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**Food allergy prevalence in two population-based UK cohorts born 12 years apart.**

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**Author contributions**

CV and WF wrote the first draft of different sections of the paper. MV and WF extrapolated the data and calculated percentages. KPN performed all other analyses. All authors read and edited versions of the paper.

31 **Key words**

32 FA, prevalence, temporal changes, pediatrics, childhood

33

34 **Key messages:**

35           ➤ Reported adverse reactions to foods have remained stable between 1989 -  
36           2001/2002.

37           ➤ Sensitization rates remained stable during the first 10 years of life.

38           ➤ Food allergy rates remained stable during the first 10 years of life.

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41

42 **Abstract**

43 Background: Adverse food reactions include food allergy (FA; immune mediated) and food  
44 intolerances (non-immune mediated). FA are classified into IgE and non-IgE mediated FA.

45 There is limited information available about changes in FA prevalence over time.

46 Methods: Two cohorts of children were evaluated, born on the Isle of Wight (IOW) 12 years  
47 apart. The IOW birth cohort (IOWBC; 1989 – 1990) and the FA and Intolerance Research  
48 birth cohort (FAIRBC; 2001 – 2002). We compared the prevalence of parental reported  
49 reactions to foods (adverse food reactions), allergic sensitization to foods and FA between  
50 the IOWBC and FAIRBC, at ages 1, 2, 3-4 and 10 years. FA included both IgE and non-IgE  
51 mediated FA.

52 Results: Reported adverse reactions to food and sensitization rates remained stable  
53 between the two cohorts. For example, FA at age 3-4 years was reported in 9.1% (95% CI  
54 7.5, 10.7) in IOWBC and 8.3% (95% CI 6.5, 10.1) in FAIRBC (P=0.57) and food sensitization  
55 by skin prick test at age 3-4 years was found in 3.2% (95% CI 2.1, 4.3) in IOWBC and 4.5%  
56 (95% CI 2.9, 6.1) in FAIRBC (P=0.20). Confirmed FA prevalence was lower in FAIRBC than  
57 IOWBC at ages 1, 2 and 3-4, but these differences were not significant after adjustment for  
58 multiple comparisons. For example, FA at age 3-4 years was confirmed in 5.0% (95%CI 3.8,  
59 6.2) in IOWBC and 3.0% (95% CI 1.9, 4.2) in FAIRBC (P=0.03, significance threshold after  
60 Bonferroni correction  $P < 0.004$ ). Confirmed cow's milk allergy rate was higher in IOWBC  
61 than FAIRBC at 3 years ( $< 0.001$ ) but not at other timepoints.

62 Conclusion: Our data show no evidence of changes in rates of adverse reactions to foods,  
63 food sensitization or food allergy during the first 10 years of life between two cohorts born  
64 in England in 1989-90 and 2001-2.

65

66

67 **Introduction**

68 Adverse food reactions include food allergy (FA) (immune mediated) and food intolerances  
69 (non-immune mediated). FA are classified into IgE and non-IgE mediated FA.(1) To fully  
70 understand the epidemiological data around FA prevalence, information regarding  
71 reported rates of FA, sensitization data and clinical FA needs to be considered.

72  
73 In Europe, two systematic reviews have investigated reported reactions to foods,  
74 sensitization to food allergens based on skin prick test (SPT) and FA in children. Risk of bias  
75 was assessed for all studies included in these meta-analyses. It is however important to  
76 consider that study methodologies differed and that it was not always clear how many  
77 children suffered from IgE and non-IgE mediated FA.

