# T07034: An Investigation into Trends of Peanut Allergy Incidence in the Last 15 Years in England Using Sequential Childhood Cohorts

# Final Technical Report

## 1. Title

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| Project Code | **T07034** |
| Project Title | **An Investigation into Trends of Peanut Allergy Incidence in the Last 15 Years in England Using Sequential Childhood Cohorts** |
| Lead Contractor | **University of Portsmouth (Institute of Medicine, Health and Social Care)** |
| Project Leader | **Dr. T. Dean** |
| Project Dates | **1st April 2003 – 31st March 2006** |
| Report Date | **31st March 2006** |

## 2.Executive Summary

Research Requirements Document (Issue 8, April 2002) stated that in the light of Department of Health's COT report (published in 1998) on peanut allergy, there is a need to establish whether the advice offered in the report has led to a change in incidence of peanut allergy. In addition there is a requirement to establish what impact, if any, this advice has had on the maternal consumption of peanut during pregnancy and breast-feeding.

This project utilised three cohorts of children born on the Isle of Wight over a 12-year period to address this area.

Using a prospective cohort approach with a validated food frequency questionnaire, maternal dietary intake during pregnancy and breast-feeding were assessed. 445 (47.5%) women reported complete avoidance of peanuts, another 57 (6.1%) did not exclude peanut but never actually ate any and 360 (38.4%) did eat peanut. It is quite likely that women who reported complete avoidance were actually exposed to traces/hidden nuts. The majority of the pregnant women consumed milk (88.7%) and wheat (91.5%) frequently and white fish moderately (83.5%). With regards to egg intake, the question on egg intake showed a low validity and reliability and was therefore not included.

Data collected during the breast-feeding period indicated that in total, 265/614 (43.1%) mothers avoided one or more foods from their diets. These included a wide variety of foods such as the major food allergens, citrus, meat, spicy foods, onion, brassica family, shellfish and strawberries. Of the 265 mothers, 173 avoided some of the main allergenic foods, with 39 avoiding more than one of the main food allergens.

We investigated the influence of maternal diet during pregnancy and breast-feeding on FHS and sensitisation in the infant during the first two years of life. We found that maternal dietary intake during pregnancy, and breast-feeding duration did not appear to influence the development of sensitisation to food allergens or FHS. Fruit and vegetable intake (≥ 5 portions per day) during pregnancy were however significantly associated with reduced FHS at age one and two. In addition fewer children whose mothers avoided a food, became sensitised or developed FHS to that particular food compared with those who did not. However as the numbers of children who were sensitised and/or had FHS were relatively small these findings cannot be regarded definitive and need to be explored further.

As nearly half of the mothers reported avoiding peanuts, we also investigated the impact this may have had on their lives and that of their families. We interviewed mothers who had avoided peanuts as well as mothers who did not avoid peanut during

pregnancy and breast-feeding. Emergent themes included: variations in information provision and the range of avoidance tactics adopted by participants; a lack of clarity in relation to information and advice about peanut avoidance, the risks entailed and the introduction of peanuts to the developing child's diet; the importance of experience of atopy in influencing participants' decisions to avoid peanuts and the importance of individuals' choice in the decision making process.

In this part of the project we concluded that improvements to the experience of avoidance and/or non-avoidance were primarily focused around provision of information and advice. In particular, a need for clear, consistent factual information and advice about the real risks associated with peanut consumption during pregnancy/lactation, and to whom these risks apply.

The project also addressed the question of whether there has been a change on sensitisation rate and symptomatic allergy to peanuts during the last decade or so. This was done by comparing the birth cohort born between 2001-2002 (post COT report) and reviewed at 3 years of age to two cohorts born prior to the publication of the COT report (a cohort of children born in 1989 and reviewed at 4 years of age, and a cohort born between 1994-1996 and reviewed at 3 years of age). With regards to changes in clinical allergy we compared the cohort born between 1994-1996 to the cohort born between 2001-2002. There was no significant change in the rate of peanut allergy between the cohorts ($p=0.146$, Fishers Exact Test).

