

Age-related differences in clinical outcomes for acute asthma in the United States, 2006-2008

Chu-Lin Tsai, MD, ScD,^a Wen-Ya Lee, MS, MPH,^a Nicola A. Hanania, MD, MS,^b and Carlos A. Camargo, Jr, MD, DrPH^c *Houston, Tex, and Boston, Mass*

Background: Little is known about the effect of age on acute asthma outcomes.

Objective: We sought to investigate age-related differences in the emergency department (ED) presentation and clinical outcomes for patients with acute asthma.

Methods: We analyzed the 2006-2008 Nationwide Emergency Department Sample, the largest, all-payer, US ED and inpatient database. ED visits for acute asthma were identified with a principal diagnosis of International Classification of Disease, ninth revision, Clinical Modification code 493.xx. Patients were divided into 3 age groups: children (<18 years), younger adults (18-54 years), and older adults (≥55 years). The outcome measures were in-hospital all-cause mortality, near-fatal asthma-related events (noninvasive or mechanical ventilation), hospital charges, admission rates, and hospital length of stay. **Results:** There were an estimated 1,813,000 visits annually for acute asthma from approximately 4,700 EDs. The estimated overall annual number of in-hospital asthma-related deaths was 1,144 (0.06%); 101 died in the ED, and 1,043 died as inpatients. By age group, there were 37 asthma-related deaths per year in children, 204 in younger adults, and 903 in older adults. Compared with younger adults, older adults had higher mortality, had higher rates of near-fatal asthma-related events, had higher hospital charges, were more likely to be hospitalized, and had a longer hospital length of stay ($P < .001$ for all). After adjusting for comorbidities, older asthmatic patients had a 5-fold increased risk of overall mortality (adjusted odds ratio, 5.2; 95% CI, 4.0-6.9), compared with younger adults.

Conclusions: Older adults with acute asthma have a substantial burden of morbidity and mortality. With the US population aging, there is an urgent need for targeted interventions for this

high-risk population. (*J Allergy Clin Immunol* 2012;■■■■:■■■■-■■■■.)

Key words: Acute asthma, age, emergency department, outcomes

Asthma is an important public health problem in the United States. The most recent estimates indicate that there were 1.75 million asthma-related emergency department (ED) visits and 456,000 asthma-related hospitalizations in 2007.¹ Asthma prevalence remains at historically high levels, affecting 25 million Americans in 2007.¹ Asthma mortality, however, appears to have peaked in 2000 ($n = 5,667$) and has decreased each year since then.²

Despite the significant morbidity and mortality associated with acute asthma, relatively few multicenter studies have examined ED presentation or hospital course among patients with acute asthma.³⁻⁸ None of these studies have examined both clinical settings and thereby offered a longitudinal view of acute asthma. The Agency for Healthcare Research and Quality (AHRQ) recently released a national database containing information on both ED presentation and hospital course.⁹ This enables asthma researchers to examine important topics in acute asthma with short-term follow-up, such as age-related differences in ED presentation and hospital course.

Asthma affects individuals across the entire age spectrum from infants to older adults. Childhood asthma is a different phenotype from adult asthma, with higher morbidity (ED visits and hospitalizations) but much lower mortality.¹⁰ On the other end of the spectrum, asthma in older adults is less studied.¹¹ Data on older adults with acute asthma are even scarcer. The only multicenter study of which we are aware is an ED-based study that showed older adults with asthma were less responsive to bronchodilators and more likely to be admitted compared with younger adults.¹²

Given these knowledge gaps in the literature, the objective of the present analysis was to investigate the age-related differences in ED presentation and clinical outcomes in patients with acute asthma by using a nationally representative database. We hypothesized that older patients would experience higher mortality, more near-fatal asthma-related events, higher charges, higher admission rates, and longer hospital length of stay (LOS) compared with younger adults. We also hypothesized that children with acute asthma would be associated with lower mortality, less near-fatal asthma-related events, lower charges, lower admission rates, and shorter hospital LOS compared with younger adults.

METHODS

Study design and setting

We conducted a retrospective cohort study using data from the 2006-2008 Nationwide Emergency Department Sample (NEDS),¹³ a component of the

From ^athe Division of Epidemiology, Human Genetics and Environmental Sciences, University of Texas School of Public Health, Houston; ^bthe Section of Pulmonary and Critical Care Medicine, Department of Medicine, Baylor College of Medicine, Houston; and ^cthe Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston.

Supported by grant no. R03HS020722 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality.

Disclosure of potential conflict of interest: C. A. Camargo, Jr, is a consultant for Dey, Genentech, Merck, Novartis, and Pfizer and has received research support from GlaxoSmithKline and Sanofi-Aventis. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication November 4, 2011; revised January 23, 2012; accepted for publication January 27, 2012.