78  
79 The first systematic review with meta-analysis where possible summarized prevalence  
80 data from 2000 – 2012, with a follow-up systematic review summarizing data from 2012 –  
81 2021.(2, 3) During 2000 – 2012, the pooled overall lifetime prevalence of self-reported FA  
82 was 17.3% and 19.8% during the period 2012- 2021.(2, 3)The overall pooled estimate for  
83 prevalence of FA based on a positive OFC or DBPCFC to any food was 0.9% during 2000–  
84 2012 and 0.4% during 2012–2021 in children and adults. (2, 3)The overall pooled estimate  
85 for prevalence of any FA based on a clinical history or food challenge, either a positive  
86 open food challenge (OFC) or a positive double-blind placebo-controlled (DBPCFC) was  
87 2.6% in children during the period 2000-2012, and 2.5% during the period 2012 – 2021,  
88 indicating no evidence to support changes in FA prevalence across Europe.(2, 3)

89  
90 For specific foods, another systematic review reported the point prevalence of  
91 sensitization rates as 0.7% for cow's milk and egg, and 2.2% for peanut but data were not  
92 separated between adults and children (2012 – 2021).(4) The corresponding numbers for  
93 the earlier period (2000 – 2012) were 0.3% for cow's milk, 0.8% for egg, and 1.7% for  
94 peanut. Sensitization rates to milk and peanut seem to have increased over time, while egg  
95 sensitization rates remained similar. (4)

96 Based on a clinical history or an oral food challenge, the point prevalence of cows milk  
97 allergy (CMA) (2012 – 2021) was 1.8%, egg allergy 0.6%, and no data were available for  
98 peanut allergy across Europe.(3) In 2000 – 2012, the point prevalence of CMA was 1.6%,  
99 egg allergy 1% and peanut allergy 1.6%.(2) The prevalence of CMA, seems to have  
100 remained stable or slightly increased whereas egg allergy prevalence seems to have  
101 increased.

102

103 In this paper we primarily aimed to compare the prevalence of reported adverse reactions  
104 to food, sensitization rates to all foods tested (cows' milk, hen's egg, wheat, soya, cod, and  
105 peanut) and sensitization to single foods (cow's milk, egg and peanut). Second, we  
106 reported on overall FA, and thirdly we reported FA to single foods cow's milk , egg and  
107 peanut between the original Isle of Wight (IOWBC)(5, 6) and the IOW FAIRBC, at 1, 2, 3-4,  
108 and 10 years of age.(7, 8) FA included both IgE and non-IgE mediated FA.

109

110 The data from this paper avoids the heterogeneity of other studies where comparative  
111 studies may not have been done in the same population and the paper is UK focused only,  
112 reflecting data from children born 1989 and 2001/2002, prior to the more recent studies. It  
113 is however important to note that data from both these cohorts were included in the  
114 European systematic reviews. (3, 4)

115

## 116 **Methods**

117 The Isle of Wight birth cohorts include the 1989 Isle Wight birth cohort (IOWBC) and the  
118 Food Allergy and Intolerance Research cohort (FAIR). (5-8)

119

### 120 *The Isle of Wight Birth cohort*

#### 121 *Inclusion criteria*

122 The IOWBC included an unselected population of children. Families of all children born on  
123 the Isle of Wight, (UK) during 1989 - 1990 were approached for study participation. A total  
124 of 1536 children were eligible to be consented Following consent, (n = 1456) children were

125 recruited into the study followed up prospectively. Demographic and reported allergy data  
126 were collected at 12 weeks' gestation, at birth and during subsequent follow ups at set  
127 time periods. The study was approved by the Isle of Wight research ethics committee  
128 (06/Q1701/34). (5, 6)

129

### 130 *The FAIR birth cohort*

131 The FAIRBC included an unselected population of children. Families of all children born on  
132 the Isle of Wight, (UK) during 2001 - 2003 were approached for study participation. A total  
133 of 1063 children were eligible to be consented. Following consent, (n = 969) children were  
134 recruited into the study followed up prospectively. Demographic and reported allergy data  
135 were collected at 12 weeks' gestation, at birth and during subsequent follow up studies at  
136 set time periods. Ethical approval was obtained from the NRES South Central -  
137 Southampton B Research Ethics Committee (REF 10/H0504/11).(7, 8)

138 Demographic information (table 1), history of allergic disease and other relevant  
139 information for both cohorts was collected using similar questionnaires developed by the  
140 team on the IOW. Information was collected as interview administered questionnaires  
141 from the parents.

