

# Accidental food-allergic reactions are associated with higher costs and more sick leave but not with quality of life

To The Editor:

The prevalence of IgE-mediated food allergy diagnosed by clinical history and positive serology in adults across Europe ranges from 0.3–6%.<sup>1</sup> Almost half of the food-allergic adults are confronted with accidental allergic reactions yearly.<sup>2</sup> Especially moderate and severe reactions require medical consultation and treatment, which can have a high impact on economic costs.<sup>3</sup> A retrospective study in the United States showed that food-induced allergic reactions are a financial burden, were ambulatory visits are responsible for more than half of the costs.<sup>4</sup> More insight into the impact of accidental food-allergic reactions on economic costs seems important to develop effective and efficient health care policies and guidelines.<sup>5</sup> Having food allergy impairs HRQL.<sup>6</sup> It is unknown to what extent the occurrence of accidental allergic reactions contribute to this. Since almost half of the food-allergic adults' experiences on average two accidental allergic reactions per year,<sup>2</sup> it is important to have insight in the impact of these reactions on costs, sick leave and HRQL. Therefore, we investigated the influence of food-induced accidental allergic reactions during 1 year on costs, sick leave and HRQL in adults.

A prospective cohort study with 1-year follow-up was conducted in a tertiary referral centre for food allergy in the Netherlands. In this study, forty-six adults with a doctor-diagnosed food allergy were included. Of them, forty (87%) patients had a severe food allergy. The most common food allergies were for tree nuts (76%, 35/46) and peanut (70%, 32/46). Patient characteristics are shown in Table S1. Patients reported every food-induced accidental allergic reaction using an online questionnaire. Furthermore, patients completed questionnaires about HRQL at baseline and after 12 months and about costs after 12 months. Differences between patients with and without accidental allergic reactions regarding total yearly direct, indirect and intangible costs, sick leave due to accidental allergic reactions and specific and generic HRQL were analysed using descriptive statistics and the Mann-Whitney *U* test. For details on the methods of the study, see Data S1.

A total of 121 accidental allergic reactions was reported during the 1-year follow-up. Of all patients, 36 (78%) patients reported one or more accidental allergic reactions (range: 1–19), with varying severity: 22% (27/121) mild, 59% (71/121) moderate and 19% (23/121) severe.

Patients with accidental allergic reactions during the 1-year follow-up ( $n = 36$ ) had higher total yearly direct and indirect costs compared to patients without accidental allergic reactions ( $n = 10$ ) (mean €1186 [bootstrap 95% CI: €609–1845] vs €158 [bootstrap 95% CI: €68–266],  $p = .01$ ). In all subcategories (primary care consultations, outpatient consultations, hospital admissions, travel costs to health care facilities and sick leave costs due to accidental reactions) patients with accidental allergic reactions had higher costs than patients without accidental allergic reactions. (Table 1) Three patients had extremely high-costs due to hospital admissions or high numbers of primary care or outpatient consultations. (Table S2) When excluding these three patients, the total yearly direct and indirect costs were still significantly higher in patients with accidental allergic reactions compared to patients without accidental allergic reactions (mean €673 [bootstrap 95% CI: €414–967] vs €158 [bootstrap 95% CI: €69–280]),  $p = .03$ ). With regard to intangible costs, patients with accidental allergic reactions reported more problems on all EQ-5D dimensions compared to patients without accidental allergic reactions: mobility (19% vs 0%), self-care (6% vs 0%), usual activities (28% vs 0%), pain/discomfort (50% vs 20%) and anxiety/depression (19% vs 0%). (Table 1).

Of the patients who experienced accidental allergic reactions, 22% (8/36) reported sick leave due to a total of eleven accidental allergic reactions during the 1-year follow-up: five patients reported sick leave for one reaction and three patients for two reactions. Severity of accidental allergic reactions in which sick leave was reported, was in 8 cases moderate (duration of sick leave: few hours [ $n = 6$ ], 1 day [ $n = 1$ ], >2 days [ $n = 1$ ]) and in 3 cases severe (duration of sick leave: few hours [ $n = 1$ ], 1 day [ $n = 2$ ]).

At baseline, there was no difference in food allergy specific and generic HRQL between patients with and without accidental allergic reactions. After 1-year follow-up, there were still no significant differences in either food allergy specific HRQL (total score FAQLQ-AF, domain Risk of accidental exposure) and generic HRQL (physical functioning, social functioning, physical role limitations, emotional role limitations, mental health, vitality, pain, general health and health change). (Table 2).