The rate of sensitisation to peanuts for the two cohorts born prior to the publication of the COT reports was 1.1% and 3.3% respectively. This represented a significant increase in rates of sensitisation to peanut in this relatively short period. The rate of sensitisation to peanuts for the cohort born after the publication of the COT report was 2.0%. Analysing the trend over time revealed a statistically significant non-linear pattern with the peak occurring in the second cohort born between 1994-1996. It is tempting to postulate that the observed decline in sensitisation rate could be due to the impact of the COT recommendation. However, we feel the strength of this evidence is weak as the data is subject to a number of biases such as recall and accuracy bias on peanut consumption information obtained from the cohort born after the publication of the COT report. Additionally, we did not collect any information on peanut consumption during pregnancy and breast-feeding from the mothers of cohorts born prior to the publication of the COT report and a direct comparison cannot be made.

In conclusion this three-year project met all its objectives. The findings of this project resulted in four international presentations. Two peer-reviewed papers have already been published and a further two are being prepared.

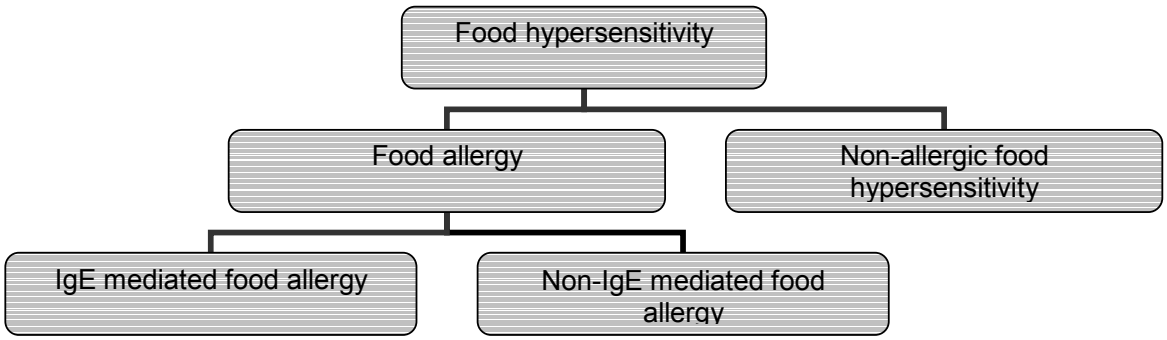
## 3.Glossary and Abbreviations

| | |
|---|---|
| COT | Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment |
| FHS | Food hypersensitivity |
| IgE | Immunoglobulin E |
| FFQ | Food frequency questionnaire |
| DBPCFC | Double blind placebo controlled food challenge |
| SPT | Skin prick test |
| OFC | Open food challenge |
| IgG | Immunoglobulin G |

## 4.Aims and Objectives of the investigation

An European Academy of Allergy and Clinical Immunology task force (1) has recently suggested that any adverse reactions to food should be called food hypersensitivity (Fig. 1). When immunological mechanisms have been demonstrated, they suggest that the appropriate term is food allergy. Where the role of IgE is confirmed, it is suggested that it is known as IgE-mediated food allergy. They suggest that other reactions, previously sometimes referred to as 'food intolerance' should be referred to as non-allergic food hypersensitivity. Severe, generalised allergic reactions to food are classified as anaphylaxis (1).

**Figure 1: Proposed nomenclature for food hypersensitivity.**




The term food hypersensitivity (FHS) will be used throughout this report.

This research aimed to establish whether a change in the incidence of peanut allergy has taken place between 1989 to 1994-1996 (Pre COT report) and between1994-1996 to 2004-2005 (Post COT report). We explored whether peanut allergy is associated with the maternal consumption of peanut during pregnancy and breast-feeding. Additionally we investigated the impact this recommendation has had on the daily life of mothers who avoided peanut and peanut products. Three sequential whole population cohorts were utilised to establish the study objectives listed below which collectively addressed the study aims.