142

### 143 *Outcome definitions used in the cohorts*

#### 144 Reported rates of adverse food reactions

145 Similar questionnaires based on the International Study of Asthma and Allergies in  
146 Childhood (ISAAC) studies, were used in both cohorts.(9)

147

#### 148 Skin prick test

149 For both cohorts, SPTs were performed with standardized methods and extracts (ALK-  
150 Abello, Hørsholm, Denmark) to a panel of common aeroallergens and food allergens. Food  
151 allergens included cows' milk, hen's egg, wheat, soya, cod, and peanut. A positive SPT was  
152 defined as a positive reaction to 1 or more food allergens with a mean wheal diameter of 3  
153 mm or larger elicited by the negative control at 15 minutes. In the IOWBC, SPTs were

154 performed at 1 and 2 years of age in symptomatic children only and at 4 and 10 years of  
155 age in all consenting participants. (5, 6) In the FAIR cohort SPTs were performed at 1,2, 3,  
156 and 10 years of age in all consenting participants.(7, 8) Skin prick tests in both cohorts  
157 were performed by the same team of nurses with standardized methodology.

158

### 159 Food allergy

160 For IOWBC, data collected over the course of the study were retrospectively reviewed to  
161 make a diagnosis of FA. No OFCs were performed. Three criteria were defined a priori, and  
162 all three needed to be met for the diagnosis of FA.(5) 1) A parental reported reaction to a  
163 food allergen, such as allergy to cow's milk, hen's egg, wheat, soya, peanuts, other nuts,  
164 fish, and shellfish; 2) a report of recognized allergic symptoms, such as: localized  
165 symptoms: itching, stinging/burning of the lips, mouth or throat, urticaria/hives, or  
166 angioedema; abdominal symptoms: nausea, vomiting, crampy/colicky abdominal pain,  
167 and diarrhea; respiratory symptoms: wheeze, stridor, watery rhinitis, and redness of  
168 eyes/nose; skin symptoms: urticaria, itching, flushed skin, and worsening eczema; or  
169 systemic reactions: anaphylaxis, 3) temporal relationship: symptoms developing within 4  
170 hours of food ingestion. Children were defined as having a FA if 1, 2 and 3 were met.

171

172 In the FAIRBC, children were invited for oral food challenges (OFC) according to predefined  
173 criteria. Based on their prior history and results of the SPT during the first 3 years of life, the  
174 following children were invited to undergo oral food challenges.(7, 8) 1) Those with a positive  
175 SPT to a food that they had not knowingly eaten previously or 2) those who indicated a  
176 previous adverse reaction to foods (regardless of their SPT data). Conversely, children with  
177 a positive SPT to a food that they have previously consumed and tolerated with no prior  
178 reaction were not invited for an OFC.

179

180 Food challenges were conducted with all foods from 6 months of age, except for peanut  
181 and sesame, which were conducted once the children were 3 years old, as it was  
182 considered that infants should not be exposed to these foods in the first few years of life in

183 line with guidance at the time.(10) Some children were excluded from food challenges  
184 because their SPT diameter was above the 95% positive predictive levels.(11) OFCs at 1, 2  
185 and 3 years were performed following a previously published algorithm. (7, 8, 12) All  
186 eligible children underwent open OFCs. Those with a history of immediate symptoms from  
187 prior ingestion of the food underwent a hospital challenge. Children of all ages who had a  
188 positive open OFC either at hospital or at home were invited to participate in a double-  
189 blind, placebo-controlled, food challenge (DBPCFC) to confirm the positive open OFC.(13)  
190 At 10 years of age the PRACTALL recommendations for food challenge doses were  
191 followed for IgE mediated FA.(14) FA was defined as a positive food challenge or a positive  
192 SPT and a convincing clinical history, as previously reported. (7, 8, 12) For non-IgE  
193 mediated FA, a normal portion of the food was given. FA was defined as positive food  
194 challenge as previously reported. (7, 8, 12)

195

196 A diagnosis of food allergy included both IgE and non-IgE mediated FA.

197 Differences in the study methodologies included that not all children in the IOWBC  
198 underwent SPT to the offending foods, whereas all consenting children in the FAIRBC  
199 underwent SPT. To make a diagnosis of FA, For reactions were reported up to four hours  
200 post ingestion in the IOWBC and up to days post ingestion which allows in the FAIR cohort.  
201 This did however allow for inclusion of both IgE and non-IgE mediated FA in both cohorts.

