

Review

Economic burden of food allergy

A systematic review

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Key Messages

- Countries without single-payer (universal) health insurance have higher mean direct medical costs than those with single-payer health insurance.
- Household-level estimates of lost opportunity costs impose the largest economic burden of food allergy, with mean costs of \$4881 across several studies.
- Standardized instruments and methods are necessary to fully understand the economic effect of food allergies across the world.
- Out-of-pocket costs, including the costs of special diets, are an important component of the economic burden in several studies.

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ABSTRACT

Objective: To assess the economic burden of food allergy (FA) worldwide.

Data Sources: PubMed MEDLINE, Embase, and Cochrane Central Register of Controlled Trials on the Wiley platform were searched to identify literature that assessed direct, out-of-pocket, and opportunity costs of FA. All databases were searched back to their inception, and no language or date limits were applied.

Study Selections: We included primary studies that examined direct medical, out-of-pocket, or opportunity costs and/or lost labor productivity in food allergic adults and/or children and their families.

Results: Eleven papers met our inclusion criteria, of which 7 addressed direct medical, 7 addressed out-of-pocket, and 5 addressed opportunity costs. Estimates were based on data that reflected costs for a patient with FA (individual level) or costs for a household with a food allergic patient (household level). The mean individual-level direct medical costs (\$2081) were much higher than the mean household-level costs (\$806). The mean individual-level out-of-pocket (\$1874) and opportunity (\$1038) and opportunity cost were lower than the mean household-level out-of-pocket (\$3339) and opportunity (\$4881) costs. Household-level estimates of lost opportunity costs imposed the largest economic burden attributable to FA.

Conclusion: Most of the economic burden studies reviewed measured components of economic burden that are unique to individuals with FA but did so in noncomparable ways. Addressing cost burdens and measuring them using standardized instruments and methods will be critical to better understand the economic burden of FA globally.

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Introduction

Food allergy (FA) is a life-threatening condition that is an increasing health concern worldwide. Currently in the United States, 8% of children have a parent-reported FA.¹ Much of the

epidemiologic work on FA has focused primarily on children; however, recent estimates have found that 10.8% of adults in the United States have a self-reported FA.² Furthermore, numerous studies have estimated the prevalence of FA in children from countries across Europe, including France (6.7%),³ Greece (5.2%),⁴ and Sweden (6.8%).⁵

FA imposes a significant cost to the health care system as well as to families. Studies of the economic burden of diseases such as FA, also known as cost-of-illness studies, can vary greatly in terms of perspective and methods.^{6,7} The societal perspective reflects costs beyond those directly affecting the individuals and families with the condition and is generally the most comprehensive. The health care system perspective reflects only medical costs incurred by the health care system for the treatment of a particular disease. The patient and family perspective is one that reflects costs borne by the family directly or costs to the overall household income in terms of lost opportunities.

Methodologic approaches also vary and include top-down, bottom-up, and econometric approaches.⁶ A top-down approach is one where a population-attributable fraction is used to allocate aggregate costs to a total population with a disease. A bottom-up approach is one where individual-level costs per person with a disease are multiplied by the total number of individuals in the population with the disease to estimate a mean cost per person. The econometric approach is one that compares the costs for a cohort of individuals with the disease to a cohort without the disease. From the comparison, an incremental cost of the disease can be described.

Regardless of perspective and methodologic approach, economic burden studies typically quantify direct and indirect costs of the disease. In the case of FA, direct health care costs related to the condition include those stemming from emergency department (ED) visits, hospitalizations, and office visits. Out-of-pocket costs related to FA are those costs borne by the patient or the patient's family and include items such as special allergen-free foods, copayments for health insurance and medications, transportation costs, and costs for safe child care. Compared with countries that offer public health insurance for all residents, the costs of health insurance copayments for health care encounters and prescription medications can be substantial. Finally, opportunity costs are those that refer to the cost of opportunities or time lost stemming from the condition. In the case of FA, opportunity costs can arise when parents of children with FA give up a job or restrict career choices to care for the food allergic child as well as lost wages from visits to health care professionals.

Few studies have described the economic burden of FA, and among those that have, there is a lack of consensus regarding costs to the health care system and families. Therefore, the purposes of this study were to systematically review the literature measuring the costs of FA and summarize direct medical costs, out-of-pocket spending, and opportunity costs of childhood and adult FAs across studies.

