

Estimating the economic burden of food-induced allergic reactions and anaphylaxis in the United States

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Background: Food allergy is reported to affect 4% to 6% of children and 1% to 2% of adults in the United States. Every year, allergic reactions result in visits to physicians, emergency departments, and hospitals. However, the economic burden of food-induced allergic reactions is unknown.

Objective: We sought to estimate the direct medical costs and indirect costs of food-induced allergic reactions and anaphylaxis in the United States.

Methods: Costs were estimated with a bottom-up approach from a societal perspective: the average cost of illness per patient was calculated and multiplied by reported prevalence estimates. Patients with an inpatient admission, emergency department admission, office-based physician visit, or outpatient visit for a food-induced allergic reaction were identified from a list of federally administered 2006 and 2007 databases by using International Classification of Diseases, ninth revision, codes. Indirect costs were quantified by estimating lost productivity in terms of lost earnings caused by absenteeism and mortality of patients or caregivers. Sensitivity analyses were conducted to measure the robustness of the estimates.

Results: For 2007, direct medical costs were \$225 million, and indirect costs were \$115 million. Office visits accounted for 52.5% of costs, and the remainder was split between emergency visits (20%), inpatient hospitalizations (11.8%), outpatient visits (3.9%), ambulance runs (3%), and epinephrine devices (8.7%). Simulations from probabilistic sensitivity analyses suggested mean direct medical costs were \$307 million and indirect costs were \$203 million.

Conclusions: The economic burden of allergic reactions caused by food and anaphylaxis was an estimated half a billion dollars in 2007. Ambulatory visits accounted for more than half of the costs. (*J Allergy Clin Immunol* 2011;■■■:■■■-■■■.)

Key words: Food allergy, food anaphylaxis, economic burden, direct medical costs, indirect costs, cost of illness

Abbreviations used

CCS: Clinical Classifications Software
CPT: Current Procedural Terminology
ED: Emergency department
FAA: Food allergy and anaphylaxis
HCUP: Healthcare Cost and Utilization Project
ICD-9: International Classification of Diseases, ninth revision
NEDS: Nationwide Emergency Department Sample
NIS: Nationwide Inpatient Sample

Food-induced allergic reactions are acute medical events resulting primarily from abnormal immunologic responses to food proteins. The 8 most common food allergen triggers are peanuts, soy, milk, eggs, fish, shellfish, wheat, and tree nuts.¹ Adverse food reactions can result in acute onset of symptoms, including serious allergic reactions (anaphylaxis).² Food allergens are responsible for up to 50% of reported anaphylaxis cases presented to emergency departments (EDs) in developed countries, such as the United States.³⁻⁵ In children and young adults food triggers are the leading cause of anaphylaxis outside the hospital setting.^{6,7}

Food allergy awareness is increasing.⁸ The prevalence of food allergies in the United States is estimated to be 5% to 6% in young children and 3.7% in adults.⁹⁻¹¹ A recent report from the Centers for Disease Control and Prevention indicated an 18% increase in food allergy among children in the past decade.¹² Diagnosis of food allergy is challenging and complicated because most *in vitro* assays and skin tests have poor accuracy, and therefore misdiagnosis often occurs. Once a diagnosis of food allergy has been established, the only proved therapy is strict elimination of the offending allergen.

Food allergies can substantially burden patients and families by negatively affecting finances, social relationships, and personal perceptions of health.^{9,10} Patients and their families must be educated to avoid accidentally ingesting food allergens and to recognize early symptoms of an allergic reaction.¹³ Some activities of daily living, such as grocery shopping, can become time-consuming and expensive endeavors for these families. Moreover, allergic subjects and their families might experience anxiety and other stresses that affect quality of life given the risk of severe reactions and lack of control over those risks.¹⁰

The effect of food allergies is not limited to subjects and their families. Food allergies can lead to a significant economic effect on society and the health care system. Food-induced anaphylaxis can result in prehospital emergency care by ambulance personnel, ED visits, hospitalizations, or even death.¹⁴ It is estimated that 150 to 200 people die of food-induced anaphylaxis per year.^{10,15} Moreover, mild reactions, diagnostic tests, and regular checkups can require private clinic and hospital outpatient visits.

