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ORIGINAL ARTICLE

Out-of-hospital health care costs of childhood food allergy in Australia: A population-based longitudinal study

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Abstract

Background: Australia has one of the highest prevalence of childhood food allergy in the world, but there are no data on its economic burden in Australia.

Methods: We used data from the HealthNuts study, a population-based longitudinal study undertaken in Melbourne, Australia. Infants were recruited at age 12 months between Sept 2007 and Aug 2011 with food allergy diagnosed using oral food challenges. Health care costs of out-of-hospital services were collected through data linkage to Australia's universal health insurance scheme Medicare. Two-part model was used to compare costs after controlling for potential confounders.

Results: 2919 children were included, and 390 (13.4%) had challenge-confirmed food allergy at age 1 year. Compared with children without food allergy, children with food allergy had significantly higher costs for GP visits, specialist visits, tests, and prescriptions in the first four years of life. The total Medicare cost associated with food allergy from age 1 to 4 years was estimated to be AUD\$889.7 (95% CI \$566.1–\$1188.3) or €411.0 (95% CI €261.5–€549.0) per child. This was projected into an annual Medicare cost of AUD\$26.1 million (95% CI \$20.1–\$32.3 million) or €12.1 (95% CI €9.3–€14.9 million) based on population size in 2020.

Conclusions: Childhood food allergy causes considerable Medicare costs for out-of-hospital services in the first four years after birth in Australia. These findings can help anticipate the financial impact on the health care system associated with childhood food allergy, act as a useful costing resource for future evaluations, and inform management of childhood food allergy internationally.

KEYWORDS

burden, child, food allergy, health care costs

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1 | BACKGROUND

The prevalence of hospital presentations for food-related anaphylaxis in children has increased rapidly in the last few decades, making it a growing public health concern worldwide.¹ Australia has one of the highest prevalence of childhood food allergy in the world, with the condition affecting more than 10% of infants.^{2,3} It has been reported that in Australia, compared with the overall population, 0 to 4-year-old children had the highest rates of hospital admissions for anaphylaxis caused by food allergy,^{4,5} as well as the highest rates of adrenaline autoinjector prescription.⁶

With this magnitude of childhood food allergy, it is important to understand its cost implication on the healthcare system to inform resource allocation and policies. A few studies have investigated the economic burden of childhood food allergy in the US⁷ and in some European countries⁸⁻¹⁰ and reported significant direct medical costs for the healthcare system. Despite food allergy representing one of the most common chronic health conditions in children,¹¹ no such study has been conducted in Australia.

In this study, using a longitudinal population-based cohort of infants with challenge-confirmed IgE-mediated food allergy outcomes (the HealthNuts study),¹² linked with administrative health data, we estimated the out-of-hospital health care costs for childhood food allergy in Australia. The aim is to understand the out-of-hospital costs for children with food allergy and with different types of food allergy from birth to 4 years old and to estimate the relevant economic burden in Australia at the population level.

2 | METHODS

2.1 | Study design and sample

The HealthNuts study is a single-centre, multi-wave, population-based, longitudinal food allergy study undertaken in Melbourne, Australia. Detailed study methods have been published previously.¹² In brief, infants were recruited between September 2007 and August 2011 when presenting for their routine scheduled 12-month vaccinations at immunization clinics. They were invited to undertake SPT screening to 4 common food allergens: egg, peanut, sesame, and either cow's milk or shrimp. Any infant with a detectable SPT wheal (≥ 1 mm) to egg, peanut, or sesame was invited for a food challenge, repeat SPT, and blood test to measure serum-specific IgE at Melbourne's Royal Children's Hospital. As described previously, food challenges were not undertaken for cow's milk or shrimp (Supplementary material S1).^{2,3}

The cohort was followed up at age 4 years. Parents completed a mailed questionnaire or short telephone questionnaire to capture information on their child's current allergy status.

Children born after 1st June 2007 (the earliest date for available healthcare cost data linkage), with a valid linkage to healthcare cost data, with nonmissing food allergy information at year 1 were included in this study as the health economics sample. Healthcare

Key Message

This is the first study in Australia estimating the costs of childhood food allergy and projecting its economic burden at the population level. The results show that although infant food allergy in many cases resolves in the first few years of life, it causes considerable costs to the health system including out-of-hospital services. The findings can act as a useful costing resource for future evaluations focusing on preventive and treatment strategies for children with food allergy, and can inform the management of childhood food allergy internationally.

service utilization and costs from 1 June 2007 till 1 December 2011 were collected.

