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ORIGINAL RESEARCH



Evaluation of the healthcare resource use and the related financial costs of managing peanut allergy in the United Kingdom

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ABSTRACT

Aims: We aimed to estimate the resource use and associated costs for patients with peanut allergy (PA) compared to matched controls.

Methods: This was a retrospective cohort study using data from the UK Clinical Practice Research Datalink and Hospital Episode Statistics. PA patients were matched to two control cohorts: the first (simple-matched) were matched 1:1 on year of birth, general practice, gender and registration year. The second (atopy-matched) were matched on the same characteristics plus presence/absence of an atopic condition. Prescriptions and primary and secondary care contacts were compared between cases and controls.

Results: 15,483 peanut-allergic patients were identified: 13,609 (87.9%) were simple-matched and 9,320 (60.2%) atopy-matched. The total per person annual incremental health-care costs associated with PA were £253 (atopy-matched) and £333 (simple-matched). For those with PA and a prior anaphylaxis incremental costs were £662, for those prescribed an epinephrine autoinjector incremental costs were £392. Extrapolated to the U.K. population, total excess costs of PA were between £33 and 44 million in 2015.

Conclusions: Patients with PA had increased health-care contacts and consequently increased associated costs compared to controls. Observation bias should be considered in interpretation, but this study suggests that PA presents significant burden to health-care systems.

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KEYWORDS

Peanut; allergy; anaphylaxis; healthcare resource use; costs

1. Introduction

Peanut allergy (PA) is characterized as an adverse immune reaction to peanuts via an immunoglobulin E (IgE) pathway [1,2]. PA reactions vary in severity and can be life-threatening [3]. PA is commonly detected in early childhood and, unlike many other food allergies, is rarely outgrown [4]. The prevalence of PA is estimated at approximately 1.3% of adults and 2.1% of children in the US [5] and between 0.22% and 1.74% in Europe (discounting prevalence of peanut IgE positivity of 8.58%, as on its own this criterion is not typically sufficient for a clinical diagnosis of PA) [6]. Prevalence estimates vary widely due to many factors including ethnicity, age group, location, study design and method of case ascertainment [7]. In a parallel study by this group, using the same health-care records databases as in this study, the prevalence of PA, in the UK specifically, was estimated to be 202 per 100,000 or 0.2% in the general population, and 635 per 100,000 or 0.6% in those under 18 years [8].

Allergic reactions to peanuts commonly include symptoms involving the skin, gastrointestinal and respiratory systems that can range from mild to severe [9]. PA is one of the leading causes of food-induced anaphylaxis in the USA, UK and Australia [10] and accounts for the majority of food allergy-related deaths [11]. The current standard of care for peanut-allergic patients is strict avoidance and the use of adrenaline in the event of an allergic reaction on accidental exposure. Several forms of immunotherapy are currently under investigation for the treatment of food allergies and recent studies

have demonstrated that oral immunotherapy may induce desensitization in peanut-allergic patients [12].

Research on the quality of life and economic impact of PA is limited. Currently, available data suggests that food allergy can lead to social isolation, depression, underperformance at school and anxiety about allergic reactions [13]. The burden of food allergy does not only affect the patients and their caregivers but has an economic effect on the healthcare system [14]. Unsurprisingly, estimates of the economic impact vary widely depending on study method and setting. In a 2007 study using medical records and claims databases it was reported that annual costs to the US health-care system attributed to food allergy were \$225 million [14], 52% of which were related to office visits, 20% for emergency department visits, 12% for hospital admissions, 4% for outpatient appointments, 3% for ambulance services and 9% for adrenaline prescriptions [15]. In contrast, a food allergy caregiver survey study conducted in the US (where PA was the most common food allergy) reported a total annual medical cost of \$724 per child, and \$4.3 billion overall [13]. Another case-control patient survey study conducted in Europe as part of the European Commission funded EuroPrevall project reported a mean, annual difference in healthcare cost of (\$1)927 international dollars between cases with food allergy and their controls [16].

There are limited data characterizing the financial costs of PA in the UK. The National Institute for Health and Care Excellence (NICE) developed a costing report for food allergy

to support implementation of its guidance on food allergy in children and young people (CG116, 2011). For a skin prick test to be conducted for the diagnosis of food allergy (including cost of staff and equipment), the total cost was estimated at £47 per test. Diagnosis by oral food challenge in a secondary care setting was estimated to cost £516, based on the need for two specialist appointments[17].