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Currently, no data exist on the economic burden of allergic reactions because of food allergy and anaphylaxis (FAA) in the United States. Having a monetary value on the effect of FAA could assist private and governmental decision makers in formulating public health policies and clinical guidelines. By using federal health care databases, we estimated the direct medical costs and indirect costs associated with FAA.

METHODS

Study design

This was a retrospective analysis of 2006 and 2007 data (the latest available) from published literature and 4 national databases maintained by federal agencies. A societal perspective was used as an approach because it has been found to be more comprehensive in assessing the costs attributable to a disease.¹⁶ Economic costs were estimated by using a prevalence-based approach, which involves measuring the costs of an illness in one period, usually a year, regardless of the date of disease onset.¹⁶ This approach was considered suitable because allergic reactions caused by food and food-induced anaphylaxis are acute illnesses. Direct medical costs were estimated by using a bottom-up approach, which involved calculating the average cost of treatment of the illness and multiplying it by the prevalence.¹⁶ Indirect costs from productivity loss caused by absenteeism or mortality were measured with the human capital approach by assigning an economic cost (eg, salary and benefits lost) for each day.

Data sources

Nationwide hospitalizations were captured with the Healthcare Cost and Utilization Project's (HCUP) Nationwide Inpatient Sample (NIS).¹⁷ The HCUP Nationwide Emergency Department Sample (NEDS) was used to estimate costs from ED visits.¹⁸ The National Ambulatory Medical Care Survey database was used to determine physicians' office visits, and the National Hospital Ambulatory Medical Care Survey–Outpatient Department database was used to estimate hospital outpatient visits. For assessing indirect costs from morbidity and mortality, the methods and data values described by Haddix et al¹⁹ were used.

Subject selection

Patients with allergic reactions caused by food or with food-induced anaphylaxis were identified from the databases by using the International Classification of Diseases, ninth revision (ICD-9), codes listed in Table 1. These codes, which are consistent with those used in the published literature, define subjects with IgE-mediated food allergy and not food intolerance.^{12,20,21} The study included patients with primary diagnoses and some patients with nonprimary diagnoses having primary diagnoses related to food allergy. For patients with secondary diagnoses of FAA, inclusion decisions were based on referencing the common symptoms from food allergy from the published literature.^{9,22,23} Consequently, if the description of a primary code was judged to be similar to one of the listed food allergy symptoms, the patient was included. Details on the inclusion of patients with nonprimary diagnoses of FAA can be found in the Methods section of this article's Online Repository at www.jacionline.org.

Measuring direct medical costs

Inpatient admission. The HCUP-NIS dataset provided total charges billed by facilities for the full inpatient stay, procedures and laboratory tests, or ED visits. This eliminated the need for tracking individual procedures and laboratory tests prescribed for the patient. Charges were converted to costs by using the hospital-specific cost/charge ratio, which was provided in a separate file with the dataset. Physicians' service fees were determined for the initial inpatient visit (Current Procedural Terminology [CPT] code 99222) and discharge visit lasting 30 minutes (CPT code 99238)²⁴ by using Medicare reimbursement for CPT codes and added to each discharge value.

TABLE 1. List of ICD-9 codes for food allergy and food-induced anaphylaxis

ICD-9 code	Description
995.6x	Anaphylaxis due to a variety of food items
477.1	Allergic rhinitis due to food
558.3	Allergic gastroenteritis and colitis
692.5	Contact dermatitis and other eczema due to food in contact with skin
693.1	Dermatitis due to food taken internally
995.7	Other adverse food reactions not elsewhere classified

Total inpatient costs were computed by first multiplying the final cost for each patient discharge by his or her patient-visit "weight" (provided by the database) and then by summing the results. The "weight" is an adjustment variable that is essential to generate national estimates of similar patient visits. Cost estimates for the years 2006 and 2007 were combined and averaged to generate cost estimates for 2007. A similar calculation procedure was repeated for all other cost categories.

ED visit without hospitalization. The HCUP-NEDS dataset provided total charges billed by facilities for the ED visit similar to NIS. However, NEDS does not provide the hospital-specific cost/charge ratio, and hence the charges were converted to costs by using an average ratio of 0.53 estimated from publicly available Medicare cost report data.²⁴ Physicians' visit fees were obtained by using Medicare reimbursement for CPT code 99284 (ED evaluation of a patient) and then were added to the costs. Total ED costs were computed by using a similar procedure as described under the inpatient admission methodology above.

