

Fatal anaphylaxis in the United States, 1999-2010: Temporal patterns and demographic associations

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Background: Anaphylaxis-related deaths in the United States have not been well characterized in recent years.

Objectives: We sought to define epidemiologic features and time trends of fatal anaphylaxis in the United States from 1999 to 2010.

Methods: Anaphylaxis-related deaths were identified by using the 10th clinical modification of the International Classification of Diseases system diagnostic codes on death certificates from the US National Mortality Database. Rates were calculated by using census population estimates.

Results: There were a total of 2458 anaphylaxis-related deaths in the United States from 1999 to 2010. Medications were the most common cause (58.8%), followed by “unspecified” (19.3%), venom (15.2%), and food (6.7%). There was a significant increase in fatal drug-induced anaphylaxis over 12 years: from 0.27 (95% CI, 0.23-0.30) per million in 1999 to 0.51 (95% CI, 0.47-0.56) per million in 2008 to 2010 ($P < .001$). Fatal anaphylaxis caused by medications, food, and unspecified allergens was significantly associated with African American race and older age ($P < .001$). Fatal anaphylaxis to venom was significantly associated with white race, older age, and male sex ($P < .001$). The rates of fatal anaphylaxis to foods in male African American subjects increased from 0.06 (95% CI, 0.01-0.17) per million in 1999 to 0.21 (95% CI, 0.11-0.37) per million in 2008 to 2010 ($P < .001$). The rates of unspecified fatal anaphylaxis decreased over time from 0.30 (95% CI, 0.26-0.34) per million in 1999 to 0.09 (95% CI, 0.07-0.11) per million in 2008 to 2010 ($P < .001$).

Conclusion: There are strong and disparate associations between race and specific classes of anaphylaxis-related mortality in the United States. The increase in medication-related deaths caused by anaphylaxis likely relates to increased medication and radiocontrast use, enhanced diagnosis, and coding changes. (J Allergy Clin Immunol 2014;■■■:■■■-■■■.)

Key words: Fatal anaphylaxis, drug, food, venom, death certificate, epidemiology

Abbreviation used

ICD-10: International Classification of Diseases 10th revision

Anaphylaxis has been dubbed “the latest allergy epidemic.”¹ The United States and Australia have some of the highest rates of severe anaphylaxis among developed countries.² Analyzing fatal anaphylaxis trends is challenging in the United States because unlike the United Kingdom,³ it does not have a national registry for anaphylaxis-related deaths. There is a voluntary registry of fatal food-induced anaphylaxis, which documented 32 cases of fatal anaphylaxis caused by food between 1994 and 1998 and an additional 31 cases between 2001 and 2006.^{4,5} Anaphylaxis admissions have increased over time in the United States, Australia, and the United Kingdom for both food- and non-food-related causes.⁶⁻¹¹ In Australia the incidence of fatal anaphylaxis doubled between 2002 and 2004 compared with that between 1997 and 2001.⁹ It has been suggested that overall rates of fatal anaphylaxis in the United States are stable⁶; however, little is known about changes in anaphylaxis-related mortality rates by cause and how they differ among racial/ethnic groups and by age and sex. Furthermore, although racial disparities have been reported for other allergic conditions, such as food allergies and asthma,¹²⁻¹⁴ it is not clear whether the same tendencies exist in fatal anaphylaxis.

The *International Classification of Diseases, 10th revision* (ICD-10), system introduced drug-related anaphylaxis as a new category and also added specific codes that allow for more exact identification of the cause of anaphylaxis. This enabled the identification of medications involved in anaphylactic shock in the United Kingdom and probable causes of fatal anaphylaxis in Australia.^{11,15}

To understand the features and time trends in fatal anaphylaxis, we analyzed the National Mortality Database in the United States between 1999 and 2010 using ICD-10 coding of US death certificates. With this study, we characterized recent trends in fatal anaphylaxis and its associations with demographic characteristics, such as age, sex, race, and geographic distribution, in the United States.

METHODS

Case identification and selection

Mortality data were obtained from the Vital Statistics Database of the National Center for Health Statistics' Multiple Cause of Death Data,¹⁶ which contains the codes provided on all annually reported death certificates from the United States. Data were analyzed for the time period starting 1999 (the first year ICD-10 codes were used)¹⁷ through 2010 (the last year for which data were available in the Vital Statistics database at the time of the analysis). All mortality data for this period were entered from death

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certificates into the database by using the Automated Mortality Medical Data System.¹⁸

Categories were assigned by using specific anaphylaxis codes (food, drug, serum, and unspecified) and certain causality codes (eg, venom and medications; see [Table E1](#) in this article's [Online Repository](#) at [www.jacionline.org](#)).

In the Multiple Cause of Death Database, anaphylaxis is disallowed as the underlying cause of death,¹⁹ and therefore anaphylaxis-related deaths were defined as all deaths that had at least 1 anaphylaxis code among the remaining cause-of-death fields. Additional deaths that fulfilled algorithmic definitions of anaphylaxis were identified (see [Table E2](#) in this article's [Online Repository](#) at [www.jacionline.org](#)).^{20,21}

The following groupings were identified as probable causes of fatal anaphylaxis¹⁵:

- *Drug-related anaphylaxis*: T88.6 (anaphylactic shock due to an adverse effect of correct drug or medicament properly administered) with or without medication-specific codes Y40.0 through Y59.0 and/or T88.7 (specific or unspecified adverse drug reactions, including allergic) or T78.2 (anaphylactic shock, unspecified) if recorded in combination with Y40.0-Y59.0 or T88.7.
- *Anaphylactic shock caused by serum*: T80.5;
- *Food-related anaphylaxis*: T78.0 (anaphylactic shock due to adverse food reaction) and/or T78.1 (other adverse reaction [including allergic] to ingested food) if it was recorded in combination with T78.2;
- *Venom-related anaphylaxis*: T63.4 (toxic effect of contact with venom of other arthropods [insect bite or sting]), X23 (contact [accidental] with bees, wasps, hornets, including yellow jacket), X25 (contact [accidental] or sting by venomous arthropod, insect, or ants), if it was recorded in combination with T78.2; and
- *Unspecified anaphylaxis*: T78.2 in the absence of other anaphylaxis codes or X/Y codes.

Anaphylaxis-related deaths were further analyzed for the place of death: (1) medical facility (including nursing home or hospice) as an inpatient (inpatient); (2) outpatient medical facility or emergency department (outpatient); or (3) decedent's home, other, or dead on arrival (community).

Anaphylaxis-related deaths were analyzed for the presence of asthma,²² angioedema, or hypotension on death certificates (see [Table E2](#)).

Data and statistical analysis

Each of the above categories (drug, venom, food, or unspecified) was evaluated by age, sex, and race. Race was specified based on categories used by the US Census Bureau, and race information was obtained from death certificates. Race and ethnicity groupings were created as follows: white, African American, Hispanic, and "other."²³ Age was grouped by 20-year intervals: 0 to 19 years, 20 to 39 years, 40 to 59 years, 60 to 79 years, and 80 years and older. Three-year time intervals were used as follows: 1999 to 2001, 2002 to 2004, 2005 to 2007, and 2008 to 2010.

Per-person rates were calculated by using US Census population data. For the years 2000 and 2010, the actual population counts were used. Population estimates were used for the remaining years.²⁴ Mortality rates by age, sex, race, and time period per million persons were calculated. Rates were not calculated for "other" race because of the small number of cases in each category and a heterogeneous mix.

Ninety-five percent CIs were calculated for each time point of the analysis by applying the gamma method for estimates based on fewer than 100 deaths.²⁵⁻²⁷ Negative binomial regression models (including all of the predictors) were used to assess the predictor effects of age, sex, race, time, and region on anaphylactic deaths. A dichotomous race variable was used in regression models as either white versus nonwhite, African American versus non-African American, or Hispanic versus non-Hispanic for each of the 4 anaphylaxis-related death groups. Information on US Census geographic regions (Northeast, Midwest, South, and West)²⁸ was available only for 1999 through 2004.¹⁶ Modeling that included geographic region was performed as a subset analysis. STATA 11.2 (StataCorp, College Station, Tex) and SAS 9.3 (SAS Institute, Cary, NC) software were used for statistical

analysis. The study was classified as exempt by the Albert Einstein College of Medicine Institutional Review Board.

RESULTS

General characteristics of anaphylaxis-related deaths

From 1999 through 2010, there were 2458 fatal anaphylaxis cases of all causes, with an overall prevalence of 0.69 persons per million. Among anaphylaxis causes, medications were the most common cause of fatal anaphylaxis in the United States, followed by unspecified anaphylaxis, venom-induced anaphylaxis, and food-induced anaphylaxis. The demographic characteristics for each anaphylaxis cause are shown in [Table I](#).

Drug-induced anaphylaxis (including serum)

There were 1446 anaphylaxis-related deaths attributable to medications, comprising 58.8% of the anaphylaxis-related deaths in the United States during the 12 years of the study. Forty-nine (3.4%) of the fatalities were in persons aged 19 years or less. Most deaths (58.6%) occurred in inpatient facilities ([Table I](#)).