Methods

Search strategies were determined collaboratively by the study team using various terms related to FA and costs. A librarian conducted the searches in the following databases: PubMed, MEDLINE, Embase (embase.com), and Cochrane Central Register of Controlled Trials (CENTRAL) on the Wiley platform. All databases were searched back to their inception, and no language or date limits were applied. The complete search strategies used are available in [eAppendix 1](#).

Two independent reviewers screened selected abstracts using Covidence software with the following inclusion criteria: primary studies examining direct medical cost, out-of-pocket cost,

opportunity cost, and/or lost labor productivity in food allergic adults and/or food allergic children and their families. We excluded studies that examined projected future costs related to allergy and studies that examined other food hypersensitivities, allergic rhinitis, eosinophilic esophagitis, food protein–induced enterocolitis syndrome, or other related disorders. We also excluded studies that examined quality-adjusted life-years because these units would not be comparable to other costs. The references of key articles were also checked for additional articles, and none were found.

Data extraction and quality assessment were undertaken by 2 independent reviewers. Several items were extracted, including citation and source information, demographic characteristics of the studied population, research design, sample size, study period, objectives, and economic costs, as noted in the inclusion criteria. This information is presented in [Table 1](#). Finally, 2 independent reviewers assessed the final set of articles included in the review for any potential selection and reporting bias and/or methodologic concerns using the Cochrane Risk of Bias Comparison.¹⁹

Search Results

A total of 1373 references were found in the 3 databases. After deduplication using EndNote software and secondary deduplication using Covidence, 898 references were left to screen. During the initial title and abstract screening phase, 868 citations were excluded based on the inclusion and exclusion outlined earlier, leaving the full text of 30 articles to be screened. A total of 11 articles were selected for inclusion. Reasons for exclusion are included in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram ([Fig 1](#)).

With respect to quality assessment, most of the 11 articles were from validated surveys, although many of the studies used small, clinically based samples that were not representative of the general populations of children and adults with FA.

Among the 11 papers included in the review, study design and methodologic approaches varied greatly. Four of the articles were part of the EuroPrevall project, a large, multinational initiative to better understand the effect of FA.^{11,13,15,18} All 4 of the EuroPrevall articles included in the review used a questionnaire developed specifically for household-level economic burden studies using a case-control design.^{11,13,15,18} Individuals with FA included in EuroPrevall had positive IgE test results or a positive food challenge result with symptoms or a history of FA. The cases were households that contained adults or parents of children with FA, while the controls were those households without an individual with FA. For cases, estimates of annual direct medical, out-of-pocket, and opportunity costs were not necessarily specific to the FA and instead represent total household costs; however, the difference in costs between cases and controls could be interpreted as the incremental cost of FA within the sample. The EuroPrevall articles yielded household-level incremental costs of FA in Sweden, Greece, Iceland, Poland, and Spain. All costs were extracted for analysis and converted to 2018 US dollars.

Of the 7 articles that were not part of EuroPrevall, all described individual-level or societal-level costs of FA, and 4 surveyed parents of children with FA to measure costs. The studies by Gupta et al¹⁴ and Bilaver et al¹⁰ used the same sample of 1643 US caregivers of children with FA to determine annual per patient health care use, out-of-pocket spending, and lost opportunities stemming from the child's FA. Two articles from Finland^{8,9} and 1 from France¹² also yielded individual-level costs of direct medical costs, out-of-pocket spending, and opportunity costs. Miller et al¹⁶ used data from the Medical Expenditure Panel Survey (MEPS) to examine direct medical costs only for children with FA. Data from each of these