202

### 203 *Statistical analysis of outcomes*

204 Demographic, environmental, and allergic characteristics of participants were compared  
205 between cohorts with Chi-Square tests. Prevalence of sensitization and allergy were  
206 calculated with 95% confidence intervals (CI) and assessed for differences between  
207 cohorts at each year where both were available independently with either Chi-Square tests  
208 or Fisher's exact tests dependent on cell size. Significance level was set at 0.05 for  
209 descriptive tables but was adjusted using a Bonferroni approach to  $0.05/4 = 0.01$  for  
210 reported adverse reactions,  $0.05/8 = 0.006$  for sensitization rates and  $0.05/14 = 0.004$  for  
211 food allergy rates to account for multiple comparisons.



212 **Results**

213 **Participants**

214 Demographic, environmental and allergic characteristics of participants in the IOWBC and  
215 the FAIRBC are shown in Figure 1 and Table 1. We compared demographic information in  
216 the two cohorts at 10 years of age. The cohorts were similar in terms of male:female ratio  
217 ( $p=0.35$ ), reported atopic dermatitis at one year ( $p=0.07$ ), aero-allergen sensitization at 10  
218 years ( $p=0.49$ ), maternal history of FA ( $p=0.14$ ), and maternal smoking during pregnancy  
219 ( $p=0.12$ ). IOWBC had a significantly higher follow-up rate at 10 years ( $p<0.001$ ), more  
220 children consented to SPT( $p<0.001$ ) and reported asthma at 10 years( $p<0.001$ ). However,  
221 significantly less children in IOWBC ever suffered from allergic rhinitis ( $p<0.001$ ) and had a  
222 maternal history of asthma ( $p=0.01$ ). Both cohorts had aeroallergen sensitization rates at  
223 10 years of 24-26% ( $p = 0.49$ ).

224

225 **Reported FA**

226 At one year of age, reported adverse reactions to foods was 8.5% (95% CI: 7.0, 10.1) in the  
227 IOWBC and 7.2% (95% CI: 5.5, 8.9) in FAIRBC ( $p = 0.31$ ). At two years of age, the reported  
228 reactions were 9.2% (95% CI: 7.5, 10.8) in the IOWBC and 8.4% (95% CI: 6.5, 10.3) in the  
229 FAIRBC at two and three years of age ( $p=0.61$ ). At three years of age, it was 9.1% (95% CI:  
230 7.5, 10.7) (IOWBC) and 8.3% (95% CI: 6.5, 10.1) (FAIRBC) ( $p=0.57$ ).

231

232 At 10 years of age, it was 8.6% (95% CI: 7.1, 10.0) in the IOWBC and 9.3% (95% CI: 7.3,  
233 11.3) in FAIRBC. ( $p = 0.6$ )(table 2 and figure 2).

234

235 **Sensitization status**

236 Sensitization rates (table 3 and figure 2) based on SPT  $\geq$  3mm are presented for peanut,  
237 egg, milk and all food allergens. No statistical differences between IOW and FAIR cohorts  
238 were reported at three/four ( $p= 0.20$ ) and 10 years of age ( $p= 0.11$ ) for overall food allergen  
239 sensitization status.

