

1 **The prevalence, natural history and time trends of peanut allergy over the**
2 **first 10 years of life in two cohorts born in the same geographical location**
3 **12 years apart**

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30 **first 10 years of life in two cohorts born in the same geographical location**
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32

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34

35 **Abstract**

36 *Background:* The aim of this study was to explore the natural history of peanut
37 allergy in childhood in two birth cohorts from the same geographical region in
38 the South of England.

39

40 *Methods:* The FAIR birth cohort was established on the Isle of Wight (UK)
41 between 2001-2002 (n = 969). Children were followed up prospectively, skin
42 prick tested (SPT) to peanut allergens at 1, 2, 3 and 10 years and food challenges
43 performed. The Isle of Wight (IOW) Birth cohort was established in 1989 (n =
44 1456). SPTs were performed at 1, 2, 4 and 10 years. Peanut allergy was based on
45 positive SPT and a good clinical history.

46

47 *Results:* In the FAIR cohort, the prevalence of sensitization to peanut was 0.4%,
48 2.0%, 2.0% and 2.4% at 1,2,3 and 10 years respectively. At 10 years of age,
49 12/828 (1.5%) children were diagnosed with peanut allergy. One child (8%)
50 outgrew her peanut allergy between 3 and 10 years and two children (15%)
51 presented with new onset peanut allergy. Over the first ten years of life, 13/934
52 (1.4%) children were diagnosed with peanut allergy. In the IOW cohort, 6/1034
53 (0.58%) were diagnosed with peanut allergy at 10 years. We found no significant
54 differences between the FAIR and the IOW birth cohort for any of the time points
55 studied.

56

57 *Conclusion:* Peanut allergy appears to be stable over the first ten years of life in
58 our cohorts. There was no significant difference in peanut sensitization or
59 clinical peanut allergy between 1989 and 2001.

60

61 Key words: birth cohort, food allergy epidemiology, peanut allergy, prevalence,
62 time trends

63

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67

68 **Introduction**

69 Prevalence, incidence and time trends of peanut allergy in older children remain
70 unclear. Furthermore, it is not known if the prevalence and/or natural history of
71 peanut allergy during childhood has changed in the last decade, although
72 sensitization rates to peanut are reported to be stable (1). A systematic review
73 reported an overall pooled estimate for all age groups of food-challenge-defined
74 peanut allergy of 0.2% (0.2–0.3) (2). In the USA a systematic review (3) based
75 their prevalence figures of 0.6% in 6-10 year olds and 0.2% in 11-17 year olds,
76 mainly on data by Sicherer et al. (4,5).

77

78 In terms of the natural history of peanut allergy, we know from cohorts recruited
79 from hospital based clinics, that a small proportion (20%) of children with
80 peanut allergy outgrow it by adolescence and occasionally a relapse may occur
81 (6). Less is known however about the natural history of peanut allergy in
82 unselected, population based birth cohorts (7). Recently, Peters et al. (8)
83 reported a prevalence rate of 1.47% at 4 years in the HealthNuts study. However
84 this was not a birth cohort as children were recruited at 1 year.

85

86 We recently reported prevalence of peanut allergy (0.58%) and sensitization
87 (1.3%) at 10 years of age in a cohort born in 1989 (Isle of Wight (IOW) birth
88 cohort) (7). In another cross-sectional study, peanut sensitization rates of 3.7%
89 was reported on the Isle of Wight at 11 years (9). These children (different from
90 the two birth cohorts analyzed in this study) were born in 1991/1992 and
91 assessed at only 11 years of age during a school visit. We have also reported on
92 the time trends of peanut allergy using data from three different cohorts on the
93 Isle of Wight when followed up between the ages of 3-4 years (10), who were
94 born in 1989 (IOW Birth cohort), 1994–1996 (FAB cohort), and 2001–2002
95 (FAIR birth cohort). Skin prick test (SPT) positivity to peanut and clinical peanut
96 allergy in children aged between 3-4 years increased significantly from 1993 to
97 1998/2000, but with no significant change was seen from 1998/2000 to
98 2004/2005. We now present prevalence and natural history data of peanut
99 allergy up to 11 years of age in the FAIR birth cohort, born in 2001-2002. In
100 order to describe time trends of peanut allergy, we have compared the FAIR

101 cohort to the IOW birth cohort (born in 1989-90) at 1, 2, 3-4 and 10 years of age.