Table 1
Summary of Included FA Economic Studies

Study	Country	Currency	Study design	No. of participants	Age	Inclusion and exclusion criteria	Outcomes
Alanne, ⁸ 2012	Finland	Euros	Questionnaire-based self-reported survey	23	6 months to 2 years	Children without FA at ages 6, 12, and 24 months	Estimation of dietary costs on the basis of dietary records was possible but challenging. In infancy, cost differences were quite small. In those infants with more severe allergy, hydrolyzed formulas are the main reason for increased costs.
Alanne et al, ⁹ 2012	Finland	Euros	Prospective mother-infant study	60	0-2 years	Mothers with possible development of allergic disease; in the infants, diagnosis of FA between the ages of 0 and 24 months	Cow's milk allergy emerged as the most expensive allergic disease, especially for the society, and concurrent asthma in particular further increased the costs.
Bilaver et al, ¹⁰ 2016	United States	Dollars	Cross-sectional survey	1643	0-17 years	Caregivers of children with FA in the United States	Disparities exist in the economic effect of FA based on socioeconomic status. Affordable access to specialty care, medications, and allergen-free foods are critical to keep all children with FA safe, regardless of income and race.
Cerecedo et al, ¹¹ 2014	Spain and Poland	Geary-Khamis international dollar	Prospective, longitudinal cost analysis study	42 (31 children, 11 adults)	Children and adults (ages undefined)	Individuals with FA	Double-blind, placebo-controlled food challenge has an effect on indirect and direct costs of living.
Flabbee et al, ¹² 2007	France	Euros (€)	Retrospective cohort study	402 (96 children, 152 adults)	Children and adults (ages undefined)	Individuals diagnosed with food anaphylaxis	The prevalence was underestimated because of many biases, leading to underestimation of the national cost. Additional studies would be necessary to evaluate the value of preventive strategies.
Fox et al, ¹³ 2013	Greece, Iceland, Poland, and Spain	Geary-Khamis international dollar	Case-control study	1682: (843 children, 839 adults)	Children (7-11 years) and adults (20-54 years)	Individuals with IgE diagnosed FA	Individuals with FA had higher health care costs than controls. FA is associated with higher health care costs. Severity of allergic symptoms is a key explanatory factor.
Gupta et al, ¹⁴ 2013	United States	Dollars	Cross-sectional survey	1643	0-17 years	Caregivers of children with FA in the United States	Caregivers of children with FAs were asked to quantify the direct medical, out-of-pocket, lost labor productivity, and related opportunity costs.
Jansson et al, ¹⁵ 2014	Sweden	Euros	Case-control study	81	19-78 years	Adults with a history of FA, who had been diagnosed by a food challenge or IgE test	Swedish adults with allergy to staple foods have higher total costs determined as direct, indirect, and intangible costs using the disease-specific socioeconomic questionnaire.
Miller et al, ¹⁶ 2016	United States	Dollars	Secondary analysis (Medical Expenditure Panel Survey)	8034 (had one of 5 chronic conditions including FA)	0-18 years	Children aged 0-18 years, with FAs, asthma, diabetes, or epilepsy compared with children without these conditions	Management and prevention of chronic conditions in children and adolescents can maximize health outcomes and reduce unnecessary health care use and costs.
Patel et al, ¹⁷ 2011	United States	Dollars	Retrospective analysis	38216 (undefined distribution)	Children (0-18 years) and adults (≥18 years)	Patients with allergic reactions caused by food or with food-induced anaphylaxis	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.
Protudjer et al, ¹⁸ 2015	Sweden	Euros	Case-control study	144	0-17 years	Children with a history of FA, who had been diagnosed by a food challenge or IgE test	Households with a child and/or adolescent with objectively diagnosed allergy to staple foods have higher total household costs than controls. Direct and indirect costs were significantly higher for cases vs controls among children only.

Abbreviation: FA, food allergy.