2.2 | Ethical conduct in human research

Approval to conduct the HealthNuts study was obtained from the Victorian State Government Office for Children (reference no. CDF/07/492), the Victorian State Government Department of Human Services (reference no. 10/07), and the Royal Children's Hospital Human Research Ethics Committee (reference no. 27047). Parents provided written informed consent for study participation, and separate written informed consent to access their child's Medicare data for use in this study.

2.3 | Costs

We investigated direct healthcare costs from a healthcare sector perspective. Out-of-hospital healthcare costs were collected through data linkage to the Medicare data, which covers study children's Medicare records from birth till December 2011. Medicare is Australia's universal health insurance scheme, which guarantees all Australians access to a wide range of health services at low or no cost. It has two components: the Medicare Benefits Schedule (MBS), which covers medical services (visits to health professionals, diagnostic and pathology services) mainly outside the hospital setting, and the Pharmaceutical Benefits Scheme (PBS), which covers prescription medications. All out-of-hospital MBS and PBS services were covered in the analysis, with MBS costs categorized into general practitioner (GP) visits, specialist visits (including visits to pediatricians and all other types of specialists), tests and all others, and PBS costs categorized into adrenaline autoinjectors, nutrition products (including infant formula), dermatologic medicines (e.g., emollients, antihistamines, corticosteroids, etc.) and all others. Details of the included services and prescription medicines and codes used to identify these categories are provided in Supplementary material S2. Costs were inflated to 2019/20 Australian dollars using the total

health price index constructed by the Australian Institute of Health and Welfare.¹³ The 2020 Purchasing power parities were used to exchange the Australian dollars into euros.

2.4 | Definitions

We identified children with food allergy and other allergic diseases using the HealthNuts data: Food allergy at age 1 was defined as an oral food challenge-confirmed allergy to egg, peanut, or sesame, in the context of an SPT ≥ 2 mm or specific IgE ≥ 0.35 kU/L to that food. Food-allergic children were further classified as having peanut allergy alone, egg allergy alone, or peanut and other food allergy (with co-existing egg or sesame food allergy). These classifications were selected to reflect the differences in the natural history of peanut vs egg allergy.¹⁴ We were not able to separate out sesame allergy for analysis in this study due to the small sample size with this food allergy type.

Since food allergy often co-exists with other allergic diseases such as eczema and asthma, which may contribute to higher health-care costs among children with food allergy, we also identified eczema and asthma in the analysis. These allergic diseases were defined as a patient-report history of doctor-diagnosed eczema or asthma at any time in the first 4 years of life.

2.5 | Statistical analysis

We compared characteristics of children included and not included in the health economic sample, with differences tested using Chi-square. Inverse probability weights were generated using logistic regression to adjust for potential bias caused by differences in child sex, socioeconomic status, and parents' country of birth between the health economic sample and the whole HealthNuts sample. We compared the MBS and PBS costs by age between children with and without food allergy, and across food-allergic children from different socioeconomic groups. Only a proportion of study children had a full follow-up for 4 years when the data linkage closed (1st December 2011). As a result, costs were aggregated into half-year intervals by age in the calculation. Annual and total four-year MBS and PBS costs were estimated by summing over the half-year interval costs with confidence interval (CI) generated using nonparametric bootstrapping with 1000 replications. Two-part model, a frequently used model to analyze cost data with a logistic regression part to estimate the likelihood of having any cost and a linear part to estimate costs when positive costs were predicted, was used to test whether the cost differences would vary after controlling for potential confounders (child sex, socioeconomic status, and parents' country of birth).¹⁵ To understand the source of the cost differences, we decomposed the total four-year MBS and PBS costs into different types of services, and compared them between children with and without food allergy and across children with different types of food allergy. To understand how other allergic diseases may contribute to children's

food allergy costs, we compared the MBS and PBS costs between children with and without food allergy among those with or without asthma and eczema, respectively.

