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Health sector costs of self-reported food allergy in Europe: a patient-based cost of illness study

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Introduction: Food allergy is a recognized health problem, but little has been reported on its cost for health services. The EuroPrevall project was a European study investigating the patterns, prevalence and socio-economic cost of food allergy. **Aims:** To investigate the health service cost for food-allergic Europeans and the relationship between severity and cost of illness. **Methods:** Participants recruited through EuroPrevall studies in a case–control study in four countries, and cases only in five countries, completed a validated economics questionnaire. Individuals with possible food allergy were identified by clinical history, and those with food-specific immunoglobulin E were defined as having probable allergy. Data on resource use were used to estimate total health care costs of illness. Mean costs were compared in the case–control cohorts. Regression analysis was conducted on cases from all 9 countries to assess impact of country, severity and age group. **Results:** Food-allergic individuals had higher health care costs than controls. The mean annual cost of health care was international dollars (I$)2016 for food-allergic adults and I$1089 for controls, a difference of I$927 (95% confidence interval I$324–I$1530). A similar result was found for adults in each country, and for children, and was not sensitive to baseline demographic differences. Cost was significantly related to severity of illness in cases in nine countries. **Conclusions:** Food allergy is associated with higher health care costs. Severity of allergic symptoms is a key explanatory factor.

Introduction

Immunoglobulin E (IgE)-mediated food allergy has been identified as a public health problem in several European countries.[1–3] IgE-mediated food allergies are adverse responses to food caused by the immune system mistakenly identifying proteins in foods as harmful to the body, triggering an allergic response. The allergic response can range from mild symptoms, such as rashes, to severe symptoms, such as anaphylactic shock, which can be fatal. Population-based data on food allergies are limited.[3–7] Previous studies have shown that while up to 35% of individuals report adverse reactions to foods, the prevalence of IgE-mediated food allergies is much lower when diagnosis is confirmed. Hospital admissions in the UK where systemic allergic reactions, including food allergy, were coded as the diagnosis increased between 1990 and 2001.[8] Currently, the only treatment is avoidance of the causative food(s), which can have

unintended consequences, including childhood malnutrition.[9] Even where an allergic person consciously avoids specific foods, traces may be consumed accidentally. For people who have a clinically diagnosed allergy, a reaction may result in administration of adrenaline, seeking further medical help, and sometimes admission to hospital. A recent burden of illness study in the USA[10] estimated the national direct health care cost of food-allergic reactions treated in the health system to be ~$300 million. However, there has been a lack of information about the health service costs imposed by food allergies in Europe.[7,8,11,12]

The economic impact of food allergy may be widespread, affecting many sectors of society both directly and indirectly.[12] Estimates of costs associated with any illness depend on which decision maker's perspective is adopted. For health policy makers, understanding more about the cost of the use of health services that arises from food allergy is the first step toward planning access to appropriate, efficient and effective services and preventive strategies in future. A range of theoretical backgrounds and modelling approaches have been used to study how and why people seek and use health services,[13] with use of health services depending on a variety of factors common to different illnesses. These include availability of services, patients' estimation of need, cost and various demographic factors. Such studies have also shown that while the majority of relatively healthy people with chronic conditions use no health services, the overall cost and use of services is most strongly predicted by severity of illness.[14] As a consequence of the complexity of interacting factors, it has been suggested that cost-of-illness studies should adopt a case–control approach.[15]

This article presents the findings of an economic study, which offered an opportunity to assess, from the perspective of health care commissioners, potential additional direct health care costs for providing services to people with food allergy compared with those with no adverse reactions to food, and to assess whether the severity of adverse reactions to foods had any impact on these costs, in cohorts of adults and school-aged children across Europe. The economic study was carried out within a European Commission Framework 6 Integrated Project, EuroPrevall, which aimed to assess the prevalence, cost and basis of food allergy in Europe.

Methods

The protocols for the EuroPrevall epidemiologic studies are described fully elsewhere.[5,6] A flowchart of the integration of the economic study is available in Supplementary Appendix 1. To summarize, random samples of local populations of primary school–aged children and working-age adults in defined catchment areas around the capital cities of 12 European countries were recruited into the EuroPrevall Project using locally relevant sampling frames, such as General Practitioners' patient lists, city council registration databases, local health authority/hospital databases and, for the child survey, primary schools.

