

Outcomes of Emergency Department Anaphylaxis Visits from 2005 to 2014



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What is already known about this topic? Emergency department (ED) anaphylaxis visits are increasing.

What does this article add to our knowledge? The proportions of ED anaphylaxis patients being admitted for observation or inpatient hospitalization and for intensive care unit admission increased from 2005 to 2014. Furthermore, the proportion of ED anaphylaxis patients undergoing endotracheal intubation increased during this time period.

How does this study impact current management guidelines? Physicians, scientists, and health care policy makers should be aware of these rising trends so that efforts can be made to identify and mitigate the underlying causes.

BACKGROUND: Although the incidence of anaphylaxis appears to be increasing, trends in anaphylaxis-related health care utilization are not well understood.

OBJECTIVE: To better understand the potential increasing health care burden, we analyzed the changes in anaphylaxis-related health care utilization, including emergency department (ED) discharges, observation stays, inpatient admissions, intensive care unit admissions, and endotracheal intubations.

METHODS: We conducted an observational study examining outcomes of anaphylaxis-related ED visits between January 1, 2005, and December 31, 2014. We analyzed administrative claims data from OptumLabs Data Warehouse, which includes more than 100 million Medicare Advantage and privately insured enrollees in the United States. We studied trends in the proportions of ED-related anaphylaxis visits based on demographic characteristics, triggers, and ED disposition for our study population.

RESULTS: Among 56,212 anaphylaxis-related ED visits during a 10-year period, the proportion of patient observation/inpatient

admissions increased by 37.6% ($P = .02$), from 13.2% of anaphylaxis-related ED visits in 2005 to 18.2% in 2014. The proportion of patients admitted to the intensive care unit increased by 27.4% ($P = .001$), from 4.5% in 2005 to 5.8% in 2014. Proportions of endotracheal intubation increased by 145.2% ($P < .001$).

CONCLUSIONS: The increasing proportions of observation/inpatient admissions, intensive care unit admissions, and endotracheal intubations suggest an increase in anaphylaxis severity. Enhanced awareness of these trends among patients, practitioners, and the community is necessary to create effective strategies to prevent anaphylaxis and decrease associated adverse consequences. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2018;6:1002-9)

Key words: Anaphylaxis; Hospitalization; Trends; United States

Anaphylaxis is “a serious allergic reaction that is rapid in onset and may cause death.”¹ Anaphylaxis can present with a broad range of signs and symptoms with varying levels of severity.² A recent national survey³ estimated that at least 1.6% of the US population has a history of anaphylaxis, and studies suggest that the rates of anaphylaxis-related hospitalizations are increasing. A study by Lin et al⁴ found a greater than 4-fold increase in the rate of anaphylaxis-related hospitalizations in New York state from 1990 to 2006. Ma et al⁵ reported a substantial increase in rates of anaphylaxis-related hospitalizations in the United States from 21.0 per million population in 1999 to 25.1 per million in 2009.

Few epidemiologic studies of anaphylaxis in the United States have been reported, and comparisons between studies have been limited by several factors, including the use of different methods and small population sizes.^{4,6,7} Through the use of OptumLabs Data Warehouse (OLDW), a national database including administrative claims data on more than 100 million enrollees in the United States, we recently reported a 101% increase in emergency department (ED) visits for anaphylaxis between 2005 and 2014.⁸ Although prior studies⁴⁻⁸ have suggested an increasing incidence of anaphylaxis, it is unclear if these changes

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Abbreviations used

ACE- Angiotensin-converting enzyme

ED- Emergency department

ICU- Intensive care unit

OLDW- OptumLabs Data Warehouse

represent true increases in severity or are primarily reflective of the overall rise in the incidence of anaphylaxis.

The objective of our study was to examine time trends in anaphylaxis-related ED visit outcomes, including observations, inpatient (non-intensive care unit [ICU]) admissions, ICU admissions, and endotracheal intubations from 2005 through 2014 reported as proportions of ED anaphylaxis visits. Evaluating outcomes as proportions of ED anaphylaxis visits rather than overall rates provides a more accurate depiction of trends in anaphylaxis severity.

METHODS

Data source

An observational study was performed using the OLDW, which includes administrative data for both Medicare Advantage enrollees and privately insured patients in the United States,⁹ along with longitudinal health information for more than 100 million enrollees over the past 20 years. Data originate from geographically diverse regions across the United States and include enrollee demographic information and medical claims.¹⁰ This study was exempt from institutional review board approval because all data were preexisting and were deidentified before analysis.

