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A Population Based Epidemiological Study of Emergency Department Visits for Anaphylaxis in Florida

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Abstract

Background—Previous population-based analyses of emergency department (ED) visits for anaphylaxis have been limited to small populations in limited geographic areas, focused on children, or have included patients who had allergic conditions other than anaphylaxis. The objective of this study was to describe the epidemiology and risk factors among patients with anaphylaxis presenting to Florida EDs.

Methods—2751 patients with anaphylaxis were identified for 2005-2006 within ED records using the *International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM) and a validated ICD-9-CM based algorithm. Age and sex specific rates were calculated. Regression analyses were used to determine relative risks for anaphylaxis due to various triggers (food, venom, medication), and risk factors (age, gender, race, ethnicity).

Results—The highest observed rates were among the youngest males (8.2/100,000 Floridians age 0-4) and among adult females (15-54 years) grouped in 10-year age categories (9.9-10.9/100,000 Floridians). Males and Blacks were 20% and 25%, respectively, more likely to have a food trigger than females and Whites. Whites, males and older individuals were more likely to have an anaphylaxis ED visit due to insect stings. Venom-induced anaphylaxis was more likely in August-October. Children were less likely than those >70 years (referent) to have medication-induced anaphylaxis ($p < 0.03$).

Conclusion—This is the only ED based population study in a lower US latitude state. The overall rate is considerably lower than other US ED population-based studies. The rates of anaphylaxis by age groups were different by gender. Males and Blacks were more likely to have a food trigger.

Keywords

Anaphylaxis; epidemiology; emergency; ICD-9-CM

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Introduction

The epidemiology of ED visits for anaphylaxis in the US has not been adequately investigated. The one previous US population-based study of the epidemiology of anaphylaxis in the ED was carried out in Rochester, Minnesota in 1993 and described an incidence rate of 90/100,000 person years.¹ This study involved a small population which was racially homogeneous. These factors limit the ability to extrapolate these Minnesota-derived rates to other areas in the US. Other reports of anaphylaxis in an ED setting presented case-series or ED rates based on all ED visits and did not analyze the various risks factors associated with anaphylaxis treated in an ED.²⁻⁵ Furthermore, the incidence of anaphylaxis treated in an ED in a lower latitude US region has not been evaluated. Recent studies have suggested that there are differences in the burden of anaphylaxis which are dependent on the latitude of the region.⁶⁻⁸ Two large scale population-based studies of anaphylaxis have been previously conducted in Florida. One examined hospitalizations⁹ and the other examined mortality using death certificate data¹⁰. Because the majority of anaphylaxis cases are seen as outpatients in the ED, the present study addresses the gap in the epidemiologic knowledge of anaphylaxis in Florida by determining the age, race and gender incidences of anaphylaxis based on presentation in EDs. Finally, the use of a diagnostic algorithm for identifying anaphylaxis cases in conjunction with anaphylaxis specific ICD-9-CM codes yields a more accurate and complete case ascertainment methodology.

Methods

The methods used to obtain the dataset and create the variables used in this analysis have been previously reported.¹¹ A brief summary follows.

Source Population and Inclusion Criteria

ED data for 2005 and 2006 were obtained from the Florida Agency for Health Care Administration (AHCA), which collects clinical and demographic data on all individuals treated in non-federal Florida EDs. For each record AHCA permits the reporting of one primary diagnosis, nine secondary diagnoses (total of ten diagnosis fields), and three external injury codes (Ecodes) all of which were used in case identification.

Anaphylaxis cases were defined in one of two ways—*International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM) codes specific to anaphylactic shock [anaphylactic shock due to food (995.60-995.69) and other anaphylactic shock (995.0)] and a validated ICD-9-CM based diagnostic algorithm^{11,12}. Using the algorithm, anaphylaxis was identified if 1) respiratory compromise or skin-mucosal involvement was found in conjunction with shock due to anesthesia; 2) respiratory compromise or reduced blood pressure (BP) were found in conjunction with skin-mucosal involvement; or 3) a combination of two of the following: gastrointestinal symptoms, respiratory compromise, reduced BP, or skin/mucosal involvement were found in conjunction with a potential causal allergen or toxic exposure (e.g. venom, drugs, or biological substance).

