

The Impact of Double-Blind Placebo-Controlled Food Challenge (DBPCFC) on the Socioeconomic Cost of Food Allergy in Europe

I Cerecedo,^{1*} J Zamora,^{2*} M Fox,³ J Voordouw,⁴ N Plana,⁵ E Rokicka,⁶ M Fernandez-Rivas,⁷ S Vázquez Cortés,⁷ M Reche,⁸ A Fiandor,⁸ M Kowalski,⁹ G Antonides,¹⁰ M Mugford,¹¹ LJ Frewer,⁴ B de la Hoz¹

¹Servicio de Alergología, Hospital Universitario Ramón y Cajal, Madrid, Spain

²Unidad de Bioestadística Clínica, Hospital Universitario Ramón y Cajal, CIBER de Epidemiología y Salud Pública (CIBERESP), Madrid, Spain

³University of East Anglia, Health Economics Group, School of Medicine, Health Policy and Practice, Norwich, UK

⁴Wageningen University, Marketing and Consumer Behaviour Group, Wageningen, The Netherlands

⁵CIBER de Epidemiología y Salud Pública (CIBERESP), Unidad de Bioestadística Clínica, Hospital Universitario Ramón y Cajal, Madrid, Spain

⁶University of Lodz, Institute of Sociology, Lodz, Poland

⁷Servicio de Alergología, Hospital Universitario Clínico San Carlos, Madrid, Spain

⁸Servicio de Alergología, Hospital Universitario La Paz, Madrid, Spain

⁹Lodz University, Department of Immunology, Rheumatology and Allergy, Faculty of Medicine, Lodz, Poland

¹⁰Wageningen University, Economics of Consumers and Households group, Wageningen, The Netherlands

¹¹University of East Anglia, Health Economics Group, School of Medicine, Health Policy and Practice, Norwich, UK

*These authors contributed equally to this study

■ Abstract

Background: Double-blind placebo controlled food challenge (DBPCFC) is the gold standard diagnostic test in food allergy because it minimizes diagnostic bias.

Objective: To investigate the potential effect of diagnosis on the socioeconomic costs of food allergy.

Methods: A prospective longitudinal cost analysis study was conducted in Spain and Poland within the EuroPrevall project. Food-allergic patients were enrolled into the study and in all cases diagnosis was confirmed through a standardized DBPCFC. Data were collected through a self-administered survey on all aspects of health and social care resource use, costs of living, and costs of leisure activities. Costs were measured before and 6 months after the DBPCFC and reported in international dollars with 2007 as the benchmark year.

Results: Forty-two patients were enrolled. Twenty-one patients had a negative DBPCFC and the suspected food was reintroduced into their diet. Comparing total direct costs before and after the DBPCFC, the reactive group spent a significantly higher amount (median increase of \$813.1 over baseline), while the tolerant group's spending decreased by a median of \$87.3 ($P=.031$). The amount of money spent on food 6 months after diagnosis was also significantly higher in the reactive group ($P=.040$). Finally, a larger, but not statistically significant, decrease in total indirect costs was observed in the tolerant group compared with the reactive group (\$538.3 vs \$32.3).

Conclusion: DBPCFC has an impact on indirect and direct costs of living. The main contribution to this increase was money spent on food.

Key words: Food allergy. Double-Blind Placebo-Controlled Food Challenge. Diagnosis. Socioeconomic impact.

■ Resumen

Introducción: La provocación oral doble ciego controlada con placebo (PODCCP) es prueba diagnóstica "gold standard" en alergia a alimentos.

Objetivo: El objetivo de este estudio es investigar el efecto del diagnóstico en los costes socioeconómicos de la alergia a alimentos (AA).

Métodos: Estudio prospectivo longitudinal de análisis de costes llevado a cabo en España y Polonia en el contexto de proyecto EuroPrevall. Se seleccionaron pacientes con AA y en todos los casos el diagnóstico fue estandarizado a través de una PODCCP estandarizada. Se utilizaron cuestionarios autoadministrados para recoger datos del uso de recursos sociosanitarios, coste de vida y coste de actividades de ocio. Los costes se midieron en dos puntos, antes y 6 meses después de PODCCP, expresados en dólares internacionales (nivel de costes 2007).