Study objectives

I. Description and analysis of the maternal dietary exposures of a birth cohort during pregnancy and lactation
II. Establish the lived-in experience of mothers who have avoided peanuts during pregnancy and/or breast feeding
III. Establish peanut sensitisation and clinical reactions at 1, 2 & 3 year of age
IV. Explore associations between dietary exposures of mothers to peanuts and peanut sensitisation and clinical reactions of their children
V. Compare the peanut sensitisation rates and clinical reactions to peanuts using the three sequential birth cohorts

The study approach and the results for each objective are described below.

## 5. Objective I: Description and analysis of the maternal dietary exposures during pregnancy and lactation

### *5.1 Study Approach*

#### 5.1.1 Recruitment of the birth cohort

A whole population birth cohort was established on the Isle of Wight to address this objective. Approval for the study was obtained from the Isle of Wight, Portsmouth and South East Hampshire Local Research Ethics Committee (Ref 09/01).

All pregnant mothers with an estimated delivery date of September 2001 to August 2002 were approached at antenatal clinics. Following consent, information regarding family history of allergy (parental or sibling), parental smoking, socio-economic status and household pets was obtained (Recruitment Questionnaire, Appendix 1).

#### 5.1.2 Development and validation of the Food Frequency Questionnaire

A number of studies using food frequency questionnaires (FFQ) in pregnant women (2-4) have reported the FFQ to be a useful tool in determining food intake during pregnancy.

The strengths of FFQs are that highly trained interviewers are not required, administration is simple, customary eating habits are not influenced, the response rates are high, the respondent burden is light and, in principle, the relationship between dietary intake and disease development can be measured (5). As there was no validated FFQ which could be utilised a FFQ was developed and validated as follows.

The FFQ was developed mainly to determine frequency of intake of the major food allergens (European Union, 2003) namely milk and milk products, egg, wheat, fish (oily and white), shellfish, nuts (peanuts and tree nuts) and seeds. The frequencies used included never, moderate (≤3 time per week), frequently (≥4 time per week) or uncertain. The FFQ also aimed to assess the frequency of avoiding certain foods such as soya and food additives. In addition, questions regarding fruit and vegetable intake (6), oily fish and food supplements such as fish oils (7) were included. Information on the type of diet (normal/vegetarian/vegan/special medical condition) pregnant women were following, their use of vitamin or mineral supplementation, medication use, smoking habits and exposure to environmental tobacco smoke was also recorded. In order to obtain the general information, a tick list with 11 dichotomous (yes/no) response variables were used. Three open ended questions were used to determine information on type of medical diet followed e.g. diabetic diet, any other foods avoided from diet, and number of cigarettes smoked per day.

Once developed, the FFQ was pre-tested using 6 pregnant women. The purpose of the pre-testing was to test the comprehension of the FFQ, to check for ambiguity and to assess the utility of the different response categories (8). A copy of the developed FFQ is attached in appendix 2.

A separate group of pregnant women (not those who contributed to the birth cohort) were approached at the ante-natal clinic of St. Mary's Hospital, Isle of Wight during 12-13 weeks of pregnancy for the validation study. An independent group of pregnant women (>20 weeks gestation) were approached for the reliability study. Once the study information was discussed, written consent was obtained from those who were willing to participate in the study.

At recruitment, detailed information on history of allergic disease and food hypersensitivity, number of previous pregnancies and level of education, was obtained. This information enabled us to ensure the women recruited for the validation and reliability studies were not significantly different from the pregnant women who had participated in the birth cohort study.

Validation of the FFQ

In order to validate the FFQ, responses were compared to information recorded in 7-day food diaries completed on 4 occasions during pregnancy (at week 12 – 16, week 20, week 28 and week 32 (9,10). In other words, 4 diaries consisting of 7 days (Monday to Sunday) were used. Participants were asked to give a detailed description of the foods eaten, but amounts of foods eaten were not required as we wanted to establish frequency of exposure rather than amounts eaten.

In order to validate intake of food supplements, avoidance of foods related to pregnancy and foods avoided due to own preference, we asked the following questions on the food diary:

- Are you taking any supplementation and if so what?
- Are you avoiding any foods, ingredients or supplements and if so, what?

In order to determine whether the pregnant women did eat products that “may contain traces of nuts” all women were asked to keep a note of brand names when possible and questions regarding avoidance of hidden nuts and foods that “may contain traces of nuts” were asked.