Outpatient visit. Total costs for office-based physician and hospital outpatient visits were computed by aggregating the reimbursement costs for physicians' fees, diagnostic procedures, laboratory tests, and medications prescribed. Physicians' visit fees were obtained by using Medicare reimbursement for CPT code 99241 (15 minutes with physician). Reimbursements for FAA-related procedures were determined by using Ambulatory Payment Classification codes, which are maintained and used by the Center for Medicare and Medicaid Services.²⁵ For laboratory services, the Medicare Lab Schedule Reimbursement file was used; the file is freely available from the Center for Medicare and Medicaid Services Web site.²⁶ Reimbursements for medications were based on the average wholesale prices published in the Red Book.²⁷ Facility charges, which were obtained from published literature, were included in estimates of hospital outpatient visit costs.²⁸ Total ED costs were computed by using a similar procedure as described under the inpatient admission methodology above.

Ambulance runs. National estimates for ambulance runs in response to FAA were obtained from the study by Clark et al.²⁹ These estimates were multiplied by the mean Medicare reimbursement for an ambulance run, which was obtained from a Government Accountability Office report.³⁰

Epinephrine self-injectable autoinjector use. National estimates for epinephrine autoinjector use after a suspected allergic reaction caused by a food were obtained from the published literature,^{15,31,32} which suggested that between 30% and 86% of patients at risk for a severe allergic reaction are prescribed an epinephrine autoinjector and have it available at the time of their reaction for use. Based on this, a baseline estimate of 55% (as a percentage of subjects with food-induced allergic reactions that use an epinephrine autoinjector to treat the reaction)^{31,32} was multiplied by the average unit cost of an epinephrine autoinjector based on the average wholesale price obtained from the Red Book. An assumption was made that all patients who were given diagnoses of food allergy and had documented symptoms associated with a severe episode were prescribed and provided an epinephrine autoinjector.

Measuring indirect costs

Morbidity. Indirect costs caused by morbidity accounted for lost wages from work absenteeism. For inpatients, absenteeism was defined as their

TABLE II. Key variables and ranges used in sensitivity analyses

Variables	Baseline	Range	Source
Common variables			
Daily wage, men (USD)	\$164	\$131-\$197	†
Daily wage, women (USD)	\$109	\$87-\$131	†
Present value for future productivity lost (mortality costs)	Varies with age at death	Mean (SD) = 892,153 (453,180)*	Haddix et al ¹⁹
Inpatients			
Mean (SD) inpatient cost (USD)	\$4,719 (\$9,136)*		NIS dataset
No. of inpatients	11,508	9,620-21,713	Clark et al ³³
No. of inpatient deaths	15	15-150	Sampson et al ⁵ Bock et al ¹⁵
Days lost from work	3	Mean (SD) = 2.6 (4.1)*	NIS dataset
ED visits			
Mean (SD) ED visit cost (USD)	\$551.3 (439)*		NEDS dataset
No. of ED visits	163,876	131,071-309,200	Clark et al ³³
No. of ED deaths	8	8-150	Sampson et al ⁵ Bock et al ¹⁵
OPD visits			
Mean OPD visit costs	279	223-335	†
No. of OPD visits	66,849	53,479-126,130	Clark et al ³³
Office-based physician visits			
Mean visit costs	\$190	\$152-\$228	†
No. of office-based visits	1,168,101	934,481-2,203,964	Clark et al ³³
Ambulance runs			
Cost per ambulance run (USD)	\$470	\$376-\$563	†
No. of ambulance runs	29,498	24,581-40,969	Clark et al ³³
Epinephrine self-injectable device			
Cost of each device	\$51	\$41-\$61	†
No. of devices used	775,684	423,100-1,212,887	McLean-Tooke et al ³¹ Sicherer et al ³²

Note: All estimates used are combined values of years 2006 and 2007. *OPD*, Outpatient department; *USD*, US dollars.

*Means and SDs were used to generate the range by using a gamma distribution. We used uniform distribution in the remaining variables for Probabilistic Sensitivity Analysis.

