

Favorable trends in the frequency of U.S. emergency department visits for food allergy, 2001–2009

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ABSTRACT

Several studies suggest an increase in both the prevalence of food allergy and in the frequency of emergency department (ED) visits for food-related allergic reactions, including anaphylaxis. This study evaluates time trends in the frequency of ED visits for food allergy, with a focus on possible differences by age. Data from two multicenter ED-based studies were used to identify the proportion of patients assigned to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes with actual food-related acute allergic reaction and the proportion of these patients with food-induced anaphylaxis. We multiplied these proportions against counts from nationally representative data (2001–2009) to estimate the number of U.S. ED visits for each ICD-9-CM code with likely food allergy. Over the 9-year study period, there were ~1,892,000 ED visits for food allergy. The number of ED visits for food allergy did not significantly change among children aged <18 years (77,000 visits in 2001 versus 92,000 visits in 2009; $p = 0.85$), but among adults aged ≥ 18 years, there was a decline (147,000 visits versus 97,000 visits; $p = 0.046$). Looking across all ED visits (any cause), the proportion of ED visits for food allergy was stable for children (0.29% versus 0.28%; $p = 0.22$) but decreased for adults (0.18% versus 0.09%; $p = 0.01$). The number of U.S. ED visits for food-related acute allergic reactions is significantly higher than prior reports. These results also suggest that the frequency of ED visits for food allergy was stable or decreased from 2001 to 2009, despite reports suggesting an ongoing rise in the prevalence of food allergy.

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Estimates of the burden of food allergy have been reported across various health care settings, including ambulatory care,¹ hospitalizations,² and the emergency department (ED).^{3–7} Food-induced anaphylaxis, defined as an IgE-mediated hypersensitivity reaction to an ingested food that results in the rapid onset of multisystem and potentially life-threatening symptoms, has been cited as the most frequent cause of anaphylaxis treated in the ED.⁵ In earlier work, we found that there were an estimated 1,015,000 ED visits (during 2001–2005) for food-related acute allergic reactions in the United States, of which 448,000 would be classified as anaphylaxis.⁸ These results suggested that the number of U.S. ED visits for food-related acute allergic reactions was significantly higher than the

number cited in prior reports.^{1,4,5} Timely and appropriate treatment is necessary to prevent progression of reactions,⁹ with delays in treatment associated with poor outcomes,¹⁰ suggesting the need for training and resources for patients and providers.

In addition to the burden on the acute health care system, there is longstanding concern about the rising prevalence of food allergy in the general population,^{11–13} which presumably drives reported increases in ED use¹⁴ and hospitalizations^{2,15} for food allergy. Differences in the prevalence and trends of food allergy between children and adults also have been reported.^{4,16} To that end, we have updated our earlier estimates of the frequency of ED visits for food allergy including National Hospital and Ambulatory Medical Care Survey (NHAMCS) that has recently become available. We also evaluated time trends in the frequency of ED visits for food allergy and examined differences in the frequency and trends of these reactions between children and adults.

METHODS

Data from two multicenter ED-based studies were used to identify the proportion of patients assigned to each International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code that was later determined by expert chart review to be a likely case of food-related acute allergic reaction.^{17,18} We then used the same approach to identify the proportion of

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Table 1 ICD-9-CM codes used to identify food-related acute allergic reactions, including anaphylaxis

ICD-9-CM Codes	Description
477.1	Allergic rhinitis due to food
558.3	Allergic gastroenteritis and colitis
692.5	Contact dermatitis due to food in contact with skin
693.1	Dermatitis due to food taken internally
708.x	Urticaria
988.0	Toxic effect of fish and shellfish
989.0	Toxic effect of hydrocyanic acid and cyanides
989.9	Toxic effect of unspecified substance
995.0	Other anaphylactic shock
995.1	Angioneurotic edema
995.2	Unspecified adverse effect of drug, <i>etc.</i>
995.3	Allergy unspecified
995.4	Shock due to anesthesia
995.60–995.69	Anaphylactic shock due to adverse food reaction with specific codes for unspecified food, peanuts, crustaceans, fruits and vegetables, tree nuts and seeds, fish, food additives, milk products, eggs, and other specified food
995.7	Other adverse food reactions not elsewhere classified
999.4	Anaphylactic shock to serum