The data obtained from the food diaries were transferred onto a FFQ (FFQV1). At 36 weeks of pregnancy, the women were asked to complete a copy of the FFQ (FFQV2)

and the information obtained from this FFQ was compared against the diary information.

Reliability of the FFQ at 36 weeks gestation

Reliability may be defined as the reproducibility of a measurement tool i.e. the degree to which the FFQ produces identical responses each time it is used.

Study participants completed one FFQ at 30 weeks gestation (FFQR1) and another at 36 week's gestation (FFQR2). In allowing 6 weeks between FFQR1 and FFQR2, we aimed to determine reproducibility of the FFQ. By allowing a much longer period of time, changes in dietary habits may be measured rather than reproducibility, especially as it is known that taste and food preferences change over the course of the pregnancy.

Statistical analysis - All data was double entered into SPSS, compared and verified. The frequency of food intake was classified into four categories: Never, Moderate (up to three times a week), Frequently (more than three times a week) or Uncertain. The number of subjects who provided identical responses to both validity and both reliability assessments was used to produce percentage agreement. We acknowledged misclassification errors, and assumed that these would be minimal. A clinical decision was made that agreement of 75% or above indicated good validity or reliability. Kappa statistics were also calculated to provide alternative indices of reliability and validity adjusting for chance agreement.

5.1.3 Development of standard data collection tool for maternal dietary practices during breast-feeding

Whilst the FFQ was used to assess maternal dietary practices during pregnancy, standard forms were developed to obtain prospective information regarding maternal dietary practices during breast feeding as well as information on formula feeding, weaning practices and reported problems to foods. A copy of these data collection tools is shown in appendices 3-5.

Ethical approval

Approval for the study was obtained from the Isle of Wight, Portsmouth and South East Hampshire NHS Local Research Ethics Committee (Ref 04/Q1701/18).

*5.2 Results*

5.2.1 Validation of the FFQ

Characteristics of participants in the validation and reliability study

Fifty-seven women completed the validity study by completing the four food diaries transferred onto a FFQ (FFQV1) and a FFQ at 36 weeks gestation (FFQV2). Ninety-one pregnant women completed questionnaires at 30 and 36 weeks (FFQR1 and FFQR2) for the reliability study. All women were Caucasian.

The characteristics of the recruited women for the validation and reliability study are shown in Table 1.

**Table 1: Characteristics of pregnant women in the Validity (n=57) and Reliability (n=91) Study**

| Characteristics | Validity study number (%) | Reliability study number (%) |
|---|---|---|
| **Age range** | 20 - 44 years | 18 - 44 years |
| **First child** | 31 (54) | 37 (41) |
| **Pregnant women with reported FHS*** | 9 (16) | 9 (10) |
| **Intention to breast feed** | 43 (75) | 68 (75) |
| **Normal diet** | 54 (95) | 84 (92) |
| **Reported peanut avoidance during pregnancy** | 31 (54) | 42 (46) |
| **Education level (further and higher)** | 41 (72) | 64 (70) |

Validity data

The data was divided into two sections, the first of which included general information relating to intended method of feeding, type of diet followed, avoidance of pregnancy

related food. The second section recorded the frequency of food intake. Tables 2 and 3 summarise the results of the validity study.

