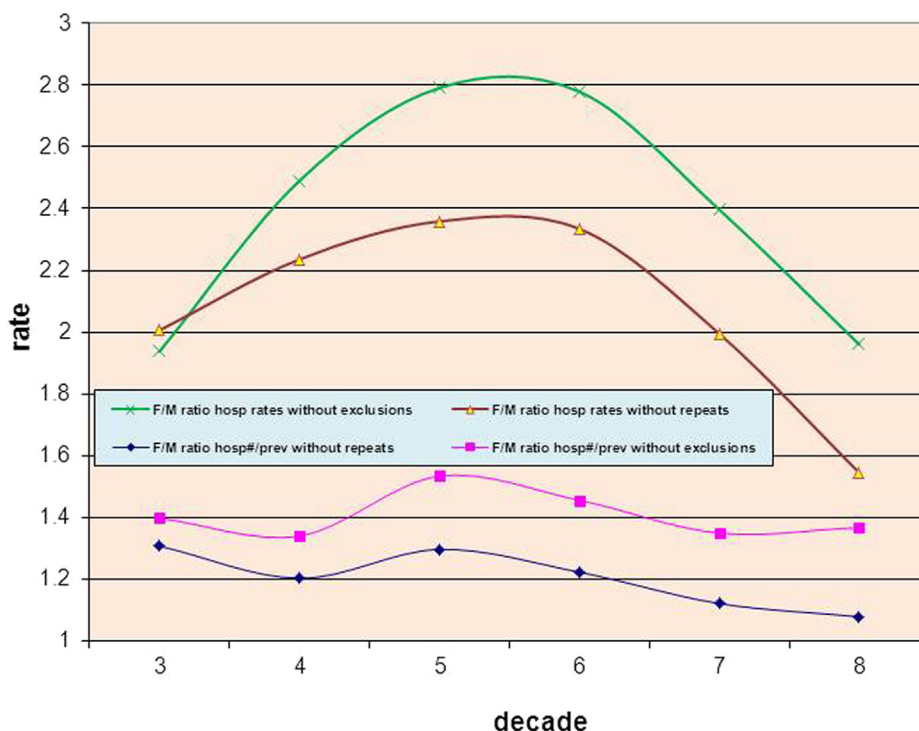


Figure 3. Ratio of hospitalization rates(hosp rates) for men and women in specific decades. Ratio of female to male asthma hospitalizations divided by estimated number of persons with current asthma for specific age decades and corresponding gender(hosp#/prev).

There has been interest in identifying severe asthma phenotypes.²¹ Certainly, hospitalization for asthma is a marker of asthma severity. In a recent cluster analysis,²² one of the severe asthma phenotype characteristics included a cluster with women with late-onset asthma and obesity. The European Network For Understanding Mechanisms Of Severe Asthma compared patients with severe asthma with patients with mild-to-moderate disease.²³ Patients with severe asthma were more likely to be female, overweight, and nonatopic. Indeed, our data support the notion of females predominating asthma hospitalizations in the fifth and sixth decade of life but did not find that this age-related sex difference was dependent on obesity. Although it is not known how long the patients in this study had asthma, the data support the concept that age, sex, and asthma severity have defined relationships.

Although incomplete and/or inaccurate coding is one limitation of database studies, in the United States studies have found good specificity for obstructive lung disease with respect to non-ICD-9-CM code validation measures.^{24,25} The current study used ICD-9-CM codes to profile asthma hospitalization patterns using a national hospital database. This approach has been successfully used to examine asthma hospitalization patterns and associations in several countries.^{26–29} Although the current study also has limitations, including not being able to definitively identify additional admissions for the same individual (and probably underestimating the proportion of additional admissions in the same year), it shows a striking pattern of fifth to sixth decade sex disparity peak in asthma hospitalizations for the entire United States for the second millennium. We furthermore found that the association between this defined age group and female asthma hospitalizations remained after adjusting for many demographic factors and clinical comorbid conditions. The more than 2-fold higher hospitalization rate in women from the fourth through the sixth decade of life suggests that efforts for better asthma control could be more focused on this subgroup of asthmatic adults with potential national cost savings.

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