Study population

We used 2 validated methods to identify ED anaphylaxis visits from January 1, 2005, to December 31, 2014.¹¹ Codes for anaphylactic shock (995.60-995.69) were used to identify patients for Method 1. An algorithm of International Classification of Diseases, 9th Revision, Clinical Modification codes of symptom combinations was used to identify patients for Method 2.¹¹ Each method was performed separately, with a combination of both methods performed to identify and exclude duplicate cases. Patients were required to have at least 30 days of medical coverage before the ED visit. The total number of enrollees with medical coverage for at least 30 days in the given calendar year was used as the denominator for percentage calculations.

Patient characteristics

We obtained patients' baseline characteristics, including age, sex, race, census region, and anaphylaxis trigger. We also analyzed outcomes that included ED discharge, observations (including ED observation unit admissions and hospital observations), non-ICU hospital admission, ICU admission, and endotracheal intubation (Current Procedural Terminology code 31500; International Classification of Diseases, 9th Revision, Clinical Modification codes 96.04, 96.05).

Methods and measurements

This study adheres to the RECORD (REporting of studies Conducted using Observational Routinely-collected health Data) Statement.¹² We examined trends over time for demographic characteristics, triggers, and ED disposition for our study population. Age groups were stratified into 5 categories to identify patient subgroups: 0-4 years (infant, toddler, and preschool-aged children),

5-17 years (school-aged children), 18-34 years (young adult), 35-64 years (middle adulthood), and 65 years and older (retirement age and older). Race was grouped into 5 categories: Asian, black, Hispanic, white, and unknown (includes missing).

Statistical analysis

Patient characteristics (age, sex, race, census region, and trigger) were reported using descriptive statistics, as appropriate for the data distribution. Annual proportions were calculated by using the number of outcomes as the numerator and total number of ED anaphylaxis visits as the denominator. We compared proportions across time using regression models (trend analysis). We calculated percentage change in proportions from 2005 to 2014 among anaphylaxis ED visits for observations/inpatient admission, ICU admission, and endotracheal intubation by age group and by trigger. The denominator for these calculations was the total number of visits for the specified age group or trigger. Change in proportions was analyzed with the χ^2 test. All significance tests were 2-sided, and $P < .05$ was considered statistically significant. SAS software version 9.4 (SAS Institute Inc., Cary, NC) was used for all statistical analysis.

We planned an *a priori* sensitivity analysis by excluding patients taking angiotensin-converting enzyme (ACE) inhibitors, because intubations in these patients could have been secondary to ACE inhibitor-induced angioedema and not anaphylaxis.

RESULTS

During the 10-year study period, we identified a total of 56,212 ED visits for anaphylaxis (Fig 1).⁸ At the time of the ED visit, the median (interquartile range) age was 36 (17-52) years; approximately one-fourth of the patients were younger than 18 years.⁸ The majority of patients were female (57.5%), and slightly more than half the cohort was white (51.3%). After an evaluation in the ED, the majority (77.1%) of the patients were dismissed home (Table E1, available in this article's Online Repository at www.jaci-inpractice.org). Other outcomes are described below (Table I, Fig 2).

Observation and inpatient (non-ICU) admissions

A total of 9881 patients (17.6%) seen in the ED for anaphylaxis were observed (either in ED observation units or in hospital beds) or admitted to a non-ICU hospital unit (Table E1, available in this article's Online Repository at www.jaci-inpractice.org). The proportion of observation/non-ICU admissions increased significantly during the study period by 37.6% ($P = .02$), from 13.2% of ED anaphylaxis visits in 2005 to 18.2% in 2014 (Table I). The proportions of observation/non-ICU admissions increased the greatest amount in those aged 0 to 4 years (94.9%; $P = .03$) (Fig 3, A). Proportions of observation/non-ICU admissions significantly increased in patients with a food ($P = .04$) or unspecified trigger ($P = .01$) (Table I).

ICU admissions

Over the 10-year study period, 5.3% ($n = 3000$) of those seen in the ED for anaphylaxis were admitted to the ICU (Table E1, available in this article's Online Repository at www.jaci-inpractice.org). Proportions of patients admitted to the ICU increased by 27.4%, from 4.5% in 2005 to 5.8% of ED anaphylaxis visits in 2014 ($P = .001$). Of all triggers, anaphylaxis due to an unspecified trigger leading to ICU admissions increased the most (51.8%; $P < .001$). Proportions of those