†Range of $\pm 20\%$ was used in the absence of specific data from published literature.

length of stay. For patients with only an ED or outpatient visit, an absence of 1 day was estimated from the datasets. In cases of FAA in children, an absence of 1 day was assumed for 1 parent acting as a caregiver. The lost days of work were multiplied with the mean wage value of a lost day (Table II)^{5,15,19,31-33} based on the Current Population Survey conducted by the US Census Bureau, which was obtained from Haddix et al.¹⁹ These estimates were for the year 2000 and were adjusted upward to 2007 estimates by using average annual earnings increases reported by the Bureau of Labor Statistics.³⁴

Mortality. Indirect costs caused by mortality were projected based on the value of future lifetime earnings. For every patient who died, lost earnings were estimated based on their age and sex, with a discount rate of 3%.^{35,36} Mortality-related costs included earnings estimates and household production estimates, which refers to the value of household services performed by household members who do not receive pay for these services.¹⁹ These cost values were obtained from previously published mortality-related productivity tables.¹⁹

Sensitivity analyses

Sensitivity analyses were conducted to account for uncertainty in the estimated data. One-way sensitivity analyses were performed on cost and prevalence estimates by varying the value of 1 variable at a time through a range of plausible values while keeping the other variables constant. These analyses helped identify variables having the greatest effect on direct and indirect costs. Table II lists the baseline values and ranges along with their sources for all variables used in the sensitivity analyses. Probabilistic sensitivity analyses were also conducted by varying all key variables simultaneously and examining the effects on final costs.

Clark et al³³ reported that about 47% of patients are missed if ICD-9 codes alone are used for patient identification. This estimate was used to generate the

upper range for the number of inpatient, ED, and ambulatory visits in the sensitivity analysis. Although this estimate was based on ED visits only, in the absence of any other published reports, it was used for the analysis of other types of visits as well.

All data analyses were performed with SAS version 9.1 software (SAS Institute, Inc, Cary, NC) and Predictive Analytical Software (PASW version 17.0, previously known as SPSS; SPSS, Inc, Chicago, Ill). Sensitivity analysis was done with MS Excel 2007.

Some additional subgroup analyses were done with the food-induced anaphylaxis patient cohort (ICD-9 code 995.6x) to determine the prevalence and compare costs with nonanaphylactic patients. Also, patients in each cohort were categorized into 7 age groups, and annual direct medical costs were calculated for each group. Throughout the analyses, patients aged less than 18 years were defined as children.

RESULTS

In 2006 and 2007, an estimated 1.4 million medical encounters caused by FAA occurred in the United States. Table III provides a description of the demographic and clinical characteristics of these patients in the 4 different datasets.

Direct medical costs

Total annual direct medical costs caused by FAA reactions were estimated at \$225 million (year 2007 US dollars, Table IV). Office visits accounted for 52.5% of costs, and the remainder were split between ED visits (20%), inpatient

TABLE III. Demographic and clinical characteristics of patients with FAA (2006 and 2007 combined)

Characteristics	Inpatients (NIS)	ED visit (NEDS)	OPD visit (NHAMCS-OPD)	Office-based physician visit (NAMCS)
No. of visits				
Sample count*	2,259	35,907	24	26
Weighted count	11,000	164,000	67,000	1,168,000
Age (y), mean (SD)	25.8 (26.3)	26.6 (20.1)	8.0 (15.1)	23.4 (26.4)
Children (<18 y), no. (%)	1,142 (50.6)	13,796 (38.4)	22 (91.7)	16 (61.5)
Sex, male/female (%)	48.8/50.5	44.6/55.4	54.2/45.8	53.8/46.2
Race, no. (%)†				
White	894 (39.6)	NA	10 (41.7)	16 (61.5)
African American	378 (16.7)	NA	10 (41.7)	5 (19.2)
Hispanic	272 (12)	NA	3 (12.5)	5 (19.2)
Asian/Pacific Islander	67 (3.0)	NA	1 (4.2)	0
Other	109 (4.8)	NA	0	0
Asthma, no. (%)	495 (21.9)	2,270 (6.3)	6 (25)	6 (23.1)
Mortality, no. (%)	7 (0.3)	2 (0.006)	0	0
Length of stay (d), mean (SD)	2.5 (4.2)	NA	NA	NA

Note: Weighted counts were rounded to the nearest thousand. NA, Not available; NAMCS, National Ambulatory Medical Care Survey; NHAMCS-OPD, National Hospital Ambulatory Medical Care Survey–Outpatient Department; OPD, outpatient department.

*Records with missing cost values were excluded.

†Few patients had missing information on this variable.