240

241 **FA status**

242 Overall FA

243 No significant differences in overall FA were seen between cohorts at any time period  
244 based on a Bonferroni correct p-value of 0.004. At one year, all FA were 5.3% (95% CI: 4.1,  
245 6.5) in the IOWBC and 3.0% (95% CI: 1.9, 4.1) in the FAIRBC (p=0.01). At 2 years, it was  
246 4.4% (95% CI: 3.2, 5.6) in the IOWBC and 2.4% (95% CI: 1.4, 3.5) in the FAIRBC (p=0.03).  
247 At 3 years, all FA were 5.0% (95% CI: 3.8, 6.2) in the IOWBC and 3.0% (95% CI: 1.9, 4.2) in  
248 the FAIRBC (p=0.03). At 10 years, all FA were 2.6% (95% CI: 1.7, 3.4) in the IOWBC and  
249 3.6% (95% CI: 2.4, 4.9) in the FAIRBC (p=0.2).

250

251 Cow's milk allergy

252 At one year, (table 4 and figure 2) cow's milk allergy (CMA) was 3.5% (95% CI: 2.5, 4.5) in  
253 the IOWBC and 2.4% (95% CI: 1.4, 3.5) in the FAIRBC (p=0.21). At 2 years, milk allergy was  
254 1.6% (95% CI: 0.9, 2.4) in the IOWBC and 1.2% (95% CI: 0.4, 1.9) in the FAIRBC (p=0.49). At  
255 3 years, milk allergy was 2.6% (95% CI: 1.7, 3.5) in the IOWBC and 0.4% (95% CI: 0, 0.9) in  
256 the FAIRBC, which was a significant decrease from the earlier to the later cohort (p<0.001)  
257 and the only significant result seen for CMA. At 10 years, milk allergy was 0.5% (95% CI:  
258 0.1, 0.9) in the IOWBC and 0.4% (95% CI: 0, 0.8) in the FAIRBC (p=0.75).

259

260 Egg allergy

261 At one year, egg allergy was 1.1% (95% CI: 0.5, 1.7) in the IOWBC and 1.8% (95% CI: 0.9,  
262 2.6) in the FAIRBC (p=0.23). At 2 years, egg allergy was 1.3% (95% CI: 0.6, 1.9) in the  
263 IOWBC and 1.3% (95% CI: 0.5, 2) in the FAIRBC (p=1). At 3 years, egg allergy was 1.4%  
264 (95% CI: 0.7, 2.1) in the IOWBC and 1.0% (95% CI: 0.4, 1.7) in the FAIRBC (p=0.55). At 10  
265 years, egg allergy was 0.6% (95% CI: 0.2, 1) in the IOWBC and 0.7% (95% CI: 0.1, 1.3) in the  
266 FAIRBC (p=0.3). No significant differences were seen.

267 Peanut allergy

268 At one year and 2 years respectively, peanut allergy was 0.1% (95% CI: 0, 0.2) and 0.2%  
269 (95% CI: 0, 0.4) in the IOWBC. Data in the FAIRBC was not available. At 3 years, peanut

270 allergy was 0.5% (95% CI: 0.1, 0.9) in the IOWBC and 1.2% (95% CI: 0.5, 2) in the FAIRBC  
271 (p=0.10). At 10 years, peanut allergy was 0.4% (95% CI: 0.1, 0.8) in the IOWBC and 1.5%  
272 (95% CI: 0.6, 2.3) in the FAIRBC (p=0.02). No significant differences were seen.

273

#### 274 **Other FA at 10 years**

275 In the IOWBC FA to wheat (0.1%), shellfish (0.2%), tree nuts (0.2%), fruits (0.3%), kiwi  
276 (0.1%), vegetables/tomatoes (0.3%) and other miscellaneous foods (0.2%) were also  
277 reported at 10 years.(2) In the FAIRBC, other FA that were diagnosed at 10 years of age,  
278 included wheat (0.5%), sesame (0.7%), Brazil nut (0.5%), almond (0.2%), hazelnut (0.4%),  
279 cashew nut (0.4%), pistachio nut (0.4%), and walnut (0.1%). No fruit and vegetable  
280 allergies were diagnosed in this cohort at 10 years of age.