As new treatments may become available for peanut allergy in the near future, it is important for policymakers and other decision-makers to understand the burden of peanut allergy from multiple perspectives, including the estimated cost to the healthcare system. Given the paucity of data on this subject, the objective of this study was to compare the difference in financial costs of healthcare between a cohort of patients with PA and two separately matched control groups, as well as to explore potential higher cost sub-groups of patients.

2. Methods

2.1. Data source

The data used for this study was from the Clinical Practice Research Datalink (CPRD) and Hospital Episode Statistics (HES). CPRD is a renowned database with data from over 14 million people in the UK[18]. It contains details of patients' medical history, test results, hospital referrals, and other demographic details. Clinical data are recorded in CPRD using the Read classification [19]. Quality assurance is provided by an acceptability flag, which ensures patient records meet certain criteria, and an up-to-standard at practice date, which identifies when a practice's data quality is sufficient to be used for research purposes. Approximately 60% of patients from CPRD are eligible for linkage to the HES dataset, providing data on secondary care contacts (inpatient, outpatient and accident and emergency). This study was granted CPRD independent Scientific Advisory Committee approval (ISAC 17_116).

2.2. Study design

The study design was a retrospective matched cohort study comparing healthcare resource use and costs between those with PA and two reference groups. A sub-analysis was conducted on a subset of patients with an epinephrine autoinjector or anaphylaxis event and their matched controls versus a subset with no epinephrine autoinjector or anaphylaxis event and their controls, as it was hypothesized that costs would be higher in these sub-groups.

2.3. Patient selection

Patients with Read codes (see Appendix) for positive PA diagnosis or a positive peanut-specific radioallergosorbent (RAST) blood test (assessing peanut-specific IgE levels) in CPRD were included in the analysis. Those patients with a negative peanut RAST test were excluded, regardless of presence of a diagnostic code for PA.

The cohort index date was set as the earliest of first diagnosis of PA or positive peanut-specific RAST or ICD-10 codes for non-specific food allergy or anaphylaxis (See appendix). If

the cohort index date was prior to the patient's registration date or up-to-standard date, then the index date was set to the latter of the two, with the end of CPRD follow-up being the patient's censor date.

Matched controls were selected from patients with no history of food allergies to compare health-care costs between peanut-allergic population and the general population. The first group (simple-matched) was matched 1:1 on their year of birth, general practice, sex, linkage status to corresponding datasets and registration year. The second group (atopy-matched) was matched on the same characteristics plus atopic status; that is, whether a patient had a diagnosis of asthma, eczema and/or allergic rhinitis identified by Read codes in CPRD and ICD-10 codes in HES inpatient data.

Patients who were HES eligible were selected for costing of secondary care resources. Those who were treated with adrenaline and antihistamines were also identified and the estimated cost of prescriptions were calculated from the Prescription Cost Analysis (PCA) for England 2015[20]. If a prescription cost was missing, costs were obtained from the most recent version of the PCA listing a cost and adjusted to 2015 costs using the HM Treasury GDP deflator index. Inpatient admissions were processed using the HRG-4 grouper to categorize into Healthcare Resource Groups[21], which were linked to the National Tariff 2015[22], allowing for the nature of the admission and excess length of stay. Where inpatient costs could not be calculated, mean cost by specialty and nature of admission (day, elective or emergency) were used. Primary care contacts were split into staff and consultation type using the 2015 Unit Cost of Health and Social Care report and each contact was attributed a cost[23]. In cases where cost was not listed, the average length of consultation for the staff role was obtained from the UK general practitioner (GP) workload survey [24] and the average cost per consultation was calculated.

2.4. Statistical analysis

Baseline characteristics and comorbidity were summarised for all cases, matched cases and controls for both the simple-matched group and the atopy-matched group.

The per person year (PPY) costs of primary care contacts, hospital admissions, prescriptions, outpatient admissions, and accident & emergency (A&E) admissions were calculated for cases and controls and compared using a Wilcoxon signed-rank test.

The sub-analysis involved calculating health-care costs associated with four different sub-groups and their matched controls in the simple cohort. Cohort 1 was peanut-allergic patients with an anaphylaxis event (and their matched controls), cohort 2 was peanut-allergic patients without an anaphylaxis event (and their matched controls), cohort 3 was peanut-allergic patients with an epinephrine autoinjector and cohort 4 was peanut-allergic patients without an epinephrine autoinjector. As above the PPY costs of primary care contacts, hospital admissions, prescriptions, outpatient admissions, and accident & emergency (A&E) admissions were calculated and compared using a Wilcoxon signed-rank test.