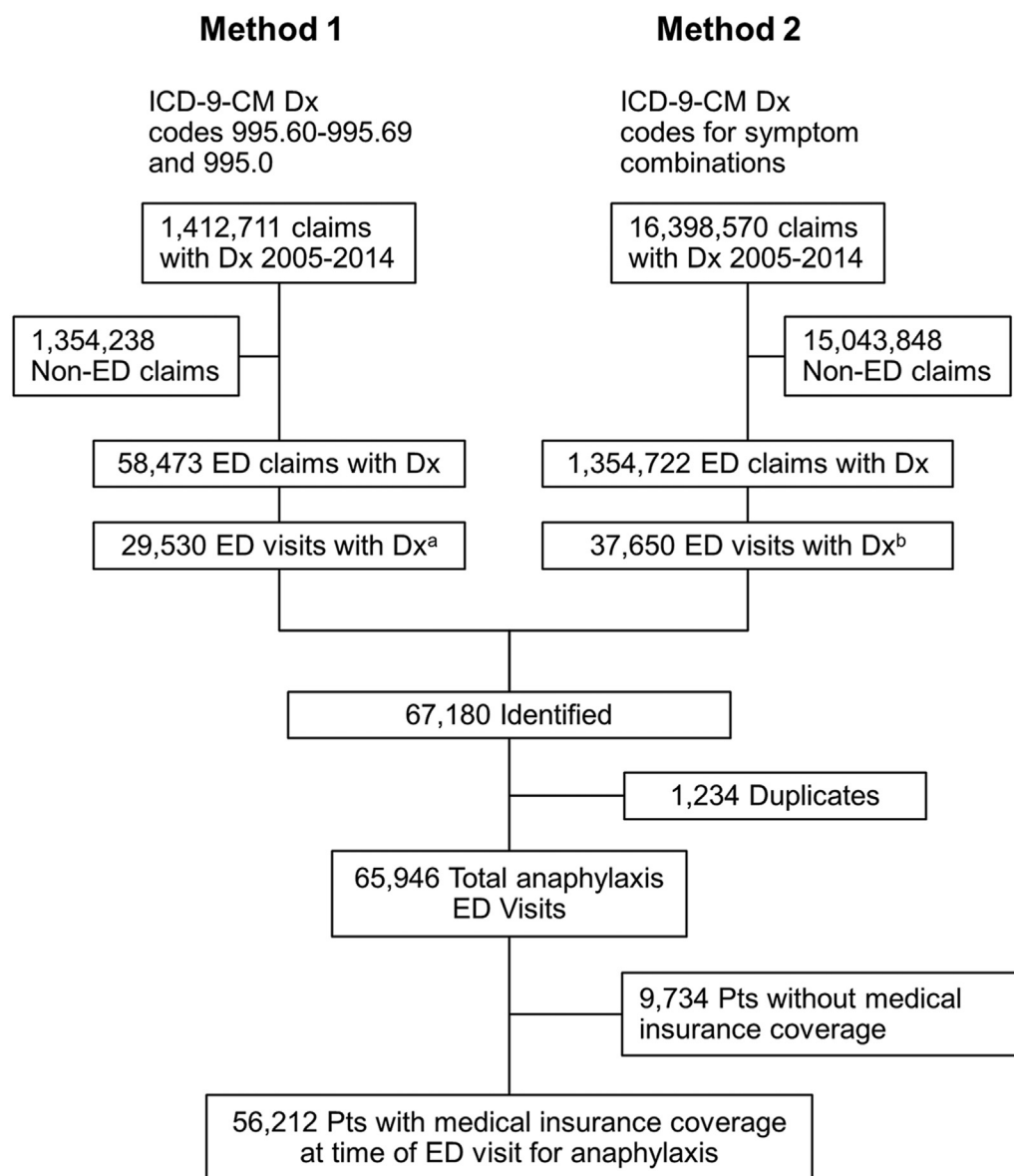


FIGURE 1. Flow chart of cohort identification. *Dx*, Diagnosis; *ED*, emergency department; *ICD-9-CM*, International Classification of Diseases, 9th Revision, Clinical Modification; *Pts*, patients. ^aMore than 1 claim can be associated with a single ED visit; of the 58,473 claims, only 29,530 represented unique visits. ^bMore than 1 claim can be associated with a single ED visit; of the 1,354,722 claims, only 37,650 represented unique visits. Adapted with permission from Motosue et al.⁸

admitted to the ICU due to medication related anaphylaxis increased by 20.3% between 2005 and 2014 ($P = .03$). A minority of cases admitted to the ICU was due to venom anaphylaxis, and proportions did not significantly change. The largest increase in ICU admissions was among patients aged 65 years or older (28.4%; $P = .003$) (Fig 3, B).