281

#### 282 **Discussion**

283 In this paper we aimed to compare the prevalence of reported adverse food reactions,  
284 sensitization status and FA in the IOWBC and the FAIRBC. Our main findings indicated that  
285 reported adverse reactions to food, sensitization rates and food allergy rates showed no  
286 significant evidence of change between the cohorts over the course of follow up. Fruit and  
287 vegetable allergies were reported in IOWBC but not in the FAIRBC. Tree nut allergies were  
288 reported in both cohorts. Sesame allergy was reported in the FAIR cohort but not in the  
289 IOWBC. Neither cohort reported any allergies to soy or corn. There are very few population-  
290 based studies with reported FA, sensitization rates and clinical FA available from the  
291 literature.

292

#### 293 *Overall FA*

294 Gupta et al.(15) reported overall parental reported clinician diagnosed IgE mediated FA  
295 prevalence of; 8.8% at one year, 10% at 2 years, 8.3% at 3-5 years of age and 8% at 6-10  
296 years. The HealthNuts study from Australia (2008) reported overall IgE mediated FA  
297 prevalence of >10% at 1 year and 4% at 4 years based on OFC. At six and ten years, these  
298 participants were diagnosed with IgE mediated FA, based on an algorithm of sensitization

299 status, OFC or history occurred in 6.4% of 6-year olds and 6.3% of 10-year-olds.(16) A  
300 study from South Africa diagnosed 2.5% of 1-3 year old with FA, based on OFC.(17)

301  
302 Our data of the IOWBC and FAIRBC showed a lower rate of overall FA compared to Gupta  
303 et al. (15) and the HealthNuts study,(16) but is higher than the data from South Africa.(17)

304  
305 In Europe, the overall pooled estimate for prevalence of any FA based on a clinical history  
306 or food challenge, was 2.6% in children during the period 2000-2012,(2) and 2.5% during  
307 the period 2012 – 2021,(3, 4) indicating no evidence to support changes in FA prevalence.  
308 We however, noticed no significant decrease in overall FA between the the 2 cohorts at 1  
309 year (p=0.01), 2 years (p=0.03), 3 years (p=0.03) and 10 years (p=0.02) after the Bonferroni  
310 corrections.

311  
312 The overall FA prevalence peaked at 1 year in IOWBC (5.3%) and at 3 years in the FAIRBC  
313 (3.9%). This is different from the data presented by Gupta et al. (15) and HealthNuts(16)  
314 but in the IOW cohorts, this finding was associated with a large decrease in egg allergy.

315  
316 The systematic reviews reported that overall, the pooled estimate for the point prevalence  
317 of a positive SPT to any food allergen was 4.5% in children (2000 – 2021). (4) The overall  
318 pooled estimate for prevalence of any FA based on a clinical history or food challenge,  
319 either a positive open food challenge (OFC) or a positive double-blind placebo-controlled  
320 (DBPCFC) was 2.6% in children during the period 2000-2012,(4) and 2.5% during the period  
321 2012 – 2021, indicating no changes in FA prevalence across Europe.(3)

322  
323 *Overall FA sensitization*

324 We did not see any significant changes in overall food allergen sensitization between the 2  
325 cohorts from the IOW. The European systematic reviews demonstrated an increase in SPT  
326 positivity to any food allergen from 2.7% in 2000–2012(4) to 6.9% during 2012–2021.(3)

327

328 *Peanut allergy*

329 In terms of childhood parental reported clinician diagnosed peanut allergy at ages 1, 2, 3-5,  
330 and 6-10 years in a US population, Gupta et al.(15) reported a prevalence of 2.2%, 2.4%,  
331 2.1% and 2.6%. Overall, the point prevalence of peanut allergy at each respective age was  
332 lower than Gupta et al. (15) in both IOWBC and FAIR studies. A third cohort born on the Isle  
333 Wight in 1997, showed a peanut allergy prevalence rate of 1.4% at 4 years of age and also  
334 showed lower rates than reported by Gupta et al.(18)