Different follow-up periods were selected for each type of health contact due to the availability of the contributory data sources. For primary care contacts patients were followed from index date. For secondary care contacts patients were followed from the latter of index date and the date that secondary care data were available; 01/04/1997 for inpatients, 01/04/2003 for outpatients and 01/04/2007 for accident and emergency. Patients were followed until the earliest of the date the patient left the practice, last data-collection date for the practice or, for the secondary care analyses, the last date the data were collected (31/12/2017).

3. Results

3.1. Baseline characteristics

Baseline characteristics were presented for patients with a PA and matched cases for both matching groups and compared to controls (Table 1). There were 15,483 cases of PA in total, 51% were males with a mean age of 17.1 (SD 15.2, median = 13) years old at index date (Table 1).

Of the identified cases, 13,609 (87.9%) could be matched to controls based on the simple-matching criteria and 9,320 (60.2%) could be matched using the atopy-matching criteria. The simple-matched cohort was 51% male with a mean age at index date of 16.1 years old (SD 14.3, median = 12). Significant differences were observed between cases and simple-matched controls for atopic diseases: 30.8% of cases had asthma compared to 6.9% of controls ($p < 0.0001$), 28.8% of cases had eczema compared to 8.9% of controls ($p < 0.0001$) and 8.2% of cases had allergic rhinitis compared to 3.1% of controls ($p < 0.0001$, Table 1).

In the atopy-matched group, 52% of patients were male with a mean age of 15.1 (SD 14.3) years old. There were 1,623 (17.4%) cases with asthma compared to 1,545 (16.6%) controls ($p = 0.1332$). The respective figures were 2,258 (24.2%) versus 2,196 (23.6%) for eczema ($p = 0.2948$) and 453 (4.9%) versus 494 (5.3%) for allergic rhinitis ($p = 0.1822$, Table 1 | Baseline characteristics split by simple-matched and atopy-matched cohorts).

The overall annual incremental health-care costs for those with PA compared to those without were £253 (atopy-matched) and £333 (simple-matched, Table 2). Scaled up to the UK population, assuming prevalence of 6,973 and a population of 3,446,500, the excess costs attributed to people with a PA are estimated to be £44 million compared with age and gender-matched controls. When allowing for prevalent co-morbid atopic conditions, this excess is reduced to an estimated £33 million.

3.2. Primary care contacts

In the simple-matched group, the rate of all-cause primary care contacts for patients identified with a PA was 7.58 GP contacts PPY, where 5.45 contacts PPY were sourced from GP surgery (Table 3), compared to 4.80 PPY for controls, respectively ($p < 0.0001$, Table 2). The cost of primary care contacts was also significantly higher in cases with a £105 increase compared to controls (£287 PPY versus £182 PPY, $p < 0.0001$, Table 2).

Table 1. Baseline characteristics for patients with peanut allergy and simple-matched and atopy-matched cohorts.

	Cases	Simple-matched cases	Simple-matched controls	p-value	Atopy-matched cases	Atopy-matched controls	p-value
Patients, n (%)	15,483 (100)	13,609 (100)	13,609 (100)		9,320 (100)	9,320 (100)	
Male, n, %	7,917 (51.13)	7,000 (51.44)	7,000 (51.44)	1	4,878 (52.34)	4,878 (52.34)	1
Age (years), median, IQR	13 (5–25)	12 (4–24)	12 (4–24)	1	10 (4–23)	10 (4–23)	1
Age (years), mean, sd	17.07 (15.19)	16.06 (14.32)	16.06 (14.32)	1	15.06 (14.25)	15.06 (14.25)	1
Primary care contacts (prior 365 days), median, IQR	2 (0–6)	2 (0–6)	2 (0–4)	<0.0001	2 (0–6)	2 (1–5)	0.6491
Atopic conditions							
Asthma, n, %	4,783 (30.89)	4,190 (30.79)	932 (6.85)	<0.0001	1,623 (17.41)	1,545 (16.58)	0.1332
Eczema, n, %	4,211 (27.20)	3,912 (28.75)	1,208 (8.88)	<0.0001	2,258 (24.23)	2,196 (23.56)	0.2948
Allergic rhinitis, n, %	1,271 (8.21)	1,111 (8.16)	420 (3.09)	<0.0001	453 (4.86)	494 (5.30)	0.1822

Table 2. Summary of health-care costs and contacts for each cohort.