Based on age-specific population size in 2020,¹⁶ food allergy prevalence in Australia estimated in previous studies,^{14,17} and the cost differences and uncertainties estimated between children with and without food allergy in this study, total extra Medicare out-of-hospital costs caused by food allergy among 0- to 4-year-old children were projected for Victoria and Australia through simulation with 1000 replications (Supplementary material S3). Based on Osborne 2012,¹⁷ a lower food allergy prevalence was assumed in North Australia compared with South and Central Australia in the calculation (Supplementary material S3).

3 | RESULTS

In total 2919 children were included in this study, with 390 (13.4%) having challenge-confirmed allergy at year 1. Compared with children who participated in the HealthNuts study but were not included in the current analysis, the health economics study sample included more males, less families from the lowest and highest socioeconomic quintiles, more families with both parents born in Australia, and more children with challenge-confirmed food allergy at year 1 (Table 1).

After adjusting for potential selection bias using inverse probability weights, compared to children without food allergy at age 1, children with food allergy had significantly higher costs for MBS medical services from the second year after birth, and significantly higher costs for PBS prescriptions from birth up to age four years, with the adjusted results similar to the observed ones (Table 2). The total healthcare costs associated with food allergy from age 1 to age 4 years were estimated to be AUD\$586.3 (95%CI: \$305.2–\$855.0) or €270.9 (95%CI: €141.0–€395.0) for MBS services, AUD\$303.4 (95%CI: \$194.5–\$420.2) or €140.2 (95%CI: €89.9–€194.1) for PBS services, and AUD\$889.7 (95%CI: \$566.1–\$1188.3) or €411.0 (95%CI: €261.5–€549.0) for all Medicare out-of-hospital services. There was no significant difference detected in total MBS costs and PBS costs among children with food allergy across different socioeconomic groups (Supplementary material S4).

Costs by category of services for children with and without food allergy and with different types of food allergy are presented in Figure 1. Compared to children without food allergy, children with food allergy incurred significantly more healthcare costs for GP visits (difference = AUD\$151.1 or €69.8), specialist visits (difference = AUD\$242.9 or €112.2), tests (difference = AUD\$127.4 or €58.9), as well as on adrenaline autoinjectors (difference = AUD\$148.3 or €68.5), nutrition products (difference = AUD\$109.3 or €50.5), and dermatological medications (difference = AUD\$27.7 or €12.8) in the first four years of life (Figure 1A,B). The cost differences across different food allergy groups mainly come from adrenaline autoinjectors, with children only allergic to peanut incurring AUD\$144.5 or €66.8 more on adrenaline autoinjectors than children with egg

	Non-health economic sample N = 2357	Health economic sample ^a N = 2919	p value
Child's sex			
Male	1148 (49.1%)	1517 (52.2%)	.024
Female	1191 (50.9%)	1388 (47.8%)	
Quintiles of Socio-Economic Indexes for Areas (SEIFA) disadvantage ^b			
Lowest 1	535 (22.8%)	527 (18.1%)	<.001
2	430 (18.3%)	620 (21.3%)	
3	459 (19.6%)	643 (22.1%)	
4	436 (18.6%)	583 (20.0%)	
Highest 5	487 (20.7%)	541 (18.6%)	
Parents' country of birth			
Both Australia	1209 (54.8%)	1814 (62.8%)	<.001
One East Asia	98 (4.4%)	121 (4.2%)	
Both East Asia	163 (7.4%)	153 (5.3%)	
Other	738 (33.4%)	802 (27.8%)	
Any challenge-confirmed food allergy at year 1			
0	1844 (92.6%)	2529 (86.6%)	<.001
1	148 (7.4%)	390 (13.4%)	

^aChildren born after 1 June 2007 (the earliest date for available healthcare cost data linkage), with a valid linkage to healthcare cost data, with nonmissing food allergy information at year 1 were included in this study as the health economics sample.

^bSocio-Economic Indexes for Areas (SEIFA) is a product developed by the Australian Bureau of Statistics that ranks areas in Australia according to relative socioeconomic advantage and disadvantage. The indexes are based on information from the five-yearly Census.