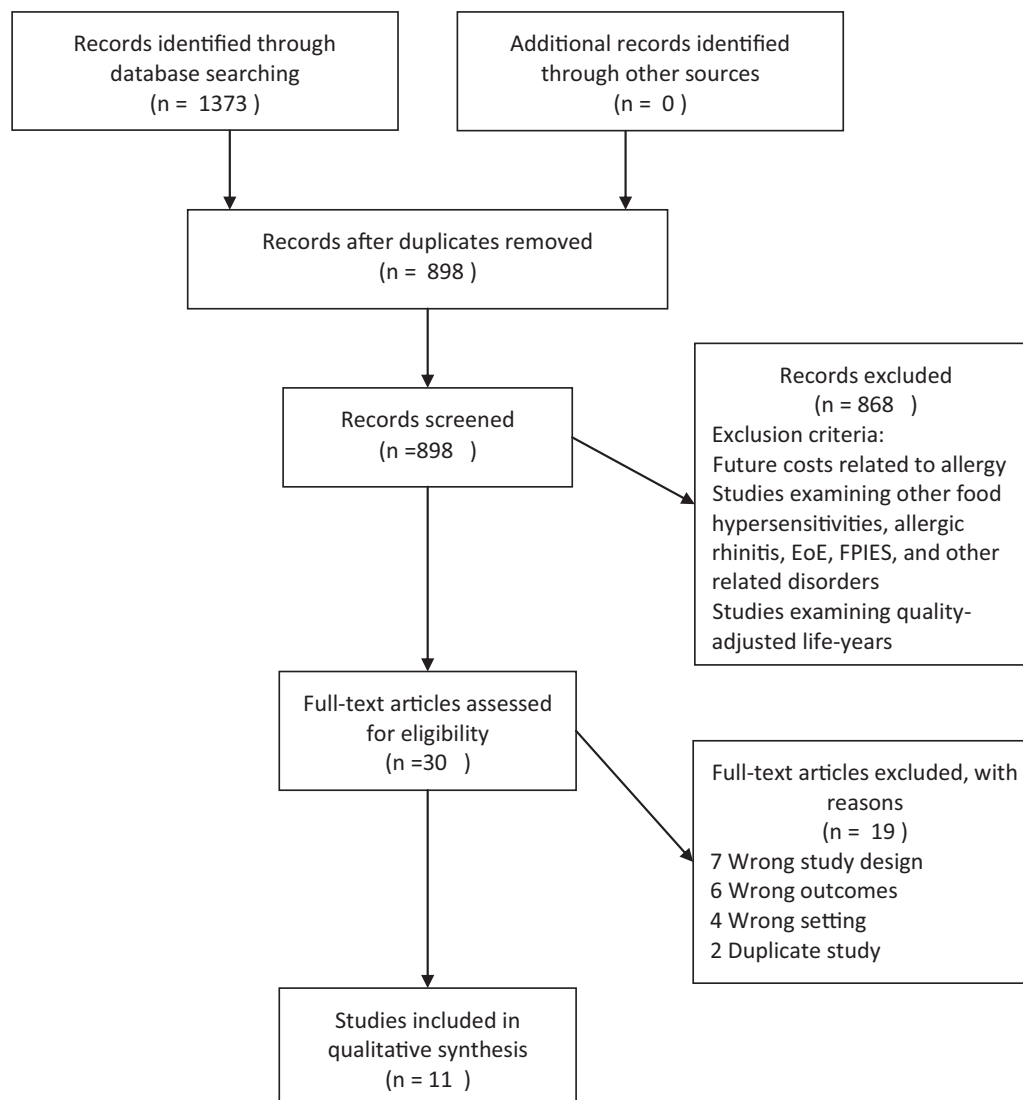


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram displaying the search methods followed to arrive at 11 articles. EoE, eosinophilic esophagitis; FPIES, food protein–induced enterocolitis syndrome.

studies were extracted for analysis and converted to 2018 US dollars. Patel et al¹⁷ used nationally representative surveys and a bottom-up approach to identify total annual direct costs to the US health care system and opportunity costs to society. The societal-level estimates could not be compared with the individual- or household-level estimates from the other studies with the data provided in the study.

Results

Direct Medical Costs

Seven of the 11 articles presented estimates of the direct medical costs of FA borne to the health care system. In all but 1 case,¹⁶ a unit cost of health services, including outpatient visits, inpatient hospitalization, ambulance transports, epinephrine autoinjectors, and ED visits, was multiplied by the number of individuals with FA in the study sample using the specific health service.

Table 2 presents study specific data on individual-level and household-level direct medical costs. Mean (SD) individual-level direct medical costs totaled \$2081 (\$1003) across 5 studies,

which was much higher than the mean (SD) household-level cost of \$806 (\$744) across 8 samples in 1 study. Gupta et al¹⁴ and Bilaver et al¹⁰ estimated parent-reported use of outpatient visits to pediatricians, allergists, pulmonologists, nutritionists, and alternative practitioners, inpatient hospitalizations, and ED visits as a result of the child's FA in the past year. The study found that inpatient hospitalizations had the highest mean annual per patient cost in dollars (\$352.39) followed by outpatient visits to allergists (\$212.11) and ED visits (\$144.77). Direct medical costs totaled \$4.3 billion (2011) annually in the United States, with a mean annual per patient cost of \$812.51. Bilaver et al¹⁰ found that annual per patient direct medical costs varied by race/ethnicity but not by household income. Using the MEPS, Miller et al¹⁶ found that the mean annual direct medical expenses per child aged 0 to 17 years with FA totaled \$1113.74. Direct medical expenses in the MEPS refer to total payments for medical expenditures (not charges) and include out-of-pocket and health insurer payments. Patel et al¹⁷ did not report mean annual per patient direct medical costs but instead reported total annual costs, which are therefore not included in Table 2. The authors found \$225 million in direct medical expenses in 2007, with the largest proportion stemming from office-based physician visits (\$118 million).