Resultados: Se incluyeron 42 pacientes. 21 pacientes tuvieron una PODCCP negativa y se reintrodujo el alimento. Comparando los costes directos antes y después de PODCCP, el gasto en el grupo de pacientes reactivos fue significativamente mayor (mediana de incremento \$813,1 a los 6 meses), mientras que en el grupo de pacientes tolerantes disminuyó una mediana de \$87,3 ($p=0,031$). Los pacientes con una provocación positiva gastaron también más dinero en comida a los 6 meses del diagnóstico ($p=0,040$). Por último, los costes indirectos disminuyeron, aunque de forma no estadísticamente significativa, en el grupo de pacientes tolerantes comparado con los reactivos (\$ 538,3 versus \$32,3).

Conclusión: La PODCCP tiene un impacto en los costes directos e indirectos, en su mayor parte debido al dinero gastado en comida.

Palabras clave: Alergia a alimentos. Provocación oral doble ciego controlada con placebo. Diagnóstico. Impacto socioeconómico.

Introduction

Food allergy is a major health problem affecting all age groups. Between 1% and 2% of adults and 5% and 8% of children are estimated to have food allergy. These rates increase to 30% in studies where self-perceived food allergy is reported [1-5]. Once diagnosis is established, the only treatment consists of strict avoidance of the offending food, and patients return for regular follow-up visits and re-evaluation [6,7]. Allergic individuals need to learn to identify and avoid products containing the problematic foods and ingredients, and be taught to deal with a reaction. This dietary management may have a considerable impact on social and family life due to the need for continuous vigilance [8].

The aim of EuroPrevall [9], a European Union-funded integrated project, is to provide information about the prevalence of food allergy. An important aspect of the project is to assess the socioeconomic impact of food allergy by linking clinical data with data related to economic costs [10]. This is a very relevant part of the project, as prior to EuroPrevall, very little was known about the socioeconomic consequences of food allergy [11,12].

Miles et al [12] developed a framework for the assessment of social and economic costs of food allergy. The authors were unable to identify previous work investigating such costs, although costs analyses have been performed for other allergic conditions, such as asthma, allergic rhinitis, eczema, latex allergy, and drug allergy. While some costs may be similar in food allergy and other allergic conditions, others may be specific to food allergy. Fox et al [11,13] developed a questionnaire for measuring costs of food allergy at the individual and household level. The questionnaire is available in Bulgarian, Czech, Dutch, French, German, Greek, Icelandic, Italian, Lithuanian, Polish, and Spanish.

Double-blind placebo-controlled food challenge (DBPCFC) is considered the gold standard diagnostic test in food allergy [14] because it minimizes bias [15,16], although it is not used routinely in most clinical settings. One of the

benefits of a positive challenge is the establishment of a conclusive diagnosis of food allergy, which goes hand in hand with the need for continued counselling regarding avoidance. Unlike the diagnosis of allergic conditions such as asthma, rhinitis, and hymenoptera venom allergy, a diagnosis of food allergy after a reaction has to be considered as merely presumptive, even in the presence of a positive skin prick test (SPT) or specific IgE (sIgE) [17]. Apart from confirming diagnosis, a positive DBPCFC also reduces anxiety about whether an individual is allergic or not, and validates patients' or parents' efforts to avoid problematic foods [8,18]. A negative DBPCFC is followed by an open exposure to the suspected food, allowing the patients to realize that they are tolerant and that avoidance is no longer necessary. Consequently, their diet is expanded, nutrition is improved, and the patient's quality of life is enhanced. The main hypothesis of this paper is that the direct and indirect costs of living and of seeking health care will also change following confirmation of food allergy by DBPCFC.

Methods

Study Population

To assess the effect of DBPCFC on socioeconomic costs, patients recruited to participate in the EuroPrevall cross-sectional study in Madrid, (Spain) and Lodz (Poland) were in addition invited to enrol in this prospective longitudinal study nested in EuroPrevall. Recruitment occurred between October 2007 and June 2009. Patients were evaluated in allergy clinics following the same protocol as those used in the clinical studies carried out in the EuroPrevall project [10,19]. A clinical history and blood samples for sIgE were obtained in all cases and SPTs were also performed. Diagnosis was subsequently established through a standardized DBPCFC.