TABLE IV. Direct medical costs and indirect costs (USD 2007 values)

Type of costs	Direct medical costs		Indirect costs
	Mean costs per patient (SD)	Total annual costs (in millions)	Morbidity/mortality (in millions)
Inpatients	\$4,719 (\$9136)	\$26.6	\$2.0/\$12.2
ED visits	\$553 (\$462)	\$44.8	\$10.9/\$4.8
Office-based physician visits	\$193 (\$119)	\$118.2	\$80.2/\$0
OPD visits	\$280 (\$89)	\$8.7	\$4.8/\$0
Ambulance runs	\$469.5*	\$6.9	NA
Epinephrine self-injectable autoinjector	\$50.7*	\$19.7	NA
Total	NA	\$224.9	\$114.9

NA, Not available; OPD, outpatient department; USD, US dollars.

*These are unit costs per ambulance run or epinephrine autoinjector, and hence there are no SDs for these values.

hospitalizations (11.8%), outpatient department visits (3.9%), ambulance runs (3%), and epinephrine devices (8.7%). Children accounted for 46.6% of the total inpatient costs, 31.5% of the ED visit costs, 67.3% of the office-visit costs, and 97.7% of the total outpatient department visit costs. Additional breakdown of annual medical costs was conducted by age group and is presented in Table V.

Food-induced anaphylaxis (ICD-9 code 995.6x) was reported for 44% of the hospitalized patients and 10.6% of ED patients. Mean costs incurred by hospitalized anaphylactic patients (\$4,445) were found to be significantly lower than costs for similar nonanaphylactic patients with food allergy (\$4938; $P = .003$, Kruskal-Wallis test). This differs from the ED-visit population sample, in which food-induced anaphylactic patients incurred significantly higher costs (\$749) than nonanaphylactic allergic patients (\$527; $P < .001$, Kruskal-Wallis test).

Indirect costs

Morbidity-related costs were dominant, accounting for 85% of the indirect costs. These costs primarily resulted from disease-related sick days. Among morbidity-related indirect costs, office visits comprised the majority proportion (82%, Table IV). Indirect costs associated with mortality were relatively minor in the base case assessment.

Sensitivity analyses

A series of 1-way sensitivity analyses revealed the most influential variables in the cost models. Prevalence estimates and mean costs for office, inpatient, and ED visits had the largest effect on direct costs. For instance, a $\pm 20\%$ variation in the office-visit prevalence resulted in a $\pm \$120$ million effect on direct costs. For indirect costs, changes in the number of food allergy-related deaths and office-visit prevalence estimates had the largest effect on estimates.

A probabilistic sensitivity analysis was conducted by using all of the variables within the ranges specified in Table II. This analysis ran 10,000 simulations of the model by using random selections of all model variable values within their specified ranges. The findings of this sensitivity analysis are reported in Table VI and depicted in Fig E1 (available in this article's Online Repository material at www.jacionline.org).

DISCUSSION

This is the first study to provide estimates of the economic burden of FAA in the United States. In our analysis of more than 35,000 patients with food-induced allergic reactions, estimated direct medical costs were \$225 million and indirect costs were \$115 million for 2007. Given irregularities in reporting and diagnosing food allergy, these values might be an underestimation. Simulations from probabilistic sensitivity analyses generated mean direct medical costs of \$307 million and indirect costs of \$203 million, and these can be considered more robust estimates.

More than 50% of the total costs came from office-based physician visits, primarily because the national estimate for the

TABLE V. Total annual medical costs categorized by patients' ages

Age groups	Annual direct medical costs (in millions USD)				
	Inpatient	ED	Office visit	OPD	Total
<4 y	10.0	7.1	42.8	7.3	67.1
5-11 y	1.3	3.3	34.8	1.3	40.6
12-18 y	1.3	4.7	1.8	0.03	7.7
19-34 y	2.7	11.7	—	0.04	14.4
35-49 y	4.0	9.5	21.2	—	34.7
50-64 y	4.3	6.0	9.5	—	19.8
>65 y	3.2	2.8	7.9	0.1	13.9

OPD, Outpatient department; USD, US dollars.

number of office visits was large. The cost values are based on a sample size of fewer than 30 and hence should be interpreted with caution. It was anticipated that ED visits would account for the largest sample proportion; however, the data revealed otherwise.