Table 2
Direct Medical Costs (Borne by the Health Care System) of FA^a

Study	Country	Direct Medical Costs per Patient With FA Per Year, 2018 US\$									
		Primary care consultations	Private specialists and examination	Inpatient hospital stays	ED visits	Hospital outpatient care	Medication	Travel costs	Infant formula	Disability allowance	Total
Gupta et al, ¹⁴ 2013	United States	103.25	212.11	352.39	144.77	NR	NR	NR	NR	NR	812.51
Miller et al, ¹⁶ 2016	United States	NR	NR	NR	NR	NR	NR	NR	NR	NR	1113.74
Alanne et al, ⁹ 2012 (first year of life)	Finland	91.76	108.04	NR	NR	627.50	47.36	185	1011.38	238.28	2309.32
Alanne et al, ⁹ 2012 (second year of life)	Finland	7.40	158.35	NR	NR	741.45	47.36	187.95	1712.30	688.17	3542.98
Flabbee et al, ¹² 2007 (children)	France	NR	NR	NR	NR	NR	NR	NR	NR	NR	2624.59
Fox et al, ¹³ 2013 (children)	Multiple countries	NR	NR	NR	NR	NR	NR	NR	NR	NR	Greece: 153.41 Iceland: –112.01 Poland: 1654.58 Spain: 1199.24 Greece: 253.24 Iceland: 1065.31 Poland: 2208.55 Spain: 233.76
Fox et al, ¹³ 2013 (adults)	Multiple countries	NR	NR	NR	NR	NR	NR	NR	NR	NR	

Abbreviations: ED, emergency department; FA, food allergy; NR, not reported.

^aDirect medical costs are those borne by the health care system associated with the prevention, diagnosis, and treatment of food allergies. The article by Bilaver et al¹⁰ is excluded from the table because it focuses on direct costs by race, ethnicity, and income and uses the same database as the articles by Gupta et al.¹⁴ The article by Patel et al¹⁷ is excluded from the table because individual-level direct medical costs attributable to FA were not reported. All costs were converted to 2018 US dollars. Individual-level mean (SD) summary costs across studies^{9,12,14,16} are \$2081 (\$1003). Household mean (SD) summary cost across study samples¹³ is \$860 (\$744).

Two small studies from Europe measured a range of direct medical costs, including inpatient, outpatient, and medication costs.^{9,12} The article by Flabbee et al¹² specifically estimated the mean per patient costs for severe food- and drug-related anaphylaxis in France. The authors estimated a mean annual per patient cost of \$2624.59. They did not report a separate amount for the 248 patients with FA. Alanne et al⁹ reported the median direct medical costs for a very small ($n = 23$) cohort of infants with FA by 2 years of age. The authors reported a mean cost of \$2309.32 for the mean annual per patient cost of these services between birth and 1 year of age as well as \$3542.9 between 1 and 2 years of age. The young age of this small cohort makes it difficult to compare this estimate to any of the other studies.

Finally, Fox et al¹³ used the EuroPrevall questionnaire and a case-control design to estimate the total cost of health care use, which included use of primary and outpatient services, hospital inpatient stays, use of ambulances, and prescribed medications. The cost of health services used for the past year (for any reason) were calculated using the WHO-CHOICE databases.²⁰ The authors found that parents of children with FA in Iceland had the lowest household-level incremental annual direct medical cost (–\$112.01), whereas adults with FA in Poland had the largest cost (\$2208.55).

Out-of-Pocket Costs

Out-of-pocket costs measure expenses associated with the burdens of disease that are not covered by insurance, such as deductibles, coinsurance, copayments, and any added services. Because of the variety of expenditures recorded among the articles reviewed, this literature review refers to out-of-pocket costs as all health care and non-health care–related costs borne by patients, such as cost of travel to the physician or hospital, insurance copayments, cost of living, medications, diet or food, health insurance premiums, counseling, and special child care arrangements.

