

Increasing Emergency Department Visits for Anaphylaxis, 2005-2014



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What is already known about this topic? Anaphylaxis is a potentially life-threatening systemic allergic reaction that is frequently managed in the emergency department. Although estimates vary, recent studies suggest that the frequency of anaphylaxis is increasing.

What does this article add to our knowledge? This retrospective study using administrative claims data found that emergency department visits for anaphylaxis increased by 101% between 2005 and 2014 with a disproportionate increase among children.

How does this study impact current management guidelines? The findings of this study highlight that children represent a vulnerable patient population and additional studies are needed to optimize the diagnosis and management of anaphylaxis in young patients.

BACKGROUND: Anaphylaxis is a potentially life-threatening systemic allergic reaction. Studies suggest that the incidence of anaphylaxis is increasing; however, recent trends in emergency department (ED) visits for anaphylaxis in the United States have not been studied.

OBJECTIVE: To examine trends in the incidence and rates of anaphylaxis-related ED visits from 2005 through 2014.

METHODS: We retrospectively analyzed data from a national administrative claims database including commercially insured and Medicare Advantage patients. We identified all ED visits for anaphylaxis and calculated rates as number of anaphylaxis-related ED visits per 100,000 enrollees. Rates were compared over time and by age and trigger.

RESULTS: During the 10-year time period, 56,212 ED visits for anaphylaxis were identified. The median (interquartile range)

age was 36 (17-52 years) years, and 58% were female. Most cases (57%) were due to unspecified triggers, 27% were associated with food, 12% were medication related, and 4% were due to insect venom. The overall rate of anaphylaxis per 100,000 enrollees increased by 101%, from 14.2 in 2005 to 28.6 in 2014 ($P < .001$). Rates of ED visits for anaphylaxis increased in all age groups, but the greatest increase was in children aged 5 to 17 years (196% increase; $P < .001$). The rate of food-related anaphylaxis increased by 124% ($P < .001$), and the rate of medication-related anaphylaxis increased by 212% ($P < .001$). **CONCLUSIONS:** ED visits for anaphylaxis increased between 2005 and 2014. Increases in ED visits were greatest among children. © 2016 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;5:171-5)

Key words: Anaphylaxis; Emergency department; Epidemiology; Time trends

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Anaphylaxis is a potentially life-threatening acute systemic allergic reaction.¹ A study of emergency department (ED) visits for acute allergic reactions from 1993 to 2004 reported that the number of allergy-related ED visits remained relatively stable and represented about 1% of all ED visits.² Although estimates vary, recent studies suggest that the frequency of anaphylaxis is increasing.³⁻⁶ Rates of anaphylaxis fatalities, however, have not increased,^{4,5} and it remains unclear whether the incidence of anaphylaxis is truly increasing or whether apparently increasing rates are due to increased recognition, diagnosis, and coding of anaphylaxis.

Most cases of anaphylaxis are managed in the ED.⁷⁻⁹ Thus, the ED serves as a front line for the diagnosis and treatment of anaphylaxis and remains an important research setting in the study of anaphylaxis. To our knowledge, no recent studies have investigated the incidence of anaphylaxis-related ED visits. Furthermore, rates of ED visits for anaphylaxis may be a more accurate reflection of trends in the incidence of anaphylaxis than

Abbreviations used

ED- emergency department

ICD-9-CM- International Classification of Diseases, 9th Revision,
Clinical Modification

OLDW- OptumLabs Data Warehouse

studies of rates of hospitalizations due to anaphylaxis because the decision to admit a patient to a hospital is multifactorial. Thus, there is currently a gap in knowledge related to time trends of anaphylaxis-related ED visits in recent years.

The objective of our study was to evaluate contemporary trends in anaphylaxis rates by evaluating anaphylaxis-related ED visits from 2005 to 2014 using a large nationwide administrative claims database.