TABLE 1 Characteristics of children included and not included in the health economics analysis sample

	No food allergy N = 2529	With food allergy ^a N = 390	Difference (95% confidence interval)	Adjusted ^b difference (95% confidence interval)
MBS costs				
Year 1	845.5	919.1	73.6 (-25.3, 174.6)	89.2 (-13.6, 188.5)
Year 2	484.9	624.4	139.5 (76.8, 211.6)	157.0 (94.6, 218.9)
Year 3	401.4	529.4	128.1 (37.2, 228.4)	143.5 (59.8, 225.0)
Year 4	394.0	589.1	195.0 (11.0, 431.4)	196.6 (24.5, 360.4)
Total	2125.8	2661.9	536.2 (236.0, 862.2)	586.3 (305.2, 855.0)
PBS costs				
Year 1	26.4	129.6	103.2 (40.6, 178.5)	102.5 (39.7, 177.6)
Year 2	13.1	97.5	84.4 (55.9, 117)	84.5 (55.6, 117.3)
Year 3	12.6	72.7	60.1 (40.1, 84.6)	59.9 (39.4, 80.2)
Year 4	10.8	73.2	62.4 (28.8, 104.7)	56.5 (23.0, 90.5)
Total	62.9	372.9	310.0 (201.2, 434.3)	303.4 (194.5, 420.2)

Note: Results were inverse probability weighted.

^aAmong which 79 children had patient-reported history of doctor-diagnosed asthma, 237 had patient-reported history of doctor-diagnosed eczema in the first 4 years of life.

^bAdjusted by child's sex, socioeconomic status, and parents' country of birth using the two-part model.

TABLE 2 Out-of-hospital Medicare Benefits Schedule (MBS, medical services) and Pharmaceutical Benefits Scheme (PBS, prescriptions) cost for children with and without challenge-confirmed food allergy at year 1 (2020 AUD\$), by year after birth