Endotracheal intubations

A total of 810 patients (1.4%) underwent endotracheal intubation during the study period (Table E1, available in this article's Online Repository at www.jaci-inpractice.org). Proportions of endotracheal intubations among those seen in the ED for anaphylaxis increased by 145.2% ($P < .001$), from

0.8% of ED anaphylaxis visits to 1.9% over the study period (Table 1). Proportions of endotracheal intubations increased for food-related anaphylaxis by 81.8% ($P = .003$), for medication-related anaphylaxis by 140.2% ($P = .009$), and for anaphylaxis due to an unspecified trigger by 188.0% ($P < .001$). In contrast, proportions of endotracheal intubations for venom-related anaphylaxis did not significantly change during the study time frame. Among the age groups, the proportion of patients requiring endotracheal intubations increased the most among older patients, with a 167.8% increase among patients aged 35 to 64 years ($P = .001$) and an 80.3% increase among patients aged 65 years or older ($P = .008$) (Fig 3, C).

TABLE I. Proportions of outcomes among ED anaphylaxis patients, 2005-2014

Category	Year*										P value	% change
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014		
Total ED visits												
ED discharge	82.25	79.06	78.14	78.63	75.90	76.40	75.84	76.42	76.04	76.04	.003	−7.5
ED observation/inpatient admission	13.20	16.73	17.56	16.69	18.26	18.09	18.72	17.70	18.16	18.17	.02	37.6
ICU admission	4.54	4.21	4.31	4.68	5.84	5.52	5.44	5.88	5.81	5.79	.001	27.4
Intubation	0.77	0.98	0.64	0.95	1.57	1.58	1.58	1.83	1.68	1.88	<.001	145.2
Age, y												
0-4	8.46	8.84	8.66	9.01	7.97	7.81	7.90	8.43	8.84	7.70	.21	−9.0
5-17	15.42	13.59	15.31	14.59	14.94	15.78	17.69	18.61	19.20	19.68	<.001	27.6
18-34	23.68	25.13	22.13	23.98	21.96	21.88	21.47	22.38	22.26	23.20	.15	−2.0
35-64	48.33	48.00	48.06	45.81	46.36	43.94	41.96	39.51	38.64	37.10	<.001	−23.2
≥65	4.12	4.43	5.85	6.61	8.78	10.59	10.99	11.08	11.07	12.34	<.001	199.7
Trigger												
Food	25.92	25.89	24.54	25.34	25.56	25.01	28.07	28.71	29.29	29.09	.005	12.2
Medication	6.53	8.96	14.40	14.97	14.60	13.76	12.92	12.09	10.48	10.20	.65	56.3
Venom	5.79	4.92	4.46	3.70	3.84	3.89	3.27	3.52	3.53	4.40	.03	−24.0
Unspecified	61.76	60.23	56.60	55.99	56.00	57.34	55.74	55.68	56.70	56.30	.028	−8.8
ED discharge												
Age, y												
0-4	87.92	81.72	81.89	79.25	78.52	77.23	75.56	76.95	80.47	79.03	.04	−10.1
5-17	88.40	85.77	81.96	86.91	80.90	83.62	82.15	83.46	84.30	83.32	.17	−5.7
18-34	87.89	85.28	86.03	87.04	85.31	85.60	84.70	86.43	85.76	86.26	.37	−1.9
35-64	78.91	75.82	76.01	75.89	74.66	75.94	74.91	75.10	73.58	74.00	.003	−6.2
≥65	54.48	53.04	50.19	47.94	47.98	47.92	52.10	48.64	47.18	49.51	.07	−9.1
Trigger												
Food	85.65	82.21	80.56	82.44	79.37	81.47	79.09	80.04	79.91	80.93	.04	−5.5
Medication	73.48	73.50	73.31	75.46	73.18	70.04	72.35	71.15	71.00	72.81	.10	−0.9
Venom	80.88	84.08	82.18	81.82	78.46	83.02	86.34	82.88	82.72	80.00	.92	−1.1
Unspecified	81.89	78.12	78.00	77.54	74.84	75.26	74.39	75.28	74.55	73.80	<.001	−9.9
ED observation/inpatient admission												
Age, y												
0-4	10.40	17.45	16.33	19.35	20.49	21.13	23.84	22.40	18.80	20.28	.03	94.9
5-17	10.50	13.33	16.60	11.94	17.52	15.22	17.04	15.29	14.21	15.80	.15	50.5
18-34	9.47	12.38	12.18	11.30	12.10	12.56	12.70	11.68	12.89	12.02	.11	26.9
35-64	15.45	18.67	18.93	18.70	19.78	19.27	20.18	19.32	21.11	21.22	.002	37.3
≥65	24.14	29.28	30.94	29.21	24.89	26.64	23.95	24.57	24.77	23.03	.07	−4.6
Trigger												
Food	11.28	15.61	16.65	14.67	18.17	16.34	18.58	17.25	17.52	16.64	.04	47.5
Medication	21.30	21.86	22.39	19.64	20.08	23.30	21.48	21.04	22.80	20.92	.82	−1.8
Venom	14.22	15.42	13.86	15.91	16.92	13.68	11.22	14.79	13.60	17.27	.95	21.5
Unspecified	13.06	16.55	17.01	16.87	17.92	17.90	18.60	17.40	17.91	18.53	.01	41.9
ICU admission												
Age, y												
0-4	1.68	0.83	1.79	1.40	0.99	1.64	0.61	0.65	0.73	0.69	.04	−58.7
5-17	1.11	0.90	1.44	1.15	1.58	1.16	0.81	1.25	1.49	0.88	.95	−20.3
18-34	2.64	2.34	1.80	1.66	2.60	1.84	2.60	1.90	1.34	1.73	.14	−34.6
35-64	5.64	5.51	5.06	5.41	5.56	4.80	4.90	5.58	5.31	4.78	.16	−15.2
≥65	21.38	17.68	18.87	22.86	27.13	25.43	23.95	26.79	28.05	27.46	.003	28.4
Trigger												
Food	3.07	2.18	2.79	2.90	2.46	2.20	2.33	2.72	2.57	2.43	.36	−20.8
Medication	5.22	4.65	4.29	4.91	6.74	6.66	6.17	7.81	6.20	6.28	.03	20.3
Venom	4.90	0.50	3.96	2.27	4.62	3.30	2.44	2.34	3.68	2.73	.81	−44.4
Unspecified	5.06	5.33	4.99	5.59	7.24	6.84	7.01	7.32	7.54	7.68	<.001	51.8