Data were collected through a patient self-administered expenditure and cost survey; in the case of pediatric patients, their parents completed the questionnaire. A detailed

description of the development of this questionnaire is provided elsewhere [11]. The questionnaire gathered structured information on all aspects of health and social care resource use, cost of living, and cost of leisure activities.

The questionnaire was distributed before and after the DBPCFC. Patients were invited to participate on the first day of the DBPCFC (baseline) and were re-evaluated 6 months later using the same instrument. After the challenge, new instructions were given to the patient. In the case of a negative result, they were told to include the previously suspected food in their diet and that avoidance was no longer necessary, and in the case of a positive result, they were advised to adhere to an avoidance diet.

Survey

This cost analysis was approached from the patient's perspective. To compare costs across countries, costs were calculated using the purchasing power parity (PPP) of the Geary-Khamis, or international, dollar with 2007 as the benchmark year [20]. Indirect costs were calculated using a method that assigns a monetary value to time loss due to household production. In the opportunity cost method each individual's market wage rate was used to calculate this value [21]. The opportunity cost method is widely used in the literature and is well validated [22]. When a person was not in paid employment, the minimum wage rate of the patient's country was used. When the person reported that they were working, but did not state their income, the national average wage was used. Total direct cost was calculated by adding all out-of-pocket cost items from the questionnaire. When no direct or indirect costs were incurred, zero cost was used in the analysis. When in previous questions it was stated that costs were incurred on a particular item without mentioning the amount, the cost item was entered as a missing value.

Direct costs included medical treatment costs not covered by insurance (and thus paid by the individual); travel costs to obtain medical treatment; medication costs, including over-the-counter (OTC) and prescription medicines (hydrolyzed formula was included in the cost of medication as it is covered by the national health system in both countries and hence is not considered a food cost); and costs of living, including food, holidays, leisure activities, equipment required to prepare safe meals, and outside domestic help. Indirect costs included lost working days, loss of education or working opportunities, lost leisure time, lost earnings, lost human capital, and time spent on shopping, cooking, household tasks, searching for information on health-related issues, and obtaining medical treatment (e.g., travel and visit time).

Ethics

All participants received written information on the study together with the questionnaire. Participation was voluntary and independent of the individual's contribution to the rest of the EuroPrevall protocols. All questionnaires were assigned unique codes to provide a data set with anonymous records. Only the researcher was able to match the unique codes with the personal data of the participants. Ethical approval was obtained from the participating centers in Spain and Poland.

Statistical Analysis

Direct and indirect costs were compared before and after the DBPCFC to detect possible differences between tolerant and reactive patients (or parents of tolerant and reactive children). Categorical variables were described using both absolute and relative frequencies. The distribution of cost data was strongly skewed and was therefore described by median and interquartile range (IQR). The effect of the DBPCFC was assessed by computing the difference between pre- and post-DBPCFC questionnaires. In other words, a positive value was interpreted as a cost increment. This difference was compared between the tolerant and reactive groups by means of the Mann-Whitney U test. All the tests were 2-tailed and the significance level was set a *P* value of .05. SPSS version 15.0 was used for all statistical analyses.

Results

Forty-two patients were followed up after the DBPCFC and information on costs was collected before the challenge and 6 months afterwards. The majority of patients (*n*=31) were children, with a median age of 3 years; the median age of respondents (including adult patients and parents) was 35 years and the majority of households were formed by 2 adults and 1 or 2 children. The most frequently tested food was milk followed by egg (Table 1). In our cohort none of the patients were allergic to more than 2 foods.

Table 1. Characteristics of Study Patients (*n*=42)^a

Food used in DBPCFC	Egg	8 (19)
	Milk	21 (50)
	Shrimp	1 (2.4)
	Hazelnut	5 (11.9)
	Peanut	1 (2.4)
	Fruit (apple/peach)	6 (13.59)
Result of DBPCFC	Positive	21 (50)
	Negative	21 (50)
Sex	Male	15 (35.7)
	Female	27 (64.3)
Median age, y	Adults ^b	35
	Children	3
Country	Spain	36 (85.7)
	Poland	6 (14.3)

^aResults are reported as number (%) of patients, unless otherwise indicated.

^bIncludes parents with an allergic child (*n*=31) and adult allergic patients (*n*=11).