Sampling was carried out in three stages in each centre. In Stage 1, a short screening questionnaire was posted to a random sample of 3000 households in the population to recruit the adult sample, and via primary schools to recruit a sample of 3000 children, to collect information about adverse reactions to food and willingness to participate in the study's second stage. In Stage 2, a random sample of adults (aged 20–54 years) and children (aged 7–11 years) responding to the screening survey and agreeing to take part in Stage 2 were invited to take part in the age-specific case–control studies; the cases within Stage 2 were categorized as respondents with 'possible food allergy'. All respondents were invited to complete a detailed questionnaire about the potential risks and exposures to food allergens, and to undergo a blood test to allow serological analysis to establish patterns of sensitization and test for presence of specific IgE against 24 selected foods.[5] Respondents with both positive IgE results and reported symptoms of food allergy were categorized as respondents with 'probable food allergy'. A random sample of 30 respondents with probable food allergy in each centre, with mild reactions to foods, were invited to a full clinical evaluation that included double-blind placebo controlled food challenge in Stage 3 of the clinical study.

The economic data were collected from cases with possible food allergy and controls identified in four of the eight EuroPrevall centres (Greece, Iceland, Poland and Spain) and from cases with probable food allergy in seven centres (Poland, Spain, Czech Republic, France, Italy, The Netherlands and UK). Data collection took place between January 2007 and July 2009. In the following sections of the article, the respondents in the economic study will be referred to either as cases with possible or probable food allergy or controls.

The development of the Food Allergy Economic Questionnaire (FA-ECOQ), used to collect the data for this study, is described elsewhere.[16] A copy of the English language version of the questionnaire is attached as Supplementary Appendix 3. A power calculation based on data collected in the pilot studies in the development of the FA-ECOQ suggested that a minimum sample of 100 cases and 100 controls would be needed to show a statistical difference in direct health care costs.[16]

Respondents to the FA-ECOQ are asked how often in the previous 12 months did they (or the study child) visit family doctors or other professionals; whether they had used an ambulance, had been prescribed medication or had been admitted to hospital; and if so, how many times and how many days they spent in hospital. For this analysis, cases and controls were included in analyses only if they had reported data on the relevant variables.

The data were analysed in two ways to meet the aims of this study. First, data collected from participants in Stage 2 of the case–control clinical study were analysed to assess any differences in health resource use between cases with possible food allergy and controls. Second, to assess whether the severity of symptoms had any impact on the health care costs for allergic people in the two age ranges, the data from cases with possible and probable food allergy were analysed by four categories of severity (mild, mild to moderate, moderate and severe), controlling for demographic characteristics.

Severity of symptoms in cases was classified into four categories using the Mueller clinical severity grading scale.[17] If mild symptoms (e.g. skin rashes) were reported, severity was categorized as Grade 1; gastrointestinal symptoms or angio-oedema were categorized as Grade 2; respiratory symptoms were categorized as Grade 3. The most severe category was Grade 4 and included reported cardiovascular symptoms and anaphylactic shock. Each centre was granted ethical approval to participate in the economic study from their local research ethics committee.

Costs of reported health services used over the previous year by each respondent in all participating countries were calculated using unit costs of service derived from the WHO-CHOICE database.[18] This database uses the I$ (also known as the Geary–Khamis dollar) to estimate unit costs of services. The I$ is an average unit of cost derived by adjusting exchange rates between the US dollar and the local currency to compare values of different currencies based on purchasing power parity and the average commodity prices within each country. Further details of the method are presented in Supplementary Appendix 2. The outcome measure was 'cost of healthcare use (in previous year)'. This was derived by counting the number of primary and outpatient services visited, hospital inpatient stays by number of days admitted, use of ambulances and prescribed medicines as quantities of health care resource use. The quantities were multiplied by the relevant unit costs and summed to create the 'cost of health care use' variable.

To assess difference in health care resource costs, a *t*-test based on log-transformed cost variables or the χ^2 test of the mean total cost of health care use between cases with possible food allergy and controls in each survey in each country was controlling for demographic and social characteristics of households (household size and

household income), gender of respondent, gender of person with allergy, employment status ('head' of household) and final educational level of the respondent (this was measured as primary school, secondary school, technical college or university degree levels of education relevant for each country).

Analysis of the effects of severity in cases of allergy (including both possible and probable diagnoses) included estimation of the impact on costs of different levels of severity (tests of means based on *t*-test and analysis of variance based on log-transformed cost variable). Linear regression analysis was applied, including three variables: the two age groups surveyed (adults aged 20–54 years, children aged 7–11 years), country and severity. This aimed to assess whether there were significant effects of these variables on combined health care costs. The reference groups for the regression analysis were the following: for adult–child comparison, 'adults with food allergy'; for the country comparison, 'Poland'; and for severity comparisons, 'mild symptoms.'