Corresponding author: Chu-Lin Tsai, MD, ScD, Division of Epidemiology, Human Genetics and Environmental Sciences, University of Texas School of Public Health, 1200 Herman Pressler, Suite W610, Houston, TX 77030. E-mail: cltsai@post.harvard.edu. 0091-6749/\$36.00

© 2012 American Academy of Allergy, Asthma & Immunology
doi:10.1016/j.jaci.2012.01.061

Abbreviations used

AHRQ: Agency for Healthcare Research and Quality
 COPD: Chronic obstructive pulmonary disease
 ED: Emergency department
 HCUP: Healthcare Cost and Utilization Project
 ICD-9-CM: International Classification of Disease, ninth revision, Clinical Modification
 IQR: Interquartile range
 LOS: Length of stay
 NEDS: Nationwide Emergency Department Sample
 OR: Odds ratio

Healthcare Cost and Utilization Project (HCUP) sponsored by the AHRQ. The HCUP-NEDS is nationally representative of all community hospital-based EDs in the United States, which is defined by the American Hospital Association as all nonfederal, short-term, general, and other specialty hospitals.¹⁴ The NEDS was constructed by using administrative records from the HCUP State Emergency Department Databases and the State Inpatient Databases. The State Emergency Department Databases capture information on ED visits that do not result in an admission (ie, treat-and-release visits or transfers to another hospital); the State Inpatient Databases contain information on patients initially seen in the ED and then admitted to the same hospital. Taken together, the resulting NEDS represents all ED visits regardless of disposition and contains information on short-term outcomes for patients admitted through the ED. The NEDS is the largest all-payer ED and inpatient database in the United States. The NEDS represents an approximately 20% stratified sample of US hospital-based EDs, containing more than 26 million records of ED visits from approximately 1,000 hospitals each year. ED and discharge weights are available to obtain national estimates at the ED and visit level. Additional details of the NEDS can be found elsewhere.¹³ The Committee for the Protection of Human Subjects at the University of Texas Health Science Center classified this analysis of de-identified data as exempt (protocol number: 11-0254).

Study population

Patient visits were included in this analysis if they carried a primary ED diagnosis of asthma (International Classification of Disease, ninth revision, Clinical Modification [ICD-9-CM]¹⁵ code of 493.xx). Patients with a primary ICD-9 code of 493.2x were classified as having “obstructive asthma” (9.5%) and were considered to have potential overlap of chronic obstructive pulmonary disease (COPD) and asthma. Patient visits with any of the 3 COPD codes (491.xx, 492.xx, and 496.xx) listed in nonprimary diagnosis fields were also identified and considered as having coexisting COPD; however, these observations accounted for only 0.7% of the study population.

Patient age

The primary exposure variable was patient age. For the purposes of characterizing the sample, patients were categorized into 3 age groups, children (<18 years), younger adults (18–54 years), and older adults (≥55 years), according to their age at ED presentation.

Patient- and ED-level variables

The NEDS contains information on patient demographics, national quartiles for median household income based on the patient's ZIP code, payment sources, ICD-9-CM diagnoses and procedures, ED disposition, hospital LOS, and hospital disposition. Hospital characteristics include annual visit volume, trauma center designation, urban-rural status, ownership, teaching status, and US region. Geographic regions (Northeast, South, Midwest, and West) were defined according to Census Bureau boundaries.¹⁶ Annual volume of asthma cases for each ED was calculated, and EDs in the top quartile of asthma volume were labeled as high-asthma-volume EDs. To adjust for confounding by

patient mix, Elixhauser comorbidity measures were derived based on the ICD-9 codes using the AHRQ's Comorbidity Software.¹⁷ Each patient record was assigned up to 29 comorbid conditions. This risk adjustment tool has been derived and validated extensively.¹⁸ We used ICD-9 codes for tobacco use (305.1 or V15.82) to identify ever smokers.

Outcome measures

The outcome measures were in-hospital all-cause mortality (ED, inpatient, and overall), near-fatal asthma-related events (inpatient and overall), hospital charges (ED and overall), admission rates, and hospital LOS. Near-fatal asthma-related events were defined as asthma visits involving noninvasive or mechanical ventilation identified by using Clinical Classification Software procedure code 216 or Current Procedural Terminology codes 94660 or 31500. Of note, about 20% of the ED visits are missing information on ED charges in the NEDS each year.¹³ Furthermore, data on intensive care unit admission, ED LOS, and actual costs are not available in the NEDS.

Statistical analysis

Summary statistics are presented as proportions (with 95% CIs), means (with SDs), or medians (with interquartile ranges [IQRs]). Bivariate associations were examined by using Student *t* tests, Kruskal-Wallis tests, and χ^2 tests, as appropriate.

Multivariable logistic (for mortality, admissions, and near-fatal asthma) and linear (for hospital LOS and charges) regression modeling was performed to adjust for baseline patient and ED characteristics that might have confounded the relationship between patient age and clinical outcomes. Although the LOS data were skewed, we did not transform the data because parametric methods are robust to nonnormality with large samples.¹⁹ Model variables were selected *a priori*²⁰ or based on review of the medical literature.^{4,6,21–23} Model variables included patient characteristics (age, sex, quartiles for median household income, weekend admission, insurance status, season, calendar year, and comorbid conditions) and ED characteristics (high asthma volume, urban/rural and teaching status, and US region). The model was fit by using generalized estimating equations to account for the effect of clustering of patients within EDs.²⁴ ED and discharge weights were used to obtain national estimates at the ED and visit level. At all other times (eg, stratified analyses and multivariable modeling), the unweighted asthma cohort was analyzed because weights are generally not advised for multilevel modeling in the HCUP data.²⁵ To better characterize the potential nonlinear relationship between age and clinical outcomes, we fit a multivariable restricted cubic spline model, and adjusted probabilities of overall mortality were predicted and plotted against the entire age spectrum.²⁶

All odds ratios (ORs) and β coefficients are presented with 95% CIs. All analyses were performed with Stata 12.0 software (StataCorp, College Station, Tex). All *P* values are 2-sided, with a *P* value of less than .05 considered statistically significant.