**Table 2: Summary of general information from Validation questionnaires**

| Questionnaire item | Number (%) responding yes | | | Validity index | |
|---|---|---|---|---|---|
| | FFQV1 (n=57) | FFQV2 (n=57) | Both V1 &V2 (n) | % Agreement* | Kappa |
| **No. of cigarettes smoked per day** | 6 | 6 | 2 | 40 | NA (Numeric data) |
| **Taken Folic acid** | 28 (49) | 53 (93) | 30 | 53 | 0.1 |
| **Excluding pregnancy related foods** | 40 (70) | 53 (93) | 42 | 74 | 0.2 |
| **Taken Iron** | 21 (37) | 24 (42) | 44 | 77 | 0.5 |
| **Claim to exclude peanuts** | 26 (46) | 31 (54) | 45 | 79 | 0.6 |
| **Exclude foods due to personal choice** | 2 (4) | 11 (19) | 46 | 81 | 0.1 |
| **Taken Calcium** | 12 (21) | 9 (16) | 48 | 84 | 0.5 |
| **Taken 0ther supplements** | 3 (5) | 7 (12) | 51 | 90 | 0.4 |
| **Taken Multi-mineral** | 19 (33) | 16 (28) | 52 | 91 | 0.8 |
| **Eaten ≥ 5 portions fruit & vegetables daily** | 6 (11) | 9 (16) | 52 | 91 | NA |
| **Normal diet** | 54 (95) | 54 (95) | 53 | 93 | 0.3 |
| **Normally smoke** | 5 (9) | 9 (16) | 53 | 93 | 0.7 |
| **Taken Multivitamin** | 20 (35) | 24 (42) | 53 | 93 | 0.9 |
| **Excluded additives** | 0 | 2 (4) | 55 | 97 | NA |
| **Following medical diet** | 0 | 1 (2) | 56 | 98 | NA |
| **Excluded soya** | 0 | 1 (2) | 56 | 98 | NA |
| **Average (min – max)** | | | | 83.3 (40 – 98) | 0.5 (0.1 – 0.9) |

*% agreement: Number of participants providing the same answer to both FFQV1 and FFQV2/total number of participants.

With regards to the general information, number of cigarettes smoked per day had the lowest agreement.

Frequency of intake of foods commonly "hidden" in foods such as eggs and seeds and foods eaten infrequently such as tree nuts, produced poor agreement. Oily fish, peanut, shellfish, milk, wheat and white fish intake showed much better agreement (≥ 75%) (Table 3).

**Table 3: Summary of food intake from Validation questionnaires.**

| Food item | Questionnaire | Frequency of consumption (n=57) | | | | Validity index | |
|---|---|---|---|---|---|---|---|
| | | Never N (%) | Moderate[α] N (%) | Frequently[β] N (%) | Uncertain N (%) | % Agreement | Kappa |
| **Egg** | FFQV1 | 0 | 14 (25) | 43 (75) | 0 | 49 | 0.2 |
| | FFQV2 | 0 | 43 (75) | 14 (25) | 0 | | |
| **Tree nuts*** | FFQV1 | 18 (32) | 37 (65) | 2 (4) | 0 | 67 | 0.3 |
| | FFQV2 | 11 (19) | 40 (70) | 5 (9) | 0 | | |
| **Seeds** | FFQV1 | 28 (49) | 29 (51) | 0 | 0 | 67 | 0.4 |
| | FFQV2 | 15 (26) | 40 (70) | 0 | 2 (4) | | |
| **Citrus fruits** | FFQV1 | 1 (2) | 32 (56) | 24 (42) | 0 | 67 | 0.5 |
| | FFQV2 | 1 (2) | 34 (60) | 21 (37) | 1 (2) | | |
| **Oily fish** | FFQV1 | 33 (58) | 24 (42) | 0 | 0 | 75 | 0.5 |
| | FFQV2 | 28 (49) | 27 (47) | 1 (2) | 1 (2) | | |
| **Peanuts*** | FFQV1 | 33 (58) | 22 (39) | 2 (4) | 0 | 77 | 0.6 |
| | FFQV2 | 31 (54) | 26 (46) | 0 | 0 | | |
| **Shellfish** | FFQV1 | 34 (60) | 23 (40) | 0 | 0 | 79 | 0.6 |
| | FFQV2 | 36 (63) | 21 (37) | 0 | 0 | | |
| **Milk** | FFQV1 | 0 | 0 | 57 (100) | 0 | 91 | NA |
| | FFQV2 | 0 | 5 (9) | 52 (91) | 0 | | |
| **Wheat** | FFQV1 | 0 | 0 | 57 (100) | 0 | 95 | NA |
| | FFQV2 | 0 | 3 (5) | 54(95) | 0 | | |
| **White fish** | FFQV1 | 4 (7) | 53 (93) | 0 | 0 | 95 | 0.5 |
| | FFQV2 | 3 (5) | 54 (95) | 0 | 0 | | |
| **Mean (min – max)** | | | | | | 76% (49 – 95) | 0.4 (0.2 – 0.6) |

* Of the pregnant women who reported that they never ate peanuts, only 1 avoided traces of nuts and 6 avoided hidden nuts.