	Contacts PPY		Costs PPY (£)		Difference in cost (£)
	Cases	Controls	Cases	Controls	
Primary care					
Simple	7.58	4.80	286.67	181.50	105 (p < 0.0001)
Atopy	6.91	5.19	262.27	194.11	68 (p < 0.0001)
Inpatient					
Simple	0.25	0.18	185.16	140.82	44 (p < 0.0001)
Atopy	0.20	0.14	175.91	131.02	45 (p < 0.0001)
Prescription					
Simple	13.10	4.90	146.34	47.83	99 (p < 0.0001)
Atopy	11.19	6.12	124.25	53.38	71 (p < 0.0001)
Outpatient					
Simple	1.60	1.00	195.31	117.84	77 (p < 0.0001)
Atopy	1.50	1.00	181.03	116.85	64 (p < 0.0001)
A&E					
Simple	0.40	0.30	33.47	25.73	8 (p < 0.0001)
Atopy	0.40	0.30	32.02	27.15	5 (p < 0.0001)
Total					
Simple	23.25	11.48	846.95	513.72	333 (p < 0.0001)
Atopy	20.20	12.80	775.49	522.51	253 (p < 0.0001)

Table 3. Summary of number of visits and assigned costs of primary care contacts for simple-matched cases and controls.

	N with visit	contacts per person (mean)	Contacts PPY	Cost/contact	Cost PPY (£)
Simple-matched cases' characteristics					
GP	458,056	33.66			272.05
surgery	400,793	29.45	5.45	44.46	242.48
clinic	14,461	1.06	0.20	65.36	12.86
telephone	26,003	1.91	0.35	26.98	9.55
home	9,968	0.73	0.14	43.32	5.88
triage	6,831	0.50	0.09	13.80	1.28
Nurse	89,641	6.59			13.22
surgery	55,545	4.08	0.77	12.14	9.31
clinic	26,817	1.97	0.37	8.85	3.23
telephone	3,785	0.28	0.05	6.19	0.32
home	358	0.03	0.01	14.79	0.09
triage	3,136	0.23	0.04	6.10	0.26
Other	9,049	0.67			1.40
surgery	6,375	0.47	0.08	12.39	1.01
clinic	2,421	0.18	0.03	12.67	0.35
telephone	141	0.01	<0.01	6.85	0.01
home	83	0.01	<0.01	22.02	0.02
triage	29	<0.01	<0.01	10.04	0.00
Total			7.58		286.67
Simple-matched controls' characteristics					
GP	267,221	19.64			172.32
surgery	234,676	17.24	3.48	44.46	154.72
clinic	6,788	0.50	0.10	65.36	6.58
telephone	15,116	1.11	0.22	26.98	6.05
home	6,381	0.47	0.09	43.32	4.10
triage	4,260	0.31	0.06	13.80	0.87
Nurse	51,687	3.80			8.31
surgery	31,998	2.35	0.48	12.14	5.87
clinic	15,155	1.11	0.23	8.85	1.99
telephone	2,107	0.16	0.03	6.19	0.19
home	173	0.01	0.00	14.79	0.05
triage	2,254	0.17	0.03	6.10	0.20
Other	5,106	0.38			0.87
surgery	3,457	0.25	0.05	12.39	0.61
clinic	1,450	0.11	0.02	12.67	0.22
telephone	104	0.01	<0.01	6.85	0.01
home	84	0.01	<0.01	22.02	0.02
triage	11	<0.01	<0.01	10.04	<0.01
Total			4.80		181.50

In the atopy-matched group, the rate of contacts for cases was 6.91 PPY, where 5.00 contacts PPY were sourced from GP surgery (Table 4), in comparison to 5.19 PPY for controls (p < 0.0001, Table 2). This is reflected in the costs where cases had a £68 increase in cost compared to controls (£262 PPY versus £194 PPY, respectively, p < 0.0001, Table 2).

3.3. Hospital inpatient care

The rate of admissions was 0.25 PPY for cases compared to 0.18 PPY for controls in the simple-matched cohort (p < 0.0001). In the atopy-matched group, admission rates were 0.20 PPY compared to 0.14 PPY for controls (p < 0.0001, Table 2).

Table 4. Summary of number of visits and assigned costs of primary care contacts for atopy-matched cases and controls.