102

103 **Methods**

104 *FAIR birth cohort*

105 A birth cohort born on the Isle of Wight (UK) (n = 969) between 2001-2002 was
106 followed up prospectively (11). Children were clinically examined and SPT were
107 performed to milk, wheat, egg, cod, peanut and sesame (ALK Abello) at 1, 2, 3
108 and 10 years of age. Children were invited for food challenges when indicated at
109 three and ten years of age. The Committee on Toxicity advice (UK)(12), which
110 recommended the avoidance of peanut until 3 years in high risk families, was
111 still relevant at the time. Children were therefore first challenged to peanut at 3
112 years of age.

113

114 Peanut allergy was defined as a positive food challenge or a positive SPT and a
115 thorough clinical history, as previously reported (7). At 10 years sensitization
116 was also measured using specific IgE to whole peanut protein and individual
117 components (ThermoFisher, Uppsala, Sweden). Lupin sensitization and allergy
118 was determined at 10 years only, using Stallergens SPT solution.

119

120 *The IOW Birth cohort*

121 The IOW birth cohort was born in 1989 (13). SPTs were performed at 1, 2, 4 and
122 10 years of age using ALK Abello diagnostic extracts. 1034 children were seen at
123 10 years of age (7). Peanut allergy was defined as a positive SPT and a thorough
124 clinical history (14).

125

126 In both cohorts SPT was performed using standardised allergen reagents and
127 methodology by the same research team (15). Allergic sensitization was defined
128 by a positive SPT, indicated by a mean wheal diameter of 3 mm or greater than
129 the negative control (saline).

130

131 Specific IgE tests in the FAIR cohort

132 All children in the FAIR cohort were invited to undergo a blood test, n=246
133 consented. Specific IgE tests to peanut were performed using ImmunoCap

134 (ThermoFisher). Component resolved diagnostic (CRD) tests using ImmunoCap
135 (ThermoFisher) were performed in all children with a positive specific IgE test to
136 peanut; these included: Ara h1, Ara h2, Ara h3, Ara h8 and Ara h9 components.

137

138 *Food challenges in the FAIR cohort*

139 Food challenges were performed with 2.5g of peanut protein at 3 years of age
140 followed by a normal age-appropriate portion, calculated from national
141 consumption data for young children from the UK National Diet and Nutrition
142 Survey databases (16). At 10 years of age, the PRACTALL (17) recommendations
143 were in place, therefore challenge doses were adapted to comply with these (i.e.
144 3.443g of protein). At younger ages in the FAIR cohort, challenges were
145 performed as double blind placebo controlled food challenge, however at age 10
146 parents consented to open food challenges only as their children already had
147 prior diagnosis of peanut allergy. Food challenges were considered positive
148 based on an adapted version of the PRACTALL (17) recommendations, which is
149 used as standard clinical practice at the David Hide Asthma and Allergy Clinic on
150 the Isle of Wight.

151

152 **Statistical methods**

153 All data were double entered by different operators on SPSS versions 20 and 21
154 and were verified (SPSS Inc, Chicago, USA). Prevalence rates were computed,
155 together with 95% confidence intervals, using the method of Clopper and
156 Pearson. Numbers indicating loss of follow-up were clearly stated. Fisher's exact
157 tests, Odds Ratio and Mann Whitney tests were used to assess risk factors for the
158 development of peanut allergy. A logistic regression model was used to assess
159 factors that could independently determine development of peanut allergy.