335

336 The HealthNuts study reported a peanut allergy prevalence of 3% at one year and 1.4% at 4  
337 years based on oral food challenges. At 6 and 10 years, peanut was the most common FA  
338 (3.1%, and 2.9%) based on a diagnostic algorithm.(16) Compared to the Healthnuts study,  
339 the IOWBC data was lower (0.1%) at one, 4 (0.5%) and 10 years (0.4%) using their  
340 predefined criteria.(5) The FAIR birth cohort showed similar rates at 3 years (1.2%) and  
341 lower at 10 years (1.5%) using OFC outcomes and/or a clinical history with supporting  
342 sensitization status. (7, 8)

343

344 The European systematic review indicated that point prevalence peanut allergy based on  
345 an oral food challenge decreased from 0.2% (2000 – 2012)(2) to 0.03% (2012 – 2021) ,  
346 although only a few studies were available for 2012–2021.(3) At 10 years of age there was  
347 no difference in the prevalence of food allergy between the two cohorts after Bonferroni  
348 correction.

349

350 *Peanut sensitization*

351 The sensitization rates to peanut at 10 years of age was 1.7% in the IOWBC, and 2.4% in  
352 the FAIRBC, with no significant difference ( $p=0.48$ ). This correlates with findings of a  
353 systematic review and meta-analysis within Europe describing no significant changes in  
354 peanut SPT positivity between 2000-2012 (1.7%, 95% CI: 0.99-2.98) and 2012-2021 (2.0%,  
355 95% CI: 1.57-1.92).(4) There are few studies that have looked at peanut sensitization in  
356 children at 10 years of age. Two European studies described higher rates of sensitization

357 than the IOW cohorts. De Jong et al. (19) reported a point prevalence of peanut  
358 sensitization at 10 years in the Netherlands of 3.2%. Erhard et al.(20) described a positive  
359 SPT and or specific IgE prevalence in children aged 8-9 to be 11.5%.

360

#### 361 *Egg allergy*

362 For egg allergy, Gupta et al.(15) reported a parental reported clinician diagnosed  
363 prevalence of 2% at one year, 1.4% at 2 years, and 1.3%, between ages of 3-5, and 0.9%  
364 between the ages 6-10 years. These figures are similar to our analysis of egg allergy  
365 prevalence in children of the same age groups of both birth cohorts. However, our data  
366 (IOWBC 1.1% and FAIRBC 1.78% at one year)(5, 12) demonstrates much lower rates of egg  
367 allergy than the 8.9% of egg allergy reported at one year in the Australian HealthNuts  
368 cohorts. (16) It is important to note that of those with raw egg allergy in the Healthnuts  
369 study, 80.3% could tolerate baked egg. The FAIRBC oral food challenges were performed  
370 with boiled egg which may explain the discrepancy. Interestingly, only 0.6% were  
371 diagnosed with egg allergy in the Healthnuts cohort at 10 years of age which is similar to  
372 the data from Gupta et al. (15) but still higher than both of the IOW cohorts. Within Europe  
373 egg allergy based on OFC or a clinical history decreased from 1.0% to 0.6%, between 2000  
374 – 2012 to 2012 -2021 but the form of the egg used in the studies were not specified.(4) Our  
375 data did not indicate any significant changes in egg allergy over time.

376

#### 377 *Egg sensitization*

378 In Europe, the SPT positivity of egg decreased from 0.8% to 0.4% from 2000-2012 to 2012-  
379 2021.(4)Our data did not indicate any significant changes over time.

380

#### 381 *Cow's milk allergy*

382 CMA is the most complex FA of childhood, often presenting as both IgE and non-IgE  
383 mediated CMA. The Diagnosis and Rationale for Action Against CMA(DRACMA) guidelines  
384 estimate the prevalence of world-wide CMA to be 1.9 – 3% during the first few years of  
385 life.(21) Gupta et al. (15) reported a prevalence of IgE mediated CMA of 3.3% at 1 year,