(continued)

TABLE I. (Continued)

	Year*										P value	% change
Category	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014		
Intubation												
Age, y												
0-4	0.34	0.55	0.00	0.23	0.00	0.23	0.00	0.00	0.00	0.17	.09	−50.0
5-17	0.18	0.00	0.14	0.14	0.13	0.35	0.09	0.22	0.27	0.00	.75	−100.0
18-34	0.84	0.49	0.20	0.18	0.81	0.40	0.37	0.43	0.18	0.23	.16	−72.6
35-64	0.59	1.17	0.74	1.05	1.06	1.21	1.10	1.56	1.78	1.58	.001	167.8
≥65	5.52	5.52	3.77	5.71	10.09	8.48	9.29	9.75	8.10	9.95	.008	80.3
Trigger												
Food	0.33	0.38	0.27	0.41	0.54	0.51	0.40	0.57	0.58	0.60	.003	81.8
Medication	0.87	0.55	0.92	0.56	1.75	0.93	1.23	1.47	1.49	2.09	.009	140.2
Venom	0.98	0.00	0.00	0.00	0.51	0.47	0.49	0.00	0.37	0.00	.46	−100.0
Unspecified	0.92	1.38	0.78	1.35	2.07	2.27	2.32	2.68	2.36	2.65	<.001	188.0

ED, Emergency department; ICU, intensive care unit.

*Values are percentage of anaphylaxis-related ED visits.

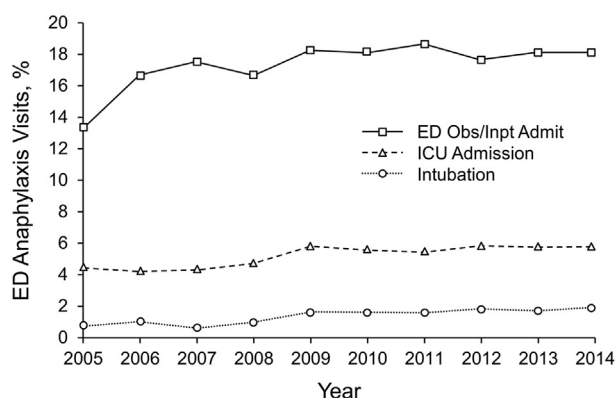


FIGURE 2. Proportions of outcomes among ED anaphylaxis visits (ED Obs/Inpt Admission $P = .02$, ICU Admission $P = .001$, Intubation $P \leq .001$). *Admit*, Admissions; *ED*, emergency department; *ICU*, intensive care unit; *Inpt*, inpatient; *Obs*, observation.

Sensitivity analysis

Over the study period, 810 patients seen in the ED for anaphylaxis underwent endotracheal intubation (Table E1, available in this article's Online Repository at www.jaci-inpractice.org). It is possible that some patients who had endotracheal intubation actually had angioedema secondary to an ACE inhibitor but may have met criteria for inclusion in the anaphylaxis cohort using Method 2. Therefore, we performed a sensitivity analysis of the data excluding 317 patients who were taking an ACE inhibitor within 90 days of the index event (Table E2, available in this article's Online Repository at www.jaci-inpractice.org). Multivariable analysis of the 493 remaining intubated patients led to similar findings, with an overall increasing trend in endotracheal intubations (116.7%, $P = .002$), a predominance among older patients (≥ 35 years), and the greatest rates among patients with an unspecified trigger. The increasing trend among medication-related anaphylaxis, however, was no longer significant ($P = .10$).