160

161 Ethical approval for the FAIR study was obtained from the NRES South Central -
162 Southampton B Research Ethics Committee (REF 10/H0504/11). Ethical
163 approval for the IOW study was obtained from the Isle of Wight Local Research
164 Ethics Committee (Ref 18/98). All parents consented and children provided
165 assent.

166

167 **Results**

168 *Prevalence and cumulative incidence of peanut allergy in the FAIR birth cohort*

169 969 children were recruited and 900/969 (92.9%), 858/969 (88.5%), 891/969
170 (91.6%) and 827/969 (85%) were assessed at 1, 2, 3 and 10 years of
171 age. Prevalence of sensitization to any of the predefined foods was 1.9%, 3.8%,
172 4.5% and 2.7% at these ages. Prevalence of sensitization to peanut at these ages
173 was 0.4%, 2.0%, 2.0% and 2.4% (Table 1).

174

175 At 3 years of age 11/891 (1.2%; 95% CI: 0.6 – 2.2%) children were diagnosed
176 with peanut allergy. At 10 years of age, 12/828 (1.5%; 95% CI: 0.8 – 2.5%)
177 children were diagnosed with a peanut allergy. SPT at either 1, 2, 3 or 10 years
178 was available for 849 children. Over the first ten years of life, 27/849 (3.2%;
179 95% CI: 2.0% - 4.4%) children were sensitized to peanut. Information on peanut
180 allergy was available for 934 children at either 1, 2, 3 or 10 years. 13/934 (1.4%;
181 95% CI: 0.6 - 2.2%) children were diagnosed with a peanut allergy over the first
182 ten years.

183

184 Looking at peanut specific IgE levels at 10 years, 29 children were sensitized to
185 peanut using a cut off of 0.35 kUA/l, 31 using 0.2 kUA/l as a cut off point¹⁷ and 36
186 using 0.1 kUA/l¹⁷ as a cut off point. All children with a positive SPT to peanut (n =
187 14) who consented to a blood test (n = 10) showed levels of specific IgE above
188 0.35 kUA/l.

189

190 *Natural history of peanut allergy in the FAIR birth cohort over the first 10 years of*
191 *life*

192 Table 2 summarizes all 27 children who were sensitized to peanut at some point
193 during their first 10 years of life. They showed a variable time course, from early
194 sensitization to late sensitization, with some cases of sensitization in specific
195 time points only. Table 3 summarizes the 13 children with clinical peanut allergy
196 over the first 10 years of life, and their sensitization status measured by SPT, as
197 well as specific IgE. One child (8%) outgrew peanut allergy between 3 and 10
198 years of age. Two children (15%) presented with new onset peanut allergy. The
199 CRD results of these children showed 5 of the 8 children having levels of Ara h2 >

200 0.35 kUA/l. Of the 12 children diagnosed with peanut allergy at age 10 years, five
201 children had positive Ara h2 levels > 0.35 kUA/L, two children had Ara h2 levels
202 < 0.35 kUA/l and five children did not have blood tests.

203

204 *Time trends in peanut allergy in the FAIR and IOW birth cohorts*

205 Although both sensitization and clinical allergy were clearly higher in the FAIR
206 cohort, the differences were not statistically significant. Looking at peanut
207 allergy in the two cohorts the data shows a prevalence of 0.62% versus 1.2% at
208 3-4 years and 0.58% vs. 1.5% at 10 -11 years (Figures 1 and 2).