Table 2 and Table 3, respectively, show the direct and indirect costs at baseline. Tolerant and reactive patients were comparable in terms of total direct costs and individual costs of living and leisure activities. Tolerant patients spent more on OTC medication (*P*=.024). No differences were found for total indirect costs, lost leisure time, or costs assigned to time spent seeking health care or information. There were,

Table 2. Total Direct Annual Costs at Baseline in Geary-Khamis Dollars for the 42 Study Participants

	Median	25th Percentile	75th Percentile
Health care			
Health care attention (travel+visits) ^a	2.7	.0	18.8
Paid prescription medicines	22.0	.0	72.0
Paid over-the-counter (OTC) medicines	161.5	.0	414.5
Total (prescription+OTC)	247.3	24.0	542.4
Costs of living			
Food ^b	2252.5	1217.8	3592.4
Leisure activities			
Holidays	352.2	.0	942.1
Total direct costs^c	3289.8	1079.3	4553.9

^aTravel includes money spent on transportation (public transport or own car; a cost of 0 was applied to patients traveling on foot or by bicycle) and corresponds to the amount paid by the patient, not the cost for the health care system.

^bTotal food cost includes the cost of food at home and in restaurants, take-away food, and food purchased at work. Participants were also asked about money spent on outside help with domestic duties (aids or appliances) but the median amount spent was 0.

^cThis total includes additional costs (see Methods section for details). These additional costs are not fully detailed in this table because they were incurred by just 1 or 2 patients.

Table 3. Total Indirect Annual Costs at Baseline in Geary-Khamis Dollars for the 42 Study Participants^a

	Median	25th Percentile	75th Percentile
Health care seeking	87.3	36.5	36.5
Time spent on household tasks	4739.1	3454.4	9572.5
Loss of leisure time (holidays)	37.7	6.8	78.5
Time spent on information seeking	127.5	81.4	408.2
Total indirect costs	5094.4	3727.4	9799.9

^aThe participants were also asked about the value of time spent off work, but the median result was 0.

however, differences in the value assigned to time spent on household tasks ($P=.047$), which was higher in the tolerant group. Direct costs were divided into health care costs, costs of living, and leisure activity costs. The median of total direct costs was \$3289.8 annually (IQR, \$13.60-\$11 207.60). The median amount spent on medication was \$22.0 for prescription medication and \$161.5 for OTC medication. Only 2 patients had private medical insurance. Regarding costs of living, \$2252.5 was spent on food per year on each individual (\$134 was spent in restaurants, and money spent on items such as take-away food or food at work was minimal in this group of patients). Respondents did not report spending money on outside help with domestic duties or the purchase of special devices or supplies. The median amount spent on holidays away from home was \$352 (including \$89.7 spent on food during this period).

The median amount for total indirect costs was \$5094.4 (IQR, \$80-\$17 713.6); the vast proportion of this was time spent on household tasks, such as cleaning, cooking, shopping, gardening, and childcare (\$4739.1). The cost assigned to time

spent on information seeking was \$127.5. Lost working days, loss of education or working opportunities, and lost earnings were not included in the analysis because they were valued as 0 or not reported by the majority of patients. In summary, there were no significant differences in total direct and indirect costs at baseline. With respect to some individual costs, OTC medication and time spent on household tasks were slightly higher in the tolerant group than in the reactive group (Tables 2 and 3).

Effect of Diagnosis: Costs After the DBPCFC

We also analyzed changes in costs between reactive and tolerant patients 6 months after the DBPCFC (Tables 4 and 5). Twenty-one patients had a negative challenge and food was reintroduced into their diets. Comparing costs before and after the DBPCFC, total direct costs were significantly higher in the reactive group (an increase of \$813.1 compared with baseline) than in the tolerant group (a reduction of \$87.3) ($P=.031$) (Table 4). The amount spent on food was also significantly different ($P=.040$). A similar trend was also observed in the amount spent on medicines but the difference was not statistically significant. No change was observed in money spent on holidays. Tolerant patients also incurred lower indirect costs (Table 5). A greater reduction in total indirect cost was obtained in the tolerant group compared with the reactive group (\$538.3 vs \$32.3), although the difference was not statistically significant.