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

patients with a likely acute reaction who had likely food-induced anaphylaxis.^{17–19} Next, we multiplied these two proportions against counts from the 2001–2009 NHAMCS to estimate the national number of ED visits for each ICD-9-CM code with food-related acute allergic reaction and with food-induced anaphylaxis. A list of ICD-9-CM codes selected because of their importance in earlier studies^{1,17–19} is shown in the Table 1. Each study included cases where the ICD-9-CM codes of interest were indicated for the primary or secondary diagnosis. The proportions of likely cases were different for children, adults, and overall (19, 13, and 16%, respectively, for food-related acute allergic reactions; 37, 43, and 46%, respectively, for food-induced anaphylaxis). Therefore, when these proportions were multiplied by weighted NHAMCS totals to estimate the national numbers of ED visits due to food-related

acute allergic reactions or food-induced anaphylaxis, the estimated totals for visits by children and visits by adults do not add up to the overall number of visits (they would have added up only if all proportions had been the same).

The first ED-based study was a multicenter retrospective cohort study performed at 21 North American EDs to examine ED visits for food allergy; ICD-9-CM codes 693.1, 995.60, 995.61 to 995.69, 995.0, and 995.3 were used to identify cases of food allergy.¹⁹ Physician investigators at each of the participating sites determined whether the ED visit was caused by food allergy. The second ED-based study was a multicenter retrospective cohort study performed at three Boston EDs to describe the management of food-related acute allergic reactions in children¹⁷ and adults.¹⁸ In the second study, all ED visits identified by ICD-9-CM codes 995.60, 995.61–995.69, 995.0, 693.1, 995.7, 558.3, and 692.5 and a random sample of the codes 995.3, 995.1, and 708.x were reviewed by two physicians, including an allergist, to determine whether the ED visit was caused by food allergy. In both studies, a food-related acute allergic reaction was defined as an acute episode of symptoms consistent with an IgE-mediated response in which the onset was temporally related (<2 hours earlier) to a known or suspected food allergen. For example, symptoms of an IgE-mediated response could include any one of the following: skin (itching, hives, and swelling), trouble swallowing and/or hoarse voice, respiratory (difficulty breathing, wheezing, and stridor), gastrointestinal (nausea, vomiting, abdominal pain/cramps, and diarrhea), or cardiovascular (dizziness and fainting).²⁰ The working definition of anaphylaxis resembled national diagnostic criteria established by the Second Symposium of the National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network.²⁰ Specifically, food-related anaphylaxis was defined as an acute allergic reaction involving two or more organ systems or hypotension alone. Hypotension was defined as a systolic blood pressure of <100 mmHg for adults and <90 mmHg for children between the ages of 10 and 17 years. For children <10 years old, hypotension was defined as a systolic blood pressure <70 mmHg plus (age multiplied by 2).²⁰

NHAMCS, the third study, is a nationally representative four-stage probability sample of visits to noninstitutional general and short-stay hospitals, excluding federal, military, and Veterans Affairs hospitals, in the United States. NHAMCS is conducted annually and covers geographic primary sampling units located in all 50 states and the District of Columbia. At each sampled hospital, trained hospital staff collect data during a randomly assigned 4-week data period, and a U.S. Census Bureau field supervisor reviews the data collection. The nonresponse rate for most items is <5%

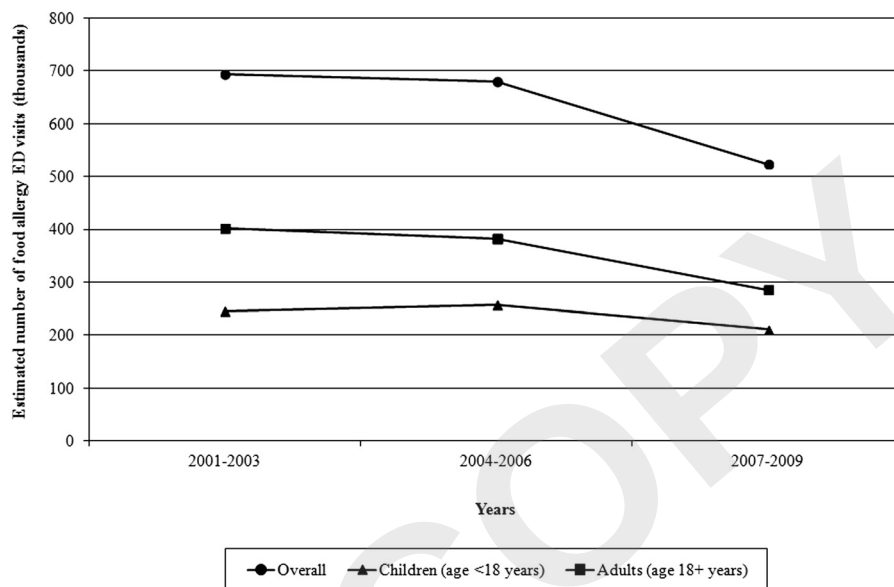


Figure 1. Estimated number of emergency department (ED) visits for food-related acute allergic reactions, 2001–2009.