209

210 Table 1: Sensitization patterns in the FAIR cohort over the first ten years of life

Sensitisation	1 year (n=763)	2 years (n=658)	3 years (n=642)	10 years (n=588)	Specific IgE at 10 years (n=246) ²¹¹
	n (%)	n (%)	n (%)	n (%)	n (%)
Any of the predefined allergens	20 (2.6)	54 (8.2)	76 (11.8)	145 (24.7)	124 (50.4)
Any of the predefined food allergens (milk, egg, cod, wheat, peanut, sesame)	17 (1.9)	25 (3.8)	29(4.5) 23 (3.6)	87 (14.6) 16 (2.7%)	fx5 56 (22.8)
Any of the predefined aero-allergens	8 (1.1)	42 (6.4)	70 (10.9)	99 (16.8%)	Aero-allergen 113 (45.9)
Peanut	3 (0.4)	13 (2.0)	13 (2.0)	14(2.4)	29/57 (50.9) Ara h8: 6/33 (18.2) Ara h1:2/33 (6.1) Ara h2: 6/33 (18.2) Ara h3: 2/33 (6.1) Ara h9: 1/33 (3.03)
Lupin				4 (0.68)	3/57 (5.3)

216 Table 2: Natural history of sensitization and clinical allergy in 27 children of the FAIR cohort over the first 10 years of life

Participant	Sensitized at 1 year	Sensitized at 2 years	Sensitized at 3 years	Peanut allergic at 3 years	Sensitized at 10 years	Peanut allergic at 10 years
1	No	Yes	Yes	Yes	Yes	Yes
2	No	NA	Yes	Yes	NA	Yes
3	No	Yes	Yes	Yes	Yes	Yes
4	NA	Yes	Yes	Yes	NA	Yes
5	NA	NA	Yes	Yes	Yes	Yes
6	NA	NA	Yes	Yes	Yes	Yes
7	No	No	No	No	Yes	Yes
8	No	Yes	Yes	Yes	Yes	Yes
9	No	No	Yes	Yes	NA	Yes
10	No	Yes	Yes	Yes	Yes	Yes
11	No	Yes	NA	Yes	No	No
12	No	NA	No	No	Yes	Yes
13	Yes	Yes	Yes	Yes	Yes	Yes
14	Yes	No	No	No	No	No
15	Yes	Yes	No	No	No	No
16	NA	Yes	No	No	No	No
17	No	Yes	Yes	No	No	No

18	No	Yes	No	No	No	No
19	No	Yes	No	No	No	No
20	No	NA	Yes	No	NA	No
21	No	NA	Yes	No	NA	No
22	No	No	NA	No	Yes	No
23	No	No	No	No	Yes	No
24	No	No	No	No	Yes	No
25	No	No	No	No	Yes	No
26	No	NA	No	No	Yes	No
27	No	Yes	No	No	No	No

217
218
219

No = negative skin prick test or food challenge. Yes= positive skin prick test or food challenge. NA= not applicable (i.e. declined test)

220 Table 3: Natural history of peanut allergy in the FAIR cohort over the first 10 years of life
 221

Participant	SPT wheal size (mm) at 1 year	SPT wheal size (mm) at 2 years	SPT wheal size (mm) at 3 years	Peanut allergy at 3 years	SPT wheal size (mm) at 10 years	Peanut allergy over the first 10 years of life	Specific IgE at 10 years (kUA/L)	CRD at 10 years
1	0	7.75	5.5	Yes	6	Yes (Positive OFC)	Fx5 15.2 Peanut 13.5	Ara h8 0.09 Ara h1 0.05 Ara h2 13.0 Ara h3 0.07 Ara h9 0.28
2	1.75	NA	4.25	Yes	NA	Yes (positive SPT plus history of reactions)	NA	NA
3	0	9.25	8.75	Yes	8.5	Yes (positive OFC in past and SPT > 8 mm)	Fx5 3.5 Peanut 0.4	Ara h8 0.01 Ara h1 0.02 Ara h2 0.32 Ara h3 0.18 Ara h9 0.04
4	NA	9.5	7.75	Yes	NA	Yes (positive SPT > 8 mm plus history of reactions)	NA	NA
5	NA	NA	6	Yes	10.75	Yes (positive SPT > 8 mm plus history of reactions)	Fx5 264 Peanut 264.5	Ara h8 0.07 Ara h1 13.6 Ara h2 138 Ara h3 2.07 Ara h9 0.11