We showed that accidental allergic reactions in food-allergic adults are associated with higher direct and indirect costs. In our study, primary care consultations, outpatient consultations and hospital

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TABLE 1 Mean yearly costs in patients with and without accidental allergic reactions

	Total	Patients with allergic reactions (n = 36)	Patients without allergic reactions (n = 10)
	Mean (bootstrap 95% CI)	Mean (bootstrap 95% CI)	Mean (bootstrap 95% CI)
Total costs	€962 (505–1476)	€1186 (609–1845)	€158 (68–266)
<b>Direct costs</b>			
Consultations			
Primary care consultations	€360 (179–550)	€443 (233–689)	€64 (34–102)
Outpatient consultations	€270 (114–483)	€322 (124–628)	€81 (17–166)
Hospital admissions	€241 (47–522)	€308 (57–663)	€0 (0–0)
Travel costs to healthcare facilities	€42 (25–59)	€50 (29–74)	€13 (5–24)
<b>Indirect costs</b>			
Sick leave costs due to accidental allergic reactions	€49 (3–115)	€62 (5–149)	€0 (0–0)
	n (%)	n (%)	n (%)
<b>Intangible costs</b>			
Frequency of reporting problems per EQ-5D dimension <sup>a</sup>			
Mobility	7 (15)	7 (19)	0 (0)
Self-care	2 (4)	2 (6)	0 (0)
Usual activities	10 (22)	10 (28)	0 (0)
Pain/discomfort	20 (44)	18 (50)	2 (20)
Anxiety/depression	7 (15)	7 (19)	0 (0)

<sup>a</sup>Reporting problems: EQ-5D level 2 (some problems) + 3 (extreme problems).

admissions were responsible for relatively comparable amounts of costs, whereof the highest costs came from primary care consultations. Patel et al.<sup>4</sup> reported that in the United States more than half of the costs of food-induced allergic reactions come from office-based physician visits and that almost half of the costs come from acute treatment. In addition, in the Netherlands patients visit a general practitioner just as often as an emergency department in case of accidental allergic reactions.<sup>7</sup> Furthermore, we found that the occurrence of accidental allergic reactions is an important factor that even leads to sevenfold higher health care costs. Assuming that 2.1% of the Dutch adults has food allergy,<sup>1</sup> whereof, 46% experiences accidental allergic reactions yearly,<sup>2</sup> a rough estimation of the total yearly costs for all food-allergic Dutch adults with accidental allergic reactions would be 160 million euro and without accidental allergic reactions 25 million euro. This shows the large economic burden of accidental allergic reactions. There are several causes for accidental allergic reactions, of which the most important are: not adequately managing the elimination diet, incorrect and confusing food labelling caused by, for example, the limited credibility of precautionary labelling and misunderstandings in restaurants.<sup>2</sup> Investment in more preventive strategies to avoid accidental allergic reactions, for example, by giving more dietary advice and by improving regulation of the food industry and restaurants, seems important to reduce the occurrence of accidental allergic reactions and related economic impact.

We demonstrated that patients with accidental allergic reactions reported more problems with regard to mobility, self-care, usual

activities, pain/discomfort and anxiety/depression compared with patients without accidental allergic reactions. This suggests that patients with accidental allergic reactions might have higher intangible costs. More research with a larger sample size is required to confirm this.

We demonstrated that 22% of the patients who experiences one or more accidental allergic reaction per year report sick leave due to 1–2 accidental allergic reactions. There is no literature about the extent to which workplace circumstances contribute to accidental allergic reactions. Further investigation into sick leave due to accidental allergic reactions and the influence of workplace circumstances would make a valuable contribution to the current knowledge on this subject.

Food-allergic patients have an impaired HRQL.<sup>6</sup> The food allergy specific HRQL in our study population was lower, compared with the Dutch food-allergic population showed by Goossens et al.<sup>8</sup> ( $p = .04$ ). This difference might be caused by the higher percentage of milk allergic patients in our study population compared with Goossens et al.<sup>8</sup> (35% vs 15%), which is known as a predictor for greater HRQL impairment.<sup>9</sup> Scores of our study population on generic HRQL were comparable with the Dutch food-allergic population<sup>10</sup> with exception of the RAND-36 dimension General health which was less impaired in our study ( $p = .037$ ). We found that experiencing accidental allergic reactions has no additional impact on HRQL. In our study, most patients had food allergy for a long period (mean: 24 years), which probably led to a relatively stable HRQL.

TABLE 2 Scores FAQLQ-AF and RAND-36 in patients with and without accidental allergic reactions