	N with visit	contacts per person (mean)	Contacts PPY	Cost/contact	Cost PPY (£)
Atopic-matched cases' characteristics					
GP	288,680	30.97			249.36
surgery	252,305	27.07	5.00	44.46	222.25
clinic	8,847	0.95	0.18	65.36	11.46
telephone	16,792	1.80	0.33	26.98	8.98
home	6,406	0.69	0.13	43.32	5.50
triage	4,330	0.47	0.09	13.80	1.18
Nurse	54,547	5.85			11.67
surgery	33,442	3.59	0.67	12.14	8.17
clinic	16,531	1.77	0.33	8.85	2.90
telephone	2,413	0.26	0.05	6.19	0.30
home	147	0.02	0.00	14.79	0.06
triage	2,014	0.22	0.04	6.10	0.24
Other	5,651	0.61			1.23
surgery	3,896	0.42	0.08	12.39	0.93
clinic	1,578	0.17	0.02	12.67	0.27
telephone	100	0.01	<0.01	6.85	0.01
home	59	0.01	<0.01	22.02	0.02
triage	18	<0.01	<0.01	10.04	0.01
Total			6.91		262.27
Atopic-matched controls characteristic					
GP	202,803	21.76			183.62
surgery	177,711	19.07	3.70	44.46	164.37
clinic	5,534	0.59	0.12	65.36	7.52
telephone	11,293	1.21	0.23	26.98	6.34
home	4,908	0.53	0.10	43.32	4.42
triage	3,357	0.36	0.07	13.80	0.96
Nurse	42,320	4.54			9.53
surgery	25,947	2.78	0.55	12.14	6.68
clinic	12,772	1.37	0.27	8.85	2.35
telephone	1,730	0.19	0.04	6.19	0.22
home	128	0.01	0.00	14.79	0.05
triage	1,743	0.19	0.04	6.10	0.22
Other	4,282	0.46			0.95
surgery	2,826	0.30	0.05	12.39	0.65
clinic	1,300	0.14	0.02	12.67	0.26
telephone	77	<0.01	<0.01	6.85	0.01
home	63	<0.01	<0.01	22.02	0.02
triage	16	<0.01	<0.01	10.04	<0.01
Total			5.19		194.11

The increase in admission rates was reflected in costs with a significant increase in cost for cases in both the simple-matched and atopy-matched groups. Simple-matched cases cost £44 more than controls (£185 PPY versus £141 PPY, respectively, $p < 0.0001$) and atopy-matched cases cost £45 more than controls (£176 PPY versus £131 PPY, respectively, $p < 0.0001$, Table 2).

3.4. Prescription costs

In the simple-matched group, the prescription rate was 13.1 PPY in cases compared to 4.9 PPY for controls ($p < 0.0001$, Table 2). There was a significant difference in cost for cases of £99 compared to controls (£146 PPY versus £48 PPY, respectively, $p < 0.0001$) (Table 2).

In the atopy-matched group, the prescription rate for PA was 11.2 PPY compared to 6.1 PPY for controls, respectively ($p < 0.0001$, Table 2). There was a significant difference and highest rate of costs were associated with the matched cases when compared with controls (£124 PPY versus £53 PPY, respectively, $p < 0.0001$), with a £71 increased cost in the cases (Table 2).

3.5. Outpatient costs

The rate of outpatient admissions PPY in the simple-matched group was 1.6 and 1.0 for case and controls, respectively

(Table 2). The outpatient cost in the simple-matched group was £195 PPY for case in comparison to £118 PPY in the controls ($p < 0.0001$, Table 2).

In the atopy-matched group, the rate of outpatient admissions was 1.5 PPY in the cases and 1.0 PPY in the controls (Table 2). The cost of outpatient admissions in the atopy-matched group was £181 and £117 in the cases and controls, respectively ($p < 0.0001$, Table 2).

3.6. Accident & emergency

In the simple-matched cohort, the rate of A&E admissions PPY was 0.4 and 0.3 for cases and controls, respectively (Table 2). The cost of A&E admissions in the cases was £33 PPY and £26 PPY in the controls ($p < 0.0001$, Table 2).

The rate of A&E admissions in the atopy-matched group was also 0.4 PPY for the cases and 0.3 PPY for the controls (Table 2). The costs for A&E admissions in the atopy-matched group were £32 and £27 for the cases and control, respectively ($p < 0.0001$, Table 2).

3.7. Sub-analysis

In the sub-group analysis, there were 7,570 patients with a history of an epinephrine autoinjector prescription and 6,039 without, there were also 410 patients with an anaphylaxis diagnosis and

Table 5. Summary of health-care costs for subgroups with an epinephrine autoinjector or anaphylaxis, and those without an epinephrine autoinjector or anaphylaxis and their controls in the simple cohort.