6	NA	NA	10.5	Yes	7.5	Yes (positive SPT > 8 mm plus history of reactions)	NA	
7	0	0	0	No	5	Yes (positive SPT and history of reactions)	Fx5 0.9 Peanut 1.5	Ara h8 0.01 Ara h1 0.07 Ara h2 0.15 Ara h3 0.01 Ara h9 0.01
8	0	0	12	Yes	8.5	Yes (positive SPT > 8 mm plus history of reactions)	Fx5 69 Peanut 49.7	Ara h8 0.00 Ara h1 11.8 Ara h2 29.5 Ara h3 7.79 Ara h9 0.01
9	0	0	3.5	Yes	NA	Yes (Positive OFC in past and still reacting)	NA	NA
10	0	4.75	11	13.25	√	Yes (positive OFC in past and SPT > 8 mm)	NA	NA
11	1.5	0	0	No	10	Yes (positive OFC in past and SPT > 8 mm)	Fx5 1.26 Spec IgE 2.34	Ara h8 1.47 Ara h1 0 Ara h2 1.01 Ara h3 0.001 Ara h9 0.003
12	4.5	8.75	11	Yes	5.5	Yes (Positive OFC)	Fx5 5.03 Spec IgE 4.65	Ara h8 0.01 Ara h1 0.3 Ara h2 4.65

								Ara h3 0.002 Ara h9 0.01
13	0	5.5	NA	Yes	0	X	Fx5 0.75 Spec IgE 1.93	Ara h8 0.03 Ara h1 0.01 Ara h2 0.02 Ara h3 0.17 Ara h9 0.04

222
223 √ = positive. NA = Not applicable (i.e. declined blood test). CRD = component resolved diagnostics
224

225 Table 4: Factors associated with the development of peanut allergy at age ten years of life in the FAIR cohort

	Peanut allergy at age 10 years (n=12)	No peanut allergy at age 10 years (n=935)*	Odds ratio (95% confidence interval)	Fisher's exact test
Sensitization to any allergen over 10 years (n=186)	12/12	174/835	Inf	p=0.000
Sensitization to any aero-allergen over 10 years (n=175)	10/13	165/671	Inf	p=0.000
Senitization to any FA over 10 years (n=41)	12/12	29/934	Inf	p= 0.000
Ever sensitized to grass (n=108)	8/12	100/835	16.727 (4.603 - 65.852)	p=0.001
Any IgE mediated Food Allergy (n=31)	12/12	19/934	Inf	p=0.000
Egg allergy at one year (n=16)	3/13	13/875	22.436 (4.245 - 106.953)	p=0.001
Ever suffered from asthma (n =101)	5/10	96/503	4.2 (1.041 - 17.278)	p=0.029
Ever suffered from eczema (n=258)	10/12	248/815	11.43 (2.486-52.55)	p=0.001
Ever suffered from hayfever (n=233)	7/12	226/815	3.649 (1.146-11.614)	p=0.045
Family history of allergy (n=790)	9/13	781/806	Inf	p=0.241
Any breast feeding (n= 598)	7/12	591/855	0.540 (0.142- 2.061)	p=0.000

226 * n=947 children have been seen at some point over the 10 years. Inf = infinite

227 *Factors associated with the development of peanut allergy*

228 In the FAIR cohort, the following factors were associated with the development
229 of peanut allergy at age 10 years (Table 4): sensitization over the first ten years
230 of life to any allergen, any aero-allergen, any food allergen and grass; ever
231 suffered from asthma, eczema or hayfever, any breastfeeding, as well as egg
232 allergy at one year. A family history of allergy was not however not associated
233 with the development of peanut allergy.