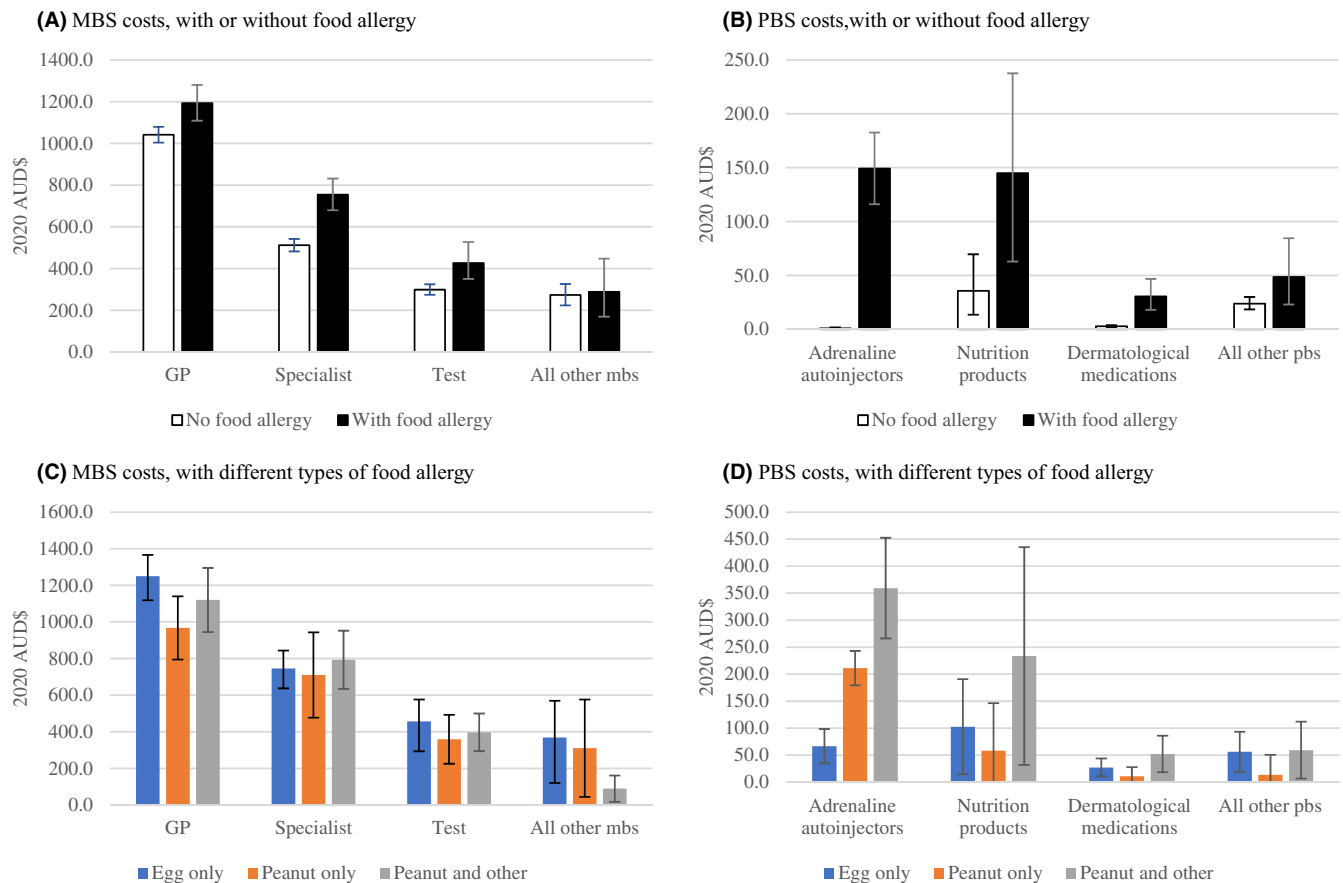


FIGURE 1 Total four-year out-of-hospital MBS (for medical services) and PBS (for prescriptions) costs for children without and with challenge-confirmed food allergy at year 1, and for children with different types of food allergy, by category of services (2020 AUD\$). Results were inverse probability weighted. The error bar represents the 95% confidence interval of the estimation. GP, general practitioner; MBS, Medicare Benefits Schedule; PBS, Pharmaceutical Benefits Scheme

allergy only (who incurred AUD\$66.6 or €30.8 on adrenaline autoinjectors), and children with multiple food allergy (peanut co-existing with other) incurring another AUD\$148.1 or €68.4 compared with children only allergic to peanut (Figure 1D).

The comparisons of healthcare costs between children with food allergy and with other allergic diseases are presented in Figure 2. Children with food allergy alone tended to incur slightly lower costs for MBS medical services compared to children with asthma alone, and higher costs for PBS prescriptions compared to children with asthma or eczema. Having food allergy co-existing with other allergic diseases tended to increase children's healthcare costs more than a purely additive way. This effect was more significant for PBS costs and for children co-existing with asthma.

Based on the age-specific MBS and PBS cost differences and uncertainties estimated between children with and without food allergy (Table 2), it was estimated that in 2020 the total economic burden on Medicare out-of-hospital services caused by food allergy among children 0–4 years old was AUD\$7.7 million (95% CI \$5.8–\$9.9 million) or €3.6 (95% CI €2.7–€4.6 million) in Victoria and AUD\$26.1 million (95% CI \$20.1–\$32.3 million) or €12.1 (95% CI €9.3–€14.9 million) in Australia, with around two-thirds of the total economic burden coming from MBS medical services and one-third from PBS prescriptions (Table 3).

4 | DISCUSSION

In this study, we estimated the Medicare out-of-hospital healthcare costs for food allergy among children 0–4 years old in Australia using a longitudinal cohort linked to administrative health data. We found that compared to children without challenge-confirmed food allergy, children with food allergy had significantly higher costs for GP visits, specialist visits, tests as well as on prescriptions. Children with peanut allergy tended to incur higher costs for adrenaline autoinjectors compared to children with egg allergy. This has translated into considerable Medicare costs for out-of-hospital services in Australia, estimated to be AUD\$26.1 million or €12.1 million among 0- to 4-year-old children in 2020.