METHODS**Data source**

We performed a retrospective study using the OptumLabs Data Warehouse (OLDW), which includes administrative claims data for privately insured and Medicare Advantage enrollees in the United States.¹⁰ The database contains longitudinal health information for more than 100 million enrollees over the past 20 years, from geographically diverse regions across the United States, with greatest representation from the South and Midwest. The data cover several domains: enrollee information (insurance plan, sex, age, race/ethnicity, and dates of eligibility); pharmacy claims (prescribing physician, pharmacy, fill data, days of supply, and dosages); medical claims (including *International Classification of Diseases, 9th Revision, Clinical Modification* [ICD-9-CM] diagnosis codes, ICD-9-CM procedure codes, Current Procedural Terminology, Version 4 procedure codes, Healthcare Common Procedure Coding System procedure codes, site of service codes, standardized costs, and provider specialty codes); laboratory results (test name, Logical Observation Identifiers Names and Codes, and results); and socioeconomic characteristics (area income, net worth, and education).¹¹ This study involved analysis of preexisting, deidentified data and was deemed exempt from institutional review board approval. The study followed the guidelines of the RECORD (REporting of studies Conducted using Observational Routinely-collected health Data) statement.¹²

Study population

To identify the analytic cohort of ED visits for anaphylaxis from 2005 to 2014, we used 2 methods validated in a previous study (Harduar-Morano algorithm).¹³ Method 1 identified patients who had ICD-9-CM diagnosis codes for anaphylactic shock (995.60-995.69 and 995.0). Method 2 identified patients through a validated algorithm of ICD-9-CM codes of symptom combinations.¹³ ED visits for anaphylaxis were included in the cohort if the patient had at least 30 days of medical insurance coverage before the ED visit. Similarly, the denominator for rate calculations included patients with medical insurance coverage for at least 30 days in the given calendar year. ED visits identified by both methods were combined, and any duplicate visits were excluded.

Statistical analysis

Patient characteristics (age, sex, race, and census region) were described using median (interquartile range) or count (percentage), as appropriate. We calculated annual rates by using the number of ED visits for anaphylaxis as the numerator and the total enrollees as the denominator. Rates were expressed as the number of ED visits

for anaphylaxis per 100,000 enrollees. We performed linear regression analysis to assess for trends by year in anaphylaxis ED visits (number of anaphylaxis ED visits per 100,000 enrollees). All significance tests were 2-sided, and a *P* value of less than .05 was considered statistically significant. All statistical analyses were performed using SAS software version 9.3 (SAS Institute Inc., Cary, NC).

RESULTS

As shown in Figure 1, 65,946 unique ED visits for anaphylaxis between 2005 and 2014 were initially identified using method 1 or method 2 of the Harduar-Morano algorithm.¹³ After excluding patients without medical coverage, 56,212 ED visits for anaphylaxis were included in our analytic cohort. The median (interquartile range) age at the time of ED visit was 36 (17-52 years) years (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). Most anaphylaxis ED visits involved patients aged 35 to 64 years (42.8%), and most patients (57.5%) were female. The cohort was primarily from the South (44.5%), followed by the Midwest (24.7%), West (15.3%), and Northeast (15.1%). Most cases were caused by unidentified triggers (56.9%), 27.1% were associated with food, 12.0% were medication related, and 4.0% were due to insect venom.

The overall rate of anaphylaxis-related ED visits increased by 101% over the study period, from 14.2 per 100,000 enrollees in 2005 to 28.6 per 100,000 in 2014 (*P* < .001 for trend) (Table I; Figure 2). Detailed data by year are presented in Table E2 in this article's Online Repository at www.jaci-inpractice.org. Rates of anaphylaxis ED visits increased in all age groups, but the greatest increase was among children aged 5 to 17 years (196% increase, 11.9 per 100,000 enrollees in 2005 to 35.2 in 2014; *P* < .01 for trend) (Table I).

Over the 10-year study time frame, rates of food-related anaphylaxis increased by 124%, from 3.7 per 100,000 enrollees in 2005 to 8.3 in 2014 (*P* < .001 for trend) (Table I). Significant increases in rates of food-related anaphylaxis were seen among all age groups except those 65 years and older, with the highest rates of increase seen in patients aged 5 to 17 years (285% increase; *P* < .001 for trend) and 18 to 34 years (150% increase; *P* < .001 for trend). The rate of medication-related anaphylaxis increased by 212% over the study period, from 0.9 to 2.9 per 100,000 enrollees (*P* < .01 for trend) (Table I). Although the highest rate of medication-related anaphylaxis was among patients aged 65 years and older (5.7 per 100,000 enrollees in 2014), significant increases in rates of medication-related anaphylaxis over the 10-year time frame were seen among all age groups (Table E2). The highest rates of increase were seen in patients aged 0 to 4 years (479% increase; *P* = .02 for trend). Rates of insect venom-related anaphylaxis also significantly increased over the study period (0.8 per 100,000 enrollees in 2005 to 1.3 in 2015; *P* < .01 for trend) (Table I). Rates of unspecified anaphylaxis ED visits are presented stratified by age in Table E2.