Higher rates of drug-related anaphylaxis were observed with increasing age and in African American subjects: 0.05 (95% CI, 0.04-0.07) per million among those aged 19 years or less versus 1.28 (95% CI, 1.09-1.50) per million among persons aged 80 years or greater and 0.54 (95% CI, 0.47-0.61) in African American subjects; results were 0.19 (95% CI, 0.15-0.23) per million in Hispanic subjects and 0.45 (95% CI, 0.43-0.48) per million in white subjects ($P < .001$ for all; [Fig 1, A and B](#), and see [Tables E3 and E4](#) in this article's [Online Repository](#) at [www.jacionline.org](#)).

The rates of drug-induced fatal anaphylaxis increased over time for all races from 0.27 (95% CI, 0.23-0.30) per million in 1999 to 2001 to 0.51 (95% CI, 0.47-0.56) per million in 2008 to 2010 ($P < .001$; [Fig 1, C](#), and see [Table E5](#) in this article's [Online Repository](#) at [www.jacionline.org](#)). There was no significant difference in rates of fatal drug-induced anaphylaxis between sexes ([Fig 1, C](#), and see [Table E5](#)).

Between 1999 and 2004, the Northeast census region had significantly lower rates of drug anaphylaxis ($P = .01$; [Fig 2, A](#)). African American race, year, and age remained significant after adjusting for region ($P < .001$ for all).

The culprit drug was not specified in 1078 (74.5%) of all drug-related anaphylaxis-induced fatalities. Among 368 (25.4%) fatalities in which a culprit drug class was identified, 40.5% were due to antibiotics (149 deaths). Of these, only 77 had a specific antibiotic class assigned. Penicillins were identified most often ($n = 35$), followed by cephalosporins ($n = 33$), sulfa-containing medications, and macrolides. The remainder were due to unspecified antibiotics.

The next most common group of specified drug-induced anaphylaxis causes consisted of reactions to radiocontrast agents (100 deaths). When combined with the adverse reactions caused by other diagnostic agents, this group comprised 112 (30.4%) deaths.

The next most frequent group was anaphylaxis-related death caused by antineoplastic drugs ($n = 46$). The remaining specified drug-induced anaphylaxis-related deaths were due to serum ($n = 10$), opiates, antihypertensive agents, nonsteroidal anti-inflammatory drugs (NSAIDs), and anesthetic agents ([Fig 1, D](#)).

TABLE I. Characteristics of fatal anaphylaxis by specific cause

Characteristic	Anaphylaxis (n = 2458)			
	Drug and serum (n = 1446 [58.8%])	Venom (n = 374 [15.2%])	Food (n = 164 [6.7%])	Unspecified (n = 474 [19.3%])
Male sex, no. (%)	701 (48.1)	301 (80.3)	97 (59.2)	238 (50.2)
Age (y), median (IQR)				
Female subjects	61 (47-73)	51 (42-64)	44 (20-60)	57 (43-71)
Male subjects	59 (47-70)	52 (44-62)	37 (22-50)	54 (40-68)
Race, no. (%)				
Non-Hispanic white	1071 (73.7)	328 (87.7)	98 (59.8)	342 (72.2)
African American	240 (16.5)	24 (6.4)	41 (25.0)	93 (19.6)
Hispanic	93 (6.4)	17 (4.6)	9 (6.0)	29 (6.1)
Place of death, no. (%)				
Inpatient	852 (58.6)	152 (40.6)	56 (34.2)	270 (57.0)
Outpatient (including ED)	429 (29.5)	154 (41.2)	86 (52.4)	134 (28.3)
Community (including dead on arrival)	156 (10.75)	67 (17.9)	21 (12.8)	64 (13.5)
Associations with asthma, angioedema, and hypotension, no. (%)				
Asthma	54 (3.7)	3 (0.8)	27 (16.5)	37 (7.8)
Angioedema	49 (3.4)	2 (0.5)	5 (3.1)	26 (5.5)
Hypotension	46 (3.2)	12 (3.2)	0	18 (3.8)

ED, Emergency department; IQR, interquartile range.

Venom-induced anaphylaxis

Three hundred seventy-four fatalities were attributed to venom-induced anaphylaxis, which comprised 15.2% of all anaphylaxis cases (Table I). Six fatalities were in persons aged 19 years or less. Venom-induced anaphylaxis had the largest proportion of deaths occurring in the community (17.9%, Table I).

Fatal anaphylaxis from venom was significantly associated with older age: 0.01 (95% CI, 0.00-0.01) per million in those aged 19 years or less versus 0.20 (95% CI, 0.17-0.25) per million among those aged 60 to 79 years ($P < .001$). Association with white race was 0.14 (95% CI, 0.12-0.15) per million in white subjects versus 0.05 (95% CI, 0.03-0.08) per million in African American subjects and 0.03 (95% CI, 0.02-0.05) per million in Hispanic subjects ($P < .001$). Association with male sex was 0.18 (95% CI, 0.16-0.21) per million for male subjects versus 0.04 (95% CI, 0.03-0.05) per million for female subjects ($P < .001$; Fig 3 and see Tables E3-E5).

There was no significant increase in venom-induced anaphylaxis rates over time (Fig 3, C, and see Table E5). Between 1999 and 2004, the South census region had significantly higher rates of fatal venom-induced anaphylaxis ($P = .02$; Fig 2, B). Age, male sex, and white race remained significant after adjusting for region ($P < .001$ for all).

Food-induced anaphylaxis

Anaphylaxis to food was identified in 164 fatalities and was the least common (6.7%) cause of fatal anaphylaxis (Table I). Thirty-seven (22.6%) deaths were in persons aged 19 years or less. This group had the highest (52.4%) proportion of deaths occurring in outpatient facilities (Table I).

Age, African American race, and male sex were significantly associated with food-induced anaphylaxis: 0.04 (95% CI, 0.03-0.05) per million among those aged 19 years or less versus 0.06 (95% CI, 0.04-0.08) among those aged 60 to 79 years ($P = .02$); 0.09 (95% CI, 0.07-0.12) in African American subjects versus 0.04 (95% CI, 0.03-0.05) per million in white subjects and 0.02 (95% CI, 0.01-0.03) per million in Hispanic subjects ($P < .001$); and 0.06 (95% CI, 0.05-0.07) per million in male

subjects versus 0.03 (95% CI, 0.02-0.04) per million in female subjects ($P < .01$; Fig 4 and see Tables E3-E5).

There was no significant overall increase in food-induced anaphylaxis over time. Analysis of time trends by race and sex subgroups suggested a time effect in African American male subjects: the rates increased from 0.06 (95% CI, 0.01-0.17) per million in 1999 to 2001 to 0.21 (95% CI, 0.11-0.37) per million in 2008 to 2010 ($P < .001$; Fig 4, C, and see Table E5).

There was no significant geographic effect on food-induced anaphylaxis (Fig 2, C).

Unspecified anaphylaxis

There were 474 (19.3%) fatal cases of anaphylaxis with no specified cause (Table I). Twenty-seven (5.7%) deaths were in persons aged 19 years or less. Most deaths (57.0%) occurred in inpatient facilities (Table I).

Unspecified fatal anaphylaxis was significantly associated with older age and African American race: 0.03 (95% CI, 0.02-0.04) per million in those aged 19 years or less versus 0.43 (95% CI, 0.32-0.56) per million in those aged 80 years or greater and 0.21 (95% CI, 0.17-0.25) in African American subjects versus 0.15 (95% CI, 0.13-0.16) per million in white subjects and 0.06 (95% CI, 0.04-0.08) per million in Hispanic subjects ($P < .001$ for all; Fig 5, A and B, and see Tables E3 and E4). The rates of unspecified fatal anaphylaxis decreased over time from 0.30 (95% CI, 0.26-0.34) per million in 1999 to 2001 to 0.09 (95% CI, 0.07-0.11) per million in 2008 to 2010 ($P < .001$; Fig 5, C, and see Table E5).

Between 1999 and 2004, there were significant geographic differences in unspecified fatal anaphylaxis. The West census region had significantly lower rates of unspecified anaphylaxis ($P = .03$; Fig 2, D). Associations between unspecified fatal anaphylaxis and age, African American race, and time remained significant after adjusting for region ($P < .001$, $P = .01$, and $P < .001$, respectively).