For sensitivity analyses

First, to minimize the potential misclassification of COPD and asthma, we repeated the main analysis on overall mortality excluding cases with a diagnosis of obstructive asthma. Second, we repeated the main analysis excluding cases with coexisting COPD listed in nonprimary diagnosis fields. Third, we repeated the main analysis by defining the older population as adults aged 65 years and older.

RESULTS**Patient and ED characteristics**

The 2006–2008 NEDS sample contained 1,195,113 ED visits for asthma from 1,813 US EDs. After the weighting procedures, there were an estimated 1,813,000 visits annually for asthma from approximately 4,700 US EDs. In the weighted analysis the mean age of patients making these visits was 29 years, and 55% were

TABLE I. Patient and hospital characteristics among patients presenting to the ED with acute asthma, 2006-2008, according to age group

	Age <18 y (n = 452,300)	Age 18-54.9 y (n = 566,974)	Age ≥55 y (n = 175,835)	P value
Patient characteristics				
Age (y), median (IQR)	6 (2-10)	36 (26-45)	66 (59-75)	<.001
Female sex (%)	38	65	69	<.001
Quartile for median household income of patient's ZIP code (%)				
\$1-\$38,999	37	38	34	<.001
\$39,000-\$47,999	26	27	26	
\$48,000-\$62,999	21	21	22	
≥\$63,000	16	14	18	
Weekend admission (%)	31	29	30	<.001
Insurance status (%)				
Medicare	0.3	8	58	<.001
Medicaid	48	25	10	
Private	38	35	23	
Self-pay	9	27	6	
Other	4	5	3	
Season (%)				
Winter (January 1-March 31)	25	26	31	<.001
Spring (April 1-June 30)	22	24	25	
Summer (July 1-September 30)	21	22	20	
Fall (October 1-December 31)	32	27	25	
Ever smokers (%)	0.6	20	20	<.001
Obstructive asthma (ICD-9 code 493.2 [%])	0.3	7	40	<.001
No. of comorbidities, median (IQR)	0 (0-0)	0 (0-1)	1 (0-2)	<.001
Selected comorbidities (%)				
Hypertension	0.1	12	47	<.001
Diabetes, uncomplicated	0.2	6	21	<.001
Fluid and electrolyte disorders	1	3	10	<.001
Obesity	0.4	4	7	<.001
Depression	0.1	3	6	<.001
Congestive heart failure	0.01	1	12	<.001
Hypothyroidism	0.1	1	7	<.001
Deficiency anemia	0.2	1	6	<.001
Psychoses	0.1	2	2	<.001
COPD	0.02	0.7	2.6	<.001
Hospital characteristics				
Total ED visit volume, median (IQR)	52,991 (34,356-78,217)	46,019 (29,505-68,427)	42,655 (27,594-63,204)	<.001
High-asthma-volume ED (%)	75	66	62	<.001
Urban/rural and teaching status (%)				
Metropolitan nonteaching	36	45	48	<.001
Metropolitan teaching	51	41	37	
Nonmetropolitan	12	15	15	
US region (%)				
Northeast	22	26	24	<.001
Midwest	19	21	17	
South	39	38	40	
West	20	16	19	

made by women. Eighteen percent were admitted to the hospital, and the mean of their hospital LOS was 3.5 days. On average, the estimated overall number of in-hospital asthma-related deaths was 1,144 (0.06%) per year. Of these, 101 (9%) died in the ED, and 1,043 (91%) died as inpatients. The estimated numbers of asthma-related deaths by age group were 37 per year in children, 204 in younger adults, and 903 in older adults. By year, the estimated numbers of asthma-related deaths were 1,176 in 2006, 1,074 in 2007, and 1,181 in 2008.

Table I shows the patient and hospital characteristics of the unweighted cohort by patient age. Children and younger adults accounted for most of the visits for acute asthma (38% and 47%,

respectively), with 15% of the visits being by older adults. The median ages for the 3 groups were 6 years (IQR, 2-10 years), 36 years (IQR, 26-45 years), and 66 years (IQR, 59-75 years), respectively. Acute asthma cases were more prevalent in male patients among children but more prevalent in female patients among adults. Median household incomes or weekend admissions did not differ much by age group, although the large sample made the differences statistically significant. Forty-eight percent of the asthmatic children had Medicaid, and 58% of the older patients had Medicare. Acute asthma occurred more frequently in the fall and winter months; however, the seasonal variation across age groups was similar. About 20% of the younger and older

TABLE II. Clinical outcomes among patients presenting to the ED with acute asthma, 2006-2008, according to age group