DISCUSSION

Over the 10-year study time frame, including more than 56,000 anaphylaxis-related ED visits, we found that the proportion of non-ICU admissions (patient observation/inpatient admissions) increased by 37.6%, the proportion of patients admitted to the ICU increased by 27.4%, and the proportion of patients undergoing endotracheal intubation increased by 145.2%.⁸ The increasing proportions of anaphylaxis-related observations/non-ICU admissions may be due to increased awareness of the diagnosis and greater guideline adherence for observation after an anaphylactic reaction.¹³ However, the increasing proportions of ICU admissions and endotracheal intubations suggest increasing anaphylaxis severity. Although the true prevalence of anaphylaxis is unknown, the trends reported here, in conjunction with prior studies⁴⁻⁸ demonstrating increasing overall anaphylaxis incidence, suggest that anaphylaxis is not as rare as previously thought,¹⁴ may be increasing in severity, and represents a condition that deserves increased attention.

In particular, we found significant trends of increasing proportions of ICU admissions and endotracheal intubations, particularly among patients aged 65 years and older and those with unspecified triggers or medication triggers. To date, few studies, if any, have examined time trends in proportions of anaphylaxis-related ICU admissions. Gibbison et al¹⁵ examined anaphylaxis-related admissions to critical care units in the United Kingdom and found that adult admissions nearly doubled from 2005 to 2009. Although anaphylaxis-related ICU admissions made up a small proportion of total critical care admissions, these findings may suggest increasing case severity. In our study, proportions of endotracheal intubations increased by 145%. To our knowledge, data regarding anaphylaxis-related endotracheal intubations are scarce and thus this represents novel data. Limited by claims data, we are unable to specify exactly why patients required intubation. However, given that proportions of intubations rose in older patients, particularly those aged 35-64 years and those 65 years and older, we suspect that comorbidities and impaired compensatory responses are likely contributing factors. Health care systems, in particular, should be aware of these trends, and efforts should be made to ensure adherence to critical care practices with current guideline recommendations.¹⁶⁻¹⁸