[α]Moderate = ≤ 3 times per week; [β]Frequently ≥ 4 times per week

We also asked a question regarding mothers' concern about weight gain as it could be argued that the "concerned" pregnant women may be under-reporting. Of the 57

pregnant women, 18 (32%) reported that they were concerned about weight gain. Of the 18 women concerned about weight gain, 16 (88%) consumed milk on a regular basis compared to 35 (90%) of the 39 women not concerned about weight gain. The difference is not statistically significant (Fisher's exact test $p > 0.999$). There was no significant difference between these two subgroups regarding frequent consumption of eggs (9/18, 50% vs 22/39, 56%, $p = 0.777$), wheat (17/18, 94% vs 34/39, 87% $p = 0.653$) or fish (1/18 5% vs 0/39, 0%, $p = 0.316$).

An additional question regarding avoidance of hidden and traces of nuts was asked on the food diaries. Only 11% (6/57) of pregnant women said that they had avoided hidden nuts and only 2% (1/57) had avoided traces of nuts.

In summary, on average 83% of responses to questions of a general nature produced identical information to that obtained from the food diaries. With regards to food intake, on average 76% of responses to questions were corroborated by data extracted from the food diaries

Reliability data

The data obtained from the two FFQs were compared and the results are summarised in Tables 4 and 5.

**Table 4: Summary of general information from Reliability questionnaires**

| Questionnaire item | Number (%) responding yes | | | Validity index | |
|---|---|---|---|---|---|
| | FFQR1 (n=91) N (%) | FFQR2 (n=91) N (%) | Both R1 &R2 N | % Agreement | Kappa |
| Excluding pregnancy related foods | 74 (81) | 70 (77) | 73 | 80 | 0.4 |
| Exclude foods due to personal choice | 15 (17) | 19 (21) | 75 | 82 | 0.4 |
| Exposed to smoke at home | 27 (30) | 27 (30) | 76 | 84 | 0.7 |
| Method of feeding: Intention to breast feed | 55 (60) | 58 (64) | 77 | 85 | 0.8 |
| Taken Iron | 30 (33) | 34 (37) | 77 | 85 | 0.7 |
| Claim to exclude peanuts | 48 (53) | 42 (46) | 79 | 87 | 0.7 |
| Exposed to smoke at work | 11 (12) | 9 (10) | 54/60 | 90 | 0.6 |
| Taken Medication | 75 (82) | 72 (79) | 82 | 90 | 0.7 |
| Eaten ≥ 5 portions fruit & vegetables | 12 (13) | 15 (17) | 83 | 91 | NA |
| Taken Multivitamin | 20 (22) | 22 (24) | 85 | 93 | 0.8 |
| Taken Multi-mineral | 11 (12) | 11 (12) | 85 | 93 | 0.8 |
| Taken Folic acid | 78 (86) | 76 (84) | 85 | 93 | 0.8 |
| Taken Calcium | 9 (10) | 8 (9) | 86 | 95 | 0.7 |
| Normally smoke | 40 (44) | 39 (43) | 86 | 95 | 0.9 |
| Stop smoke | 16 (18) | 15 (17) | 36/38 | 95 | 0.9 |
| Normal diet | 87 (96) | 84 (92) | 87 | 96 | 0.7 |
| Excluded soya | 5 (6) | 3 (3) | 88 | 97 | 0.7 |
| Excluded additives | 7 (8) | 6 (7) | 88 | 97 | 0.8 |
| Cut down on smoke | 28 (31) | 27 (30) | 28/29 | 97 | 0.8 |
| Following medical diet | 7 (8) | 9 (9.9) | 89 | 98 | 0.9 |
| Taken other supplements | 2 (2) | 1 (1.1) | 90 | 99 | 0.7 |
| Mean (min-max) | | | | 91.5 (80 – 99) | 0.8 (0.4 – 0.9) |

Agreement between responses to general questions on the two reliability questionnaires was higher than 75% for all the questions asked (Table 4).