Outcome	Age <18 y	18-54.9 y	Age ≥55 y	P value
Overall sample				
No. of patients, no.	452,300	566,974	175,835	
ED mortality, no. (%)	12 (0.003)	33 (0.01)	23 (0.01)	<.001
Overall mortality, no. (%)	22 (0.005)	135 (0.02)	608 (0.4)	<.001
Noninvasive or mechanical ventilation, no. (%)	1,601 (0.4)	3,906 (0.7)	3,261 (1.9)	<.001
Charge for ED services per visit (\$), median (IQR)*	801 (495-1,241)	951 (583-1,537)	1,161 (706-1,885)	<.001
Admission (%)	12	14	44	<.001
Admitted sample				
No. of patients admitted	54,651	79,327	77,391	
Inpatient mortality, no. (%)	10 (0.02)	102 (0.1)	585 (0.8)	<.001
Noninvasive or mechanical ventilation, no. (%)	452 (0.8)	3,016 (3.8)	3,085 (4.0)	<.001
Total charge for ED and inpatient services per visit (\$), median (IQR)	7,337 (4,704-11,920)	11,048 (6,688-18,880)	15,570 (9,218-27,105)	<.001
Hospital LOS (d), median (IQR)	2 (1-3)	3 (2-4)	4 (2-6)	<.001

*Data are available for 964,445 patients.

TABLE III. Multivariable analysis of clinical outcomes among patients presenting to the ED with acute asthma, 2006-2008, according to age group

Outcome	Adjusted OR or β coefficient (95% CI)*		
	Age <18 y	18-54.9 y	Age ≥55 y
Overall sample			
ED mortality	0.7 (0.3 to 1.4)	1.0 (reference)	2.9 (1.4 to 6.2)
Overall mortality	0.3 (0.2 to 0.5)	1.0 (reference)	5.2 (4.0 to 6.9)
Noninvasive or mechanical ventilation	0.7 (0.3 to 1.6)	1.0 (reference)	1.2 (1.007 to 1.3)
Charge for ED services per visit (\$)	-252 (-291 to -212)	0 (reference)	192 (167 to 217)
Admission	1.7 (1.6-1.8)	1.0 (reference)	2.1 (2.0-2.2)
Admitted sample			
Inpatient mortality	0.2 (0.1 to 0.4)	1.0 (reference)	3.4 (2.5 to 4.6)
Noninvasive or mechanical ventilation	0.3 (0.2 to 0.4)	1.0 (reference)	0.9 (0.8 to 0.96)
Total charge for ED and inpatient services per visit (\$)	-3,263 (-4,140 to -2,385)	0 (reference)	3,326 (2,795 to 3,857)
Hospital LOS (d)	-0.5 (-0.6 to -0.4)	0.0 (reference)	0.7 (0.7 to 0.8)

*Model adjusting for the following patient and hospital characteristics: sex, median household income, insurance status, weekend admission, season, 29 comorbid conditions, calendar year, US region, urban/rural and teaching status, and high-asthma-volume ED.

adults with asthma were ever smokers. As expected, obstructive asthma was more prevalent in older adults. With respect to comorbidities, older asthmatic adults had more comorbid conditions, such as hypertension, congestive heart failure, and obesity. Table E1 in this article's Online Repository at www.jacionline.org details the 29 comorbid conditions by age group. Asthmatic children were more likely to visit EDs with high total visit volumes and high asthma volumes, and these EDs tended to be in urban teaching hospitals. The regional differences were not prominent.

Patient age and clinical outcomes

In the overall sample asthma mortality was uncommon, and asthma-related deaths in the ED accounted for only a small portion of overall mortality (Table II). Near-fatal asthma-related events were also rare (0.7% overall); however, those who received noninvasive or mechanical ventilation had significantly higher rates of mortality than those who did not (5% vs 0.02%, $P < .001$). By age group, compared with younger adults, older adults had higher ED and overall mortality, had higher rates of near-fatal asthma-related events, had higher ED charges, and were more likely to be admitted to the hospital. On the other hand, compared

with younger adults, children with acute asthma had lower ED and overall mortality, lower rates of near-fatal asthma, lower ED charges, and were less likely to be admitted to the hospital.

Among those who were admitted to the hospital, the inpatient mortality, total charges, and rates of near-fatal asthma-related events were all higher than those in the overall sample, reflecting a more severe case mix in the inpatient population. Patients who experienced near-fatal asthma-related events had much higher mortality (6.9% vs 0.1%, $P < .001$) and a longer hospital LOS than those who did not (median LOS, 5 vs 3 days; $P < .001$). By age group, again, older asthmatic patients had the highest mortality, highest rates of near-fatal asthma-related events, highest charges, and longest hospital LOS among the 3 age groups.

These age-related differences were confirmed by using the multivariable analysis (Table III). After adjusting for potential confounders, including comorbidities, older adults continued to have a nearly 3-fold increased risk of death in the ED (adjusted OR, 2.9; 95% CI, 1.4-6.2) and a 5-fold increased risk of overall mortality (adjusted OR, 5.2; 95% CI, 4.0-6.9) compared with younger adults. By contrast, children with acute asthma had a significantly lower risk of overall mortality (adjusted OR, 0.3; 95% CI, 0.2-0.5), but the reduced ED mortality was not statistically