Results

Study participants

Overall, 1411 participants in Stage 2 of the clinical study completed an FA-ECOQ: 674 completed the adult FA-ECOQ, and 737 completed the parent FA-ECOQ on behalf of children aged 7–11 years (table 1). Additionally, 271 (165 adults and 106 parents of study children) participants of Stage 3 of the clinical study completed an FA-ECOQ (table 2).

Table 3 shows significant difference between cases and controls in characteristics of respondents to both the adult and child surveys. In the adult survey, a higher percentage of respondents were male individuals in the case group compared with the control group. Children with possible or probable food allergies, in this survey, lived in smaller households, with younger children and lower incomes than those in the control group.

Response rates varied between centres and between cases and controls, ranging between 19% of controls in the Greek child survey and a maximum of 90% for the Spanish child survey.

Costs associated with possible food allergy: case–control comparison

Table 4 presents the average number of visits to health professionals for respondents from all participating countries in the year before the survey, and for each participating country separately. The aggregate analysis shows there is a significant difference in health care resource use reported by those with 'possible' food allergies compared with controls. Adults with 'possible' food allergy visited health professionals, on average, 11.17 (SD = 16.14) times per year compared with 7.11(SD = 12.80) visits per year reported by controls. Children with 'possible' food allergy visited health professionals 10.75 times per year (SD = 13.23) compared with 6.56 (SD = 9.78) visits per year reported by controls. Within Spain and Poland, numbers of visits to health professionals are significantly higher for adults and children with possible food allergy compared with controls, respectively. Differences between the number of visits to health professionals by adults and children with possible food allergy and that by controls in Greece and Iceland do not reach conventional levels of significance for 'within country' statistical tests. There was no evidence of any heterogeneity of the difference between cases and controls in the adult survey ($P = 0.6117$). There was evidence of heterogeneity in the child survey ($P = 0.0373$), although none of the individual two-country comparisons was significant. The difference between cases and controls remained when adjusted for potential confounders.

Table 5 shows that there was a significant difference in the number of days spent in hospital in the previous year for both adults and children with possible food allergies compared with controls. Adults with food allergies spent a mean of 1.39 days in hospital each year (SD = 7.43) compared with 0.46 (SD = 2.42) days spent in hospital by controls. For children, those with possible food allergies spent 0.75 (SD = 3.04) days in hospital compared with 0.40 (SD = 2.77) days spent in hospital by controls. There was no evidence of any heterogeneity of the difference between cases and controls in the adult ($P = 0.8557$) or the child ($P = 0.2246$) surveys. The difference between cases and controls remained when adjusted for potential confounders.

Table 1 Number of respondents or parents of study children with or without possible food allergy completing FA-ECOQ

Country	Number of respondents			
	Adult[a]		Parent[b]	
	Case	Control	Case	Control
Greece	27	9	21	28
Iceland	13	14	15	31
Poland	92	232	153	170
Spain	93	194	81	238
Total	225	449	270	467

a: Adults aged between 20 and 54 years.
b: Of children aged between 7 and 11 years.

Table 2 Number of respondents or parents of study children with probable food allergy completing FA-ECOQ

Country	Number of respondents[a]	
	Adult[b]	Parent[c]
Czech Republic	4	17
France	6	5
Italy	56	–
Netherlands	67	72
UK	32	12
Total	165	106

a: Cases only—no controls in this analysis.
b: Adults aged between 20 and 54 years.
c: Of children aged between 7 and 11 years.

Table 3 Baseline characteristics of case and control respondents in the adult and child Food Allergy Survey [mean (SD)]

Baseline characteristics	Adult					Parent				
	n	Cases	*n*	Controls	*P*-value	*n*	Cases	*n*	Controls	*P*-value
Total household members	215	2.98 (1.26)	429	3.04 (1.26)	0.4936	260	3.76 (1.01)	459	4.00 (1.15)	0.0044*
Household income	207	3264 (2055)	416	3455 (3216)	0.4348	254	3106 (2146)	439	3928 (4855)	0.0108*
Age	187	38.55 (10.75)	425	39.15 (10.05)	0.5058	231	9.10 (3.98)	411	10.16 (2.22)	<0.001*
Gender (male/female)	193	70/123	430	198/232	0.023*	244	45/199	437	82/355	0.918

*Significant.