and error rates are <2% for items that required medical coding. Completed data collection forms are sent for coding using the ICD-9-CM. National estimates are obtained through use of a multistage estimation procedure and patient visit weights. A detailed description of NHAMCS procedures is available in the technical notes section of each year's NHAMCS ED survey.²¹

The institutional review boards at each of the participating hospitals approved the studies.^{17–19} The requirement for informed consent was waived for these retrospective studies. Analysis of NHAMCS data has been classified as exempt by the Partners HealthCare Institutional Review Board.

Statistical Analysis

Analyses were performed using STATA 11.2 (StataCorp, College Station, TX) and NHAMCS design variables to estimate variance. To test for trends over time, we used linear regression, logistic regression, and a nonparametric Wilcoxon-based trend test, where appropriate. The *p* values for trend were generated using all 9 data years. A two-sided value of *p* < 0.05 was considered statistically significant. For visual representation of the trend data in figures, we used 3-year groupings and then generated weighted estimates for each of the three 3-year groups.

RESULTS

Over the 9-year study period (2001–2009), there were a total of 11,900,000 U.S. ED visits (95% CI, 10,700,000–13,100,000 visits), including repeat visits, identified using the specified ICD-9-CM codes. From this starting number, we estimated that 1,892,000 visits (16%) were likely food-related acute allergic reactions.^{17–19} On average, this represents ~210,000 ED visits for food-re-

lated acute allergic reactions each year. With a total of 525,600 min/yr, this suggests, on average, an ED visit for food-related acute allergic reaction somewhere in the United States every 3 minutes. Among children aged <18 years, there were 714,000 ED visits (19%) estimated to be likely food-related acute allergic reactions, with a visit occurring in the United States an average of every 7 minutes for adults aged ≥18 years and there were 1,069,000 ED visits (13%) for food-related allergic reactions, with a visit occurring in the United States an average of every 4 minutes. Adults accounted for approximately two-thirds of all ED visits for food-related allergic reactions.

Among the 1,892,000 ED visits for food-related allergic reactions during the study period, ~866,000 visits (46%), or 96,000 visits each year, would be classified as probable anaphylaxis.^{17–19} On average, an ED visit caused by food-induced anaphylaxis occurred somewhere in the United States every 5 minutes. Considering children's ED visits for food-related allergic reactions, 261,000 of these visits (37%) were likely caused by anaphylaxis, with a visit occurring in the United States an average of every 18 minutes. Among adult ED visits for food-related allergic reactions, 457,000 of these visits (43%) were likely caused by anaphylaxis, with a visit occurring in the United States an average of every 10 minutes.

Looking at trends over the 9-year period, the estimated number of U.S. ED visits considered to be likely food-related acute allergic reactions did not significantly change for total visits (244,000 visits in 2001 versus 194,000 visits in 2009; *p* = 0.09) or for visits among children (77,000 visits in 2001 versus 92,000 visits in 2009; *p* = 0.85; Fig. 1). However, among adults, a decline in the number of ED visits was detected,