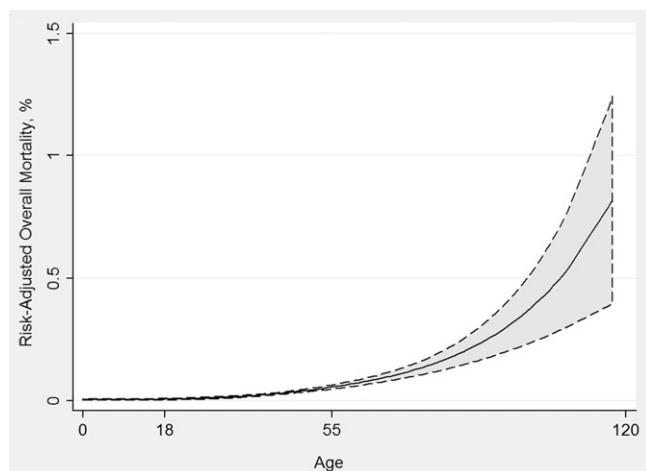


FIG 1. Risk-adjusted probabilities of overall mortality as a function of age. Data were fitted by using a multivariable restricted cubic spline model. The 95% CIs are indicated by the dashed lines.

significant. Older adults had a slightly higher risk of near-fatal asthma-related events (adjusted OR, 1.2; 95% CI, 1.007-1.3) and were about 2 times more likely to be admitted to the hospital. After adjusting for confounders, children with acute asthma were more likely to be admitted than younger adults.

Among those who were admitted to the hospital, similar age-related differences were observed for inpatient mortality and near-fatal asthma-related events, with higher inpatient mortality in older adults and similar risks of near-fatal asthma-related events in younger and older adults. Age-related differences in total charges and hospital LOS remained similar, although the differences were attenuated after multivariable adjustment.

When treating age as a continuous variable (Fig 1), there was an exponential increase in overall mortality with age, adjusting for comorbidities and other confounders. In the first sensitivity analysis, by excluding cases with a diagnosis of obstructive asthma, older adults continued to have a 3-fold increased risk of overall mortality compared with younger adults (adjusted OR, 3.1; 95% CI, 1.9-5.0). In the second sensitivity analysis, by excluding cases with coexisting COPD listed in nonprimary diagnosis fields, older adults continued to have a 5-fold increased risk of overall mortality compared with younger adults (adjusted OR, 5.3; 95% CI, 4.0-7.1). Finally, by using a different age cutoff, older adults aged 65 years and older still had a 4-fold increased risk of overall mortality compared with adults aged 18-64 years (adjusted OR, 4.1; 95% CI, 3.1-5.5).

DISCUSSION

In this nationally representative sample of more than 1 million ED visits by patients with acute asthma, we found that older patients had higher ED and overall mortality, higher ED and overall charges, higher admission rates, and longer hospital LOS compared with younger adults. These findings were partially explained by differences in comorbidities; however, in multivariable and sensitivity analyses older age remained a strong predictor of higher morbidity and mortality in ED patients with acute asthma. With the US population aging, the societal burden of asthma can be expected to increase over the coming years.

In this study the magnitude of differences in comorbidities was quite striking across the age groups. Most prior studies on elderly

asthmatic patients excluded older adults with multiple comorbid conditions²⁷⁻²⁹; thus our estimates might be closer to the true burden of comorbidity in this population. Other smaller studies using insurance claims data without exclusion criteria were able to show substantial differences in comorbidity between younger and older asthmatic patients.^{30,31} Of note, some comorbid conditions, such as congestive heart failure and obesity, might complicate the management of asthma and diminish response to treatments in older adults, leading to undertreatment of asthma and worse clinical outcomes.³²⁻³⁴ In our study the potential overlap of COPD and asthma (defined by ICD-9 code 493.2x) was also prevalent among elderly asthmatic patients, a comorbid condition that has been previously linked to poor prognosis in a Medicaid population.³⁵

Even after adjustment for comorbidities, older adults with asthma still had a 5-fold increased risk of overall mortality, suggesting that other factors might explain the higher mortality in the older population. For example, normal aging is associated with a reduction in lung elastic recoil, which might lead to increased propensity for airway collapse and reduced ability of bronchodilation or bronchoprotection through lung inflation.^{36,37}

Airway response to bronchodilators, particularly β -agonists, might also decrease with age.^{38,39} Furthermore, older adults might have decreased sensation of asthma symptoms (eg, air hunger),^{40,41} leading to their later presentation for care with more severe disease. Finally, several studies have shown that older adults with asthma are undertreated, and even when they are treated, the treatments they receive are not concordant with guideline recommendations.^{29,31,42,43} Our findings highlight the need to examine these factors that lead to poor outcomes in older adults with asthma.

Consistent with an earlier report on national surveillance for asthma,² our results suggested that older patients were responsible for a small proportion of overall ED visits for acute asthma; however, they carry disproportionately higher morbidity and mortality compared with younger patients. The data further indicated that asthma mortality was extremely rare in the ED (<10% of in-hospital asthma-related deaths), and most of the in-hospital deaths occurred as inpatients. A previous analysis using the Nationwide Inpatient Sample found 1,499 asthma-related deaths occurred when patients were inpatients in the United States for 2000,²¹ accounting for about one third of all asthma-related deaths in that year ($n = 4,483$).² Taken together, these observations indicate that most asthma-related deaths occur outside the hospital; if asthma-related deaths occur inside the hospital, they rarely happen in the ED. Interventions aiming to further reduce asthma-related deaths should focus on out-of-hospital settings.