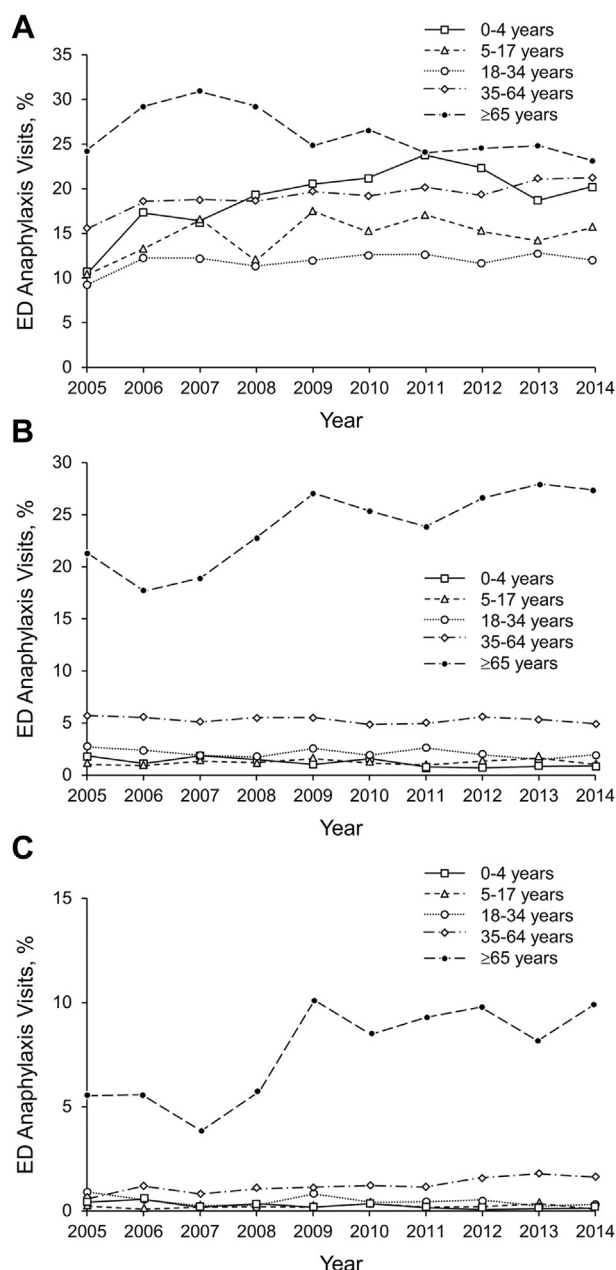


FIGURE 3. Outcomes stratified by age group. **A**, Observations/non-ICU admissions among ED anaphylaxis visits (0-4 years $P = .03$; 5-17 years $P = .15$; 18-34 years $P = .11$; 35-64 years $P = .002$; ≥ 65 years $P = .07$). **B**, ICU admissions among ED anaphylaxis visits (0-4 years $P = .04$; 5-17 years $P = .95$; 18-34 years $P = .14$; 35-64 years $P = .16$; ≥ 65 years $P = .003$). **C**, Endotracheal intubation among ED anaphylaxis visits (0-4 years $P = .09$; 5-17 years $P = .75$; 18-34 years $P = .16$; 35-64 years $P = .001$; ≥ 65 years $P = .008$). ED, Emergency department; ICU, intensive care unit.

In our study, the greatest increase in proportion of patients admitted to the ICU was among patients 65 years and older. Older age is considered a risk factor for fatal anaphylaxis.^{5,19} In older patients, the higher risk of severe and fatal anaphylaxis is frequently attributed to an impaired ability to tolerate anaphylaxis-related

complications including hypoxia, arrhythmias, and hypotension because of underlying cardiovascular or cerebrovascular disease.^{20,21} In addition, elderly patients may be taking cardiovascular medications including beta-blockers, which may increase anaphylaxis severity and decrease response to epinephrine.¹⁶

In addition, we found increasing proportions of patients admitted to the ICU and requiring endotracheal intubations among patients with medication-related anaphylaxis. Medication reactions are reported to be one of the most common causes of fatal anaphylaxis in the United States²² and elsewhere, including Australia,²³ New Zealand,²⁴ and the United Kingdom.²⁵ Medications have been associated with severe allergic reactions including cardiorespiratory compromise.^{19,26} Medications are unique in that related anaphylactic reactions can progress quickly. In a review of fatal anaphylactic reactions,²⁵ the median time to respiratory or cardiac arrest was 30 minutes for foods, 15 minutes for venom, and only 5 minutes for medication. Because antibiotics are a common culprit in many cases of medication-related anaphylaxis,²² adoption of a drug allergy educational program and antibiotic prescribing guideline, like the inpatient protocol published by Blumenthal et al,^{27,28} geared toward the outpatient setting may improve outcomes. Furthermore, studies examining the attitudes, knowledge, and practices regarding drug allergy among health care practitioners would be useful in identifying ways to optimize current management.

For venom-related anaphylaxis, proportions of ICU admissions did not significantly change, nor did endotracheal intubations during the study period. The reasons for these findings are unclear. However, venom-related anaphylaxis tends to be self-limited and is not a common diagnosis for admission. In one of the largest multicenter studies including 617 patients with allergic reactions to venom in the ED, 31% had anaphylaxis.²⁹ Most patients were discharged home, with only 3% admitted to the hospital.

In our study cohort, the majority of patients seen in the ED for anaphylaxis were discharged directly from the ED (77%). Most other patients were observed, either in an ED observation unit or in an inpatient hospital bed, or admitted to a non-ICU bed. Proportions of observation/inpatient admissions increased the greatest among the very young (0-4 years) (94.9%). This may reflect an increase in recognition, severity, and/or increasing adherence to guidelines that recommend observation after an ED visit for anaphylaxis.¹ Traditional biomarkers such as serum tryptase can often be unreliable,³⁰ and the clinical presentation of anaphylaxis in children can be as vague as increased irritability, drooling, or incontinence.³¹

Because anaphylaxis is often self-limited, a short period of observation is frequently needed. In an Australian study by Brown et al,³² 61% of patients with anaphylaxis were admitted to the observation unit, compared with 3% admitted to the general medical floor and 3% admitted to the ICU. ED observation units decrease cost and inpatient admissions and serve as a fitting venue for continued monitoring for many patients seen in the ED for anaphylaxis.³³ In addition, widespread implementation of ED observation unit protocols designed to facilitate the care of anaphylaxis patients, as was described in a study by Manivannan et al,³⁴ may be helpful. Many institutions have developed outpatient observation units as an alternative to short-stay inpatient admissions, with 36% of US EDs reporting having observation units in 2007.³⁵ In the current cohort, we could not determine whether the observation care was provided in an ED observation unit or in a

hospital bed. Because many studies of anaphylaxis have examined overall hospital admissions, future anaphylaxis studies may benefit from including time trends of ED observations.