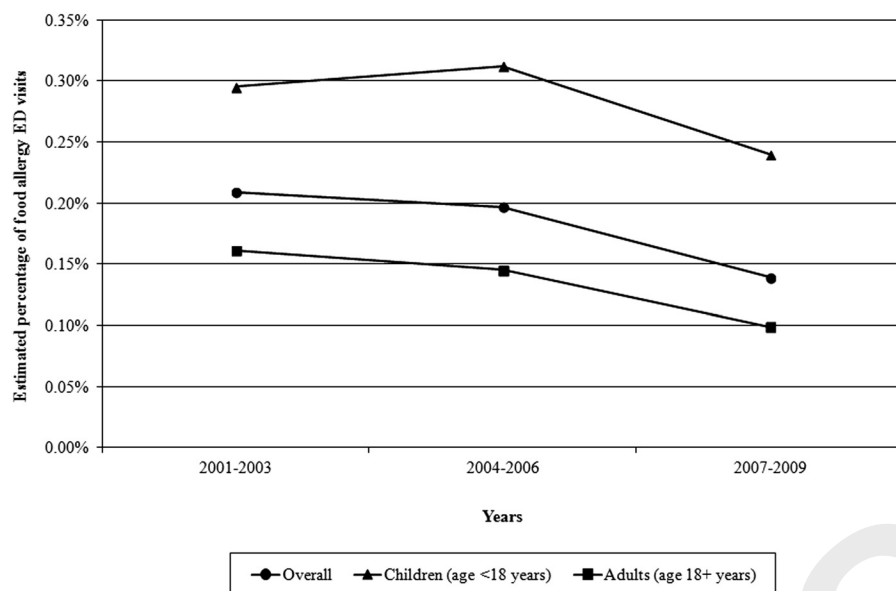


Figure 2. Estimated emergency department (ED) rates for food-related acute allergic reactions, 2001–2009.

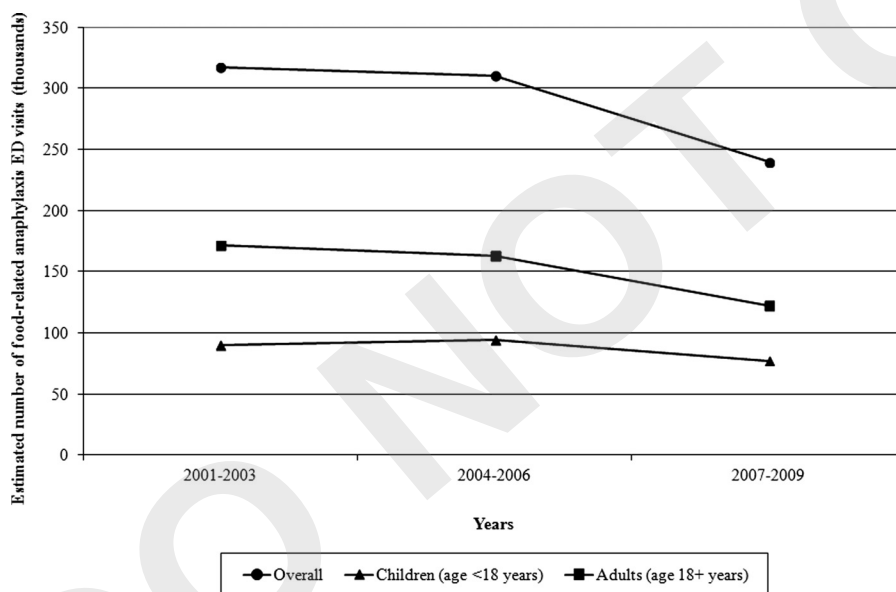


Figure 3. Estimated number of emergency department (ED) visits for food-related acute allergic reactions due to anaphylaxis, 2001–2009.

going from 147,000 visits in 2001 to 97,000 visits in 2009 ($p = 0.046$). Examining the overall rate of food-related acute allergic reactions among ED visits for any reason (Fig. 2) revealed a downward trend for total visits (0.23% of all ED visits in 2001 versus 0.14% in 2009; $p = 0.04$). This downward trend did not hold for children (0.29% in 2001 versus 0.28% in 2009; $p = 0.22$) but was present among adults (0.18% in 2001 versus 0.09% in 2009; $p = 0.01$).

Over the 9-year period, the subset of patients with likely food-induced anaphylaxis followed the same patterns (Figs. 3 and 4). The total number of ED visits for food-induced anaphylaxis went from 111,000 visits in 2001 to 89,000 visits in 2009 ($p = 0.09$) and from 28,000 visits to 34,000 visits among children ($p = 0.85$) and 63,000 visits to 41,000 visits among adults ($p =$

0.046). ED visit rates for food-induced anaphylaxis decreased in the total population (0.10% of all ED visits in 2001 versus 0.07% in 2009; $p = 0.04$) and among adults (0.08% versus 0.04%; $p = 0.013$) but was stable among children (0.11% versus 0.10%; $p = 0.22$).

DISCUSSION

This study extends our previous findings suggesting that the number of U.S. ED visits for food-related acute allergic reactions is significantly higher than prior reports.^{4,5} These results also suggest that the number of ED visits for food-related acute allergic reactions has been stable over time, despite earlier reports suggesting an increase in the prevalence of food allergies^{11–13} and an associated increase in ED visits¹⁴ and hospitalizations^{2,15} for food allergies.