DISCUSSION

In this study of more than 56,000 ED visits for anaphylaxis, we found a 101% increase in overall rates of anaphylaxis ED visits from 2005 through 2014. Furthermore, rates of ED visits for anaphylaxis increased in all age groups, with the greatest increases in children younger than 17 years and in those 65 years

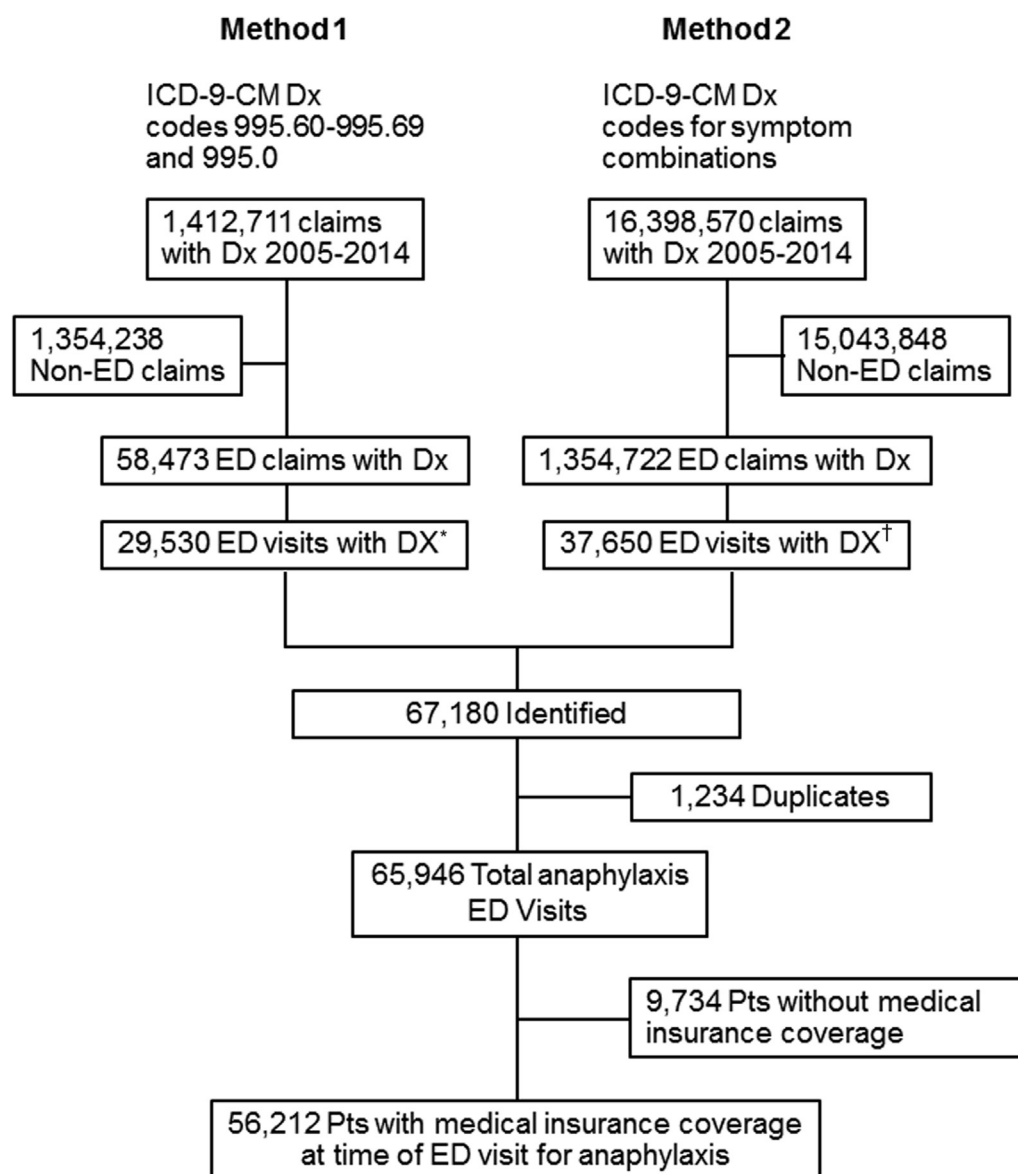


FIGURE 1. Flow chart of cohort identification. *Dx*, Diagnosis; *Pts*, patients. *More than 1 claim can be associated with a single ED visit; of the 58,473 claims, only 29,530 represented unique visits. †More than 1 claim can be associated with a single ED visit; of the 1,354,722 claims, only 37,650 represented unique visits.

and older. Rates of food-related anaphylaxis increased by 124%. The greatest increases in food-related anaphylaxis were observed in patients aged 5 to 17 years (285% increase).

The overall increase of 101% in ED visits during the study period is in contrast to the study published by Gaeta et al,² who did not find a significant change in ED visits for acute allergic reactions in the United States from 1993 to 2004. Because data presented in this study are reported rates, it is unclear whether our findings represent a true increase in the incidence of anaphylaxis or simply improved awareness and recognition of the diagnosis. However, the disproportionate increase in ED visits for pediatric and food-related anaphylaxis, in particular, mirrors the increasing rates of food allergy. According to the National Center for Health Statistics of the