Exclusion Criteria

A total of 3024 records of anaphylaxis were identified for the period 2005-2006 in Florida ED records; 1283 records from anaphylaxis specific ICD-9-CM codes and 1741 records obtained through use of the diagnostic algorithm.¹¹ Analysis was restricted to records of Florida residents; 254 non-resident records were excluded from analysis. Nineteen records were also excluded from the analysis when the envenomation, as determined through ICD-9-

CM code 989.5, was from an animal (E905.0 or E905.1) or plant (E905.6) whose venom is likely to produce signs and symptoms which result from venom toxicity (E905.2, E905.4, or E905.7) rather than anaphylaxis. There were 2751 records used in the analysis which met the inclusion and exclusion criteria.

Anaphylaxis Triggers

After case identification, variables were created for three common causes of anaphylaxis based on ICD-9-CM codes and Ecodes located in any of the diagnostic fields available: food (693.1, 995.60-995.69, 995.7), medication (693.0, 995.2, 995.4, E930-E930.9, E931-E931.9), and hymenoptera insect venom (E905.3, E905.5). The ICD-9-CM code 989.5 is often used to identify patients with hymenoptera insect stings.^{13,14} Therefore anaphylaxis patients with this code were also classified as having a venom trigger.

Demographic Factors

The demographic factors examined were age, race, ethnicity, and gender. The principal payer was used as a proxy for patients' socioeconomic status and was defined as commercial insurance, governmental insurance, and no insurance. Commercial insurance carriers were non-Medicaid HMOs and preferred provider organizations. Governmental insurance carriers included Medicare, Medicaid, Department of Veteran Affairs, and government sponsored health care plans. Patients whose principal payer was through charity, self-pay, or other were categorized as having no insurance.

Calculation of ED Visit Rates

Age and sex specific incidence rates for patients treated in Florida EDs were calculated by dividing the appropriate number of anaphylaxis cases by the sum of the stratum-specific Florida population estimates for 2005 and 2006. Population estimates were obtained from the Florida Legislature's Office of Economic and Demographic Research.¹⁵ The chi-square test for linear trend in proportions was calculated for both the male and female rates using SAS software (SAS Institute, Inc, Cary, NC). Age-adjusted rates stratified by sex were calculated using the direct method with the 2000 US standard population as the weighting factor.¹⁶ In addition, the proportion of anaphylaxis cases by month was compared with the proportion of monthly ED visits by Floridians using the chi-square goodness of fit test.¹⁷ An alpha level of 0.05 was used for all calculations. The case fatality rate was calculated as the number of anaphylaxis deaths divided by the number of anaphylaxis cases multiplied by 100.

Regression Analysis

In order to examine anaphylaxis in the general Florida population a regression analysis using all anaphylaxis cases was done. For regression purposes, non-cases were comprised of the Florida population estimate for 2005 and 2006 minus the total anaphylactic cases. An age-gender interaction was found. Therefore stratified results for this model are presented. Anaphylactic triggers were examined within the population of ED treated anaphylaxis cases. Potential risk factors included the demographic variables: age, race, ethnicity, gender, and primary payer, which was used as a proxy for socio-economic status. For each of the outcome variables a saturated model as well as a model for each individual risk factor was created.

The GENMOD procedure in SAS was used to create all regression models. The model examining anaphylaxis in the general population had a log link and binomial distribution. Due to the clustering of patients in EDs, generalized estimating equations were used to account for the potentially correlated outcome data in the anaphylaxis trigger models.^{18,19}

The generalized estimating equations models had a log link, binomial distribution, and an exchangeable correlation structure. All regression models produced a relative risk (RR) and a corresponding 95 percent confidence interval (CI). A RR was considered statistically significant if the confidence interval excluded one.

Results

Descriptive Epidemiology for Anaphylaxis Treated in Florida EDs

The total number of ED anaphylaxis cases identified among male and female Floridians during 2005 and 2006 was 1173 and 1578, respectively. This resulted in an age-adjusted incidence rate for males of 6.6/100,000 male Floridians/year (95% CI=2.8-10.4) and of 8.7/100,000 female Floridians/year (95% CI=4.3-13.0) for females. The demographic composition of individuals identified with anaphylaxis (Table 1) was slightly different from the general Florida population. Among males the highest ED anaphylaxis incidence rate was among children, ages 0 to 4 years, with a rate of 8.2/100,000 (95% CI=6.5-9.9) (Table 2). For females the highest incidence rate, 10.9/100,000 (95% CI=9.5-12.2), was among individuals age 25 to 34 years.