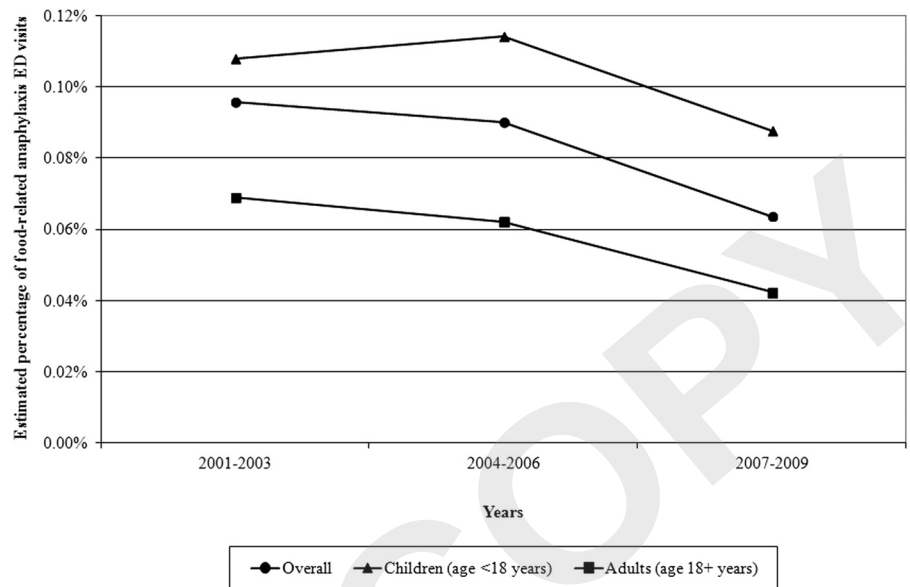


Figure 4. Estimated emergency department (ED) rates for food-related acute allergic reactions due to anaphylaxis, 2001–2009.

Recent studies, primarily among children, have shown increases in food allergy prevalence. Branum and Lukacs reported an increase in the prevalence of food allergy in the United States between 1997 and 2007 for children ≤ 17 years.^{1,2} Similarly, Hu and colleagues¹¹ performed two cross-sectional studies in China, one in 1999 and one in 2009, confirming food allergy by oral food challenge, the gold standard for diagnosis of food allergy.²² They reported a higher prevalence in 2009 compared with 1999. Peanut allergy is the most common food trigger for severe allergic reactions,¹⁰ and studies in the United States,²³ Australia,²⁴ and the United Kingdom^{12,13} have looked at this specific food allergy and observed increases in its incidence and prevalence over time.

With these reported increases in the prevalence of general food allergies and peanut allergies, specifically, one might reasonably expect associated increases in health care use for food allergy and anaphylaxis. Indeed, Branum and Lukacs examined ambulatory care visits (including ED, hospital outpatient, and physician office visits) for food allergy among children ≤ 17 years and found that the number of visits tripled between 1993 and 1997 and 2003 and 2006.¹ Although looking at only ED visits and not other ambulatory care visits, the current study did not observe an increase in the frequency of ED visits for food-related reactions. We observed a stable trend overall and among children between 2001 and 2009 and a decrease in the frequency of ED visits for food allergy among adults. These results are more consistent with earlier work by Gaeta and colleagues, also analyzing NHAMCS data, which reported a stable population rate of ED visits for allergic reactions (of any kind) between 1993 and 2004.³

Looking at more severe reactions, several studies have examined ED visits for food-induced anaphylaxis

and hospitalizations for allergic disorders.^{2,15,25,26} Similar to the current study, Bohlke and colleagues found that the rates of anaphylaxis in children were stable over time between 1991 and 1997.²⁷ Although this study did not focus on food-induced anaphylaxis alone, food was found to be the most common cause of anaphylaxis. Huang and colleagues also observed a consistent incidence of food-related anaphylaxis among children at a single New York City ED between 2004 and 2008.⁶ Rudders *et al.* recently reported a doubling of the rate of ED visits for food-induced anaphylaxis among children between 2001 and 2006 and a similar increase in hospital admissions during the same time period.¹⁴ Similarly, Gupta *et al.* reported an increase in hospital admissions for food allergy between 1990 and 1991 and 2000 and 2001 in the United Kingdom.²⁵

In addition to stable trends, overall and among children, in the frequency of ED visits for food-related allergic reactions, and a decrease in the frequency of reactions in adults, we also observed decreasing trends in ED visit rates (*i.e.*, the percentage of food allergy-related visits among all ED visits for any reason). Rates for ED visits attributed to food-related acute allergic reactions decreased between 2001 and 2009 overall and for adults, while remaining stable for children. Differences in observed trends could be attributed to geographical or practice variation. Although Branum and Lukacs^{1,2} evaluated trends using U.S. national data, Rudders (Boston, MA)¹⁴ and Bohlke (western Washington state)²⁷ focused on specific geographical areas in the United States. Gupta analyzed data from the United Kingdom,^{25,26} so differences in health care systems and diagnosis patterns should also be considered when comparing trends.