We identified 6 articles that presented individual-level or household-level out-of-pocket costs (Table 3). Mean (SD) individual-level out-of-pocket costs totaled \$1874 (\$469) across 2 studies, which was lower than the mean (SD) household-level cost

of \$3339 (\$834) across 4 samples in 3 studies. Gupta et al¹⁴ studied a broad range of costs incurred as a result of FA among US children. The annual cost per child totaled \$1405.06 and were calculated by multiplying the percentage reporting cost by the mean out-of-pocket cost. The highest proportion of out-of-pocket costs stemmed from caregiver estimates of changes in child care, special schools or camps, and counseling because of allergy (\$349.02 per patient) followed closely by the cost of special diets and allergen-free foods (\$319.84).¹⁴

Two studies measured the incremental household-level out-of-pocket cost of FA in Sweden.^{15,18} Overall out-of-pocket costs did not differ between adults and children. Similar to the US study by Gupta et al,¹⁴ the highest proportion of costs in the Swedish studies were related to the cost of living (ie, specialized diet, cost of food, additional equipment to prepare safe meals, domestic help), which was \$1427.92 annually per patient for adults,¹⁵ \$2702.48 annually per patient for children aged 0 to 12 years, and \$3504.95 annually per patient for children aged 13 to 17 years.¹⁸

In studies from Spain and Poland, Cerecedo et al¹¹ used the EuroPrevall questionnaire to measure out-of-pocket costs before and after a double-blind, placebo-controlled food challenge for 42 patients enrolled in the study. The authors calculated median out-of-pocket costs of \$4005.33 annually, with the largest proportion stemming from the cost of food, including the cost of food at home, in restaurants, or at work.¹¹

Opportunity Costs

We identified 5 articles that presented the opportunity cost of FA (Table 4). We considered opportunity cost as the loss of potential earnings that result from FA, of which some examples included decreased labor productivity, loss of leisure activity, and increased time spent on FA-related household tasks and information seeking. Mean (SD) individual-level lost labor productivity totaled \$1038 (\$1273) across 3 studies, which was much lower than the mean (SD) household-level opportunity costs of \$4881 (\$2201) across 4 samples in 3 studies.

Decreased labor productivity was measured in 2 of the included studies that yielded individual-level estimates. In the study by

Table 3
Out-of-pocket Costs of FA^a

Study	Country	Out-of-pocket Costs, 2018 US\$							
		Visits to Physician or ED (including copayments)	Travel (for visits)	Cost of living ^b	Medications	Diet and food	Health insurance	Childcare, schools, camps, and/or counseling	Total
Gupta et al, ¹⁴ 2013	United States	185.17	28.06	NR	132.43	319.84	NR	349.02	1405.06
Flabbee et al, ¹² 2007	France	NR	NR	NR	NR	NR	NR	NR	2342.45
Cerecedo et al, ¹¹ 2014	Spain and Poland	NR	3.29	NR	301.09	2742.42	NR	NR	4005.33
Jansson et al, ¹⁵ 2014	Sweden	NR	88.79	1427.92	360.01	Included in cost of living	24.33	NR	2116.02
Protudjer et al, ¹⁸ 2015 (children 0–12 years old)	Sweden	NR	56.70	2702.48	423.03	Included in cost of living	–168.3	NR	3031.03
Protudjer et al, ¹⁸ 2015 (children 13–17 years old)		NR	24.72	3504.95	543.69	Included in cost of living	85.77	NR	4204.18

Abbreviations: ED, emergency department; FA, food allergy; NR, not reported.

^aOut-of-pocket costs include those borne by patient associated with the prevention, diagnosis, and treatment of food allergies and all costs associated with protecting the child from exposure to allergens, including special child care arrangements. The article by Bilaver et al¹⁰ is excluded from the table because it focuses on out-of-pocket costs by race, ethnicity, and income and uses the same database as the article by Gupta et al.¹⁴ Both articles by Alanne et al^{12,16} are excluded from the table because they only present out-of-pocket costs related to infant's diets during a very narrow period of infancy and early childhood. All costs were converted to 2018 US dollars. Individual-level mean (SD) summary costs across studies^{12,14} are \$1874 (\$469). Household mean (SD) summary cost across studies^{11,15,18} is \$3339 (\$834).

^bIncludes the combined costs of food, additional equipment to prepare safe meals, and domestic help.