Three individuals admitted to the ED with anaphylaxis died. The ED case fatality rate was 0.11 percent. An anaphylactic trigger was not identified in any of these cases.

An anaphylactic trigger was identified in 37 percent (1016) of cases. Males were more likely than females to have an identified trigger ($p<0.001$). The most common trigger identified was food (497, 49%) followed by venomous insect stings (291, 29%) and medication (228, 22%) (Figure 1). Table E1 contains a breakdown of the specific triggers for food. The most common trigger for women (ages 0-70) was food (Table 3). Food was also the most common trigger for males ages 0-30 only, with venom as the most common trigger among those males older than 30. Among older females (>70 years) medication-induced anaphylaxis was most often identified as the trigger.

The distribution by month of ED visits due to anaphylaxis differs from the overall monthly distribution of ED visits ($p=0.0002$). However, when venom-induced anaphylactic cases are removed from the analysis, the difference in the two distributions is no longer statistically significant ($p=0.1$). The rate of venom anaphylaxis from July through September (4.29/100,000 ED visits) is greater than that of any of the other quarters (Table 4). The highest proportion of venom-induced anaphylaxis cases occurred in August (14%), September (16%) and October (12%) (Figure 1). Compared to the overall monthly distribution of ED visits, no statistically significant difference was found in the monthly anaphylaxis distributions for medication-induced ($p=0.4$), food-induced ($p=0.2$), or trigger unknown ($p=0.1$).

Predictors of ED Treatment for Anaphylaxis

The stratified results of the regression model examining anaphylaxis in the general Florida population are presented in Table 5. Among males, Blacks were less likely than Whites to have been treated for anaphylaxis in the ED (RR=0.8, $p=0.003$). This difference was not seen among females (RR=1.0, $p=0.9$). Young adult females age 18-30 were twice as likely to be treated for anaphylaxis as females age 71 years or older ($p<0.0001$) and 1.6 times as likely as female children age 0-17 ($p<0.0001$). For males less than 71 years, no difference in RRs were seen among various age groups.

Multivariate modeling results for anaphylaxis due to food compared to all anaphylaxis ED cases are presented in Table 6. The RR in the multivariate model were slightly closer to the null (RR =1) than in the crude analysis (data not shown). However, neither the direction of

the RR nor the p-value changed. There was a decreasing trend for age with pediatric patients having the greatest RR of food-induced anaphylaxis compared to the referent group of age 71 or older (RR=3.1, $p<0.0001$). Males were 20 percent more likely than females to be diagnosed with anaphylaxis with an accompanying food trigger ($p=0.01$). Race was also a statistically significant factor for food-induced anaphylaxis. Black patients were 25 percent more likely to be identified with food related anaphylaxis than White patients ($p=0.02$). Finally, individuals who used commercial insurance were more likely to be identified with food related anaphylaxis than those who used governmental insurance (RR=1.3, $p=0.008$).

Among all anaphylaxis cases, the results of the multivariate modeling for anaphylaxis due to venom can be found in Table 6. In general, the results of the multivariate model were very similar to the crude results (data not shown). Blacks are 0.4 times as likely as Whites to be identified as having anaphylaxis due to an insect sting(s). Males are almost two and half times as likely as females to be diagnosed with venom-induced anaphylaxis ($p<0.0001$). In addition, children are 0.5 times as likely as adults ages 30 to 70 years to present with venom-induced anaphylaxis ($p<0.0001$).

Table 6 also presents the results of multivariate models for anaphylaxis due to medication compared to all anaphylaxis cases. There was no difference between the crude RR (data not shown) and the multivariate results. Pediatric patients are 0.5 times as likely as patients age 71 or older to present with medication-induced anaphylaxis ($p=0.03$). Black patients are less likely than White patients to have anaphylaxis related to medication (RR=0.7, $p=0.03$). Males are 0.6 times as likely as females to be treated in the ED with medication-induced anaphylaxis ($p<0.0001$).

Discussion

A substantial portion of the existing data on the epidemiology of anaphylaxis has come from investigations that have limited-scope population sources, such as surveys^{20,21} and volunteer registries²²⁻²⁴. Further data have come from descriptive epidemiologic studies of anaphylaxis that have been conducted at specific practice venues, such as local health care settings^{2,4}. Our analysis is the only study of a large, diverse population with anaphylaxis diagnosed in EDs that includes rigorous descriptive and analytical evaluation of risk factors, such as gender, race, ethnicity and age.