Because this was the first investigation focusing on the economic burden of food-induced allergic reactions, the results could not be compared with those of other published studies of FAA. Comparisons with total medical costs in the United States of allergic rhinitis (\$1.2 billion³⁷) and asthma (\$7.8 billion³⁸) showed them to be significantly higher than the baseline estimate (\$0.23 billion) we calculated for FAA events. These dissimilarities could be due to differences in prevalence rates, and hence comparing mean cost per visit might provide a better indication of relative costs. For asthma, mean costs per ED visit (converted to 2007 US dollar value) were \$345,^{38,39} which is less than \$553 for FAA. For hospitalization, the mean cost per patient was \$4,570,^{38,39} which is also less than the \$4,719 estimate for FAA.

This analysis sought to understand the economic burden of food-induced allergic reactions and anaphylaxis. For a more accurate comparison with other diseases, future work should assess the total economic burden of food allergy. Specifically, the total economic burden of food allergy should include intangible costs, such as quality of life and the cost associated with epinephrine autoinjectors that are dispensed to subjects at risk for food allergy but that are never used during a reaction. Analyses should also include cost data associated with patients who do not seek medical attention for their food-induced reaction but incur self-treatment or other nonquantified costs. An argument can be made that the number of patients with self-perceived allergy to food who do not seek medical attention is greater among those with food allergy than other conditions, such as asthma, and hence this might have a substantial effect when comparing the economic burden of other diseases with that of food allergy.

In our analysis nationwide estimates of office-based physician visits accounted for more than 80% of FAA visits. The range used for the office-visit prevalence estimate was wide, explaining why the estimate had so much effect on the variability of direct and indirect costs. Deaths associated with FAA had a significant effect on indirect costs because of the lost productivity associated with each additional death. On average, the cost to society from the death of a working adult would be close to a million dollars. Another variable affecting indirect cost estimates was days of work lost because of an outpatient visit. Because there is a dearth of published studies on the topic, the authors assumed 1 lost day for the analysis based on expert opinion. Changing this assumption to a half day of lost productivity decreased indirect costs from

TABLE VI. Results of probabilistic sensitivity analysis (USD 2007 values)

After 10,000 simulations	Direct costs (in millions)	Indirect costs (in millions)
Mean	\$307.0	\$202.7
SD	\$89.5	\$39.7
Minimum	\$180.3	\$112.3
Maximum	\$1290.6	\$443.8
Median	\$283.1	\$197.3

USD, US dollars.

\$114.9 million to \$72.4 million, whereas changing it to zero days decreased indirect cost estimates to \$29.9 million. Future investigations should seek to replace these assumptions with actual data to obtain more accurate estimates.

Probabilistic sensitivity analysis is considered the most appropriate form of sensitivity analysis because it generates estimates by varying all variables simultaneously multiple times. The mean direct costs after 10,000 simulations were \$307 million, which was a 36% increase from the baseline value. For indirect costs, the mean estimate was \$203 million, a 76% increase from baseline. The large discrepancy between the sensitivity analysis and baseline estimates indicates that the baseline numbers are not very robust. This suggests that any reports of baseline estimates should be accompanied by sensitivity analysis estimates.

The economic burdens of diseases are often computed by using costs and prevalence estimates obtained from a variety of sources, which can introduce inaccuracies in the final estimates. Several studies have highlighted severe irregularities in the diagnosis and coding of FAA.^{33,40} This creates challenges in estimation and interpretation of costs. For instance, Clark et al³³ indicated almost half of the patients with food allergy are missed in searches that use food-specific ICD-9 CM codes alone.

Additionally, it is important to acknowledge that the positive predictive value of food allergy ICD-9 codes varies greatly. For example, a higher proportion of patients coded 995.6x (anaphylaxis caused by food items) will have true food allergy compared with those coded 995.7 (other adverse food reactions not elsewhere classified). However, the overidentification of some codes might be offset by the underidentification of other codes, which might balance the overall estimates. In this analysis codes that provide limited information on whether a patient had a true food-induced allergic reaction, such as 995.3 (allergy unspecified), were not included in the analysis.³³ This can result in further underestimation of the economic burden of food-induced allergic reactions.