Although methods for identifying cases of food-related acute allergic reactions and food-induced anaphylaxis differed across studies, potentially contributing to different trends observed across studies, several studies used similar criteria for identifying cases and still observed different trends. The current study used a broad list of ICD-9-CM codes, similar to Branum and Lukacs^{1,2} and Ridders *et al.*,¹⁴ both of which reported increasing trends over time. A strength of the current study is that it incorporates data from two multicenter studies^{17,19} that used allergist review to confirm the diagnosis of food allergy among ICD-9-CM identified cases of food allergy, adjusting NHAMCS estimates by multiplying the proportion of cases within each ICD-9-CM that are likely to be food-related acute allergic reactions or food-induced anaphylaxis.

Because food allergies have been reported to differ between children and adults, with the prevalence of food allergies reported to be higher in children^{28,29} and increasing among this age group,^{30,31} we also evaluated differences in food allergy between children and adults. Despite a higher prevalence of food allergy among children compared with adults, adults appear to account for a higher proportion of ED visits for food-related acute allergic reactions and food-induced anaphylaxis. Ross and colleagues examined age-related differences in ED visits for food allergy and found that adults accounted for 73% of ED visits for food allergy and 57% of cases classified as anaphylaxis.⁴ Brangaza and colleagues compared the incidence of anaphylaxis in their pediatric ED population¹⁶ to a report focusing on adults³² and found that the incidence of ED visits for anaphylaxis were higher among adults compared with children.^{16,32} Our results are consistent with these earlier studies with adults accounting for approximately two-thirds of likely food allergy visits and food-induced anaphylaxis visits.

Trends in hospital admissions for food allergy also have been examined across age groups. Gupta and colleagues found an increase in the frequency of food allergy hospital admissions, with rates being highest in children.²⁶ Our study also found differences between children and adults with respect to trends in food-related acute allergic reactions and food-induced anaphylaxis; however, we observed that the frequency of ED visits for food-related reactions and ED visit rates were stable over time for children and decreased significantly for adults between 2001 and 2009.

Case identification is a potential limitation of this study. The inconsistent use of diagnostic codes for food-related allergic reactions^{33,34} and the lack of a universally accepted clinical definition for anaphylaxis have complicated the study of food-related acute allergic reactions and food-induced anaphylaxis.²⁰ While identifying cases of food-related acute allergic reactions and food-induced anaphylaxis using ICD-9-CM

codes, this study incorporates findings from previous studies, one including three Boston area EDs^{17,18} and one including 21 sites across the United States,¹⁹ which used allergist review to verify diagnoses, and adjusts the national estimates of ED visits and trends of food allergy and anaphylaxis. Despite accounting for the potential use of food allergy-related ICD-9-CM codes for cases that were not likely to be food-related reactions, the current study still found that previous reports underestimated the frequency of ED visits for food-related reactions. Although NHAMCS is a nationally representative sample of U.S. ED visits, it is possible that the earlier studies used to derive the proportion of ICD-9-CM codes likely to be food allergy or anaphylaxis may not be generalizable to the United States as a whole.

Many studies have reported the need for better education about the management of anaphylaxis, particularly at discharge from the ED, including being followed by an allergist, avoiding triggers, and carrying self-injectable epinephrine.^{19,35} With numerous studies reporting an ongoing rise in food allergy prevalence,^{11–13} the observed stability in the frequency and rates of ED visits for food-related allergic reactions between 2001 and 2009 among children—and decreasing trends among adults—suggest that efforts to educate both patients and clinicians on the appropriate management of food allergy are having beneficial effects. Nevertheless, although the trend of ED visits appears to be stable or decreasing, the number of visits for food-related allergic and anaphylactic reactions is higher than previously reported; the societal burden of ED visits for food allergy is quite large. Next steps might include well-designed surveillance programs to further improve our understanding of the incidence and prevalence of food-related allergic reactions. Taken together, these efforts will continue to improve public awareness about food allergy and anaphylaxis and support efforts to improve patient outcomes.

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