Population-based studies of anaphylaxis ED visits are rare in the US. Only one such study has been conducted. That study identified anaphylaxis cases treated in an ED over a four month period in Rochester, Minnesota in 1993 through medical record review. An incidence rate of 90/100,000 persons was found. This incidence rate is most likely an overestimation as the study was conducted during the four months of summer when the vast majority of cases presented to the ED and extrapolated to estimate an annual incidence rate.²⁵ Racial differences among anaphylaxis patients were not assessed in the Rochester community, which is almost entirely of European origin. Additionally, in that brief report the investigators did not assess risk factors such as age, gender, or anaphylactic trigger. This Florida based ED study found an age-adjusted incidence rate for anaphylaxis of 7.6 ED visits/100,000 Floridians/year.¹¹ The Florida ED results were considerably lower than the results found in Minnesota. This may be due in part to the case finding methods. Another possible factor would be the north-south gradient identified in previous literature, where populations in higher latitudes were noted to have a higher rate of anaphylaxis than those in lower latitudes.⁶⁻⁸ This difference is not well understood. Prior studies examining this gradient have hypothesized that the differences may be due in part to vitamin D blood concentrations.^{6,26} Worldwide, two prior studies (both in lower latitude Brisbane) exclusively examining anaphylaxis ED visits presented population-based incidence rates.

Both studies were conducted in one ED in Brisbane, Australia. A population-based incidence rate of 26.8/100,000/year for children (<16 years)⁵ and 29.3/100,000/year for adults (>12 years)³ was estimated. As with the Rochester study, the differences in rates between the Brisbane studies and Florida may in part be due to the case identification methodology and exposure to different anaphylactic triggers. Neither these Australian studies nor the Rochester study provided population-based incidence rates or formal statistical comparisons of anaphylactic triggers stratified by race, gender or age group. Finally, hospitalization rates for anaphylaxis have been compared for New York State and Florida²⁶. Children were more likely to be hospitalized with anaphylaxis in New York than in Florida. This observation is consistent with the hypothesis that higher latitude is associated with a higher prevalence of anaphylaxis. However, adults were *less* likely to be hospitalized for anaphylaxis in New York than in Florida. This suggests that the factor(s) which might be responsible for the different anaphylaxis prevalence in higher and lower latitudes are more complex than simply differences in sun exposure and generation of vitamin D in the skin.

The higher incidence rate of anaphylaxis seen in the summer months in the present Florida based ED study is consistent with previously reported data on monthly changes in anaphylaxis rates in Olmsted County, Minnesota,²⁵ and were also consistent with incidence rates for people who were hospitalized or who died from anaphylaxis in Florida.^{10,27} As shown in our study, the seasonality of anaphylactic cases is driven purely by *Hymenoptera* insect stings. This finding was also seen in Olmsted County.²⁵ Increased awareness of the dangers of insect stings by individuals most at risk (White males >30 years of age) may lower the incidence of associated anaphylaxis presenting to the EDs.

This is the first ED study to examine the effect of race/ethnicity on anaphylaxis and anaphylactic triggers. In this study, Hispanics and Black males were less likely to be treated in the ED compared with non-Hispanics and White males, respectively. Blacks were also more likely to present with food-induced anaphylaxis than Whites and less likely to present with anaphylaxis triggered by venom or medications. Very few studies are available regarding the effect of race/ethnicity on anaphylaxis presentation but results from these studies also indicate a racial/ethnic difference.^{9,10,28,29} This disparity may be due to differences in cultural and economic factors among different racial and ethnic groups. Further analyses of racial/ethnic subgroups are required to determine the most important underlying causes.