Other limitations of the analysis that can result in further underestimation include the fact that the study did not include the cost of epinephrine autoinjector prescribing for at-risk patients and included only autoinjectors used as a result of a reaction. Also, direct nonmedical costs, such as those incurred from lifestyle changes caused by FAA, were not estimated. The costs from lifestyle changes, such as alteration in diet, are difficult to estimate from a database analysis. Future studies should consider collecting these data.

Another limitation of this analysis includes the use of the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey databases, which contain only 30,000 patient-visit records and made it difficult to find a sufficient number of records from patients with food allergy to

generate reliable estimates. The study used hospital-specific cost/charge ratios (ie, one ratio for all hospital services) rather than service-specific ratios. This might have introduced errors in the estimates because using 1 common ratio across different hospital services might overestimate or underestimate actual costs.²⁴ Also, the cost values range over 2 years, 2006 and 2007, but the results were reported for the 2007 baseline year without any adjustments. However, analysis of the data indicated the difference between 2006 and 2007 estimates to be small (<4%). Because the prevalence of FAA has increased over the last several years,¹² it might be assumed that the estimate provided by this study has also increased since then. Finally, the study did not specify the proportion of costs related to medications because the NIS and NEDS databases only provide the final charges incurred.

In summary, results from this retrospective data analysis demonstrate that FAA events are associated with a significant financial burden to society. Direct medical costs accounted for two thirds of the total economic burden. The mean costs of an ambulatory visit were less than half those of ED visits and negligible compared with the mean cost of hospitalization. Simulation results from probabilistic sensitivity analyses generated significantly higher cost estimates than baseline values and should be considered more robust. The study provided useful cost estimates for future health economic evaluations, such as cost-effectiveness analyses of new food allergy treatments.

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Key messages

- Allergic reactions caused by food in the United States result in an estimated economic burden of at least \$340 million for a given year.
- Sensitivity analyses suggest a higher estimate of \$510 million, primarily because of the uncertainty surrounding prevalence estimates of food-induced allergic reactions.
- Ambulatory visits account for more than half of costs.

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METHODS

Selection of patients with nonprimary diagnoses of FAA

Selection of patients based on only primary diagnostic codes or primary and nonprimary codes was a challenge. Including nonprimary codes would ensure that genuine patients with FAA coded as having nonprimary diagnoses for reimbursement reasons were considered for the analysis. However, it could be argued also that this fails to account for costs attributed to the primary diagnosis under situations in which the primary diagnoses were not related to FAA. After a thorough literature review and consultation with subject matter experts, it was decided to include patients with both primary and nonprimary diagnostic codes. The steps involved in subject selection are described in [Fig E2](#).

Because there were few patients (<50) in the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey–Outpatient Department datasets, the primary ICD-9 diagnostic codes for each patient with a nonprimary diagnosis were perused manually by the first author. A decision on whether the codes were related to FAA was made based on referencing the common symptoms from food allergy, a clinician's opinion, and by consensus. Hence if a primary code's description was found to be similar to one of the listed food allergy symptoms (obtained from published literature^{E1-E3}), the patient was included. The list of primary ICD-9 codes that were included are presented in [Table E1](#).

In the NIS and NEDS datasets combined, there were more than 20,000 patient records. Initial analysis revealed more than 1,000 unique ICD-9 codes for patients with nonprimary diagnoses. Examining each code was not practical, and therefore an alternative that involved using Clinical Classifications Software (CCS) codes developed by HCUP for its NIS and NEDS datasets was chosen. This classification system collapses the multitude of ICD-9 diagnostic (14,000) and procedure (3,900) codes into a smaller number (about 250) of clinically meaningful categories. For every ICD-9 code, each patient in these datasets is also assigned a matching CCS code. Hence the primary CCS codes for patients with nonprimary diagnoses were evaluated and, by using criteria as discussed above, were either included or excluded from the analysis. Along with the description of CCS codes, the list of ICD-9 codes included under the selected CCS codes was also reviewed before making the inclusion/exclusion decision. A list of primary CCS codes that were included is presented in [Table E2](#).