Algorithm-identified deaths and additional analyses

The algorithm identified 593 deaths. Combining anaphylaxis-related and algorithm-defined deaths results in a prevalence for

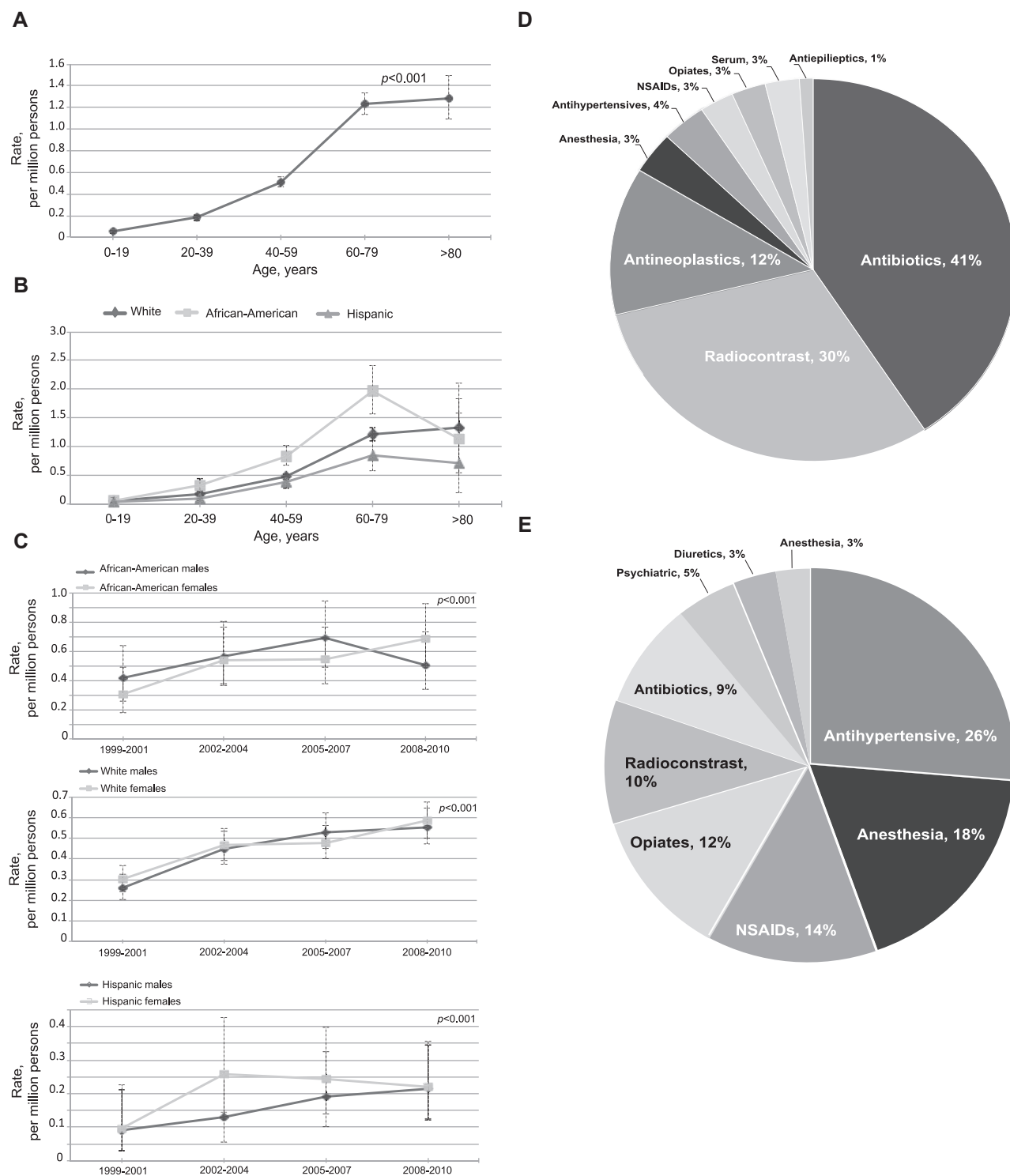


FIG 1. Fatal drug-induced anaphylaxis features. **A**, Rates by age groups, all races, and sexes combined. Drug-induced anaphylaxis was significantly associated with age ($P < .001$). **B**, Rates by race and age groups, both sexes. Drug-induced anaphylaxis was significantly associated with African American race ($P < .001$). **C**, Rates over time by race and sex. Fatal anaphylaxis to drugs significantly increased over 12 years among all races and both sexes ($P < .001$). No significant difference was observed between female and male subjects. **D**, Culprit medications in fatal drug-induced anaphylaxis with specified medications ($n = 368$). **E**, Culprit medications in fatal algorithm-identified anaphylaxis with specified medications ($n = 148$). Error bars show 95% CIs.

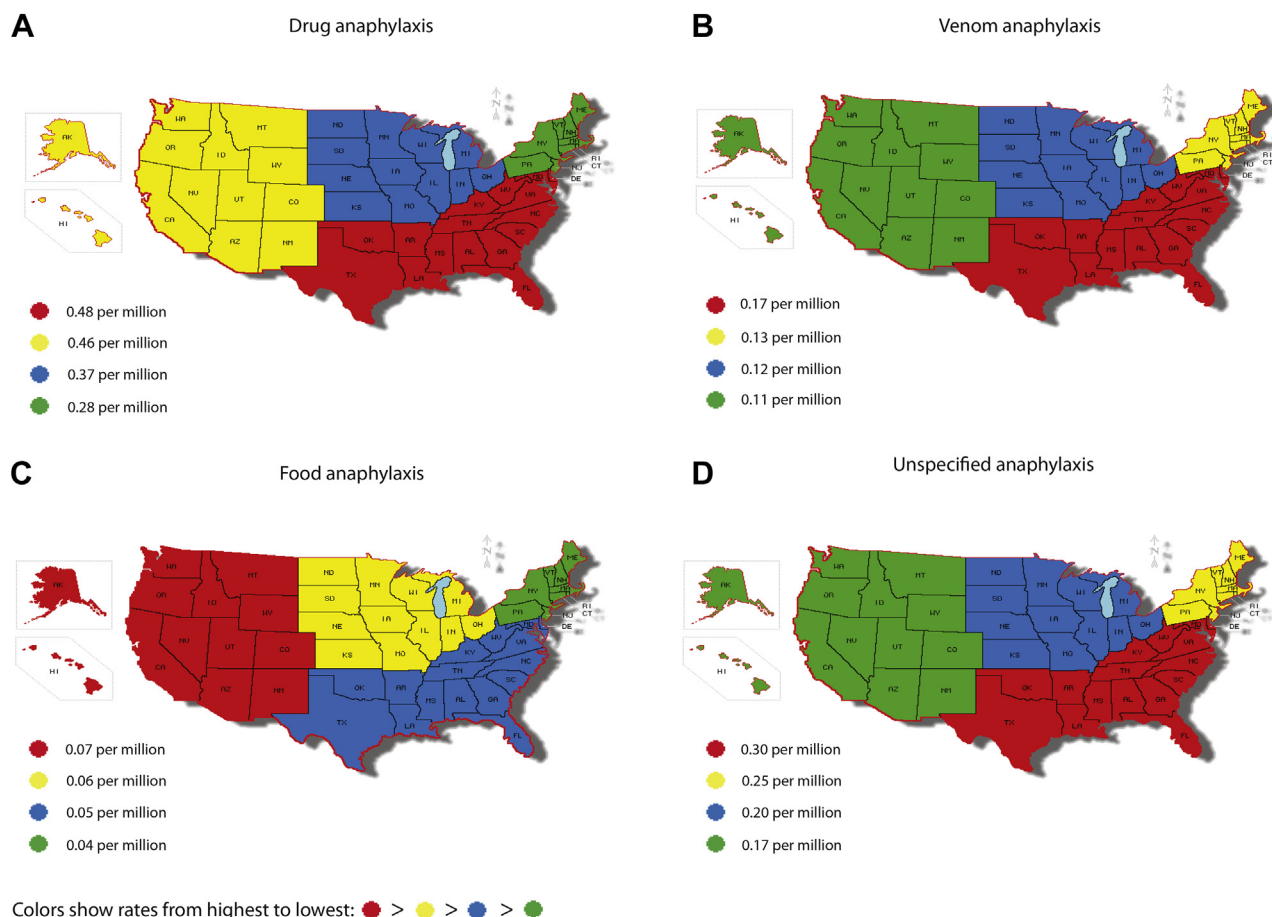


FIG 2. Fatal anaphylaxis by geographic region performed as a subset analysis, 1999-2004. **A**, Drug-induced anaphylaxis rates were lower in the Northeast census region ($P < .001$). **B**, Venom-induced anaphylaxis rates were higher in the South census region ($P < .001$). **C**, There was no significant association with geographic region for food-induced anaphylaxis. **D**, The West census region had lower unspecified anaphylaxis rates ($P = .03$). Maps were created with an interactive map tool available at <http://diymaps.net>.

fatal anaphylaxis of 0.86 persons per million. The demographic characteristics for each type of algorithm-identified death are shown in Table II. Three hundred six deaths were due to drugs, 48 to venom, 24 to food, and 215 to unspecified allergic reactions. Among drug-induced reactions, 148 (48.4%) deaths had an identified possible culprit medication (Fig 1, E). Combining algorithm-identified cases into the 4 anaphylactic groups did not result in abrogation of the age, race, sex, and time effects noted for non-algorithm-defined anaphylaxis (data not shown). More deaths occurred in the community, especially the non-drug-induced, algorithm-defined, anaphylaxis-related deaths (Table II).