Rates of medication-induced anaphylaxis were higher among adults than among children in this study. Reviews of anaphylaxis studies report that medication-induced reactions are seen more often in adults³⁰ and self-reported antibiotic allergy prevalence increases with increasing age³¹. There have been no previous population-based studies that rigorously assessed and determined the relationship of age-stratification to medication-induced anaphylaxis in ED patients. A South Carolina study, which computed pediatric rates, is the only other population-based ED study to provide age-specific ED rates for medication-induced anaphylaxis.³² The study found, using an ICD-9-CM drug-related algorithm, a medication-induced anaphylaxis rate of 1.6/100,000 among children age 0-18/year. However, as identified through medical record abstraction many of the cases were non-drug related. The authors indicate that the real rate is somewhere between the medical record abstraction rate (0.5/100,000 children/year) and the ICD-9-CM drug-related algorithm rate. These rates are slightly higher than the Florida ED study which found a rate of 0.3/100,000 among children age 0-17/year. It is important to note that the South Carolina study examined children as a group and did not assess the included age groups individually as was done in the present Florida ED study (Table 2-3).

The importance of multiple data sources for assessing the population burden of anaphylaxis has been emphasized previously.³³ Two prior studies have been conducted examining anaphylaxis among Florida residents using data sources other than ED records. The first study assessed patient hospitalizations due to anaphylaxis during 2001. An incidence rate of 2.8/100,000 Floridians/year was found basing case ascertainment on identification by ICD-9-CM codes specific to anaphylaxis⁹. This rate may be an underestimate as use of the ICD-9-CM codes alone may miss a significant portion of anaphylactic cases. Additionally, the authors only used the primary diagnosis to identify anaphylaxis patients, a search strategy that has been used by previous investigators³⁴. If the ICD-9-CM algorithm had been used, the incidence rate of anaphylaxis would have been 4.7/100,000 Floridians/year (personal communication Zuber Mulla, data obtained using the anaphylaxis algorithm⁹). The second study assessed deaths due to anaphylaxis from 1996-2005¹⁰. It reported an annual death rate of 0.05/100,000 Floridians/year based on a manual review of death certificates. Data from both of these studies (incidence rates and average number of yearly anaphylaxis hospitalizations and deaths), in addition to the present ED data, provides an estimated anaphylaxis rate of 12.4/100,000 Floridians/year with a case fatality rate for anaphylaxis in Florida of 0.42 percent. This case fatality rate estimate is similar to estimates seen in prior studies.³⁵ However, neither estimate (incidence rate or case fatality rate) takes into account that many cases of anaphylaxis are not severe enough to prompt an ED visit and thus are not included in this Florida estimate. This limitation is present in prior studies as well. If we assume that the proportion of non-severe anaphylaxis cases can be estimated as an additional 20-30 percent of all anaphylaxis cases (estimate based on previous studies)^{36,37} then the rate of anaphylaxis would range from 15.5-17.7/100,000 Floridians/year with a case fatality rate of 0.29-0.34 percent. Of note, the large number of cases found within the ED highlights this important data source. These findings support the use of multiple data sources for the determination of an accurate anaphylaxis case fatality rate and an accurate incidence rate.

In contrast to hospitalizations⁹ and deaths¹⁰ from anaphylaxis, we report that ED visits for anaphylaxis is more common in younger individuals. Females were more likely to be treated for anaphylaxis in the ED while there is no gender difference among individuals hospitalized for anaphylaxis nor among those who die from anaphylaxis in Florida. Blacks were less likely to be treated in the ED for anaphylaxis while there was no racial differences found among patients who died¹⁰ or who were hospitalized for anaphylaxis⁹. Comparing hospitalizations⁹ and ED visits, venom was the most common anaphylactic trigger identified in Florida hospitals⁹ while food-induced anaphylaxis was seen most frequently in Florida EDs (Table 7).

Both prior Florida studies reported an increase in hospitalizations and deaths from anaphylaxis with increasing age.^{9,10} This is in contrast to the ED data which identified decreasing age-specific ED visits rates with increasing age. One possible explanation for these contrasting findings is that older individuals, who may have more comorbid conditions, are less able to tolerate anaphylaxis and therefore are more likely to require hospitalization and/or die. Additionally, it is possible that the first identification of an anaphylaxis food trigger occurs in childhood with subsequent awareness of personal risk factors resulting in avoidance behaviors.