Table 4 Health care resource use by country and study participation [mean (SD)]: health care contacts

Country	Adult					Parent				
	n	Case	*n*	Control	*P*-value[a]	*n*	Case	*n*	Control	*P*-value[a]
Greece	27	1.81 (2.33)	9	1.14 (1.01)	0.693	18	3.01 (2.99)	26	2.32 (2.69)	0.521
Iceland	13	20.45 (27.27)	14	9.64 (14.68)	0.405	14	6.03 (7.27)	30	5.54 (11.15)	0.376
Poland	91	10.56 (12.14)	226	6.33 (11.47)	<0.001*	149	12.16 (15.52)	167	9.59 (13.34)	0.022*
Spain	93	13.19 (18.62)	194	8.12 (14.27)	0.007*	81	10.69 (9.68)	238	5.02(5.81)	<0.001*
Total	224	11.17 (16.14)	443	7.11 (12.80)	<0.001*	262	10.75 (13.23)	461	6.56 (9.78)	<0.001*

a: Test of log mean difference is >0 based on a linear regression model with log contacts +0.5 to allow for zero contacts.
*Significant.

Table 5 Health care resource use by country and study participation [mean (SD)]: hospital days

Country	Adult					Parent				
	n	Case	*n*	Control	*P*-value[a]	*n*	Case	*n*	Control	*P*-value[a]
Greece	19	0.32 (1.16)	6	0.50 (1.22)	0.268	16	0.81 (1.94)	24	0.13 (0.61)	0.082
Iceland	11	0.36 (1.21)	14	0.00 (0.00)	0.268	14	0.00 (0.00)	30	0.20 (0.76)	0.260
Poland	91	2.07 (9.12)	224	0.79 (3.32)	0.192	150	0.98 (3.81)	162	1.01 (4.55)	0.450
Spain	93	1.08 (6.70)	194	0.11 (0.54)	0.021*	81	0.42 (1.40)	238	0.03 (0.29)	<0.001*
Total	214	1.39 (7.43)	438	0.46 (2.42)	0.020*	261	0.74 (3.04)	454	0.40 (2.77)	0.015*

a: Test of log mean difference based on a linear regression model with log contacts +0.5 to allow for zero inpatient days.
*Significant.

Table 6 Health sector costs (I$2007 prices) for people with possible food allergy compared with controls in each country [mean (SD)]

Country	Adult					Parent				
	n	Case I$	*n*	Control I$	*P*-value[a]	*n*	Case I$	*n*	ControlI$	*P*-value[a]
Greece	27	391 (583)	9	183 (265)	0.525	21	306 (360)	28	180 (234)	0.926
Iceland	13	1429 (2280)	14	554 (1073)	0.508	15	310 (432)	31	402 (937)	0.524
Poland	92	3318 (7986)	232	1504 (3171)	<0.001	153	3074 (7043)	170	1715 (3475)	0.008*
Spain	93	1281 (2279)	194	673 (1100)	0.078	81	1379 (3876)	238	394 (1349)	<0.001*
Total	225	2016 (5443)	449	1089 (2435)	<0.001	270	2197 (5799)	467	863 (2405)	<0.001*

a: Test of log mean difference based on a linear regression model with log contacts +0.5 to allow for zero inpatient days.
*Significant.

Tables 4 and 5 also show that there are absolute differences between those with possible food allergy and controls in levels of service use between countries, with higher service use overall by adults in the Poland and the lowest service use in Greece. These differences in service use are reflected in the level of costs of health care use in different countries (table 6).

There are significantly higher costs of providing health services for adults and children with possible food allergy compared with controls for the whole sample. Overall, the mean cost of providing health care to adults with possible food allergy is I$2016 compared with I$1089 for controls, a difference of I$927 (95% confidence interval based on untransformed data of I$324–I$1530). For children aged 7–11 years, the costs are I$2197 for those with possible food allergy compared with I$863 for controls, a difference of I$1334 (95% confidence interval based on untransformed data of I$729–I$1939). There was no evidence of any heterogeneity of the difference between cases and controls in the adult survey ($P = 0.3736$) or the parent survey ($P = 0.1061$). The difference between cases and controls remained when adjusted for potential confounders.

Severity of reported allergy and health care costs

The mean average yearly cost of health care for 766 cases of possible and probable food allergy in the nine participating centres was I$1778. Table 7 shows that there is a significant gradient in costs associated with severity of food allergy (as defined by reported presence of specific clinical events and symptoms). There is evidence that the cost of health services for those with moderate food allergy (category 3) is likely to be 68% higher than for those with the mildest symptoms of food allergy. The cost of health services for those with severe food allergy (category 4) is predicted to be twice that of those with mild food allergy. These differences are significant at the 99% level of confidence, with $P \leq 0.0009$. There is also evidence that there are country-specific effects on the cost of health care. There was no significant difference in the costs of health services for children and adults.