Because drug-induced and unspecified anaphylaxis had opposing time effects, we examined the hypothetical scenario that all unspecified cases were miscoded drug cases by merging the 2 groups for regression modeling for the specified effects. No time effect was noted on the combined anaphylaxis cases: 0.55 (95% CI, 0.50-0.60) per million in 1999 to 2001 and 0.58 (95% CI, 0.53-0.63) per million in 2008 to 2010 (see Fig E1 in this article's Online Repository at www.jacionline.org).

DISCUSSION

Analysis of the US Death Database from 1999 to 2010 suggested that fatal anaphylaxis during this time period was

mostly due to the use of medications, followed by unspecified anaphylaxis, venom-induced anaphylaxis, and food-induced anaphylaxis. Based on these data, the overall prevalence of fatal anaphylaxis for recent years in the United States was 0.69 persons per million, which is similar to the prevalence found in a recent US population-based study.⁶ This prevalence is higher than that reported from the United Kingdom (0.33 per million).²² Although the rate reported from Australia is 0.64 persons per million,¹⁵ the Australian anaphylaxis data used a more expansive case by including angioedema (T78.3) and allergy, unspecified (T78.4). If algorithm-identified anaphylaxis-related deaths are included, the US mortality rate is higher than that in Australia (ie, 0.86 persons per million).

Drugs were the most common cause of fatal anaphylaxis in the United States, which is similar to reports from the United Kingdom, Australia, and New Zealand.^{3,15,29,30} Fatal drug-induced anaphylaxis in the United Kingdom has been reported to be mostly due to general anesthetics,²⁹ whereas antibiotics predominate in Australia¹⁵ and France.² Most (approximately 74%) of the drug-induced anaphylaxis-related deaths in the current study had no identified culprit drug. Among those with an identified culprit drug (368), nearly half (149) were antibiotics. This underscores the continued importance of identifying antibiotic allergy in the US population.

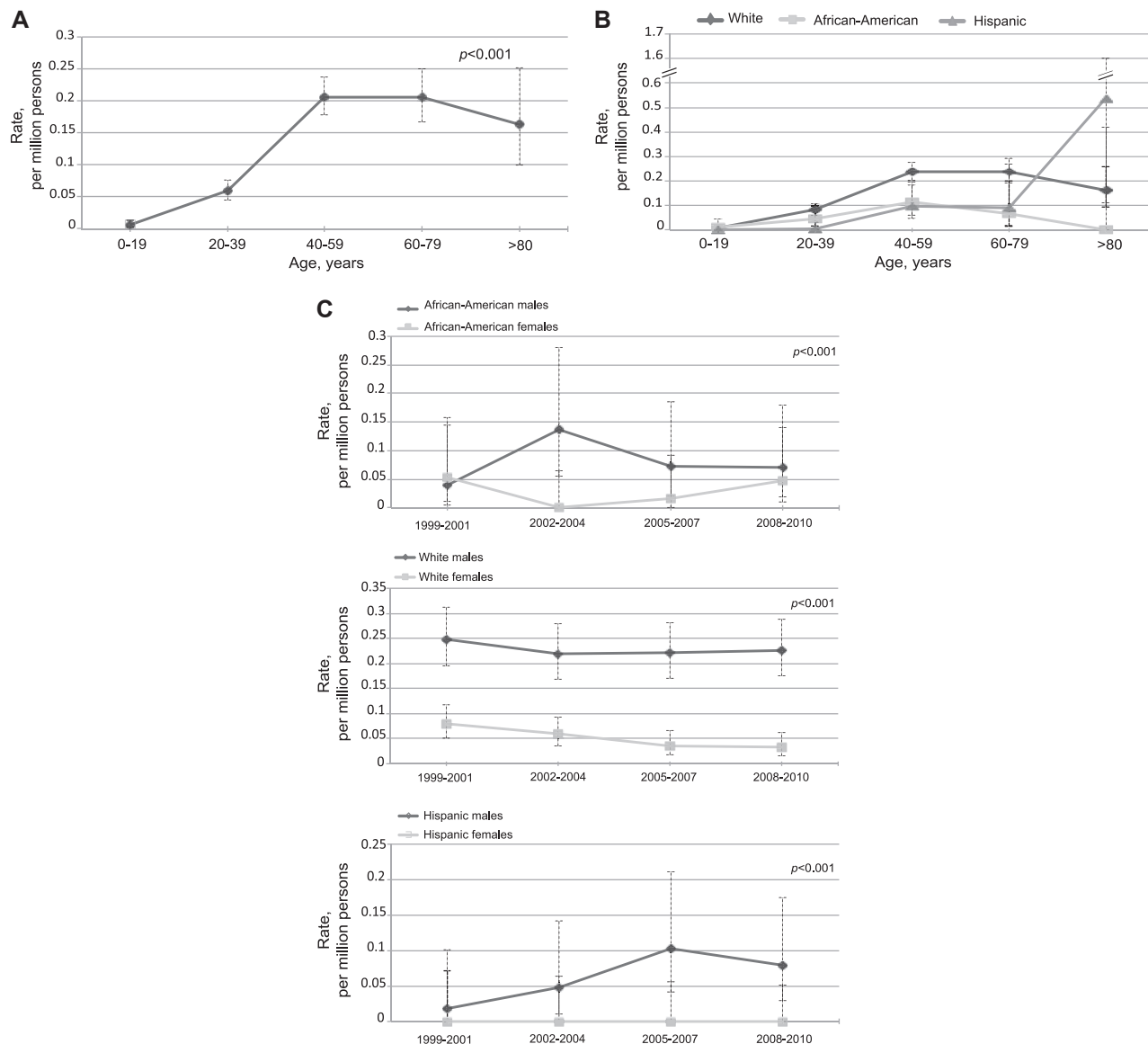


FIG 3. Fatal venom-induced anaphylaxis features. **A**, Rates by age groups, all races and sexes combined. Venom-induced anaphylaxis was significantly associated with age ($P < .001$). **B**, Rates by race and age groups, both sexes. Venom-induced anaphylaxis was significantly associated with white race ($P < .001$). **C**, Rates over time by race and sex. Venom-induced anaphylaxis was significantly associated with male sex ($P < .001$). There was no significant increase over time in fatal anaphylaxis to venom. Error bars show 95% CIs.

Among those experiencing fatal drug-induced anaphylaxis, 15% of cases in the United Kingdom, 7% of cases in Australia, and 20% of cases in New Zealand (Auckland county) with a specified drug were due to radiocontrast agents.^{15,22,30} The high number of anaphylaxis-related deaths in this study due to radiocontrast and diagnostic agents in the United States could be explained in part by the greater use of diagnostic imaging studies compared with other countries.³¹ In the United States 228 computed tomographic and 91 magnetic resonance imaging examinations were performed per 100,000 persons in 2008.³¹

Chemotherapy was another frequently identified cause of fatal drug-induced anaphylaxis. With increasing cancer prevalence predictions, especially in developed countries,³² awareness of chemotherapy-induced anaphylaxis is particularly relevant.

Drug-induced anaphylaxis-related fatalities in the United States significantly increased over the 12 years of the study period, without a significant influence of sex. A similar increase in fatal drug-induced anaphylaxis was noted in Australia.^{9,15} Over the course of the study, there was also a significant decrease in unspecified anaphylaxis. The lack of a time effect in combined drug-induced and unspecified anaphylaxis supports the possibility that at least some of the unspecified cases might have been drug related. However, unexplained death has been linked to fatal anaphylaxis caused by insect stings,^{33,34} raising the possibility that some unspecified anaphylaxis cases were due to venom.

The rates of venom-induced anaphylaxis-related deaths were relatively constant over the 12-year period. Our results are