386 4.3% at 2 years, 2.8% at 3-5 years and 1.9% at 6-10 years. This well documented decrease  
387 in both non-IgE and IgE CMA with age is similarly reflected in both our birth cohorts; CMA  
388 allergy was highest at 1 year of age (IOWBC: 3.5%, FAIR: 2.4%), and lowest at age 10  
389 (IOWBC: 0.5%, FAIR: 0.4%).(5, 12) The significant difference in CMA prevalence between  
390 the IOWBC and FAIRBC at 3 years ( $p < 0.001$ ) is most likely due to the fact that the IOWBC  
391 did not perform OFC. As the IOWBC did not distinguish between IgE and non-IgE mediated  
392 CMA, it is difficult to speculate which effect the type of CMA might have had on the  
393 prevalence figures. Within Europe CMA prevalences based on OFC or clinical history  
394 decreased of over the period 2000 – 2012 (1.56%) to 2012 – 2021 (0.75%).(4)

395

#### 396 *Cow's milk sensitization*

397 The European systematic review indicates that cow's milk sensitization has increased  
398 significantly over the period (2000 – 2012; 0.33) and (2012 – 2021; 3.82%).(4) We did not  
399 see any significant changes in cow's milk sensitization between the two cohorts.

400

401 The strength of our study is that it is the only study in Europe investigating changes in  
402 reported adverse reactions to food, food allergen sensitization status and FA in two  
403 cohorts born in the same geographical area ten years apart. The same research team led  
404 and conducted the research which increased comparability of outcomes in the same  
405 cohorts. The paper has a number of limitations. One limitation of the study is that the  
406 criteria for FA were not exactly similar in the two studies. The IOWBC used defined criteria  
407 for capturing IgE and non-IgE mediated FA. The FAIRBC based their diagnosis of FA on a  
408 clinical history plus a supportive IgE or a positive OFC irrespective of sensitization status.  
409 However, the definitions used allowed capturing the prevalence of both IgE and non-IgE  
410 mediated FA in the two cohorts. Other limitations included that the selection of who would  
411 undergo SPT varied. We could not compare sesame sensitization and allergy data as it was  
412 most likely not considered a major allergen in 1989.

413

#### 414 **Conclusions**

415 In conclusion, our data indicate that reported FA, sensitization and food allergy rates  
416 showed no significant evidence of change between two cohorts born in 2001- 2002 and  
417 1989. This is consistent with systematic reviews indicating the prevalence of FA did not  
418 substantially change over the period 2000 – 2012 and 2012 – 2021. The significance of our  
419 data is that it was derived from two cohorts in a single geographic population. We are in a  
420 unique position to compare data on reported adverse food reactions, sensitization rates  
421 and diagnosed FA between two cohorts in the same population over a period. Despite  
422 some differences in the diagnosis of FA, our data contributes to the literature by  
423 challenging high rates of FA published elsewhere. It also challenges the concept that FA  
424 rates are increasing world-wide. We highlight the need for further studies on clearly  
425 defined FA outcomes in the same population over time.

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513 **Tables and figure legends**

514 **Table 1: Descriptions of IOWBC(1989-90) and FAIRBC(2001-02) at the 10 year follow-up**

515

516 **Table 2: Reported adverse reactions to food in the IOWBC(1989-90) and FAIRBC(2001-02) with**  
517 **95% confidence intervals (CI).**

518 **Table 3: Sensitization rates in the IOWBC(1989-90) and the FAIRBC(2001-02) with 95%**  
519 **confidence intervals (CI).**

520 **Table 4: Food allergy rates in the IOWBC(1989-90) and the FAIRBC(2001-02) with 95%**  
521 **confidence intervals (CI).**

522

523 Figure 1: Summary of follow-ups of the Isle of Wight (IOW) Birth cohort and the FA and Intolerance  
524 (FAIR) birth cohort

525

526 Legend: Figure 1 summarizes the different time points of follow-up, number of children seen or  
527 tests performed at each time point.

528

529 Figure 2: Temporal changes in the reported rates of adverse food reactions, sensitization and  
530 prevalence of milk, egg, peanut and overall FA in the the  
531 IOW birth cohort and FAIR birth cohort

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533 Legend: Figure 2 describes the temporal changes in the reported rates of adverse food reactions,  
534 sensitization status, prevalence of milk, egg, peanut and overall FA in the the IOW birth cohort and  
535 FAIR birth cohort

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