Discussion

DBPCFC is recognized as the gold standard for food allergy diagnosis and has an unquestionable impact on clinical management. However, to date, very little has been reported on the economic impact of food allergy. This is the first study to analyze, using a validated instrument, the impact of DBPCFC on the socioeconomic costs of food allergy for individuals and households.

Table 4. Differences in Direct Annual Costs in Geary-Khamis Dollars Between Tolerant and Reactive Patients (n=42) 6 Months after the Double-Blind Placebo-Controlled Food Challenge

		Median	25th Percentile	75th Percentile	P
Health care					
Health care attention (travel+visits)	Reactive	.0	-3.1	.3	.596
	Tolerant	-1.3	-12.8	13.5	
Medication	Reactive	-4	-40	8	.409 ^a
	Tolerant	0	-48	6	
Paid over-the-counter (OTC) medicines	Reactive	.0	-215.3	5.4	.545
	Tolerant	-64.6	-430.7	13.5	
Paid OTC and prescription medicines	Reactive	-4.00	-293.03	47.84	.697
	Tolerant	-112.60	-329.51	109.46	
Costs of living					
Food	Reactive	1257.3	178.6	2766.3	.040 ^a
	Tolerant	.0	-533.2	753.1	
Leisure activities					
Holidays	Reactive	.0	-234.2	513.7	.584
	Tolerant	.0	-423.1	336.5	
Total direct costs	Reactive	813.1	-3.7	2879.8	.031 ^a
	Tolerant	-87.3	-521.7	211.6	

^aSignificant value.

Table 5. Differences in Indirect Annual Costs in Geary-Khamis Dollars Between Tolerant and Reactive Patients (n=42) 6 Months after the Double-Blind Placebo-Controlled Food Challenge

		Median	25th Percentile	75th Percentile	P
Health care	Reactive	.0	.0	.0	.57
	Tolerant	.0	.0	13.3	
Time spent on household tasks	Reactive	-47.5	-1940.8	2485.2	.538
	Tolerant	-415.6	-3172.7	1468.7	
Loss of leisure time (holidays)	Reactive	.0	-6.8	45.3	.275
	Tolerant	31.5	.0	75.6	
Time spent on information seeking	Reactive	-51.6	-108.5	161.3	.497
	Tolerant	28.7	-99.7	244.8	
Total indirect costs	Reactive	-32.8	-2275.8	2490.7	.606
	Tolerant	-538.3	-3499.0	1845.3	

Our study has shown that DBPCFC has an impact on direct costs. Six months after the challenge, patients with a confirmed food allergy experienced a median increase in expenditure of \$813.1 compared with baseline. The main contribution to this increase was money spent on food. No significant differences were observed in other areas of direct costs. This observation could be explained by the clinical characteristics of the patients included in the study. Around 70% of the patients were allergic to milk and egg, which were the most frequent self-reported causes of food allergy in patients referred to allergy outpatient clinics in the EuroPrevall cross-sectional study. These foods are present in many manufactured products and allergic patients need to avoid even foods that contain tiny amounts used as preservatives or enhancers. Food labeled as “milk-egg-free” tends to be more expensive and patients are usually restricted to 1 or 2 brands. Impact on food costs may be different when other

less common allergens are involved, but it is well established that manufactured products that assure they do not contain a specific food are more expensive. No impact was observed for a confirmed diagnosis of food allergy on health care-seeking costs, probably because patients included in the study were using publicly funded health care. Furthermore, they typically travelled to the health care center on foot or by public transport. Good patient education at baseline visits also helps to reduce allergic reactions and visits to the specialist office or emergency room. In addition, because of the short follow-up period, it is possible that the patients or their carers had not yet changed their use of health services.

Apart from an avoidance diet, no specific therapy is available for food allergy, contrasting with allergic rhinitis and asthma, for which immunotherapy is available. Medication is prescribed to be used in case of reactions. This medication

mainly consists of antihistamines and corticosteroids and in some cases self-injected adrenaline, which are all relatively cheap. Indirect costs were not significantly different between the groups, but tolerant patients tended to save on time spent on household tasks, which includes time spent shopping and cooking. Those activities take less time when there is no need to carefully read labels or avoid meals containing the offending allergens, for example. It was observed that loss of leisure time and the value of time spent on information seeking were higher, albeit not significantly so, in tolerant patients. This could be because patients who discover they are not allergic feel the need to reassert their new status.