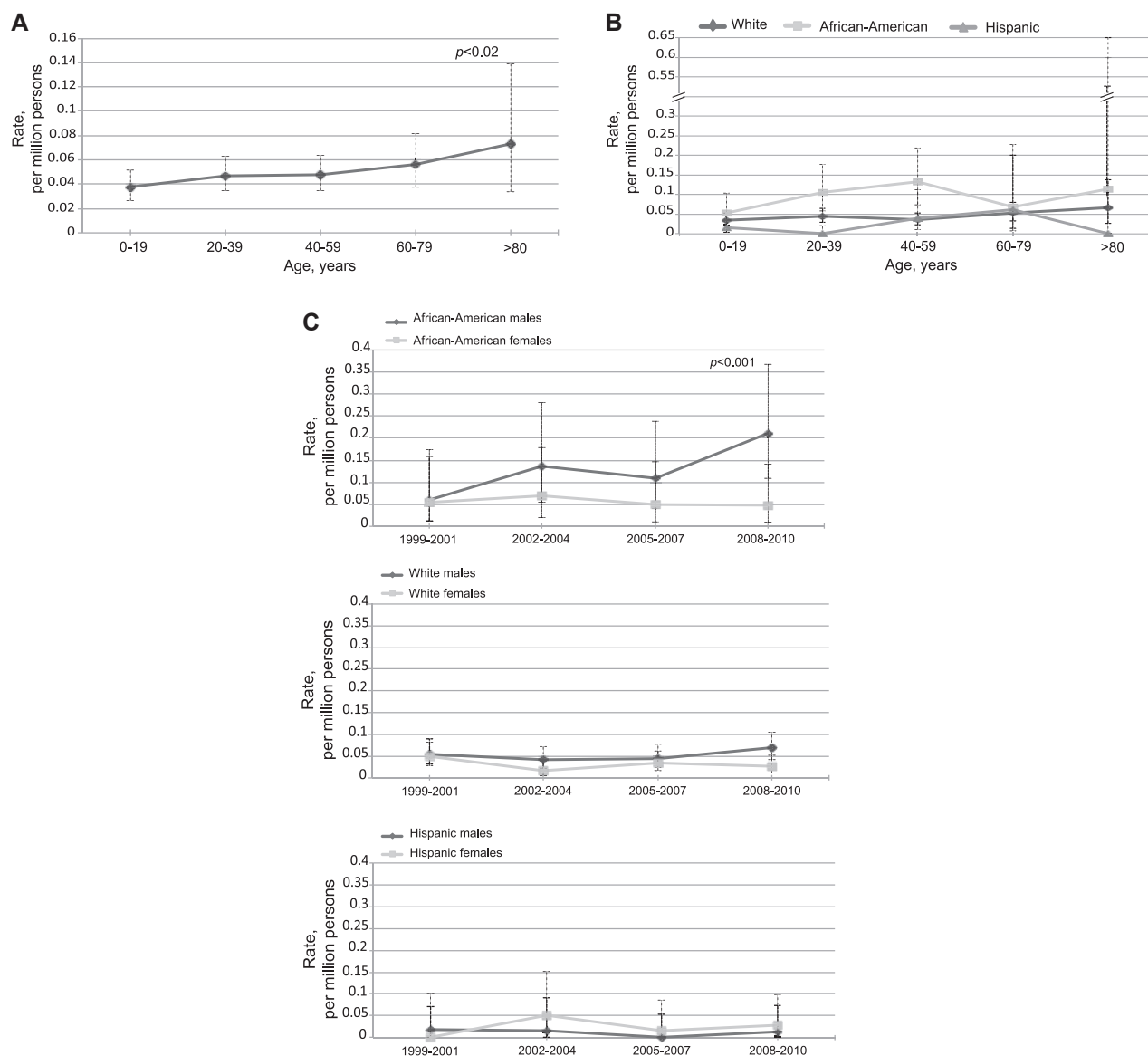


FIG 4. Fatal food-induced anaphylaxis features. **A**, Rates by age groups, all races and sexes combined. Fatal food-induced anaphylaxis was significantly associated with age ($P = .02$). **B**, Rates by race and age groups, both sexes. Food-induced anaphylaxis was significantly associated with African American race ($P < .001$). **C**, Rates over time by race and sex. There was a significant increase over time in fatal anaphylaxis to food among African American male subjects ($P < .001$). Error bars show 95% CIs.

consistent with the previously published data: earlier US reports suggested similar rates of approximately 40 deaths per year due to venom anaphylaxis.^{35,36}

Because of the lack of a specific code for venom anaphylaxis in the ICD-10, the number of anaphylaxis cases caused by venom is possibly underestimated.²⁰ Other studies reported that fatal venom-induced anaphylaxis comprises 18% to 23% of all fatal anaphylaxis cases.^{3,15,37} Not having a specific code for venom-induced anaphylaxis can result in diagnostic inaccuracies, and currently available codes reflecting venom toxic effect or venomous insect contacts are not always related to allergic reactions.

Higher rates for venom-induced anaphylaxis were observed among white male subjects. This finding is consistent with the

previously reported male predilection of fatal anaphylaxis to venom: 95% of cases of fatal anaphylaxis to venom were observed in male subjects in Australia, and significantly more male than female subjects died in Florida from Hymenoptera venom-induced anaphylaxis.^{15,37} Indolent systemic mastocytosis with insect sting-induced anaphylaxis is also significantly associated with male sex, which itself is a clinical criterion for predicting bone marrow mast cell clonality and systemic mastocytosis in the absence of skin lesions.^{38,39} White race was associated with higher rates of venom-induced anaphylaxis, possibly reflecting differential occupational exposure, outdoor exposure, or both by race.

Fatal food-induced anaphylaxis rates remained relatively unchanged over the 12-year time period. The proportion of

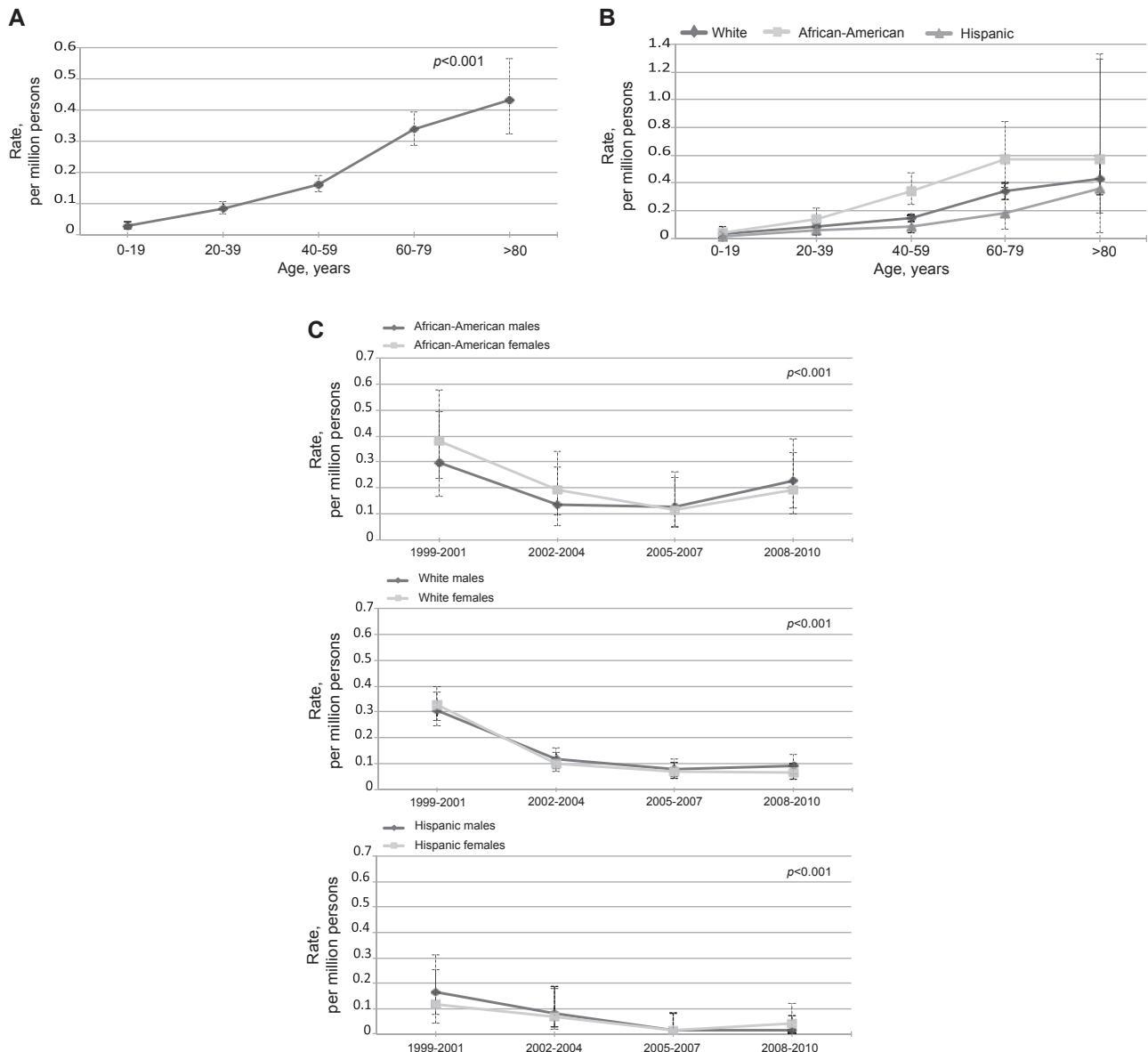


FIG 5. Unspecified fatal anaphylaxis features. **A**, Rates by age groups, all races and sexes combined. Unspecified fatal anaphylaxis was significantly associated with age ($P < .001$). **B**, Rates by race and age groups, both sexes. Unspecified anaphylaxis was significantly associated with African American race ($P < .001$). **C**, Rates over time by race and sex. There was a significant decrease over time in unspecified fatal anaphylaxis among all races and both sexes ($P < .001$).