On the other hand, children with acute asthma had very low mortality, lower ED and overall charges, and a shorter hospital LOS compared with younger adults. There were 167 asthma-related deaths among children in 2005,¹⁰ and the estimated number of in-hospital asthma-related deaths from the NEDS data was only 37 per year from 2006 to 2008. Thus our results indicate that asthma mortality in children also appears to occur more often in the out-of-hospital setting. In our study approximately half of the children had Medicaid and most of the children visited high-asthma-volume urban EDs, suggesting the persistence of the "inner-city asthma"^{44,45} phenomenon. Although asthma-related hospitalizations in children have been decreasing over the past few years,^{10,46} our study suggests that inner cities merit additional interventions to reduce asthma morbidity, thereby

fulfilling the goal of reducing asthma-related ED visits and hospitalizations in "Healthy people 2020."⁴⁷

In our study patients with near-fatal asthma represent a small proportion of ED visits; however, they had a much higher risk of mortality and were associated with a longer hospital LOS, a finding that is consistent with a previous single-center study.⁴⁸ Near-fatal asthma can be viewed as a subset of severe asthma, which is an active area of ongoing asthma research.⁴⁹⁻⁵¹ The data showed that the association of older age with near-fatal asthma-related events was largely explained by comorbidities in the multivariable analysis, suggesting that older age might not be an important phenotype in characterizing severe asthma. Indeed, a recent study showed that age of onset might be more important than age itself in characterizing severe asthma.⁵²

This study has some potential limitations. First, we used administrative rather than clinical data, and potential misdiagnosis of COPD and asthma in the elderly might exist. However, we have conducted sensitivity analyses to address this issue, and the results did not materially change. In addition, the smoking rates in the NEDS asthma population were comparable with those from our previous multicenter study of adults with acute asthma.⁵³

Second, the NEDS contains visit-level records and not patient-level records. Lack of patient identifiers precluded us from examining longer-term outcomes, such as readmissions. It is possible that a small proportion of patients might have visited the ED multiple times during the 3-year period. In this case, because mortality events are nonrecurrent, the number of deaths should not change. However, the mortality rates, especially in older adults, were likely underestimated in our study.

Third, the NEDS does not include information about asthma medications, and we were not able to further explore this potential risk factor for asthma mortality.^{54,55}

In summary, in this nationally representative combined ED and inpatient database, age had profound effects on short-term clinical outcomes in patients presenting to the ED with acute asthma. Older adults with acute asthma have substantially higher morbidity and mortality compared with younger adults. As the US population ages, clinicians will undoubtedly see a higher number of older asthmatic patients with multiple comorbidities. Asthma guidelines might require updating to address special diagnostic and treatment considerations in older adults with asthma. For policymakers, our real-world data call for advanced planning to meet the needs of the growing elderly population with asthma. Although these data support evidence of a continued decrease in asthma-related deaths,^{2,10,46} both in adults and children, interventions targeted on prehospital settings might yield further decreases in this preventable outcome.

Clinical implications: Older adults with acute asthma have a substantial burden of morbidity and mortality. With the US population aging, there is an urgent need for targeted interventions for this high-risk population.

REFERENCES

1. American Lung Association. Trends in asthma morbidity and mortality. Available at: <http://www.lungusa.org/finding-cures/our-research/trend-reports/asthma-trend-report.pdf>. Accessed September 15, 2011.
2. Moorman JE, Rudd RA, Johnson CA, King M, Minor P, Bailey C, et al. National surveillance for asthma—United States, 1980-2004. *MMWR Surveill Summ* 2007; 56:1-54.
3. Schatz M, Clark S, Camargo CA Jr. Sex differences in the presentation and course of asthma hospitalizations. *Chest* 2006;129:50-5.