	Scores at baseline				Scores after 12 months follow-up				
	Patients with reactions n = 33 (missing: n = 3)		Patients without reactions n = 10		With reactions n = 36		Without reactions n = 10		Test of difference between patients with vs without reactions
	Median (bootstrap 95% CI)	Median (bootstrap 95% CI)	Median (bootstrap 95% CI)	Median (bootstrap 95% CI)	Median (bootstrap 95% CI)	Median (bootstrap 95% CI)	p-value		
<b>FAQLQ-AF<sup>a</sup></b>									
Total score	4.3 (3.9–4.7)	3.2 (2.1–5.1)			4.1 (3.4–4.6)	3.7 (2.4–4.9)			.41
Domain Allergen avoidance-dietary restrictions	4.0 (3.5–4.6)	2.6 (2.2–4.5)			3.8 (3.0–4.5)	3.5 (2.6–4.6)			
Domain Emotional impact	4.4 (4.1–4.7)	3.1 (2.0–5.3)			4.2 (3.7–4.7)	3.7 (2.3–4.9)			
Domain Risk of accidental exposure	5.0 (4.6–5.6)	4.1 (2.4–6.1)			4.8 (14.4–5.3)	4.2 (2.4–5.8)			.50
Domain Food allergy-related health	3.0 (2.7–3.8)	2.3 (1.7–3.7)			3.0 (2.3–3.5)	2.5 (1.8–3.7)			
<b>RAND-36<sup>b</sup></b>									
Physical functioning	100 (90–100)	100 (93–100)			95 (90–100)	98 (90–100)			.35
Social functioning	88 (75–100)	100 (44–100)			50 (50–50)	50 (38–50)			.17
Physical role limitations	100 (75–100)	100 (100–100)			100 (75–100)	100 (100–100)			.25
Emotional role limitations	100 (100–100)	100 (100–100)			100 (100–100)	100 (100–100)			.72
Mental health	80 (72–88)	80 (68–88)			60 (60–66)	60 (58–64)			.72
Vitality	60 (55–70)	70 (50–90)			45 (43–50)	50 (43–55)			.34
Pain	90 (84–100)	95 (78–100)			20 (0–22)	5 (0–10)			.13
General health	65 (55–75)	73 (60–78)			50 (50–50)	50 (45–55)			.80
Health change	50 (50–50)	50 (38–50)			50 (50–50)	50 (50–50)			.63

<sup>a</sup>The total score ranges from 1 “no impairment” to 7 “maximal impairment”. MCID: 0.5.

<sup>b</sup>The total score ranges from 0 “maximum disability” to 100 “no disability”. MCID: 3–5.

A limitation of this study was the relatively small sample size. Furthermore, our study population had a relatively high percentage of patients with severe food allergy, which might be caused by our third line population. These limitations restrict the generalizability of the data to the general food-allergic population. The results were strengthened by the prospective design, use of validated questionnaires and inclusion of a well-defined patient-set. More research in a larger study population is needed to get more insight into the impact of accidental food-allergic reactions on economic costs and HRQL.

In conclusion, accidental allergic reactions are associated with higher direct and indirect costs and more sick leave, but not with HRQL.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## AUTHOR CONTRIBUTIONS

AK, ADMH, GFH, VMB and HOM designed the study. ADMH and HOM collected the data. AV, ACK, TML and HOM, analysed the data and wrote the manuscript. All authors contributed to interpretation of results and manuscript revision and approved the final version of the manuscript.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are not publicly available due to privacy or ethical restrictions.

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## REFERENCES

1. Lyons SA, Burney PGJ, Ballmer-Weber BK, et al. Food allergy in adults: substantial variation in prevalence and causative foods across Europe. *J Allergy Clin Immunol Pract.* 2019;7:1920.e11-1928.e11.
2. Michelsen-Huisman AD, van Os-Medendorp H, Blom WM, et al. Accidental allergic reactions in food allergy: causes related to products and patient's management. *Allergy.* 2018;73:2377-2381.
3. Fox M, Mugford M, Voordouw J, et al. Health sector costs of self-reported food allergy in Europe: a patient-based cost of illness study. *Eur J Public Health.* 2013;23(5):757-762.
4. Patel DA, Holdford DA, Edwards E, Carroll NV. Estimating the economic burden of food-induced allergic reactions and anaphylaxis in the United States. *J Allergy Clin Immunol.* 2011;128(1):110.e5-115.e5.
5. Chisholm D, Evans DB. Economic evaluation in health: saving money or improving care? *J Med Econ.* 2007;10:325-337.
6. Flokstra-de Blok BM, Dubois AE, Vlieg-Boerstra BJ, et al. Health-related quality of life of food allergic patients: comparison with the general population and other diseases. *Allergy.* 2010;65(2):238-244.
7. Le TM, van Hoffen E, Pasmans SG, Bruijnzeel-Koomen CA, Knulst AC. Suboptimal management of acute food-allergic reactions by patients, emergency departments and general practitioners. *Allergy.* 2009;64(8):1227-1228.
8. Goossens NJ, Flokstra-de Blok BM, van der Meulen GN, et al. Health-related quality of life in food-allergic adults from eight European countries. *Ann Allergy Asthma Immunol.* 2014;113(1):63.e1-68.e1.
9. Saleh-Langenberg J, Goossens NJ, Flokstra-de Blok BM, et al. Predictors of health-related quality of life of European food-allergic patients. *Allergy.* 2015;70(6):616-624.
10. Flokstra-de Blok BM, van der Velde JL, Vlieg-Boerstra BJ, et al. Health-related quality of life of food allergic patients measured with generic and disease-specific questionnaires. *Allergy.* 2010;65(8):1031-1038.

## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.