234

235 Logistic regression was performed to assess the impact of a number of factors on
236 the likelihood of developing peanut allergy. The model, containing four variables
237 (breastfeeding, family history, egg allergy and sensitization to any food allergen)
238 was statistically significant, predicting 98.9% of participants' peanut allergic
239 status correctly, α^2 (6, N = 854) = 75.94, $p < 0.01$. The model as a whole explained
240 between 8.5% (Cox and Snell R squared) and 66.1% (Nagelkerke R squared) of
241 the variation. Although this model was very specific, correctly predicting 99.9%
242 of non-peanut allergic participants; it had low sensitivity, correctly predicting
243 only 27% of those with peanut allergy. None of the variables made a unique
244 statistically significant contribution to the model. Sensitization to any food
245 allergen made the strongest contribution, explaining 20.8% of the variation.

246

247 **Discussion**

248 We have shown that in the FAIR cohort at 10 years of age, 2.4% of children were
249 sensitized to peanut and 1.5% clinically allergic. Between the ages of 3 and 10
250 years, one child outgrew peanut allergy and two children had new onset peanut
251 allergy, leading to a cumulative incidence of peanut allergy over the first ten
252 years of life of 3.0%. Comparing peanut sensitization and peanut allergy in two
253 cohorts of children born 12 years apart, we found no significant difference in the
254 prevalence of peanut sensitization at 1, 2, 3-4 and 10 years of age or peanut
255 allergy at 3-4 or 10 years of age. A number of factors played a role in the
256 development of peanut allergy, such as egg allergy and eczema in early life.
257 Family history of allergy and breastfeeding did not independently affect the risk
258 although they were both contributing factors in a multivariate logistic regression
259 model.

260

261 We found a sensitization rate to peanuts at 10 years of 1.8% in the IOW birth
262 cohort and 2.4% in the FAIR cohort. We have also described the prevalence of
263 peanut sensitization in a different IOW school cohort (9) to be 3.7%, which may
264 indicate either higher rates in that particular cohort or some selection bias as
265 only 47.4% of the total cohort was recruited. Very few studies have looked at
266 peanut sensitization in children of this age. Mustayev et al.(18) described the
267 prevalence of sensitization to peanut at 11 years of age in Turkish children as
268 0.7%. Asarnoj et al. (19) report a higher rate of peanut sensitization of 7.4% at
269 age eight years in a Swedish birth cohort, whilst McGowan et al (1) reported a
270 higher rate again of 10.5% in a cross sectional US population of 6-19 year old
271 children and adolescents.

272

273 Gupta et al.(20) described the prevalence of self-reported doctor's diagnosed
274 peanut allergy in 11- 13 year olds from the US to be 2.3%. Using similar
275 methodology in children 11-17 years of age, Sicherer et al. (4,5) reported
276 prevalences of 0.2% and 1.7%. In our cohort, 1.4% of children reported a
277 problem with consuming peanut, but not necessarily based on a doctor's
278 diagnosis. Only one previous study has reported peanut allergy in a prospective
279 cohort study based on oral food challenges, SPTs, and specific IgE measurements
280 (21). The HealthNuts study recruited 12 month old infants in Australia, born
281 between 2006-2009 (n = 5276). Of the 156 participants diagnosed with peanut
282 allergy at age 12 months (2.95% of cohort), 78% had persisting allergy at age 4
283 years. This is therefore a higher initial diagnosis rate and resolution rate than
284 observed in either the FAIR or IOW cohorts. In the HealthNuts study, Ara h2, tree
285 nut, and house dust mite sensitization, coexisting food allergies, eczema and
286 asthma were not predictive of persistent peanut allergy at age 4 years. In the
287 FAIR cohort, we reported that sensitization over the first ten years of life to any
288 allergen, ever having asthma, eczema, hayfever or egg allergy at one year *were*
289 associated with the development of peanut allergy by 10 years. Overall the
290 differences between studies are difficult to disentangle given the different
291 sampling time periods, ages at recruitment and factors reported. Future

292 publications from the HealthNuts study reporting data at age ten years will
293 enable more direct comparisons to be made.