Centers for Disease Control and Prevention, the incidence of food allergy in those younger than 18 years increased by 18% from 1997 to 2008.¹⁴ Currently, food allergies affect 5.9 million children (about 8%) in the United States, and more than 35% of these children have a history of severe reactions.¹⁵ In a study of the combined rates of ED visits and hospitalizations for food-related anaphylaxis in children in Illinois from 2008 to 2012, Dyer et al¹⁶ found that the rate of food-related ED visits and hospitalizations increased 29.3% annually, from 6.3 visits per 100,000 children in 2008 to 17.2 in 2012. This annual overall increase was higher than for non-food-related anaphylaxis, which increased by 23.6%.

During our 10-year study period, medication-related anaphylaxis increased by 212%. On further analysis of all ED

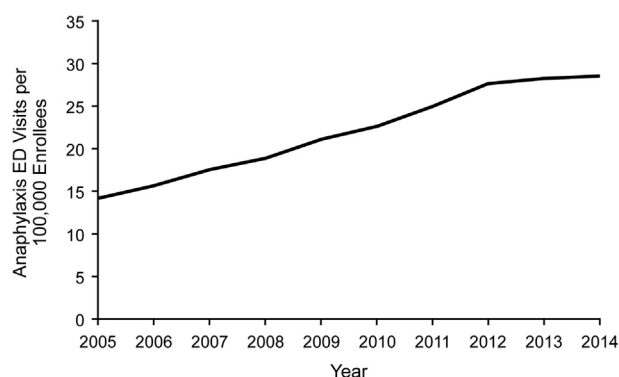
TABLE 1. Overall changes in rates of anaphylaxis ED visits, 2005-2014

Category	% Increase*	P value
All anaphylaxis ED visits	101.4	<.001
Outcome		
Discharge†	104.0	<.001
Inpatient admission	36.8	.14
ICU admission	165.6	<.001
Triggers		
Food	124.3	<.001
Medication	211.8	.009
Venom	58.5	.007
Unspecified	83.0	<.001
Age (y)		
0-4	129.8	<.001
5-17	195.8	<.001
18-34	97.7	<.001
35-64	63.8	<.001
≥65	130.5	<.001

ICU, Intensive care unit.

*Change from 2005 to 2014.

†Values represent all nonadmitted patients and include observation patients.