Gupta et al,¹⁴ annual lost labor productivity was \$2838.18 per child with FA, of which the largest proportion was attributable to a caregiver giving up a job, followed by choice of career being restricted and loss of job because of dismissal. In addition, decreased labor productivity was calculated in the Finnish study,⁹ which evaluated 23 food allergic children during the first 2 years of life. The authors estimated decreased labor productivity, amounting to \$141.96 per child during the first year of life and \$134.92 per child for the second year of life by multiplying the median hourly wage by reported hours lost.

Two studies in Sweden assessed opportunity cost using the EuroPrevall questionnaire. The first Swedish study assessed economic costs for adults with FA using lost labor productivity, time spent on information seeking, and time spent on household tasks.¹⁵ To determine total opportunity cost, the number of lost hours was multiplied by the mean wage in the geographic area of study. The total incremental number of hours lost per adult with FA was 929 hours per year, and when added to the lost earnings, the total incremental opportunity cost attributable to FA was \$7812.24.

Another Swedish study restricted the study sample to children aged 0 to 17 years and calculated opportunity cost by multiplying by the mean wage in Sweden by hours lost. Incremental lost labor productivity was \$895.49 in parents of children 0 to 12 years old and \$1256.02 in children 13 to 17 years old,¹⁸ which was higher than the amount found in Swedish adults. However, despite the comparable lost labor costs, incremental opportunity cost of FA

among Swedish adults was greater than \$5000 higher¹⁵ than parents of Swedish children. This difference was because adults with FA lost 345 hours per year because of being unable to perform domestic tasks, whereas caregivers of children with FA only lost 92 hours per year.

In Spain and Poland, Cerecedo et al¹¹ analyzed opportunity costs in adults and children with FA using the same EuroPrevall survey as the Swedish studies. They calculated the opportunity cost using an individual's market wage as well as national minimum wage for those who did not work. The cost of time spent on household tasks and information seeking was \$5769.86 and \$155.23, respectively. In addition, the total opportunity cost reported was \$6202.43 per patient per year, which was lower than the costs found by Swedish authors.

Discussion

Despite the methodologic variation across the studies included in this review, most countries reported more than 1 type of FA cost. With the exception of direct medical costs, the mean household level estimate was larger than individual-level estimates. Individual-level estimates reveal the largest economic burden stemming from direct medical costs (\$2081). On the basis of household-level estimates, lost opportunity costs imposed the largest economic burden attributable to FA, with mean costs of \$4881 across several studies; however, there was substantial variation in this estimate, with an SD of \$2201.

Table 4
Opportunity Costs of FA

Study	Country	Opportunity costs, 2018 US\$		
		Lost labor productivity	Time costs	Total lost labor productivity and/or time costs
Gupta et al, ¹⁴ 2013	United States	2838.18	NR	2838.18
Alanne et al, ⁹ 2012 (first year of life)	Finland	141.96	NR	141.96
Alanne et al, ⁹ 2012 (second year of life)	Finland	134.92	NR	134.92
Cerecedo et al, ¹¹ 2014	Spain and Poland	NR	6202.43	6202.43

Abbreviations: FA, food allergy; NR, not reported.

Direct medical costs should vary, depending on the type of health care financing system used in a country, particularly between countries with universal health care and those without. It is well documented, for example, that the cost of health care in the United States is far greater than any other industrialized nation.²¹ Although the difference in study designs obscures the comparison of direct medical costs of FA between the United States and other countries, we noted substantial variation among the 4 European countries.¹³ In comparison to Iceland, Spain, and Greece, Poland had the highest annual mean per patient direct medical cost of FA. This result was unexpected given that total health care spending in Poland is lower than the other 3 countries.²¹ Poland was the only other country outside the United States without a single payer (universal) health insurance system included in our review.

Likewise, it was expected that the United States would have higher out-of-pocket costs compared with countries that have universal health care, such as Sweden. Surprisingly, the overall out-of-pocket cost was higher in Sweden^{11,15,18} than in the United States.¹⁴ However, the higher out-of-pocket cost in Sweden may have been attributable to the questionnaire used in the EuroPrevall studies not being specific to the FA, instead asking individuals with FA questions about their overall health care use. Individuals with FAs tend to have other allergic conditions, including asthma and eczema,²² which may have led to increased health care use and therefore higher out-of-pocket cost as seen by these studies.