294

295 In terms of development of peanut allergy, our data confirm that egg allergy and
296 eczema are significant risk factors for peanut allergy, as reported previously by
297 Lack et al. (22), the recent LEAP study (23) and the HealthNuts study (21).
298 Nicolau et al. (24) reported that asthma, eczema, and food allergies were more
299 common among subjects with peanut allergy, whereas hayfever was more
300 common in peanut-tolerant children. With respect to diet during pregnancy and
301 infancy as risk factors for development of peanut allergy, our group has
302 previously demonstrated that government advice to atopic mothers to avoid
303 peanut during pregnancy was misunderstood and did not lead to a reduction in
304 peanut allergy prevalence (25). It remains to be seen whether changes to
305 national UK infant feeding guidelines will be made following the publication of
306 the LEAP (23) and Enquiring About Tolerance (EAT) studies (26).

307

308 Comparing SPT or specific IgE testing, we found SPT was a better indicator of
309 peanut allergy: 29 children had a positive specific IgE to peanut, 14 had a
310 positive SPT, with 12 found to be peanut allergic at age 10. For specific IgE, a cut
311 off of > 0.35 kUA/l performed better than 0.1 kUA/l. This is despite the fact that a
312 0.35 kUA/l cut off point reported by ThermoFisher was due to the initial analytic
313 ability of the test, and does not have a clinical basis. This cut off was reduced to
314 0.1 kUA/l as lower detection levels are now possible, but these are not clinical
315 diagnostic levels(27).

316 Children with a clinical peanut allergy were sensitised to a range of peanut
317 components. The majority was sensitised to Ara h2 as all eight children showed a
318 level of sensitisation to Ara h2; (n=7 above 0.1 kUA/l; n=5 above 0.35 kUA/l).
319 This is similar to data reported by Nicolau et al.(24) who reported that Ara h2
320 was the most important predictor of peanut allergy. However, it may not be true
321 in all populations as Restani et al. (28) identified Ara h3 as the major allergen in
322 a group of peanut allergic children.

323

324 A limitation of our study was that the IOW birth cohort were not challenged to
325 peanut, rather the diagnosis was based on a thorough clinical history and
326 positive SPT. Although all the children in the FAIR cohort at the age of 10 years
327 were offered a food challenge, only two consented, both of which were open
328 challenges. Additionally, less than 25% consented to a blood test, which may
329 affect the accuracy of the results. Another limitation is that the sample size was
330 not sufficient to detect statistically significant differences between the two
331 cohorts. Based on our data, we would require a sample size of 4207 children in
332 each group at 3 years and 1908 children per group at 10 years of age to detect a
333 difference with 80% power. Theoretically, if we use these sample sizes and
334 impute our % of peanut allergy we will find a highly significant increase in
335 peanut allergy, both at 3 years ($p=0.006$) and at 10 years ($p = 0.004$).

336

337 **Conclusion**

338 Peanut allergy appears to be stable at 1.5% over the first 10 years of life, with
339 only about 10% of children outgrowing their peanut allergy and approximately
340 20% developing new onset peanut allergy. In the 12 years between 1989-2011,
341 an increase in both peanut sensitization and clinical peanut allergy was noted
342 but this did not reach statistical significance possibly due to sample size
343 constraints. We acknowledge that in some areas of the world, some food
344 allergies seem to be on the increase (29). It is therefore probably safe to assume
345 that with sufficient numbers our peanut allergy prevalence may be significantly
346 increasing, but it is difficult to say for certain as there is such limited data on the
347 time-trends in food allergy.

348

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351 funders played no role in the study design; in the collection, analysis, and
352 interpretation of data; in the writing of the report; and in the decision to submit
353 the article for publication. The researchers acted independent of the funders.

354

355 **Conflicts of interest:** none

356

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