Discussion

This survey indicates that both working-age adults and primary school children with possible food allergy (identified as having defined symptoms of food allergy) use more health services than those without food allergy; therefore, the costs of providing health services for people with food allergies is likely to be higher than the cost of providing health service to people without food allergy within these age-specific groups.

This finding was not sensitive to baseline differences in household characteristics between the cases and controls. The result holds in all

Table 7 Effect of severity, country and whether adult or child on health care cost for people with probable food allergy[a]

Covariate	Coefficient	Exponent of coefficient (95% confidence interval)	*P*-value*
Version (adult as baseline)			
School-aged child	0.29 (−0.04 to 0.61)	1.34 (0.96 to 1.85)	0.082
Country (Poland as baseline)[b]			<0.0001*
Greece	−1.17 (−1.98 to −0.35)	0.31 (0.14 to 0.7)	
Iceland	−0.08 (−1.16 to 1)	0.92 (0.31 to 2.73)	
Spain	1.14 (0.5 to 1.78)	3.13 (1.66 to 5.92)	
Czech Republic	0.42 (−0.19 to 1.03)	1.53 (0.83 to 2.81)	
France	1.02 (−0.02 to 2.06)	2.77 (0.98 to 7.82)	
Italy	−0.53 (−1.85 to 0.8)	0.59 (0.16,2.22)	
Netherlands	0.19 (−0.47 to 0.85)	1.21 (0.63 to 2.33)	
UK	−0.14 (−0.92 to 0.63)	0.87 (0.4 to 1.88)	
Severity ('mild' as baseline			0.0009*
2	−0.02 (−0.46 to 0.43)	0.98 (0.63 to 1.54)	
3	0.52 (0.06 to 0.98)	1.68 (1.06 to 2.67)	
4	0.81 (0.28 to 1.34)	2.25 (1.32 to 3.83)	

a: Regression: log(cost) = version + country + severity.
b: Poland was chosen as the baseline because it was the country with the greatest number of cases; hence, the confidence intervals for the two-country comparisons should be minimized.
*Significant.

countries participating in the case–control study, but the small sample sizes in some countries meant there was insufficient power to show a significant difference in each participating country. Response bias is unlikely to have affected the findings, but should be considered as a possibility in some settings. In the larger studies in Poland and Spain, where local project managers were funded and supported to implement the socio-economic study, the response rates were excellent. Measurement of response was difficult in the other centres, as records were not kept of how many questionnaires were distributed. The research team sent packs of questionnaires for use, and response rate calculation was based on the assumption that all were handed out.

WHO-CHOICE unit costs were used to standardize costing methodology across countries because it was impossible to obtain local unit costs in all settings (see table A2.1 in Supplementary Appendix 2). In four countries, we also had data from local sources about unit costs of services used. A comparison of the costs from different sources is shown in Supplementary Appendix 2 (table A2.2). The costs estimated in this study are lower than the estimates of population resource use and costs published by the Organisation of Economic Cooperation and Development (OECD).[19] This may partly be due to the age distribution of population in the EuroPrevall study, which included no one aged >60 years. It is well reported that health care use is higher for people in older age categories.[20]

Health policy depends on good information about prevalence and severity of disease, appropriate care pathways and costs. We have found only one recent report of health care cost of food allergy,[10] using administrative databases in the USA, to estimate the cost of using services coded to food allergy–related illness. Our study takes a different approach, but provides a basis for modelling total direct health care costs in European countries, even taking into account the small risk of recall error that might be associated with the retrospective method of collecting data about health resource use. However, as the economic study was part of an integrated project, the methods for data collection were constrained to what was feasible within that project. EuroPrevall has described how people with food allergy use services in different parts of Europe.[4] This article provides data that can be used to estimate direct health care costs of programmes of care. Elsewhere, we report the estimated impacts on direct, indirect and intangible costs of food allergies to individuals within households.[21–25] Combined with evidence on effects of options for allergy diagnosis and care on both health and quality of life,[26] the data reported here provide a key input to estimating burden of illness and cost-effectiveness comparisons at different levels in Europe.

This study has confirmed that suspected food allergy can have a significant impact on health care costs in countries across Europe by providing evidence that the cost of health care is significantly higher for children and adults with food allergies than for those with no food allergy, and that there is a positive relationship between the severity of the symptoms of food allergy and the costs of providing health care.

Supplementary data

Supplementary data are available at *EURPUB* online.

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Key points

- Adults and children with suspected food allergies use more health care resources than those with no suspicion of food allergy.
- More severe symptoms of food allergy is associated with higher costs of providing health care than is the case for people with milder symptoms.
- Given this increased resource use, the diagnosis and management of food allergies in the European countries should be monitored and evaluated to ensure optimum and cost-effective use of health resources.

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