Although many of the studies recognized the effect of special foods on out-of-pocket costs of FA, few quantified the effect stemming from the purchase of allergen-free foods. Studies using the EuroPrevall questionnaire,^{15,18} for example, collected data that included the cost of all food summarized as part of a cost of living. In contrast Gupta et al¹⁴ specifically asked parents about the amount spent in the past year on special diets or allergen-free foods for their children with FA. Both the incremental cost of living and the cost of special diets and allergen-free foods were among the largest proportion of out-of-pocket costs measured, signaling the effect that food costs have on households affected by FA. Time spent preparing foods in households affected by FA was also recognized as a unique contributor to opportunity costs. Both the EuroPrevall and Gupta et al¹⁴ questionnaires specifically asked about time spent food shopping and preparing foods.

It is important to acknowledge that some of the studies included in this review discussed intangible costs of FA that could not be assigned a monetary value.^{14,15,18} There is an ever-increasing amount of literature that documents the effect of FA on quality of life, including psychosocial impact,^{23,24} which may have downstream consequences that can be measured in monetary terms. Examples include the cost of mental health or counseling services (possibly stemming from stress and anxiety, bullying, or marital disruption), the costs of special camps, or childcare. Because only 1 study included in the review included these costs in the calculation of out-of-pocket costs, it is important for future research on the economic burden of FA to account for these costs when designing study questionnaires.

This review has several limitations, such as the small number of studies included. In addition, almost all the studies selected for this review had different methods and were conducted in different years, resulting in a lack of comparison among the studies. A specific limitation of the articles stemming from the EuroPrevall project is that these studies provided household-level estimates, which could not address possible confounding attributable to other atopic conditions often present in individuals with FA and their family members. Cases and controls were matched based on age and sex and not on other health conditions, meaning the household costs of FA would reflect the effect of comorbid conditions on costs.

Conclusion

This review provides insight into the economic effect of direct medical, out-of-pocket, and opportunity costs to individuals and their families with FA. The review reveals that household-level lost opportunity costs were the highest across the literature and suggests the need to better understand this burden in terms of time and lost labor costs associated with FA. The EuroPrevall project made an important contribution to the literature that exists, but the case-control design allowed authors to estimate the incremental costs of households with a FA compared with those without rather than the total costs attributable to FA from the patient's perspective. In addition, most studies included in this review did not attempt to extrapolate the estimates of cost burden to the total population of individuals with FA in a country.

To our knowledge, this is the first article to review the literature on the economic burden of FA. Further research using standardized instruments and methods is necessary to fully comprehend the economic effect of FA on individuals with FA and their families around the world.

Supplementary Data

Supplementary data related to this article can be found online at <https://doi.org/10.1016/j.anai.2019.01.014>.

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eAppendix 1

PubMed, MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and Epub Ahead of Print, In-Process, and Other Nonindexed Citations, Daily, and Versions (1946 to July 23, 2018)

Search history sorted by search number ascending		
No.	Searches	Results
1	exp food hypersensitivity/ or exp egg hypersensitivity/ or exp milk hypersensitivity/ or exp "nut and peanut hypersensitivity"/ or exp nut hypersensitivity/ or exp peanut hypersensitivity/ or exp shellfish hypersensitivity/ or exp wheat hypersensitivity/	18,172
2	((food or Oral Allergy Syndrome or milk or egg or peanut or arachis hypogaea or tree nut or hazelnut or brazil nut or walnut or chestnut or pistachio or almond or legumes or wheat or rice or soy or fish or seafood or shellfish or shrimp or lobster or crab or crawfish or kiwi or apple or peach or apricot or cherry or pear or plum or tomato or green pea or potato or carrot or parsley or celery or additives) adj3 (allerg* or hypersensitiv*).ti,ab.	16,894
3	1 or 2	24,148
4	exp Models, Economic/	13,383
5	exp Health Care Costs/	58,639
6	exp Drug Costs/	14,709
7	exp BUDGETS/	13,315
8	exp absenteeism/	8500
9	exp cost of illness/	23,655
10	exp health expenditures/	19,555
11	exp sick leave/	5212
12	(health?care adj cost*).ti,ab.	8795
13	economic*.ti,ab.	223,738
14	cost*.ti,ab.	517,359
15	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	748,889
16	3 and 15	455