The Florida based ED study is unique in the fact that it utilizes all ED visits from a large, diverse population (~18 million), providing for the estimate of anaphylactic ED visits per unit of population and allowing for the statistical analysis of racial subpopulations. Additionally, this is the only population-based epidemiological study of ED anaphylaxis to calculate the relative risk of anaphylaxis on the basis of race, gender, and anaphylactic trigger. Rates determined in the Florida study are particularly inclusive and robust because two methods were used (ICD-9CM coding and a diagnostic algorithm) for case

ascertainment. Without the addition of the algorithm, 1602 cases (58%) of anaphylaxis patients would not have been identified.¹¹ The current study is the only epidemiological study of ED anaphylaxis at a lower US latitude and is one of a handful internationally at approximately the same latitude. Finally, the ED study complements the prior population-based studies of anaphylactic death¹⁰ and hospitalizations for anaphylaxis⁹ conducted in Florida.

A weakness of this study was the large proportion (67%) of anaphylactic cases without a known trigger. This is also a weakness of non-ED anaphylaxis studies even when a medical records review is conducted.^{25,36} The demographic description of individuals with unknown triggers has not previously been reported. Within this Florida based ED study the distribution of cases with an unknown trigger varied by age and gender, with triggers identified least often in elderly females. It is unclear how the differential bias (i.e. a different magnitude of bias for each demographic subgroup) of anaphylactic cases with unknown triggers may affect currently reported risk factors for anaphylaxis. For instance, within this ED study, if we were able to identify the trigger for 141 anaphylaxis cases among females with previously unknown triggers and 50 percent of these newly identified cases were food-induced then males would no longer have an increased statistically significant crude RR for food-induced anaphylaxis compared with females. The new RR would be 0.99 (95%CI=0.88-1.12).

A further weakness of this study was the inability to determine the accuracy of the coding through medical record review. The data used in the study were based on coding performed by physicians who may not be experts in the diagnosis of anaphylaxis. The addition of the diagnostic algorithm compensates for the undercoding of anaphylaxis. A weakness of the case ascertainment used in this analysis was the omission of ICD-9-CM 999.4 (anaphylactic shock due to serum). However, by not including this code only one case was omitted. In addition it is not known how often ICD-9-CM code 989.5 is used to identify patients with anaphylaxis related to hymenoptera insect stings. For this reason it is not possible to determine to what degree the estimates related to Hymenoptera anaphylaxis are biased.

This large (~18 million) population-based ED study of anaphylaxis in Florida has demonstrated that age related incidences differ by sex. Males were found to be more likely than females to have an identified trigger. An effect of race was seen among the identified triggers. Blacks were more likely to be seen in the ED with food-induced anaphylaxis while Whites were more likely to be seen with medication- and venom-induced anaphylaxis. Children were less likely to be treated for medication-induced anaphylaxis which was most common in the oldest group (>70 years). The seasonal variation in anaphylaxis ED presentation was due to venom and venom-induced anaphylaxis was most common in August, September, and October. No previous report has documented these relationships.

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Abbreviations

ICD-9-CM	<i>International Classification of Disease, Ninth Revision Clinical Modification</i>
NIAID/FAAN	National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network
AHCA	Agency for Health Care Administration
BP	Blood pressure
CI	Confidence Interval
ED	Emergency Department
Ecodes	External Cause of Injury Codes

Clinical Implications

Florida emergency department anaphylactic patients were identified for 2005-2006 by anaphylaxis ICD-9-CM codes and through an ICD-9-CM based anaphylactic algorithm. Age-adjusted ED visits = 6.6/100,000 males/year and 8.7/100,000 females/year.

Capsule Summary

In this southern US population-based ED study, anaphylaxis rates differed by age and gender. Food triggers were more common among males and Blacks; venom triggers among Whites, males and elderly; medication triggers among older individuals.

Figure 1. Proportion of anaphylaxis ED visits by month and type of trigger for the years 2005-2006 (n=2751).
Caption: Compared to the overall monthly distribution of ED visits, a statistically significant difference was found only for venom-induced anaphylaxis ($p < 0.001$).

Table 1
Demographic characteristics of patients treated for anaphylactic shock in Florida emergency departments compared to the population of Florida (2005-2006)

Type of Case Definition					
	Anaphylaxis Cases (n = 2751)		Florida Population (n = 36,459,197)		p-value
	Number	(Percentage)	Number	(Percentage)	
Age in years *	38.7	(21.46)	39.8	(0.06)	0.96
Male	1173	(43)	17,840,284	(49)	< 0.0001
Female	1578	(57)	18,618,913	(51)	
White	2190	(80)	29,491,578	(81)	0.04
Black	436	(16)	5,973,489	(16)	
Other	96	(4)	994,130	(3)	
Hispanic	391	(14)	7,126,462	(20)	< 0.0001
Non-Hispanic	2331	(86)	29,332,735	(80)	

* Reported mean (standard deviation) used z-test. Florida population mean age estimate obtained from the 2006 US Census Bureau American Community Survey.