	Cases (£)	Controls (£)	Difference in cost (£)
Primary care costs			
Peanut allergy + anaphylaxis	348.54	173.00	175.54 (p < 0.0001)
Peanut allergy – anaphylaxis	283.81	181.85	101.96 (p < 0.0001)
Peanut allergy + epinephrine autoinjector	282.99	169.26	113.73 (p < 0.0001)
Peanut allergy – epinephrine autoinjector	294.00	202.92	91.08 (p < 0.0001)
Inpatient costs			
Peanut allergy + anaphylaxis	280.66	119.52	161.14 (p < 0.0001)
Peanut allergy – anaphylaxis	180.85	141.64	39.21 (p < 0.0001)
Peanut allergy + epinephrine autoinjector	176.18	121.88	54.30 (p < 0.0001)
Peanut allergy – epinephrine autoinjector	203.17	173.00	30.17 (p < 0.0001)
Prescription costs			
Peanut allergy + anaphylaxis	196.02	44.37	151.65 (p < 0.0001)
Peanut allergy – anaphylaxis	144.03	47.97	96.06 (p < 0.0001)
Peanut allergy + epinephrine autoinjector	169.25	44.93	124.32 (p < 0.0001)
Peanut allergy – epinephrine autoinjector	100.74	52.90	47.84 (p < 0.0001)
Outpatient costs			
Peanut allergy + anaphylaxis	233.52	91.24	142.28 (p < 0.0001)
Peanut allergy – anaphylaxis	193.66	118.57	75.09 (p < 0.0001)
Peanut allergy + epinephrine autoinjector	202.65	112.03	90.62 (p < 0.0001)
Peanut allergy – epinephrine autoinjector	181.07	127.35	53.72 (p < 0.0001)
A&E costs			
Peanut allergy + anaphylaxis	53.72	22.74	30.98 (p < 0.0001)
Peanut allergy – anaphylaxis	32.67	25.84	6.83 (p < 0.0001)
Peanut allergy + epinephrine autoinjector	33.93	24.96	8.97 (p < 0.0001)
Peanut allergy – epinephrine autoinjector	32.72	27.00	5.72 (p < 0.0001)
Total healthcare costs			
Peanut allergy + anaphylaxis	1112.46	450.87	661.59 (p < 0.0001)
Peanut allergy – anaphylaxis	835.02	515.87	319.15 (p < 0.0001)
Peanut allergy + epinephrine autoinjector	865.02	473.06	391.96 (p < 0.0001)
Peanut allergy – epinephrine autoinjector	811.70	583.17	228.53 (p < 0.0001)

13,199 without. Those with a history of epinephrine autoinjector prescription had a lower age than those without (means of 12 versus 20 years, medians of 8 versus 19) and those with a history of anaphylaxis diagnosis had a slightly lower mean age than those without (15 versus 16 years, medians of 11 versus 12 years).

In the PA with epinephrine cases, total mean costs PPY for cases were £865 in comparison to £473 in the controls, an incremental cost of £392 PPY (p < 0.0001, Table 5). In the PA without epinephrine cases, total mean costs were £812 in the cases and £583 in the controls with an incremental cost of £229 (p < 0.0001, Table 5).

In the PA with anaphylaxis cases, total mean costs PPY were £1,112 compared to £451 for controls, an incremental cost of £662 PPY (p < 0.0001, Table 5). In the PA with prior anaphylaxis cases, there was an incremental cost of £319 versus controls (p < 0.0001, Table 5).

4. Discussion

This study reports an increased number of primary care visits, in- and out-patient admissions and prescriptions for patients with PA compared to their matched controls in both simple- and atopy-matched groups.

It is unsurprising that the PA group incurred higher health-care costs than the simple-matched controls given the high level of atopic comorbidities in the PA group which may be partly responsible for driving the increase in costs. However, there remains a significant increase in costs between the PA and atopy-matched groups where the impact of atopic comorbidities should effectively be excluded.

The excess costs associated with people with PA were between £211 and £333 PPY, versus atopy-matched and simple controls, respectively. Given the usually skewed distribution of costs, it is likely that a subset of peanut-allergic patients is driving most of the increased cost; perhaps those with a more severe disease or a history of reactions. The sub-analysis supports this assumption with increased costs of £662 for patients with PA and prior anaphylaxis and £392 for patients with PA and a prescription of epinephrine versus simple-matched controls. Further research into understanding potential high resource use sub-groups would be useful in order to prioritize future support and treatment. Those patients who were prescribed an epinephrine in a hospital setting would not have been recorded electronically and therefore would not be included within the epinephrine cohorts. This may affect the difference in costs between those with and without an epinephrine prescription.

To date, there is little data available regarding the cost of PA specifically to health-care systems. However, this study is in alignment with previously published cost of food allergy studies in reporting increased health-care costs in those affected in comparison to their controls [16]. The EuroPrevall case-control study reported a slightly higher mean annual incremental cost attributed to food allergy of approximately \$927 per patient in Europe with UK costs of food allergy at the low end of the range (See unit costs appendix 2 to Fox et al. 2013 [15]). The differences in study design, the focus on a wider range of food allergies and different assumptions on unit costs may have also contributed to the slightly higher costs compared to our study. For example, the EuroPrevall study assumed no differentiation in costs between GP consultations (£32.27) and nurse consultations (£32.27), which

differs to this study where the cost of nurse consultations was less than a GP consultation (£12.14 per consultation versus £44.46, respectively).