**FIGURE 2.** Overall rates of ED visits for anaphylaxis, 2005-2014.

visits for medication-related anaphylaxis, we found that rates were highest among patients who were female and older, consistent with previous studies.¹⁷⁻¹⁹ A recent study of fatal anaphylaxis in the United States demonstrated that medications were the most common cause of fatal anaphylaxis and that the rates of fatal medication-induced anaphylaxis were increasing over time and were associated with older age.²⁰ In our study, the rates of medication-related anaphylaxis increased the most among children 0 to 4 years (479% increase). This increase in medication-related anaphylaxis in children represents a novel finding. Although not specifically examined in this study, medication triggers in children include antibiotics such as penicillin, ibuprofen, and other antipyretics, along with neuromuscular blockers.²¹ Further study is needed for confirmation because drug hypersensitivity reactions in children can often be overreported by caregivers¹⁹ and confounded by other factors such as infections (eg, morbilliform rashes in patients with EBV infections treated with amoxicillin, or other common pediatric rashes).

As the disproportionate increase in anaphylaxis among children and infants suggests, these patients represent a vulnerable population. Our findings support those of other studies in Spain²² and Canada,²³ which reported rates of anaphylaxis in children aged 0 to 4 years as being 3 times greater than those among older age groups. This is concerning and further complicated in that the diagnosis of anaphylaxis in infants can be challenging. Unlike older children, infants cannot verbalize symptoms, and reactions often manifest with subtle symptoms such as irritability, clinging to caregiver, and incontinence. In addition, total mast cell tryptase, a serologic marker that can assist in the diagnosis of adult anaphylaxis, may be a less reliable marker in infants because it can be increased at baseline because of the mast cell burden that is commonly seen in an infant's developing immune system.²⁴

Anaphylaxis remains undertreated in general, and in infants it is no different. Fleischer et al²⁵ reported that only 29.9% of infants with severe anaphylaxis received epinephrine. Reasons for caregivers not administering epinephrine include epinephrine being unavailable, lack of recognition of anaphylaxis severity, and fears related to administering epinephrine. Going forward, continued biomarker research and increased efforts to improve anaphylaxis and epinephrine education of caregivers and the community will be important for addressing these issues.

Over the past decade, our understanding of the epidemiology of anaphylaxis has increased, in part through the accumulation of studies using large patient databases. Such studies rely heavily on the use of diagnostic codes, and the accuracy of these studies is dependent on the validity of those codes. In the current study, we used data that were not created or collected to answer the specific research question, and as with all studies that rely on administrative data, there is a potential for inaccuracies and lack of detail regarding individual diagnoses and codes. For example, a case of angioedema and urticaria may be diagnosed in the ED as anaphylaxis but may actually be a preluding presentation of chronic urticaria. Our methods would not be able to exclude such cases. Future efforts are needed to standardize protocols for ED-based diagnosis and management of anaphylaxis. Such standardization will not only improve ED management but also guide the refinement of diagnostic codes and improve the accuracy of future anaphylaxis epidemiology studies.

An additional limitation of our study is that most cases were from the Southern United States, with a minority in the Northeast region, which is a reflection of the geographic distribution of patients within OLDW. Previous studies^{26,27} suggest that higher rates of anaphylaxis are associated with geographic latitude such that Northeast regions have higher rates of anaphylaxis than do Southern areas, possibly related to sunlight exposure and vitamin D levels. Therefore, having most cases from the South may underestimate rates of anaphylaxis. In addition, a large subset of the cases did not have a specified trigger and, therefore, we are unable to be certain that the analysis of visits for specific triggers is fully reliable. These data might represent unknown triggers after evaluation or missing information on the triggers. Last, we could not eliminate the effects of unmeasured confounders. Despite these limitations, this study is, to our knowledge, the largest contemporary cohort study among US patients and includes a large range of visits to academic and nonacademic centers, which is closer to a "real-world" population. This factor was made possible by the large number of patients and data available in the OLDW data

set and is therefore generalizable to other commercially insured populations in the United States.

CONCLUSIONS

Our study demonstrates a 101% overall increase in ED visits for anaphylaxis from 2005 through 2014. Rates of anaphylaxis increased the most in children 5 to 17 years of age. This study provides recent trends in the rates of anaphylaxis-related ED visits in a diverse cohort of insured patients in the United States and provides further evidence of increasing incidence. Enhanced awareness of anaphylaxis prevention, diagnosis, and proper management is necessary, particularly for children and infants. Additional studies using large patient databases such as OLDW are important as we continue to provide a national perspective on the burden of anaphylaxis.