Table 2
Age specific rates and 95% confidence intervals of Florida residents treated in Florida
EDs for anaphylactic shock for the years 2005-2006 (n=2,751)*

Age group	Males	Females
	Rate/100,000 (95% CI)	Rate/100,000 (95% CI)
0 to 4	8.2 (6.5, 9.9)	6.2 (4.7, 7.7)
5 to 14	5.9 (4.9, 6.9)	5.3 (4.4, 6.3)
15 to 24	6.2 (5.2, 7.2)	10.4 (9.1, 11.7)
25 to 34	6.7 (5.6, 7.8)	10.9 (9.5, 12.2)
35 to 44	7.6 (6.5, 8.6)	9.9 (8.7, 11.1)
45 to 54	6.6 (5.5, 7.6)	10.7 (9.5, 12)
55 to 64	6.8 (5.6, 7.9)	7.8 (6.6, 9.0)
65 to 74	6.7 (5.3, 8.0)	8.0 (6.6, 9.4)
75 to 84	5.0 (3.7, 6.4)	4.7 (3.6, 5.9)
85 plus	3.2 (1.2, 5.2)	4.0 (2.3, 5.7)

* Rates were calculated using the age and gender specific Florida population for the years reported. Note that distribution for males is monotonic decreasing while the distribution for females is concave up. The two distributions are significantly different ($p < 0.0001$).

Table 3
Number and percentage of anaphylactic cases with an identified trigger treated in Florida EDs stratified by trigger type, age group, and sex, 2005-2006

All identified triggers (n=1016)		Food (n=497)		Venom (n=291)		Medication (n=228)	
Male	Number (Row Percent)*	Number	(Row Percent)	Number	(Row Percent)	Number	(Row Percent)
0-17	128 (46)	99 (77)	17 (13)	12 (9)			
18-30	89 (45)	50 (56)	28 (31)	11 (12)			
31-70	248 (41)	85 (34)	124 (50)	39 (16)			
71+	28 (31)	7 (25)	16 (57)	5 (18)			
Total	493 (42)	241 (49)	185 (38)	67 (14)			
Female							
0-17	96 (37)	72 (75)	11 (11)	13 (14)			
18-30	100 (33)	49 (49)	22 (22)	29 (29)			
31-70	292 (33)	127 (43)	64 (22)	101 (35)			
71+	35 (27)	8 (23)	9 (26)	18 (51)			
Total	523 (33)	256 (49)	106 (20)	161 (31)			

* Percentage of total anaphylactic cases with an identified trigger. Note only 37% (1016/2751) of cases had an identified trigger. A greater proportion of males age <71 years have an identified trigger compared to females <71 years (p<0.0001).

Table 4
Rate of venom-induced anaphylactic case per 100,000 Florida ED visits stratified by report quarter, 2005-2006*

Quarter	Rate/100,000	p-value
January-March	1.09	<0.0001
April-June	2.27	<0.0001
July-September	4.29	Referent
October-December	3.06	0.02

* Venom-induced anaphylactic cases = 291, ED visits = 10,898,271

Table 5
Adjusted relative risks for Floridians treated in the ED for anaphylactic shock from binomial regression models stratified by sex, 2005-2006
(n =2,751)*

	Male			Female		
	Relative Risk	95% CI	p-value	Relative Risk	95% CI	p-value
Race [†]						
Black	0.77	(0.65-0.91)	0.003	0.99	(0.87-1.14)	0.9
Other	1.11	(0.8-1.54)	0.5	1.27	(0.98-1.66)	0.07
White	1	Referent	---	1	Referent	---
Ethnicity						
Hispanic	0.70	(0.6-0.82)	< 0.0001	0.65	(0.56-0.75)	< 0.0001
Non-Hispanic	1	Referent	---	1	Referent	---
Age [‡]						
0 to 17 years	1.46	(1.15-1.85)	0.002	1.29	(1.04-1.6)	0.02
18 to 30 years	1.41	(1.1-1.81)	0.01	2.07	(1.68-2.55)	< 0.0001
31 to 70 years	1.46	(1.17-1.82)	0.001	1.87	(1.56-2.25)	< 0.0001
71 years plus	1	Referent	---	1	Referent	---

* Each RR is adjusted for the remaining variables in the table. An age/gender interaction for the relative risks (p=0.002) was found therefore results were presented stratified by gender. Note that the comparison population is the general Florida population for 2005 and 2006.