anaphylaxis-related deaths from food in the United States is similar to that reported in Australia. In this study 6.7% of all fatal anaphylaxis cases were food related, whereas an Australian study reported food being responsible for 6% of all fatal allergic reactions.¹⁵ Fatal food-induced allergic reactions are commonly caused by asthma and angioedema and are less commonly associated with shock,²² and in this study the diagnosis of asthma was more common in patients with food-related anaphylaxis. African American race has been reported to be a risk factor for food allergies,^{40,41} and in this study higher food-related fatal anaphylaxis rates were observed in African American subjects. Male sex predominated among cases of fatal food-induced anaphylaxis. This contrasts with an Australian study, which

observed that 5 of 7 food-induced fatalities were in female subjects¹⁵ and with a United Kingdom study reporting that 75% of United Kingdom fatalities in subjects with nut allergy occurred in female subjects.²² Overall, the prevalence of food-related anaphylaxis was lower than for anaphylaxis of other causes, which is consistent with findings from other fatal anaphylaxis studies.⁴²

African American race was a significant risk factor for all anaphylaxis causes, with the exception of venom-induced anaphylaxis. Previous US reports suggested racial/ethnic disparity in atopic diseases, with African American subjects more likely to be sensitized to foods, to have self-reported allergy, or to have a clinic-based diagnosis of food allergy.¹² Also,

TABLE II. Characteristics of additional algorithm-defined anaphylaxis cases by specific cause

Characteristic	Fatal allergic reactions and anaphylaxis-related deaths identified by algorithm (n = 593)			
	Drug and serum (n = 306 [51.6%])	Venom (n = 48 [8.1%])	Food (n = 24 [4.0%])	Unspecified (n = 215 [36.3%])
Male sex, no. (%)	139 (45.4)	38 (79.2)	13 (54.2)	83 (38.6)
Age (y), median (IQR)				
Female subjects	65 (49.0-79.0)	51 (39-64)	64 (25-75)	64.5 (51-79)
Male subjects	61.0 (44-75)	54.5 (45-65)	41 (34-63)	63 (50-76)
Race, no. (%)				
Non-Hispanic white	190 (62.1)	38 (79.2)	14 (58.3)	171 (79.5)
African American	93 (30.4)	7 (14.6)	3 (12.5)	31 (14.4)
Hispanic	16 (5.2)	2 (4.2)	1 (4.2)	10 (4.7)
Place of death, no. (%)				
Inpatient	210 (68.6)	11 (22.9)	8 (33.3)	95 (44.2)
Outpatient (including ED)	59 (19.3)	22 (45.8)	10 (41.7)	59 (27.4)
Community (including dead on arrival)	37 (12.1)	15 (31.3)	6 (25.0)	60 (27.9)
Associations with asthma, angioedema, and hypotension, no. (%)				
Asthma	119 (38.9)	8 (16.7)	10 (41.7)	142 (66.1)
Angioedema	99 (32.4)	10 (20.8)	12 (50.0)	45 (20.9)
Hypotension	47 (15.4)	19 (39.6)	1 (4.2)	25 (11.6)

ED, Emergency department; IQR, interquartile range.

African American subjects have higher asthma mortality than white subjects.^{43,44} Higher prevalence of fatal drug-induced anaphylaxis in African American subjects might reflect more comorbidities, greater medication use, and less access to care.

Older age was associated with increased fatal anaphylaxis rates regardless of the anaphylaxis cause. Even in food-induced anaphylaxis (which had the highest proportion of childhood fatalities), the rates nearly doubled from 0.04 per million in persons aged 19 years or less to 0.07 per million in persons aged 80 years or greater, emphasizing that coping with severe anaphylaxis is more challenging for the elderly.^{45,46}

Geography has been reported to play an important role in allergies and in anaphylaxis specifically. Latitude and solar radiation were linked to more admissions for anaphylaxis and greater sales of epinephrine autoinjectors in the United States and Australia.⁴⁷⁻⁴⁹ In this study there was no overall predominance of a geographic area associated with fatal anaphylaxis. Although drug-induced anaphylaxis was less common in the Northeast census region, unspecified anaphylaxis was less common in the West census region. Fatal venom-induced anaphylaxis was observed more in the South census region, which could relate to greater/longer exposure to venomous insects in that area. Interestingly, fatal food-induced anaphylaxis had no significant association with a geographic region. Although latitude was reported to be an important risk factor for hospital admissions for food-induced anaphylaxis,⁴⁸ it is possible that the lack of such association in this study is due to the relatively low number of food-induced anaphylaxis cases.

As previously observed, drug-induced anaphylaxis occurred more frequently among inpatients,⁵⁰ and the deaths from food anaphylaxis were more frequent in outpatient settings.⁵¹ Interestingly, the highest proportion of cases occurring in the community was due to venom. It is possible that venom-induced anaphylaxis occurs more frequently in areas remote from medical assistance, making timely treatment difficult. In addition, patients allergic to venom frequently neglect using

epinephrine autoinjectors.^{52,53} This underscores the use of venom immunotherapy as a highly effective treatment option for patients with venom allergy.⁵¹ Algorithm-identified fatal allergic reactions to food also resulted in a high proportion of deaths occurring in the community. Educating all allergic patients at risk on self-management of anaphylaxis emergencies is an important task of practicing physicians.⁵¹

This study has several limitations. Overall, there is a possibility of underreporting and misreporting of anaphylaxis-related fatalities on death certificates. Thus the presented findings should be interpreted with caution. The large number of unspecified anaphylaxis codes used in the registry necessitated the use of adverse/toxic effect or contact codes to classify etiology. Although a drug-induced anaphylaxis code was added to the ICD-10, a venom-induced anaphylaxis code was not. It is important to consider the introduction of such a code. Culprit foods in food-related anaphylaxis could not be assessed because they are coded with Z-codes in the ICD-10 system, which are considered therapeutic codes and are not reported on death certificates. It would be important to consider creating ICD-10 codes specific to anaphylaxis caused by certain foods, such as exists for serum anaphylaxis, so that the actual foods could be identified and preventive strategies implemented. Finally, there was no information on the time course of the anaphylactic events and attempted treatment. Many of the above limitations could be overcome if the United States would have a National Registry on Fatal Anaphylaxis. Although it exists for food allergies,^{4,5} other anaphylaxis causes should also be considered.

Nevertheless, the present study also has several strengths, including analysis of the National Mortality Database, which includes all anaphylaxis-related deaths from the study period. To our knowledge, this is the largest study of anaphylaxis-related mortality that is based on the entire US population during the study period and examines demographic features of fatal anaphylaxis by cause. Understanding the patterns of fatal anaphylaxis might help in identifying specific risk factors and formulating preventative approaches.

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Clinical implications: Drugs are the most frequent culprits of fatal anaphylaxis in the United States. Anaphylaxis-related deaths from medications and diagnostic agents increased over time. Practitioners should be aware of therapeutic and prevention strategies.

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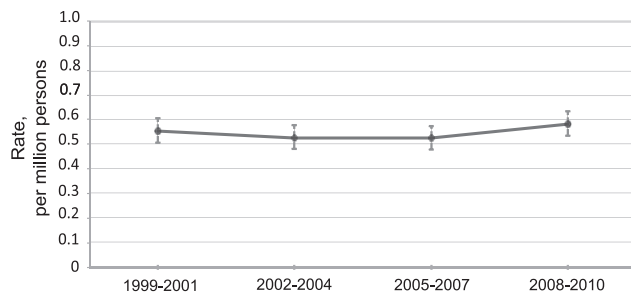


FIG E1. Analysis of the time trend on combined drug-induced and unspecified fatal anaphylaxis cases. *Error bars* show 95% CIs.