Limitations of our study included the way that PA was characterized. Using CPRD data and relying on clinical testing and medical histories in general gives rise to lower prevalence rates than those detected through self-reporting methods[4]. Some cases of PA may have been miscoded or not coded at all and we cannot quantify those missed. Additionally, Read codes where a suspicion of PA was recorded before confirmatory testing was performed may have been included in this study. Even though patients with a positive peanut RAST test were included in the PA cohort this does not necessarily confirm diagnosis, particularly in patients who had a low positive RAST test, which may have led to overestimation of the prevalence of PA. Despite this, only 34 patients were exclusively identified by a positive peanut RAST in the simple-matched cohort.

A limitation of all observational research studies selecting a cohort based on presence of a disease is the likelihood of observation bias. Patients who by definition have had at least one primary care contact will have an increased chance of other morbidities detected and recorded.

Furthermore, we did not attempt to match cohorts based on presence or absence of other food allergies due to coding issues, and separating costs across multiple food allergens would be problematic. Those with PA are more likely than controls to have other food allergies, which is likely to be contributing to the incremental costs. However, out of the total 15,483 with a PA, the majority (58.3%) were mono-allergic to peanuts, 41.7% were poly-allergic to peanuts and one or more other food allergy and 0.09% were poly-allergic to all food categories we used (milk, egg, other nuts, and other foods). Secondary care data was only available for 64.4% of patients in the simple-matched and 60% in the atopic matched. Of the patients for whom secondary care data were available, inpatient data was only available from 1997, outpatient data from 2003 and A&E data from 2007. The quality of A&E data is historically known to be poor with incomplete coverage and missing data items, this could potentially lead to an underestimate in costs. This will also have an effect on the anaphylaxis rates as we were not able to identify anaphylaxis events from this source, due to the lack of granularity in the coding system. It is likely that the rates of anaphylaxis were underestimated in this study. The accident and emergency dataset coding did not differentiate between admissions for anaphylaxis and those for allergy in general. The lack of coding of anaphylaxis in ICD-10 has been acknowledged in previous studies and showed there is intention to improve this area in the future [25–27].

5. Conclusions

Patients with PA had more frequent visits to primary care and secondary care settings and higher prescription rate in both

matched cohorts. This led to significantly higher health-care costs in those with PA compared to those without. The excess costs associated with patients with PA are between £253 and £333 per patient year and are higher in objectively defined higher-risk sub-groups. The excess costs attributed to people with a PA are estimated to be £44 million compared with age and gender-matched controls. When allowing for prevalent co-morbid atopic conditions, this excess is reduced to an estimated £33 million. However, these estimates are likely to be conservative and true incremental costs could be significantly higher given the wide range in prevalence estimates for PA.

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Declaration of interest

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References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Bruijnzeel-Koomen C, Ortolani C, Aas K, et al. Adverse reactions to food. European academy of allergology and clinical immunology subcommittee. *1995* Aug;50(8):623–635.
2. Sicherer SH, Sampson HA. Food allergy. *J Allergy Clin Immunol.* 2010;125(2 SUPPL. 2):S116–25.
3. Hourihane JO, Kilburn SA, Dean P, et al. Clinical characteristics of peanut allergy. *Clin Exp Allergy Internet.* 1997;27(6):634–639. Available from: <http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=9208183&retmode=ref&cmd=prlinks%5Cnpapers3://publication/uuid/CD02ED61-BB2D-4B28-9031-BE3533493D16>
4. Sicherer SH, Furlong TJ, Muoz-Furlong A, et al. A voluntary registry for peanut and tree nut allergy: characteristics of the first 5149 registrants. *J Allergy Clin Immunol.* 2001;108(1):128–132.
5. Sicherer SH, Munoz-Furlong A, Godbold JH, et al. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. *J Allergy Clin Immunol.* 2010;125:1322–1326.