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

Characteristic	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)	
Age at ED visit (y)	36 (18.0-49.0)	36 (19.0-50.0)	37 (18.0-51.0)	36 (18.0-51.0)	38 (19.0-53.0)	38 (18.0-53.0)	37 (17.0-53.0)	35 (16.0-52.0)	34 (16.0-53.0)	34 (16.0-53.0)	36 (17.0-52.0)
Age (y)											
0-4	298 (8.5)	361 (8.8)	392 (8.7)	429 (9.0)	405 (8.0)	426 (7.8)	495 (7.9)	616 (8.4)	681 (8.8)	577 (7.7)	4,680 (8.3)
5-17	543 (15.4)	555 (13.6)	693 (15.3)	695 (14.6)	759 (14.9)	861 (15.8)	1,109 (17.7)	1,360 (18.6)	1,478 (19.2)	1,475 (19.7)	9,528 (17.0)
18-34	834 (23.7)	1,026 (25.1)	1,002 (22.1)	1,142 (24.0)	1,116 (22.0)	1,194 (21.9)	1,346 (21.5)	1,636 (22.4)	1,714 (22.3)	1,739 (23.2)	12,749 (22.7)
35-64	1,702 (48.3)	1,960 (48.0)	2,176 (48.1)	2,182 (45.8)	2,356 (46.4)	2,398 (43.9)	2,631 (42.0)	2,888 (39.5)	2,975 (38.6)	2,781 (37.1)	24,049 (42.8)
≥65	145 (4.1)	181 (4.4)	265 (5.9)	315 (6.6)	446 (8.8)	578 (10.6)	689 (11.0)	810 (11.1)	852 (11.1)	925 (12.3)	5,206 (9.3)
Female sex	1,958 (55.6)	2,287 (56.0)	2,652 (58.6)	2,806 (58.9)	3,006 (59.1)	3,128 (57.3)	3,700 (59.0)	4,195 (57.4)	4,380 (56.9)	4,235 (56.5)	32,347 (57.5)
Race											
Asian	99 (2.8)	120 (2.9)	126 (2.8)	102 (2.1)	122 (2.4)	157 (2.9)	199 (3.2)	210 (2.9)	246 (3.2)	223 (3.0)	1,604 (2.9)
Black	247 (7.0)	333 (8.2)	352 (7.8)	470 (9.9)	547 (10.8)	543 (10.0)	652 (10.4)	746 (10.2)	769 (10.0)	765 (10.2)	5,424 (9.6)
Hispanic	242 (6.9)	311 (7.6)	334 (7.4)	380 (8.0)	393 (7.7)	433 (7.9)	517 (8.2)	531 (7.3)	533 (6.9)	541 (7.2)	4,215 (7.5)
White	1,742 (49.5)	2,124 (52.0)	2,443 (54.0)	2,522 (52.9)	2,702 (53.2)	2,958 (54.2)	3,204 (51.1)	3,693 (50.5)	3,853 (50.0)	3,587 (47.8)	28,828 (51.3)
Unknown	1,192 (33.8)	1,195 (29.3)	1,273 (28.1)	1,289 (27.1)	1,318 (25.9)	1,366 (25.0)	1,698 (27.1)	2,130 (29.1)	2,299 (29.9)	2,381 (31.8)	16,141 (28.7)
Census region											
Midwest	856 (24.3)	957 (23.4)	1,055 (23.3)	1,103 (23.2)	1,251 (24.6)	1,311 (24.0)	1,545 (24.6)	1,901 (26.0)	1,977 (25.7)	1,907 (25.4)	13,863 (24.7)
Northeast	522 (14.8)	579 (14.2)	676 (14.9)	671 (14.1)	755 (14.9)	809 (14.8)	988 (15.8)	1,102 (15.1)	1,190 (15.5)	1,219 (16.3)	8,511 (15.1)
South	1,572 (44.6)	1,861 (45.6)	2,149 (47.5)	2,217 (46.5)	2,291 (45.1)	2,434 (44.6)	2,703 (43.1)	3,216 (44.0)	3,362 (43.7)	3,191 (42.6)	24,996 (44.5)
West	555 (15.8)	667 (16.3)	633 (14.0)	751 (15.8)	756 (14.9)	867 (15.9)	988 (15.8)	1,057 (14.5)	1,156 (15.0)	1,176 (15.7)	8,606 (15.3)
Other	17 (0.5)	19 (0.5)	15 (0.3)	21 (0.4)	29 (0.6)	36 (0.7)	46 (0.7)	34 (0.5)	15 (0.2)	4 (0.1)	236 (0.4)
Trigger											
Food	913 (25.9)	1,057 (25.9)	1,111 (24.5)	1,207 (25.3)	1,299 (25.6)	1,365 (25.0)	1,760 (28.1)	2,099 (28.7)	2,255 (29.3)	2,181 (29.1)	15,247 (27.1)
Medication	230 (6.5)	366 (9.0)	652 (14.4)	713 (15.0)	742 (14.6)	751 (13.8)	810 (12.9)	884 (12.1)	807 (10.5)	765 (10.2)	6,720 (12.0)
Venom	204 (5.8)	201 (4.9)	202 (4.5)	176 (3.7)	195 (3.8)	212 (3.9)	205 (3.3)	257 (3.5)	272 (3.5)	330 (4.4)	2,254 (4.0)
Unspecified	2,175 (61.8)	2,459 (60.2)	2,563 (56.6)	2,667 (56.0)	2,846 (56.0)	3,129 (57.3)	3,495 (55.7)	4,070 (55.7)	4,366 (56.7)	4,221 (56.3)	31,991 (56.9)