TABLE E1. ICD-10 codes used in the analysis

Code	Definition
T78.2	Anaphylactic shock, unspecified
Food	
T78.0	Anaphylactic shock due to adverse food reaction
T78.1 (if recorded with T78.2)	Other adverse food reactions, not elsewhere classified
Venom	
T63.4 (if recorded with T78.2)	Toxic effect of venom of other arthropods including allergic or anaphylactic shock following venomous insect sting(s) (bee, hornet, wasp or other insect or arthropod NEC)
X23 (if recorded with T78.2)	Contacts with hornets, wasps, and bees
X25 (if recorded with T78.2)	Contacts with other venomous arthropods (including ants and caterpillars)
Drugs	
T80.5	Anaphylactic shock due to serum
T88.6	Anaphylactic shock due to adverse effect of correct drug or medicament properly administered
T88.7 and other adverse reactions codes due to medications (if recorded with T88.6 or T78.2)	Specific or unspecified adverse drug reactions (including allergic). A full list of other adverse drug reaction codes is provided below (medication-specific codes)
Medication-specific codes	
Y40.0	Penicillins
Y40.1	Cephalosporins and other beta-lactam antibiotics
Y43.1	Antineoplastic antimetabolites
Y43.2	Antineoplastic natural products
Y43.3	Other antineoplastic drugs
Y45.1	NSAIDs: salicylates
Y45.3	NSAIDs: other
Y45.8	NSAIDs: other analgesics and antipyretics
Y45.9	NSAIDs: analgesic, antipyretics and anti-inflammatory drug, unspecified
Y40.3	Macrolides
Y40.4	Tetracyclins
Y40.5	Aminoglycosides
Y40.6	Rifamycins
Y40.7	Antifungal antibiotics, systemically used
T88.2	Anesthetics: shock due to anesthesia in which the correct substance was properly administered
Y48.0	Anesthetics: inhaled anesthetics
Y48.1	Anesthetics: parenteral anesthetics
Y48.2	Anesthetics: other and unspecified general anesthetics
Y48.3	Anesthetics: local anesthetics
Y48.4	Anesthetics: anesthetic, unspecified
Y48.5	Anesthetics: therapeutic gases
Y57.5	X-ray contrast media
Y57.6	Diagnostic agents: other diagnostic agents
Y40.8	Other systemic antibiotics
Y40.9	Systemic antibiotic, unspecified
Y41.0	Sulfonamides
Y41.5	Antiviral drugs
Y41.8	Other specified systemic anti-infectives and antiparasitics, hydroxyquinoline derivatives
Y57.8	Other drugs and medicaments
Y57.9	Drug or medicament, unspecified
Y46.2	Antiepileptics: hydantoin derivatives
Y46.3	Antiepileptics: deoxybarbiturates
Y46.5	Antiepileptics: valproic acid
Y46.6	Antiepileptics: other and unspecified antiepileptics
Y47.0	Sedatives, hypnotics, and anti-anxiety drugs: barbiturates, not elsewhere classified
Y47.1	Sedatives, hypnotics, and anti-anxiety drugs: benzodiazepines
Y47.5	Sedatives, hypnotics, and anti-anxiety drugs: mixed sedatives and hypnotics, not elsewhere classified
Y47.8	Sedatives, hypnotics, and anti-anxiety drugs: other sedatives, hypnotics, and anti-anxiety drugs
Y47.9	Sedatives, hypnotics, and anti-anxiety drugs: unspecified
Y49.0	Psychotropic drugs: tricyclic and tetracyclic antidepressants
Y49.1	Psychotropic drugs: monoamine-oxidase-inhibitor antidepressants
Y49.2	Psychotropic drugs: other and unspecified antidepressants
Y49.3	Psychotropic drugs: phenothiazine antipsychotics and neuroleptics

(Continued)

TABLE E1. (Continued)

Code	Definition
Y49.4	Psychotropic drugs: butyrophenone and thioxanthene neuroleptics
Y49.5	Psychotropic drugs: other antipsychotics and neuroleptics
Y49.6	Psychotropic drugs: psychodysleptics
Y49.7	Psychotropic drugs: psychostimulants with abuse potential
Y49.8	Psychotropic drugs: other psychotropic drugs, not elsewhere classified
Y49.9	Psychotropic drugs: psychotropic drug, unspecified
Y51.6	Antihypertensive drugs: alpha-adrenoreceptor antagonists, not elsewhere classified
Y51.7	Antihypertensive drugs: beta-adrenoreceptor antagonists, not elsewhere classified
Y51.8	Antihypertensive drugs: centrally acting and adrenergic-neuron-blocking agents, not elsewhere classified, e.g. clonidine
Y52.1	Antihypertensive drugs: calcium-channel blockers
Y52.4	Antihypertensive drugs: angiotensin-converting-enzyme inhibitors
Y52.5	Antihypertensive drugs: other antihypertensive drugs, not elsewhere classified
Y54.1	Diuretics: mineralocorticoid antagonists (aldosterone antagonists)
Y54.2	Diuretics: carbonic-anhydrase inhibitors
Y54.3	Diuretics: benzothiadiazine derivatives
Y54.4	Diuretics: loop diuretics
Y54.5	Diuretics: other diuretics
Y45.0	Opioids and related analgesics
Y59	Other and unspecified vaccines and biological substances

NSAIDs, Nonsteroidal anti-inflammatory drugs.

TABLE E2. ICD-10 codes used for identification of algorithm-defined anaphylaxis cases*

Code	Meaning
Allergic reactions	
T78.4	Allergy, unspecified
Respiratory tract system	
J45.0	Predominantly allergic asthma
J45.1	Nonallergic asthma
J45.8	Mixed asthma
J45.9	Asthma, unspecified
J46	Status asthmaticus
J80	Adult respiratory distress syndrome
J96.0	Acute respiratory failure
J96.9	Respiratory failure, unspecified
R06.0	Dyspnea
R06.1	Stridor
R06.2	Wheezing
R06.3	Periodic breathing
R06.4	Hyperventilation
R06.8	Other and unspecified abnormalities of breathing
J38.4	Edema of larynx
J39.2	Other diseases of pharynx
J39.3	Upper respiratory tract hypersensitivity reaction, site unspecified
J39.8	Other specified disease of upper respiratory tract
J39.9	Disease of upper respiratory tract, unspecified
Cardiovascular system	
I95.0	Idiopathic hypotension
I95.1	Orthostatic hypotension
I95.2	Hypotension due to drugs
I95.8	Other hypotension
I95.9	Hypotension, unspecified
R55	Syncope and collapse
R57.0	Cardiogenic shock
R57.1	Hypovolemic shock
R57.8	Other shock
R57.9	Shock, unspecified
Gastrointestinal system	
K52.2	Allergic and dietetic gastroenteritis and colitis
K52.8	Other specified noninfective gastroenteritis and colitis
K52.9	Noninfective gastroenteritis and colitis, unspecified
R10.0	Pain, acute abdomen
R10.1	Pain localized to upper abdomen
R10.3	Pain localized to other parts of lower abdomen
R10.4	Other and unspecified abdominal pain
R11	Nausea and vomiting
R11.2	Heartburn
Integumentary system	
H02.8	Other specified disorders of eyelid
H02.9	Disorder of eyelid, unspecified
H11.9	Disorder of conjunctiva, unspecified
L29.8	Other pruritus
L29.9	Pruritus, unspecified
L50.0	Allergic urticaria
L50.1	Idiopathic urticaria
L50.3	Dermatographic urticaria
L50.8	Other urticaria
L50.9	Urticaria, unspecified
R23.2	Flushing
R23.8	Other and unspecified skin changes
T78.3	Angioneurotic edema

*The algorithm identifies anaphylaxis cases if respiratory compromise or skin-mucosal involvement were found in combination with shock, respiratory compromise or reduced blood pressure was found in conjunction with skin-mucosal involvement, or a combination of gastrointestinal symptoms, respiratory compromise, reduced blood pressure, or skin mucosal involvement was found in conjunction with a potential allergen (including venom, drugs, food, a biological substance, or an unspecified allergic reaction), as previously reported.²⁰

TABLE E3. Rates of fatal anaphylaxis by cause and age group

Type of anaphylaxis	Age group									
	≤19 y		20-39 y		40-59 y		60-79 y		≥80 y	
	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)
Drug	49	0.05 (0.04-0.07)	178	0.18 (0.16-0.21)	482	0.51 (0.47-0.56)	590	1.23 (1.13-1.34)	158	1.28 (1.09-1.50)
Venom	6	0.01 (0.00-0.01)	58	0.06 (0.04-0.08)	193	0.20 (0.18-0.24)	98	0.20 (0.17-0.25)	20	0.16 (0.10-0.25)
Food	37	0.04 (0.03-0.05)	46	0.05 (0.03-0.06)	45	0.05 (0.03-0.06)	27	0.06 (0.04-0.08)	9	0.07 (0.03-0.14)
Nonspecified	27	0.03 (0.02-0.04)	83	0.08 (0.07-0.10)	153	0.16 (0.14-0.19)	161	0.34 (0.29-0.39)	53	0.43 (0.32-0.56)