4. Pollack CV Jr, Pollack ES, Baren JM, Smith SR, Woodruff PG, Clark S, et al. A prospective multicenter study of patient factors associated with hospital admission from the emergency department among children with acute asthma. *Arch Pediatr Adolesc Med* 2002;156:934-40.
5. Singh AK, Cydulka RK, Stahmer SA, Woodruff PG, Camargo CA Jr. Sex differences among adults presenting to the emergency department with acute asthma. Multicenter Asthma Research Collaboration Investigators. *Arch Intern Med* 1999;159:1237-43.
6. Weber EJ, Silverman RA, Callahan ML, Pollack CV, Woodruff PG, Clark S, et al. A prospective multicenter study of factors associated with hospital admission among adults with acute asthma. *Am J Med* 2002;113:371-8.
7. Griswold SK, Nordstrom CR, Clark S, Gaeta TJ, Price ML, Camargo CA Jr. Asthma exacerbations in North American adults: who are the "frequent fliers" in the emergency department? *Chest* 2005;127:1579-86.
8. Tsai CL, Sullivan AF, Gordon JA, Kaushal R, Magid DJ, Blumenthal D, et al. Quality of care for acute asthma in 63 US emergency departments. *J Allergy Clin Immunol* 2009;123:354-61.
9. Nationwide Emergency Department Sample (NEDS) Data. Available at: <http://www.hcup-us.ahrq.gov/nedsoverview.jsp>. Accessed September 15, 2011.
10. Akinbami LJ, Moorman JE, Garbe PL, Sondik EJ. Status of childhood asthma in the United States, 1980-2007. *Pediatrics* 2009;123(suppl):S131-45.
11. Hanania NA, King MJ, Braman SS, Saltoun C, Wise RA, Enright P, et al. Asthma in the elderly: Current understanding and future research needs—a report of a National Institute on Aging (NIA) workshop. *J Allergy Clin Immunol* 2011; 128(suppl):S4-24.
12. Banerji A, Clark S, Afilalo M, Blanda MP, Cydulka RK, Camargo CA Jr. Prospective multicenter study of acute asthma in younger versus older adults presenting to the emergency department. *J Am Geriatr Soc* 2006;54:48-55.
13. HCUP Nationwide Emergency Department Sample (NEDS). Healthcare Cost and Utilization Project (HCUP). Rockville (MD): Agency for Healthcare Research and Quality. Available at: <http://www.hcup-us.ahrq.gov/nedsoverview.jsp>. Accessed April 15, 2011.
14. AHA Annual Survey Database. Available at: <http://www.ahadata.com/ahadata/html/AHASurvey.html>. Accessed April 15, 2011.
15. Department of Health and Human Services. 5th ed. The international classification of diseases, 9th revision, clinical modification: ICD-9-CM., Vol. 1. Washington (DC): Government Printing Office.
16. United States Bureau of the Census. Census regions and divisions of the United States. Available at: http://www.census.gov/geo/www/us_regdiv.pdf. Accessed April 9, 2011.
17. Healthcare Cost and Utilization Project Comorbidity Software. Available at: <http://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp>. Accessed April 15, 2011.
18. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998;36:8-27.
19. Thompson SG, Barber JA. How should cost data in pragmatic randomised trials be analysed? *BMJ* 2000;320:1197-200.
20. Tsai CL, Camargo CA Jr. Methodological considerations, such as directed acyclic graphs, for studying "acute on chronic" disease epidemiology: chronic obstructive pulmonary disease example. *J Clin Epidemiol* 2009;62:982-90.
21. Krishnan V. Mortality in patients hospitalized for asthma exacerbations in the United States. *Am J Respir Crit Care Med* 2006;174:633-8.
22. Moorman JE, Mannino DM. Increasing U.S. asthma mortality rates: who is really dying? *J Asthma* 2001;38:65-71.
23. Barnett SB, Nurmagambetov TA. Costs of asthma in the United States: 2002-2007. *J Allergy Clin Immunol* 2011;127:145-52.
24. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika* 1986;73:13-22.
25. HCUP Methods Series. Hierarchical modeling using HCUP data. Report no. 2007-01. Rockville (MD): Agency for Healthcare Research and Quality. Available at: http://www.hcup-us.ahrq.gov/reports/methods/2007_01.pdf. Accessed April 15, 2011.
26. Greenland S. Dose-response and trend analysis in epidemiology: alternatives to categorical analysis. *Epidemiology* 1995;6:356-65.
27. Huss K, Naumann PL, Mason PJ, Nanda JP, Huss RW, Smith CM, et al. Asthma severity, atopic status, allergen exposure and quality of life in elderly persons. *Ann Allergy Asthma Immunol* 2001;86:524-30.
28. Slavin RG, Haselkorn T, Lee JH, Zheng B, Deniz Y, Wenzel SE. Asthma in older adults: observations from the epidemiology and natural history of asthma: outcomes and treatment regimens (TENOR) study. *Ann Allergy Asthma Immunol* 2006;96:406-14.
29. Enright PL, McClelland RL, Newman AB, Gottlieb DJ, Lebowitz MD. Underdiagnosis and undertreatment of asthma in the elderly. Cardiovascular Health Study Research Group. *Chest* 1999;116:603-13.