[†] Black male patients were less likely than those of other race to be treated in the ED for anaphylaxis (RR=0.69, p=0.04).

[‡] Female patients age 18-30 and 31-70 years were more likely to have been treated in the ED for anaphylaxis compared to pediatric female patients (RR=1.60, p< 0.0001; RR=1.45, p<0.0001).

Table 6
Adjusted relative risks for anaphylaxis due to food, venom, or medication among patients treated in the ED for anaphylaxis shock from binomial regression models, 2005-2006 (n =2,751)*

	Food-induced [†]		Venom-induced [‡]		Medication-induced	
	Relative Risk (95% CI)	p-value	Relative Risk (95% CI)	p-value	Relative Risk (95% CI)	p-value
Sex						
Male	1.20 (1.05-1.37)	0.01	2.43 (1.95-3.03)	< 0.0001	0.56 (0.42-0.75)	< 0.0001
Female (<i>referent</i>)						
Race						
Black	1.25 (1.04-1.51)	0.02	0.37 (0.24-0.58)	< 0.0001	0.66 (0.45-0.97)	0.03
Other	1.14 (0.81-1.60)	0.5	0.92 (0.49-1.73)	0.8	0.61 (0.24-1.58)	0.3
White (<i>referent</i>)						
Ethnicity						
Hispanic	1.06 (0.88-1.28)	0.5	0.72 (0.46-1.13)	0.2	0.86 (0.57-1.28)	0.5
Non-Hispanic (<i>referent</i>)						
Health Insurance						
Commercial	1.09 (0.90-1.31)	0.4	1.07 (0.78-1.45)	0.7	0.86 (0.61-1.21)	0.4
Government	0.86 (0.69-1.08)	0.2	1.16 (0.81-1.68)	0.4	0.89 (0.58-1.37)	0.6
No Insurance (<i>referent</i>)						
Age						
0 to 17 years	3.18 (2.05-4.94)	< 0.0001	0.63 (0.35-1.14)	0.1	0.48 (0.25-0.92)	0.03
18 to 30 years	2.40 (1.53-3.77)	0.00	1.11 (0.65-1.89)	0.7	0.75 (0.47-1.19)	0.2
30 to 70 years	1.70 (1.11-2.60)	0.01	1.30 (0.82-2.07)	0.3	0.92 (0.60-1.41)	0.7
71 years plus (<i>referent</i>)						

* Each RR is adjusted for the remaining variables in the table. Note that the comparison population is all anaphylaxis cases treated in Florida EDs (2005-2006).

[†] Patients with commercial insurance were more likely to have food related anaphylaxis than patients with governmental insurance (RR = 1.26, p = 0.008).

[‡] Patients age 0 to 17 are less likely to have venom related anaphylaxis compared to patients age 31 to 70 (RR = 0.48, p < 0.0001).

Table 7
Comparison of identified anaphylactic triggers for all anaphylaxis ED visits and all anaphylaxis hospitalizations*

Trigger	ED visits(n= 1166)		Hospitalizations (n= 464)		p-value [†]
	Number	(Percent)	Number	(Percent)	
Food	409	(35)	75	(16)	< 0.0001
Venom	192	(16)	158	(34)	< 0.0001
Medication	97	(8)	54	(12)	0.04
Unknown	468	(40)	177	(38)	0.5

* Mulla and Simon analyzed hospitalizations using only the principal diagnosis code for anaphylaxis diagnosis. For the above comparison the same methodology was used for the ED data: records were determined to be anaphylaxis cases if the principal diagnosis code contained 995.0, 995.60-995.69, or 995.4. A case of anaphylaxis was also included if the principal diagnosis code contained 989.5 and one of the following codes were present E905.3 and E905.5.

[†] Pearson chi-square test was used to compare the proportion of all ED anaphylaxis cases (n=1166) with the identified trigger (e.g. food) to the proportion of all hospitalized anaphylaxis cases (n=464) with the identified trigger (e.g. food).