6. Nwaru BI, Hickstein L, Panesar SS, et al. Prevalence of common food allergies in Europe: a systematic review and meta-analysis. *Allergy*. 2014;69(8):992–1007.
 7. Christiansen ES, Kjaer HF, Eller E, et al. The prevalence of atopic diseases and the patterns of sensitization in adolescence. *Pediatr Allergy Immunol*. 2016;27(4):847–853.
 8. Scott LA, Berni TR, Jones BI, et al. Evaluation of the epidemiology of peanut-allergic in the United Kingdom (in-submission).
 9. Bruce J. Children's adverse reactions to subsequent peanut exposure were often more serious than symptoms experienced in initial reactions. *Evid Based Nurs*. 2001;4:91.
 10. Decker WW, Campbell RL, Manivannan V, et al. The etiology and incidence of anaphylaxis in Rochester, Minnesota: a report from the Rochester epidemiology project. *J Allergy Clin Immunol*. 2008;122(6):1161–1165.
 11. Bock SA, Muñoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol*. 2001;107:191–193.
 12. Anagnostou K, Islam S, King Y, et al. Assessing the efficacy of oral immunotherapy for the desensitisation of peanut allergy in children (STOP II): a phase 2 randomised controlled trial. *Lancet*. 2014;383(9873):1297–1304.
 13. Cummings AJ, Knibb RC, King RM, et al. The psychosocial impact of food allergy and food hypersensitivity in children, adolescents and their families: a review. *Allergy*. 2010;65:933–945.
 14. Gupta R, Holdford D, Bilaver L, et al. The economic impact of childhood food allergy in the United States. *JAMA Pediatr*. 2013;167(11):1026–1031.
 15. Patel DA, Holdford DA, Edwards E, et al. Estimating the economic burden of food-induced allergic reactions and anaphylaxis in the United States. *J Allergy Clin Immunol*. 2011 Jul;128(1):110–115.e5.
 16. 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 Oct;23(5):757–762.
 17. National Institute for Health and Clinical Excellence. Diagnosis and assessment of food allergy in children and young people in primary care and community settings. London: National Institute for Health and Clinical Excellence. 2011. Available from: www.nice.org.uk/guidance/CG116
 18. The Clinical Practice Research Datalink. Medicines and healthcare products regulatory authority [Internet]. cited 2016 Mar 1. Available from: <http://www.cprd.com>
 19. Herrett E, Thomas SL, Schoonen WM, et al. Validation and validity of diagnoses in the general practice research database: a systematic review. *Br J Clin Pharmacol* [Internet]. 2010;69(1):4–14. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=20078607%5Chttp://www.ncbi.nlm.nih.gov/pmc/articles/PMC2805870/pdf/bcp0069-0004.pdf
 20. Centre H and SCI. Prescription cost analysis, England [Internet]. 2016 cited 2016 Nov 7. Available from: <https://www.gov.uk/government/statistics/prescription-cost-analysis-england-2015>
 21. Centre H& SCI. HRG4 2013/14 local payment grouper [Internet]. 2013 cited 2017 Apr 28. Available from: <http://www.hscic.gov.uk/article/2580/HRG4-201314-Local-Payment-Grouper>
 22. NHS England. NHS national tariff payment system 2014/15 [Internet]. cited 2018 Mar 6. Available from: <https://www.gov.uk/government/publications/national-tariff-paymentsystem-2014-to-2015>
 23. Curtis L, Burns A Unit costs of health and social care 2015 [Internet]. 2015 cited 2016 Nov 7. Available from: <http://www.pssru.ac.uk/project-pages/unit-costs/2015/>
 24. Centre H& SCI. GP workload survey [Internet]. 2007 cited 2016 Nov 7. Available from: <http://www.ic.nhs.uk/pubs/gpworkload>
 25. Pourang D, Batech M, Sheikh J, et al. Anaphylaxis in a health maintenance organization: international classification of diseases coding and epinephrine auto-injector prescribing. *Ann Allergy Asthma Immunol*. 2017 Feb;118(2):186–190.
- **Interesting insight into the current coding of anaphylaxis.**
26. Tanno LK, Chalmers R, Bierrenbach AL, et al. Changing the history of anaphylaxis mortality statistics through the world health organization's international classification of diseases-11. *J Allergy Clin Immunol*. 2019 Jun 19;pii:S0091-6749(19)30664–5.
 27. Tanno LK, Molinari N, Bruel S, et al. Field-testing the new anaphylaxis' classification for the WHO international classification of diseases-11 revision. *Allergy*. 2017 May;72(5):820–826.
- **Shows promising advancements into coding anaphylaxis.**

Appendix

Readcode	Description
SN58200	Peanut allergy
43Y1.00	Peanut RAST test
ICD	Description
L23.6	Allergic contact dermatitis due to food in contact with skin
T78.0	Anaphylactic shock due to adverse food reaction
T78.1	Other adverse food reactions, not elsewhere classified
T78.2	Anaphylactic shock, unspecified
T78.4	Allergy, unspecified
T80.5	Anaphylactic shock due to serum