*Values are median (interquartile range) or no. of patients (%).

TABLE E2. Rates of anaphylaxis ED visits, 2005-2014

Category	Year*										P value	% Increase
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014		
All anaphylaxis ED visits	14.2	15.7	17.6	18.9	21.1	22.7	25.0	27.7	28.3	28.6	<.001	101.4
Outcome												
Discharge†	12.6	13.8	15.4	16.7	18.3	19.9	22.0	24.6	25.2	25.7	<.001	104.0
Inpatient admission	1.0	1.2	1.4	1.4	1.5	1.6	1.6	1.5	1.4	1.3	.14	36.8
ICU admission	0.6	0.7	0.8	0.9	1.2	1.3	1.4	1.6	1.6	1.7	<.001	165.6
Triggers												
Food	3.7	4.1	4.3	4.8	5.4	5.7	7.0	8.0	8.3	8.3	<.001	124.3
Medication	0.9	1.4	2.5	2.8	3.1	3.1	3.2	3.4	3.0	2.9	.009	211.8
Venom	0.8	0.8	0.8	0.7	0.8	0.9	0.8	1.0	1.0	1.3	.007	58.5
Unspecified	8.8	9.5	10.0	10.6	11.8	13.0	14.0	15.5	16.1	16.1	<.001	83.0
Sex												
Female	15.5	17.2	20.2	22.0	24.5	25.5	29.0	31.3	31.7	31.9	<.001	105.8
Male	12.8	14.1	14.8	15.8	17.5	19.8	20.9	24.1	24.9	25.2	<.001	96.9
Age (y)												
0-4	18.8	22.2	24.5	28.2	29.1	31.9	36.6	44.1	48.3	43.2	<.001	129.8
5-17	11.9	11.9	15.0	15.7	18.2	21.3	26.7	31.4	33.5	35.2	<.001	195.8
18-34	13.2	15.7	15.4	18.0	19.2	20.9	22.0	25.1	25.2	26.1	<.001	97.7
35-64	14.9	16.4	18.3	18.8	21.2	21.8	23.2	24.5	24.8	24.4	<.001	63.8
≥65	15.1	14.8	22.4	24.4	27.7	30.2	33.2	34.9	33.4	34.8	<.001	130.5
Food trigger	3.7	4.1	4.3	4.8	5.4	5.7	7.0	8.0	8.3	8.3	<.001	124.3
Sex												
Female	3.5	3.8	4.2	4.9	5.6	5.4	7.0	7.9	7.8	8.0	<.001	128.6
Male	3.9	4.4	4.4	4.7	5.2	6.0	7.1	8.0	8.8	8.6	<.001	120.5
Age (y)												
0-4	11.5	15.8	14.7	18.1	19.6	20.4	25.1	28.3	32.0	26.2	<.001	127.8
5-17	4.7	4.4	5.4	6.0	8.3	8.5	12.8	14.7	17.0	18.1	<.001	285.1
18-34	3.2	3.8	3.9	4.5	4.5	5.4	6.1	7.5	7.2	8.0	<.001	150.0
35-64	2.6	2.7	2.9	3.1	3.4	3.6	4.1	4.3	4.0	4.2	<.001	61.5
≥65	2.4	2.1	1.9	1.7	2.2	2.1	2.7	3.1	3.4	2.3	.07	-4.2
Medication trigger	0.9	1.4	2.5	2.8	3.1	3.1	3.2	3.4	3.0	2.9	.009	211.8