The conclusions of our study may be limited by the small number of patients included. Despite the considerable difference observed for indirect costs between tolerant and reactive patients, the difference did not reach statistical significance, probably because of the reduced sample size and the high variability in reported costs. In addition, the follow-up period may have been too short to capture changes in lifestyle following diagnosis. These limitations may explain the absence of impact of DBPCFC on some of the cost dimensions.

However, some strengths of the study also need to be mentioned. Firstly, our study recruited a sample of well-characterized patients, with a confirmed diagnosis of food allergy by DBPCFC. Secondly, we assessed the socioeconomic impact of food allergy on individuals and households using a validated measurement instrument in the context of the pan-European project EuroPrevall.

DBPCFC has been considered the gold standard in food allergy diagnosis for a long time, but it is absent in daily practice in most clinical settings. In Spain it has been estimated that only 13% of food allergy patients are routinely diagnosed by an oral challenge [23]. The decision to perform an oral challenge, whether blind or open, is based on clinical history, SPT results, and sIgE values, but in some centers it may also be influenced by the cost of the procedure: a trained allergist and nurses are needed for several days (at least 3 in the case of a blind challenge and 1 in the case of an open challenge). This paper covers a new aspect to be considered in the decision on whether or not an oral food challenge is indicated: a negative result will lead to a reduction in costs of living for allergic individuals and households.

Our study has focused on the economic impact of DBPCFC from a patient perspective. Future research is needed to assess the impact of DBPCFC using broader perspectives, such as quality of life impact and cost-effectiveness analyses.

Acknowledgments

We would like to thank Dr Doreen McBride for her work in coordinating the implementation of the socioeconomic questionnaires in the clinical groups of EuroPrevall; Dr Kirsten Beyer, leader of the pediatric cohorts in EuroPrevall; Dr Lourdes Sainz de los Terreros, Carmen Salazar, and Elena Sopolana at Hospital Universitario Ramón y Cajal, and Dr Isabel Reig and Dr Pablo Rodriguez at Hospital Clínico San Carlos for their help in collecting the questionnaires and performing the preliminary analyses.

Funding

This study was part of the collaborative research project EuroPrevall, an integrated project funded by the European Commission under the 6th Framework Programme (FOOD-CT-2005-514000).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

1. NDA. Opinion of the scientific panel of dietetic products, nutrition and allergies on a request from the commission relating to the evaluation of allergenic foods for labelling purposes. *The EFSA Journal*. 2004;(32):1-197.
2. Branum AM, Lukacs SL. Food allergy among U.S. children: trends in prevalence and hospitalizations. *NCHS Data Brief*. 2008;(10):1-8.
3. Pereira B, Venter C, Grundy J, Clayton CB, Arshad SH, Dean T. Prevalence of sensitization to food allergens, reported adverse reaction to foods, food avoidance, and food hypersensitivity among teenagers. *J Allergy Clin Immunol*. 2005; 116(4):884-92.
4. Rona RJ, Keil T, Summers C, Gislason D, Zuidmeer L, Sodergren E, Sigurdardottir ST, Lindner T, Goldhahn K, Dahlstrom J, McBride D, Madsen C. The prevalence of food allergy: a meta-analysis. *J Allergy Clin Immunol*. 2007; 120(3):638-46.
5. Venter C, Pereira B, Grundy J, Clayton CB, Arshad SH, Dean T. Prevalence of sensitization reported and objectively assessed food hypersensitivity amongst six-year-old children: a population-based study. *Pediatr Allergy Immunol*. 2006; 17(5):356-63.
6. Asero R, Ballmer-Weber BK, Beyer K, Conti A, Dubakiene R, Fernandez-Rivas M, Hoffmann-Sommergruber K, Lidholm J, Mustakov T, Oude Elberink JN, Pumphrey RS, Stahl Skov P, van Ree R, Vlieg-Boerstra BJ, Hiller R, Hourihane JO, Kowalski M, Papadopoulos NG, Wal JM, Mills EN, Vieths S. IgE-mediated food allergy diagnosis: Current status and new perspectives. *Mol Nutr Food Res*. 2007; 51(1):135-47.
7. Sicherer SH, Sampson HA. Food allergy. *J Allergy Clin Immunol*. 2010; 125(2 Suppl 2):S116-S125.
8. Munoz-Furlong A. Living with food allergies: not as easy as you might think. *FDA Consum*. 2001; 35(4):40.
9. Prevalence, Costs & Basis of Food Allergy Across Europe. www.europrevall.org. 2010. 10-5-2010. Ref Type: Electronic Citation
10. Mills EN, Mackie AR, Burney P, Beyer K, Frewer L, Madsen C, Botjes E, Crevel RW, van Ree R. The prevalence, cost and basis of food allergy across Europe. *Allergy*. 2007; 62(7):717-22.
11. Fox M, Voordouw J, Mugford M, Cornelisse J, Antonides G, Frewer L. Social and economic costs of food allergies in Europe: development of a questionnaire to measure costs and health utility. *Health Serv Res*. 2009; 44(5 Pt 1):1662-78.
12. Miles S, Fordham R, Mills C, Valovirta E, Mugford M. A framework for measuring costs to society of IgE-mediated food allergy. *Allergy*. 2005; 60(8):996-1003.
13. Voordouw J, Cornelisse-Vermaat JR, Fox M, Antonides G, Mugford M, Frewer L. Household and health care costs