TABLE E4. Rates of fatal anaphylaxis by cause, race, and age group

	Age group											
	≤19 y		20-39 y		40-59 y		60-79 y		≥80 y		Total	
	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)
Drug												
White	31	0.05 (0.04-0.08)	108	0.18 (0.15-0.21)	332	0.47 (0.42-0.53)	461	1.21 (1.10-1.32)	141	1.34 (1.13-1.58)	1073	0.45 (0.43-0.48)
African American	8	0.05 (0.02-0.10)	43	0.32 (0.23-0.44)	94	0.83 (0.67-1.02)	86	1.96 (1.57-2.42)	10	1.14 (0.55-2.10)	241	0.54 (0.47-0.61)
Hispanic	6	0.03 (0.01-0.07)	17	0.10 (0.06-0.15)	39	0.39 (0.27-0.53)	28	0.86 (0.57-1.24)	4	0.71 (0.19-1.38)	94	0.19 (0.15-0.23)
Overall	45	0.04 (0.04-0.07)	168	0.18 (0.16-0.21)	465	0.51 (0.46-0.56)	575	1.25 (1.15-1.36)	155	1.29 (1.10-1.52)	1408	0.42 (0.40-0.45)
Venom												
White	4	0.01 (0.00-0.02)	50	0.08 (0.06-0.11)	167	0.24 (0.20-0.28)	91	0.24 (0.19-0.29)	17	0.16 (0.09-0.26)	329	0.14 (0.12-0.15)
African American	2	0.01 (0.00-0.05)	6	0.05 (0.02-0.10)	13	0.11 (0.06-0.20)	3	0.07 (0.01-0.20)	0	0.00 (0.00- 0.42)	24	0.05 (0.03-0.08)
Hispanic	0	0.00 (0.00-0.02)	1	0.01 (0.00-0.03)	10	0.10 (0.05-0.18)	3	0.09 (0.02-0.27)	3	0.54 (0.11-1.57)	17	0.03 (0.02-0.05)
Overall	6	0.01 (0.00-0.01)	57	0.06 (0.05-0.08)	190	0.21 (0.18-0.24)	97	0.21 (0.17-0.26)	20	0.17 (0.10-0.26)	370	0.11 (0.10-0.12)
Food												
White	20	0.03 (0.02-0.05)	27	0.04 (0.03-0.06)	25	0.04 (0.02-0.05)	20	0.05 (0.03-0.08)	7	0.07 (0.03-0.14)	99	0.04 (0.03-0.05)
African American	8	0.05 (0.02-0.10)	14	0.11 (0.06-0.18)	15	0.13 (0.07-0.22)	3	0.07 (0.01-0.20)	1	0.11 (0.00-0.63)	41	0.09 (0.07-0.12)
Hispanic	3	0.02 (0.00-0.05)	0	0.00 (0.00-0.02)	4	0.04 (0.01-0.10)	2	0.06 (0.01-0.22)	0	0.00 (0.00-0.66)	9	0.02 (0.01-0.03)
Overall	31	0.03 (0.02-0.05)	41	0.04 (0.03-0.06)	44	0.05 (0.03-0.06)	25	0.05 (0.04-0.08)	8	0.07 (0.03-0.13)	149	0.04 (0.04-0.05)
Nonspecified												
White	18	0.03 (0.02-0.05)	51	0.08 (0.06-0.11)	101	0.14 (0.12-0.18)	129	0.34 (0.28-0.40)	45	0.43 (0.31-0.57)	344	0.15 (0.13-0.16)
African American	6	0.04 (0.01-0.09)	18	0.14 (0.08-0.21)	39	0.34 (0.24-0.47)	25	0.57 (0.37-0.84)	5	0.57 (0.18-1.33)	93	0.21 (0.17-0.25)
Hispanic	3	0.02 (0.00-0.05)	10	0.06 (0.03-0.10)	9	0.09 (0.04-0.17)	6	0.18 (0.07-0.40)	2	0.36 (0.04-1.29)	30	0.06 (0.04-0.08)
Overall	27	0.03 (0.02-0.04)	79	0.09 (0.07-0.11)	149	0.16 (0.14-0.19)	160	0.35 (0.30-0.41)	52	0.43 (0.32-0.57)	467	0.14 (0.13-0.15)

TABLE E5. Rates of fatal anaphylaxis over time by cause, race, and sex

Type of anaphylaxis	Time period									
	1999-2001		2002-2004		2005-2007		2008-2010		Total	
	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)	Count	Rate per million US population (95% CI)
Drug										
White										
Male	75	0.26 (0.20-0.32)	131	0.45 (0.38-0.53)	154	0.53 (0.45-0.62)	161	0.55 (0.47-0.65)	521	0.45 (0.41-0.49)
Female	91	0.30 (0.24-0.37)	142	0.47 (0.39-0.55)	143	0.48 (0.40-0.56)	176	0.58 (0.50-0.68)	552	0.46 (0.42-0.50)
African American										
Male	21	0.42 (0.26-0.64)	29	0.56 (0.38-0.81)	38	0.69 (0.49-0.95)	29	0.51 (0.34-0.73)	117	0.55 (0.45-0.66)
Female	17	0.31 (0.18-0.49)	31	0.54 (0.37-0.77)	33	0.55 (0.38-0.77)	43	0.69 (0.50-0.93)	124	0.53 (0.44-0.63)
Hispanic										
Male	5	0.09 (0.03-0.21)	8	0.13 (0.06-0.26)	13	0.19 (0.10-0.33)	16	0.21 (0.12-0.35)	42	0.16 (0.12-0.22)
Female	5	0.10 (0.03-0.23)	15	0.26 (0.14-0.43)	16	0.24 (0.14-0.40)	16	0.22 (0.13-0.36)	52	0.21 (0.16-0.28)
Overall	214	0.27 (0.23-0.30)	356	0.43 (0.39-0.48)	397	0.47 (0.43-0.52)	441	0.51 (0.47-0.56)	1408	0.42 (0.40-0.45)
Venom										
White										
Male	72	0.25 (0.19-0.31)	64	0.22 (0.17-0.28)	64	0.22 (0.17-0.28)	66	0.23 (0.18-0.29)	266	0.23 (0.20-0.26)
Female	24	0.08 (0.05-0.12)	18	0.06 (0.04-0.09)	11	0.04 (0.02-0.07)	10	0.03 (0.02-0.06)	63	0.05 (0.04-0.07)
African American										
Male	2	0.04 (0.00-0.14)	7	0.14 (0.05-0.28)	4	0.07 (0.02-0.19)	4	0.07 (0.02-0.18)	17	0.08 (0.05-0.13)
Female	3	0.05 (0.01-0.16)	0	0.00 (0.00-0.06)	1	0.02 (0.00-0.09)	3	0.05 (0.01-0.14)	7	0.03 (0.01-0.06)
Hispanic										
Male	1	0.02 (0.00-0.10)	3	0.05 (0.01-0.14)	7	0.10 (0.04-0.21)	6	0.08 (0.03-0.17)	17	0.07 (0.04-0.10)
Female	0	0.00 (0.00-0.07)	0	0.00 (0.00-0.06)	0	0.00 (0.00-0.06)	0	0.00 (0.00-0.05)	0	0.00 (0.00-0.01)
Overall	102	0.13 (0.10-0.15)	92	0.11 (0.09-0.14)	87	0.10 (0.08-0.13)	89	0.10 (0.08-0.13)	370	0.11 (0.10-0.12)
Food										
White										
Male	16	0.06 (0.03-0.09)	12	0.04 (0.02-0.07)	13	0.04 (0.02-0.08)	20	0.07 (0.04-0.11)	61	0.05 (0.04-0.07)
Female	15	0.05 (0.03-0.08)	5	0.02 (0.01-0.04)	10	0.03 (0.02-0.06)	8	0.03 (0.01-0.05)	38	0.03 (0.02-0.04)
African American										
Male	3	0.06 (0.01-0.17)	7	0.14 (0.05-0.28)	6	0.11 (0.04-0.24)	12	0.21 (0.11-0.37)	28	0.13 (0.09-0.19)
Female	3	0.05 (0.01-0.16)	4	0.07 (0.02-0.18)	3	0.05 (0.01-0.15)	3	0.05 (0.01-0.14)	13	0.06 (0.03-0.09)
Hispanic										
Male	1	0.02 (0.00-0.10)	1	0.02 (0.00-0.09)	0	0.00 (0.00-0.05)	1	0.01 (0.00-0.07)	3	0.01 (0.00-0.03)
Female	0	0.00 (0.00-0.07)	3	0.05 (0.01-0.15)	1	0.02 (0.00-0.09)	2	0.03 (0.00-0.10)	6	0.02 (0.01-0.05)
Overall	38	0.05 (0.03-0.06)	32	0.04 (0.03-0.05)	33	0.04 (0.03-0.06)	46	0.05 (0.04-0.07)	149	0.04 (0.04-0.05)
Nonspecified										
White										
Male	89	0.31 (0.25-0.38)	34	0.12 (0.08-0.16)	23	0.08 (0.05-0.12)	27	0.09 (0.06-0.14)	173	0.15 (0.13-0.17)
Female	99	0.33 (0.27-0.40)	31	0.10 (0.07-0.14)	21	0.07 (0.04-0.11)	20	0.07 (0.04-0.10)	171	0.14 (0.12-0.16)
African American										
Male	15	0.30 (0.17-0.49)	7	0.14 (0.05-0.28)	7	0.13 (0.05-0.26)	13	0.23 (0.12-0.39)	42	0.20 (0.14-0.27)
Female	21	0.38 (0.23-0.58)	11	0.19 (0.10-0.34)	7	0.12 (0.05-0.24)	12	0.19 (0.10-0.34)	51	0.22 (0.16-0.28)
Hispanic										
Male	9	0.16 (0.07-0.31)	5	0.08 (0.03-0.19)	1	0.01 (0.00-0.08)	1	0.01 (0.00-0.07)	16	0.06 (0.04-0.10)
Female	6	0.12 (0.04-0.25)	4	0.07 (0.02-0.18)	1	0.02 (0.00-0.09)	3	0.04 (0.01-0.12)	14	0.06 (0.03-0.09)
Overall	239	0.30 (0.26-0.34)	92	0.11 (0.09-0.14)	60	0.07 (0.05-0.09)	76	0.09 (0.07-0.11)	467	0.14 (0.13-0.15)