Sex												
Female	1.2	1.8	3.5	3.9	4.1	4.2	4.3	4.6	4.1	4.0	.008	233.3
Male	0.7	1.0	1.6	1.7	2.0	2.0	2.1	2.1	1.8	1.8	.01	160.9
Age (y)												
0-4	0.2	0.4	0.9	1.1	0.9	1.0	0.7	1.2	1.0	1.1	.02	478.9
5-17	0.5	0.5	1.3	1.0	1.3	1.3	1.7	1.5	1.5	1.2	.02	140.0
18-34	0.7	1.3	1.9	2.7	2.7	2.9	2.7	2.9	2.4	2.6	.01	256.2
35-64	1.2	1.9	3.3	3.4	3.7	3.5	3.7	3.8	3.5	3.3	.02	175.0
≥65	1.7	2.0	5.2	6.6	6.6	7.0	6.9	7.2	5.5	5.7	.04	235.3
Venom trigger	0.8	0.8	0.8	0.7	0.8	0.9	0.8	1.0	1.0	1.3	.007	58.5
Sex												
Female	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.7	0.8	0.9	.007	58.2
Male	1.1	1.0	1.0	0.8	1.0	1.2	1.0	1.3	1.3	1.7	.02	54.5
Age (y)												
0-4	0.3	0.5	0.4	0.4	0.6	0.0	0.7	0.6	0.3	0.5	.56	40.6
5-17	0.8	0.3	0.5	0.4	0.5	0.7	0.5	0.9	0.8	1.0	.06	26.6
18-34	0.4	0.4	0.5	0.5	0.5	0.8	0.5	0.7	0.6	0.7	.02	68.2
35-64	1.1	1.2	1.0	1.0	1.0	1.1	1.1	1.2	1.3	1.5	.07	36.4
≥65	0.7	0.6	1.1	0.7	1.6	1.0	1.2	1.2	1.7	2.3	.003	215.1
Unspecified trigger	8.8	9.5	10.0	10.6	11.8	13.0	14.0	15.5	16.1	16.1	<.001	83.0
Sex												
Female	10.3	11.2	11.9	12.6	14.2	15.4	17.1	18.1	19.0	19.0	<.001	84.5
Male	7.1	7.7	7.9	8.6	9.4	10.6	10.7	12.7	13.0	13.1	<.001	84.5

(continued)

TABLE E2. (Continued)

Category	Year*										P value	% Increase
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014		
Age (y)												
0-4	6.8	5.5	8.4	8.6	8.1	10.5	10.1	14.0	15.0	15.5	<.001	127.9
5-17	5.9	6.6	7.8	8.2	8.2	10.7	11.7	14.4	14.2	14.9	<.001	152.5
18-34	8.8	10.1	9.0	10.3	11.4	11.8	12.7	14.1	15.0	14.8	<.001	68.2
35-64	10.0	10.7	11.0	11.4	13.1	13.6	14.3	15.2	16.0	15.4	<.001	54.0
≥65	10.3	10.1	14.3	15.4	17.4	19.9	22.5	23.4	22.8	24.5	<.001	137.9

ICU, Intensive care unit.

*Values are no. of visits per 100,000 enrollees.

†Values represent all nonadmitted patients and include observation patients.

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