- associated with food allergy: an exploratory study. *British Food Journal*. 2010 (In press).
14. Sampson HA. Immunologically mediated food allergy: the importance of food challenge procedures. *Ann Allergy*. 1988; 60(3):262-9.
 15. Bindslev-Jensen C, Ballmer-Weber BK, Bengtsson U, Blanco C, Ebner C, Hourihane J, Knulst AC, Moneret-Vautrin DA, Nekam K, Niggemann B, Osterballe M, Ortolani C, Ring J, Schnopp C, Werfel T. Standardization of food challenges in patients with immediate reactions to foods. Position paper from the European Academy of Allergology and Clinical Immunology. *Allergy*. 2004; 59(7):690-7.
 16. Nowak-Wegrzyn A, Assa'ad AH, Bahna SL, Bock SA, Sicherer SH, Teuber SS. Work Group report: oral food challenge testing. *J Allergy Clin Immunol*. 2009; 123(6 Suppl):S365-S383.
 17. Sampson HA. Adverse reactions to foods. In: Adkinson NF, Yunginger JW, Busse WW, Bochner BS, Holgate ST, Simons ER et al., editors. *Allergy: principles and practice*. Philadelphia: Mosby Inc., 2003: 1619-43.
 18. Semper HM KRC. Stress in parents of severely food allergic children: Does consulting a health professional influence stress levels? *Proceedings of the British Psychological Society* 2005;(13):88.
 19. Keil T, McBride D, Grimshaw K, Niggemann B, Xepapadaki P, Zannikos K, Sigurdardottir ST, Clausen M, Reche M, Pascual C, Stanczyk AP, Kowalski ML, Dubakiene R, Drasutiene G, Roberts G, Schoemaker AF, Sprickelman AB, Fiocchi A, Martelli A, Dufour S, Hourihane J, Kulig M, Wjst M, Yazdanbakhsh M, Szépfalusi Z, van Ree R, Willich SN, Wahn U, Mills EN, Beyer K. The multinational birth cohort of EuroPrevall: background, aims and methods. *Allergy*. 2010; 65(4):482-90.
 20. Ethier W. *Modern International Economics*. 3 ed. New York/London: W. W. Norton & Comp, 1995.
 21. Kooreman P, Wunderink S. *The Economics of Household Behaviour*. London Wiltshire Great Brittan: Macmillan Press Ltd, 1997.
 22. Posnett J, Jan S. Indirect cost in economic evaluation: the opportunity cost of unpaid inputs. *Health Econ*. 1996; 5(1):13-23.
 23. Fernandez-Rivas M. Food allergy in *Alergológica-2005*. *J Investig Allergol Clin Immunol*. 2009;19 2009; 19(Suppl 2):37-4.
- *Manuscript received January 24, 2013; accepted for publication, December 12, 2013.*
- **Inmaculada Cerecedo**
- Medical Department
Laboratorios Leti S.L.Unipersona
28760 Tres Cantos, Spain
E-mail: inmaculadacerecedo@gmail.com