There are several potential limitations of our study. First, we used administrative claims, and this methodology is susceptible to coding errors. We could not validate diagnoses with medical record review, and thus we cannot verify if all cases represent true anaphylaxis. Second, the trigger was unspecified in a substantial proportion of cases, so it is unclear whether the trigger remained unknown after evaluation or was not specified in the coding information. Third, in this study, we used hospital and ICU admissions as markers of severity. However, the decision to admit and where the patient is admitted to in the hospital depends not only on severity but also influenced by local practices, resource availability, and patient preference.³⁶ Fourth, cases from the Southern United States made up approximately 45% of the total cases, whereas only 15% were from the Northeast region of the United States, which reflects the OLDW geographic distribution. Because higher rates of anaphylaxis are associated with more northerly latitude,³⁷⁻³⁹ our rates of anaphylaxis could be an underestimate. Finally, as with most observational studies, we could not eliminate potential unmeasured confounders. Nonetheless, strengths of our study include a large sample size, the inclusion of multiple academic and nonacademic institutions across the United States, and rigorous methodology followed throughout, including selection and analysis of the cases. We also followed standardized guidelines for reporting observational studies.

In conclusion, our study comprehensively evaluated hospital-based health care utilization after an ED visit for anaphylaxis. The rising trends in the proportions of observation/hospital admission, ICU admissions, and endotracheal intubations among those seen in the ED for anaphylaxis would suggest an increase in anaphylaxis severity. Practitioners, patients, and the community need to be aware of these trends because responding to these increases will require a collaborative effort. Finally, research that continues to better characterize these trends is necessary to identify strategies to improve inpatient management, prevent hospitalizations, and direct the proper allocation of resources.

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This study is a re-examination of data presented in Motosue et al⁸ to focus on outcomes.

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TABLE E1. Outcomes of ED visits for anaphylaxis, 2005-2014*

Outcome	Year										Total (N = 56,212)
	2005 (n = 3,522)	2006 (n = 4,083)	2007 (n = 4,528)	2008 (n = 4,763)	2009 (n = 5,082)	2010 (n = 5,457)	2011 (n = 6,270)	2012 (n = 7,310)	2013 (n = 7,700)	2014 (n = 7,497)	
ED outcome											
ED discharge	2,897 (82.3)	3,228 (79.1)	3,538 (78.1)	3,745 (78.6)	3,857 (75.9)	4,169 (76.4)	4,755 (75.8)	5,586 (76.4)	5,855 (76.0)	5,701 (76.0)	43,331 (77.1)
ED observation/inpatient admission	465 (13.2)	683 (16.7)	795 (17.6)	795 (16.7)	928 (18.3)	987 (18.1)	1,174 (18.7)	1,294 (17.7)	1,398 (18.2)	1,362 (18.2)	9,881 (17.6)
ICU admission	160 (4.5)	172 (4.2)	195 (4.3)	223 (4.7)	297 (5.8)	301 (5.5)	341 (5.4)	430 (5.9)	447 (5.8)	434 (5.8)	3,000 (5.3)
Endotracheal intubation	27 (0.8)	40 (1.0)	29 (0.6)	45 (0.9)	80 (1.6)	86 (1.6)	99 (1.6)	134 (1.8)	129 (1.7)	141 (1.9)	810 (1.4)

ED, Emergency department; ICU, intensive care unit.

*Values are No. of ED visits (%).

TABLE E2. Rates of endotracheal intubation among ED anaphylaxis patients (excluding 317 patients with ACE inhibitor use within 90 days)

Category	Year*										P value	% change
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014		
Overall	0.54	0.76	0.53	0.57	0.94	0.95	0.88	1.00	0.91	1.17	.002	116.7
Age, y												
0-4	0.34	0.55	0.00	0.23	0.00	0.23	0.00	0.00	0.00	0.17	.09	-50.0
5-17	0.18	0.00	0.14	0.14	0.13	0.35	0.09	0.22	0.27	0.00	.76	-100.0
18-34	0.48	0.49	0.20	0.18	0.63	0.17	0.22	0.37	0.18	0.23	.21	-52.1
35-64	0.47	0.92	0.60	0.64	0.81	0.83	0.76	0.87	1.08	1.19	.007	153.2
≥65	3.45	3.31	3.02	2.86	4.71	4.50	4.50	4.81	3.64	5.41	.02	56.8
Trigger												
Food	0.22	0.38	0.27	0.25	0.38	0.37	0.28	0.52	0.40	0.50	.02	127.3
Medication	0.87	0.27	0.61	0.28	1.21	0.53	0.74	0.90	1.24	1.05	.10	20.7
Venom	0.49	0.00	0.00	0.00	0.51	0.47	0.49	0.00	0.37	0.00	.93	-100.0
Unspecified	0.64	1.06	0.66	0.82	1.16	1.34	1.23	1.33	1.15	1.63	.003	154.7

ACE, Angiotensin-converting enzyme; ED, emergency department.

*Values given as percentage of ED anaphylaxis visits.

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