30. Diette GB, Krishnan JA, Dominici F, Haponik E, Skinner EA, Steinwachs D, et al. Asthma in older patients: factors associated with hospitalization. *Arch Intern Med* 2002;162:1123-32.
31. Hartert TV, Togias A, Mellen BG, Mitchel EF, Snowden MS, Griffin MR. Underutilization of controller and rescue medications among older adults with asthma requiring hospital care. *J Am Geriatr Soc* 2000;48:651-7.
32. Gibson PG, McDonald VM, Marks GB. Asthma in older adults. *Lancet* 2010;376:803-13.
33. Reed CE. Asthma in the elderly: diagnosis and management. *J Allergy Clin Immunol* 2010;126:681-9.
34. Chotirmall SH, Watts M, Branagan P, Donegan CF, Moore A, McElvaney NG. Diagnosis and management of asthma in older adults. *J Am Geriatr Soc* 2009;57:901-9.
35. Shaya FT, Dongyi D, Akazawa MO, Blanchette CM, Wang J, Mapel DW, et al. Burden of concomitant asthma and COPD in a Medicaid population. *Chest* 2008;134:14-9.
36. Sharma G, Goodwin J. Effect of aging on respiratory system physiology and immunology. *Clin Interv Aging* 2006;1:253-60.
37. Janssens JP, Pache JC, Nicod LP. Physiological changes in respiratory function associated with ageing. *Eur Respir J* 1999;13:197-205.
38. Connolly MJ, Crowley JJ, Charan NB, Nielson CP, Vestal RE. Impaired bronchodilator response to albuterol in healthy elderly men and women. *Chest* 1995;108:401-6.
39. Ullah MI, Newman GB, Saunders KB. Influence of age on response to ipratropium and salbutamol in asthma. *Thorax* 1981;36:523-9.
40. Connolly MJ, Crowley JJ, Charan NB, Nielson CP, Vestal RE. Reduced subjective awareness of bronchoconstriction provoked by methacholine in elderly asthmatic and normal subjects as measured on a simple awareness scale. *Thorax* 1992;47:410-3.
41. Kronenberg RS, Drage CW. Attenuation of the ventilatory and heart rate responses to hypoxia and hypercapnia with aging in normal men. *J Clin Invest* 1973;52:1812-9.
42. Navaratnam P, Jayawant SS, Pedersen CA, Balkrishnan R. Asthma pharmacotherapy prescribing in the ambulatory population of the United States: evidence of non-adherence to national guidelines and implications for elderly people. *J Am Geriatr Soc* 2008;56:1312-7.
43. Sin DD, Tu JV. Underuse of inhaled steroid therapy in elderly patients with asthma. *Chest* 2001;119:720-5.
44. Bryant-Stephens T. Asthma disparities in urban environments. *J Allergy Clin Immunol* 2009;123:1199-208.
45. Szefer SJ, Gergen PJ, Mitchell H, Morgan W. Achieving asthma control in the inner city: do the National Institutes of Health Asthma Guidelines really work? *J Allergy Clin Immunol* 2010;125:521-8.
46. Szefer SJ. Advancing asthma care: the glass is only half full! *J Allergy Clin Immunol* 2011;128:485-94.
47. Healthy people 2020 summary of objectives. Respiratory diseases. Available at: <http://www.healthypeople.gov/2020/topicsobjectives2020/overview.aspx?topicid=36>. Accessed September 15, 2011.
48. Dhuper S. Profile of near-fatal asthma in an inner-city hospital. *Chest* 2003;124:1880-4.
49. Szefer SJ. Defining asthma phenotypes: focusing the picture. *J Allergy Clin Immunol* 2010;126:939-40.
50. Moore W, Bleecker E, Curran-Everett D, Erzurum SC, Ameredes BT, Bacharier L, et al. Characterization of the severe asthma phenotype by the National Heart, Lung, and Blood Institute's Severe Asthma Research Program. *J Allergy Clin Immunol* 2007;119:405-13.
51. Moore W, Peters S. Severe asthma: an overview. *J Allergy Clin Immunol* 2006;117:487-94.
52. Moore WC, Meyers DA, Wenzel SE, Teague WG, Li H, Li X, et al. Identification of asthma phenotypes using cluster analysis in the Severe Asthma Research Program. *Am J Respir Crit Care Med* 2009;181:315-23.
53. Patel SN, Tsai CL, Boudreaux ED, Kilgannon JH, Sullivan AF, Blumenthal D, et al. Multicenter study of cigarette smoking among patients presenting to the emergency department with acute asthma. *Ann Allergy Asthma Immunol* 2009;103:121-7.
54. Abramson MJ, Bailey MJ, Couper FJ, Driver JS, Drummer OH, Forbes AB, et al. Are asthma medications and management related to deaths from asthma? *Am J Respir Crit Care Med* 2001;163:12-8.
55. Drazen JM, O'Byrne PM. Risks of long-acting beta-agonists in achieving asthma control. *N Engl J Med* 2009;360:1671-2.

TABLE E1. Comorbidities among patients presenting to the ED with acute asthma, 2006-2008, according to age group

Comorbidity (%)	Age <18 y (n = 452,300)	Age 18-54.9 y (n = 566,974)	Age ≥55 y (n = 175,835)	P value
Hypertension	0.1	12	47	<.001
Diabetes, uncomplicated	0.2	6	21	<.001
Fluid and electrolyte disorders	1	3	10	<.001
Obesity	0.4	4	7	<.001
Depression	0.1	3	6	<.001
Congestive heart failure	0.01	1	12	<.001
Hypothyroidism	0.1	1	7	<.001
Deficiency anemia	0.2	1	6	<.001
Chronic pulmonary diseases	2	3	5	<.001
Psychoses	0.1	2	2	<.001
Neurological disorders	0.3	1	3	<.001
Drug abuse	0.1	2	1	<.001
Renal failure	0.01	0.3	4	<.001
Valvular heart disease	0.03	0.4	3	<.001
Alcohol abuse	0.01	1	1	<.001
Rheumatoid arthritis/collagen vascular diseases	0.01	0.4	2	<.001
Diabetes, complicated	0	0.3	2	<.001
Pulmonary circulatory disorders	0.02	0.2	2	<.001
Peripheral vascular disorders	0	0.1	2	<.001
Liver disease	0.01	0.3	0.6	<.001
Paralysis	0.2	0.2	0.6	<.001
Coagulopathy	0.03	0.2	0.8	<.001
Solid tumor without metastasis	0.01	0.1	0.9	<.001
AIDS	0	0.2	0.1	<.001
Weight loss	0.01	0.1	0.5	<.001
Metastatic cancer	0	0.03	0.3	<.001
Blood loss anemia	0	0.1	0.2	<.001
Lymphoma	0	0.03	0.3	<.001
Peptic ulcer disease excluding bleeding	0	0	0.02	<.001