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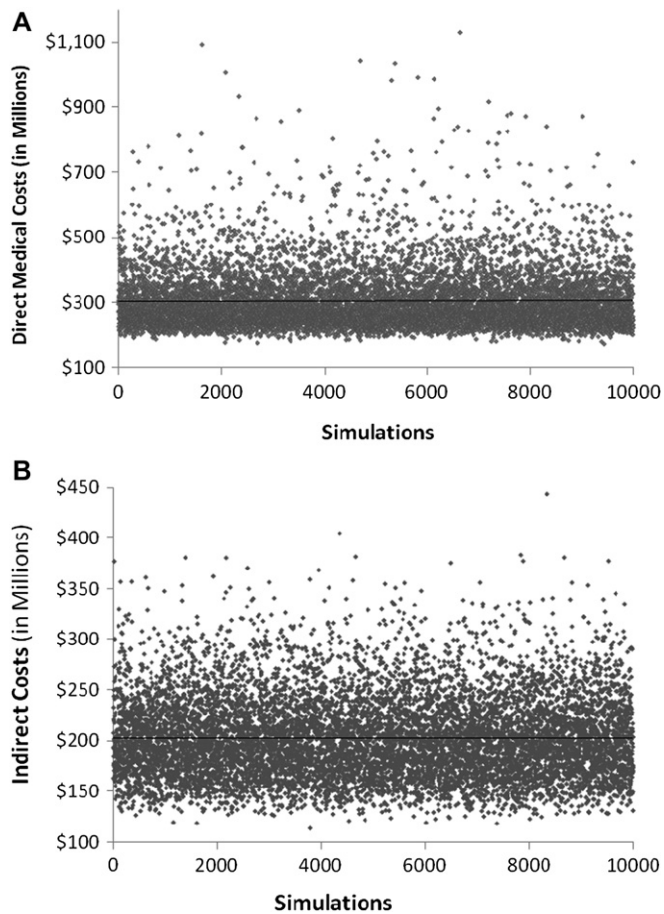
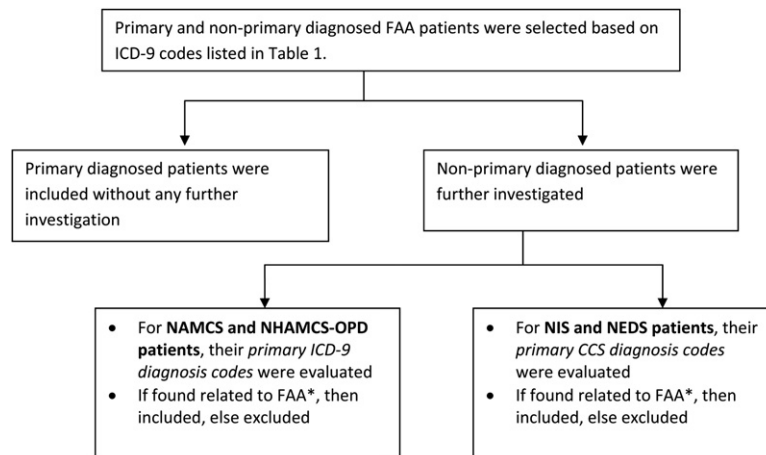


FIG E1. Scatter plot for simulation. **A**, Direct costs. **B**, Indirect costs.



*FAA related codes are described in the text below

FIG E2. Flowchart depicting how subjects with primary and nonprimary diagnostic codes were selected for the analysis.

TABLE E1. Primary ICD-9 codes for NAMCS and NHAMCS-OPD patients with nonprimary diagnoses included in the analysis

ICD-9 code	Description
692.9	Contact dermatitis and other eczema, unspecified cause
477.90	Allergic rhinitis, unspecified cause
691.80	Other atopic dermatitis and related condition
708.00	Allergic urticaria
472.00	Chronic rhinitis
708.90	Unspecified urticaria
473.90	Unspecified sinusitis (chronic)
536.90	Unspecified functional disorder of stomach
477.20	Allergic rhinitis

NAMCS, National Ambulatory Medical Care Survey; NHAMCS-OPD, National Hospital Ambulatory Medical Care Survey—Outpatient Department.

TABLE E2. Primary CCS codes for NIS and NEDS patients with nonprimary diagnoses included in the analysis

CCS code	Description
251	Abdominal pain
253	Allergic reactions
128	Asthma
93	Conditions associated with dizziness or vertigo
138	Esophageal disorders
140	Gastritis and duodenitis
250	Nausea and vomiting
154	Noninfectious gastroenteritis
155	Other gastrointestinal disorders
198	Other inflammatory condition of skin
200	Other skin disorders
131	Respiratory failure; insufficiency; arrest
245	Syncope