We found no significant difference in out-of-hospital costs for childhood food allergy across different socioeconomic groups. This is different from what was found in a US study, which identified disparities in the economic effect of food allergy based on socioeconomic status.¹⁸ It is worth noting that children in the HealthNuts cohort were all recruited from immunization clinics in greater metropolitan Melbourne.¹² This suggests that any inequality between families from the remote and the metropolitan area will not be captured in this study. Regarding different types

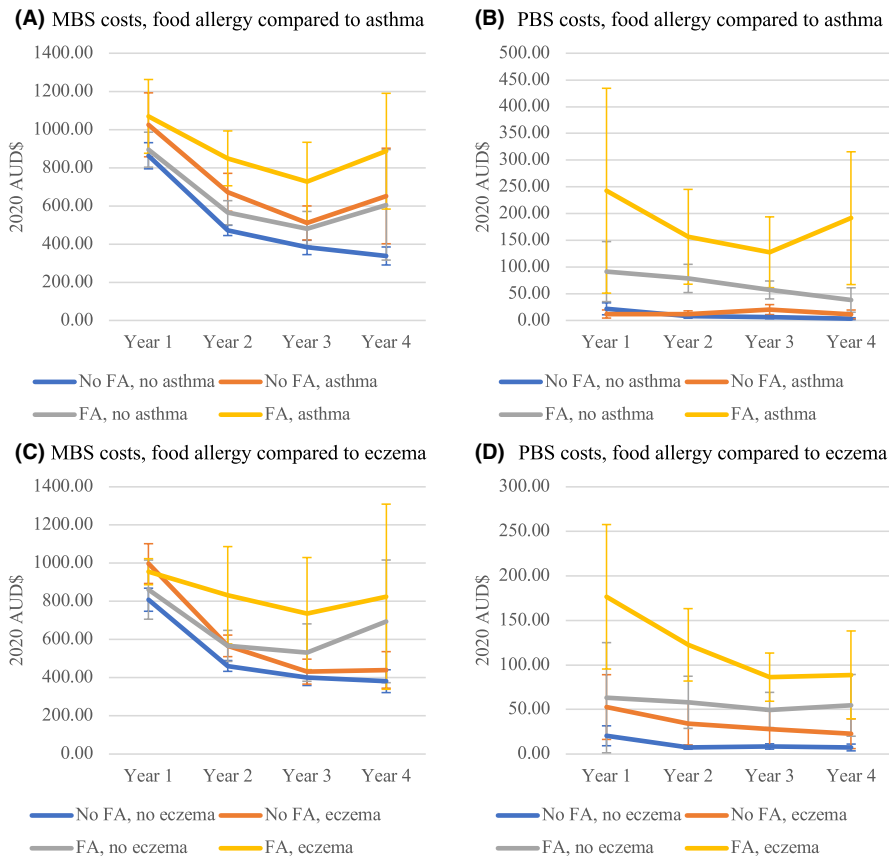


FIGURE 2 Out-of-hospital MBS (for medical services) and PBS (for prescriptions) costs for children with challenge-confirmed food allergy at year 1 and with other allergic diseases, by year after birth (2020 AUD\$). Results were inverse probability weighted. The error bar represents the 95% confidence interval of the estimation. FA, food allergy; MBS, Medicare Benefits Schedule; PBS, Pharmaceutical Benefits Scheme

of food allergy, we found a higher cost associated with the prescription of adrenaline autoinjectors among children with peanut allergy and higher prescription costs among children with food allergy co-existing with asthma. This is consistent with clinical guidelines at the time of the study, which specifically suggested considering the prescription of adrenaline autoinjectors for children with food allergies to peanuts, tree nuts, and seafood, as well as those with a history of anaphylaxis or asthma.¹⁹

This is the first study in Australia estimating the costs of childhood food allergy and projecting its economic burden at the population level. The results show that although infant food allergy in many cases resolves in the first few years of life, it causes high costs to the health system including out-of-hospital services. This is consistent with a few other studies in the United States and Finland, which have also separated out primary care, specialist visits, and examinations in the analysis.²⁰ Our estimated costs of specialist consultations and tests due to childhood allergy were significantly lower compared with the US study (US\$212 or AUD\$311 annually, 2018 price). This may be due to the GP-centred primary care services for children with food allergy in Australia. In Australia, primary care stands for the “gateway” to the wider health system including secondary specialist and tertiary hospital services.²¹ It will be useful to strengthen the role of primary care in the management of childhood food allergy, e.g., to advise on foods to avoid and deal with nonurgent food allergy reactions. This may help reduce referrals to specialists and avoid the more expensive hospital admissions and emergency department presentations.

This study represents good baseline cost data for childhood food allergy in Australia. With the ongoing effort on monitoring and reducing the incidence of childhood food allergy in Australia through primary prevention strategies such as the timely introduction of allergenic foods,²² results in this study can be useful to conduct future projections on the economic burden of childhood food allergy and guide policy decisions.

The strength of this study is the use of a longitudinal cohort with the challenge-confirmed diagnosis of childhood food allergy and linkage to administrative health data, which allows for accurate identification of the food allergy sample and the utilization of health services. The limitation is that we were not able to measure hospital admission and emergency presentation costs for children with food allergy in this study, which could represent more than half of the total healthcare costs.⁷ It will be useful for future studies with a good hospital data linkage to investigate this further. We were not able to measure any cost of items that are not covered by Medicare, for example, over-the-counter medicines and formulas that can be purchased without a prescription. This suggests that our cost estimates should be viewed as conservative.

In conclusion, in this study using a population-based longitudinal study linked to administrative health records, we quantified the out-of-hospital healthcare costs for children with food allergy from birth to 4 years of age in Australia. The findings can help anticipate the financial impact on the health care system associated with childhood food allergy, and act as a useful costing resource for future evaluations focusing on preventive and treatment strategies for children with food allergy.

TABLE 3 Total economic burden on Medicare out-of-hospital services caused by food allergy among children 0–4 years old in Victoria and Australia in 2020 (2020 AUD\$/Euro€)

	Mean	95% confidence interval
Victoria		
Extra MBS costs for medical services		
in AUD	\$5,131,726	(\$3,391,202, \$7,167,774)
in Euro	€2,370,641	(€1,566,592, €3,311,209)
Extra PBS costs for prescriptions		
in AUD	\$2,609,540	(\$1,894,234, \$3,390,647)
in Euro	€1,205,497	(€875,056, €1,566,336)
Total extra Medicare costs for out-of-hospital services		
in AUD	\$7,741,266	(\$5,807,297, \$9,925,920)
in Euro	€3,576,138	(€2,682,726, €4,585,356)
National		
Extra MBS costs for medical services		
in AUD	\$17,270,457	(\$11,761,483, \$23,271,085)
in Euro	€7,978,222	(€5,433,308, €10,750,259)
Extra PBS costs for prescriptions		
in AUD	\$8,851,188	(\$6,602,891, \$11,197,133)
in Euro	€4,088,875	(€3,050,257, €5,172,603)
Total extra Medicare costs for out-of-hospital services		
in AUD	\$26,121,645	(\$20,136,505, \$32,255,652)
in Euro	€12,067,097	(€9,302,215, €14,900,749)

Abbreviations: MBS, Medicare Benefits Schedule; PBS, Pharmaceutical Benefits Scheme.

AUTHOR CONTRIBUTIONS

Xinyang Hua: Conceptualization; Methodology; Formal analysis; Writing—original draft; Writing—review & editing; Project administration. Kim Dalziel: Conceptualization; Methodology; Supervision; Writing—review & editing; Writing—original draft; Formal analysis. Tim Brettig: Conceptualization; Methodology; Writing—review & editing. Shyamali C Dharmage: Conceptualization; Methodology; Writing—review & editing; Funding acquisition; Investigation. Adrian Lowe: Conceptualization; Methodology; Writing—review & editing. Kirsten P Perrett: Conceptualization; Methodology; Funding acquisition; Investigation; Writing—review & editing. Rachel L Peters: Conceptualization; Methodology; Investigation; Funding acquisition; Writing—review & editing. Anne-Louise Ponsonby: Conceptualization; Methodology; Writing—review & editing. Mimi LK Tang: Conceptualization; Methodology; Investigation; Funding acquisition; Writing—review & editing. Jennifer Koplin: Conceptualization; Methodology; Investigation; Funding acquisition; Writing—review & editing; Writing—original draft; Data curation; Supervision.

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CONFLICT OF INTEREST

Kirsten Perrett is Chair of the scientific advisory board for AllergyPal. Her institution has received research grants from the National Health and Medical Research Council, Immune Tolerance Network, DBV Technologies, and Novartis and consultant fees from Aravax; outside the submitted work. Other authors declare no conflict of interest. S.C.D. and A.J.L. declare they have received research funds from GSK's competitively awarded Investigator Sponsored Studies programme, for unrelated research. A.J.L. has also received donations of interventional product (EpiCeram) from Primus Pharmaceuticals for unrelated research.

PEER REVIEW

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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