As with the validity test, frequency of intake of foods commonly "hidden" in foods such as seeds, and foods eaten infrequently such as tree nuts, produced poor agreement. In addition, intake of citrus fruit showed the lowest degree of agreement (Table 5). In contrast, consumption of oily fish, peanut, shellfish, milk, wheat and white fish showed good agreement.

**Table 5: Summary of food intake from Reliability questionnaires.**

| Food item | Questionnaire | Frequency of consumption (n=91) | | | | Validity index | |
|---|---|---|---|---|---|---|---|
| | | Never N (%) | Moderate[α] N (%) | Frequently[β] N (%) | Uncertain N (%) | % Agreement | Kappa |
| **Citrus fruits** | FFQR1 | 3 (3) | 54 (59) | 34 (37) | 0 | 66 | 0.4 |
| | FFQR2 | 6 (7) | 46 (51) | 38 (42) | 1 (1) | | |
| **Tree nuts** | FFQR1 | 26 (29) | 58 (64) | 7 (8) | 0 | 67 | 0.3 |
| | FFQR2 | 29 (32) | 59 (65) | 2 (2) | 1 (1) | | |
| **Seeds** | FFQR1 | 39 (43) | 50 (55) | 2 (2) | 0 | 71 | 0.4 |
| | FFQR2 | 43 (47) | 47 (52) | 0 | 1 (1) | | |
| **Egg** | FFQR1 | 4 (4) | 74 (81) | 12 (13) | 1 (1) | 76 | 0.3 |
| | FFQR2 | 2 (2) | 74 (81) | 15 (17) | 0 | | |
| **Oily fish** | FFQR1 | 39 (43) | 50 (55) | 1 (1) | 1 (1) | 82 | 0.7 |
| | FFQR2 | 44 (48) | 45 (50) | 1 (1) | 1 (1) | | |
| **Peanut** | FFQR1 | 51 (56) | 37 (41) | 2 (2) | 1 (1) | 82 | 0.7 |
| | FFQR2 | 49 (54) | 39 (43) | 2 (2) | 1 (1) | | |
| **Wheat** | FFQR1 | 0 | 13 (14) | 76 (84) | 2 (2) | 82 | 0.3 |
| | FFQR2 | 0 | 11 (12) | 80 (88) | 0 | | |
| **Shell fish** | FFQR1 | 63 (69) | 27 (30) | 0 | 1 (1) | 84 | 0.6 |
| | FFQR2 | 65 (71) | 26 (29) | 0 | 0 | | |
| **Milk** | FFQR1 | 0 | 12(13) | 78 (86) | 1 (1) | 87 | 0.4 |
| | FFQR2 | 0 | 8 (9) | 83 (19) | 0 | | |
| **White fish** | FFQR1 | 10 (11) | 73 (80) | 6 (7) | 2 (2) | 90 | 0.7 |
| | FFQR2 | 12 (13) | 77 (85) | 2 (2) | 0 | | |
| **Mean (min – max)** | | | | | | 79 (66-90) | 0.5 (0.3 – 0.7) |

[α]Moderate = ≤ 3 times per week; [β]Frequently ≥ 4 times per week

Again, pregnant women were asked about concern over weight gain as the women who said they were concerned (yes/no answer) may be under-reporting. Of the 91 pregnant women, 30 (33%) said that they were concerned regarding weight gain. This reported rate of milk, egg, wheat and fish intake in these pregnant women was compared to the rest to test whether they were under-reporting. Of the 30 women

concerned about weight gain, 26 (87%) consumed milk on a regular basis compared to 54 (89%) of the 61 women not concerned about weight gain. The difference is not statistically significant (Fisher's exact test $p > 0.999$). There was no significant difference between these two subgroups regarding frequent consumption of eggs (6/30, 20% vs 10/61, 16%, $p = 0.272$), wheat (26/30, 86% vs 54/61, 89% $p > 0.999$) or fish (1/30, 3% vs 3/61, 5%, $p > 0.999$).

In summary, on average 92% of responses to questions of a general nature were identical on both questionnaires. With regards to questions on food intake, the average was 79%.

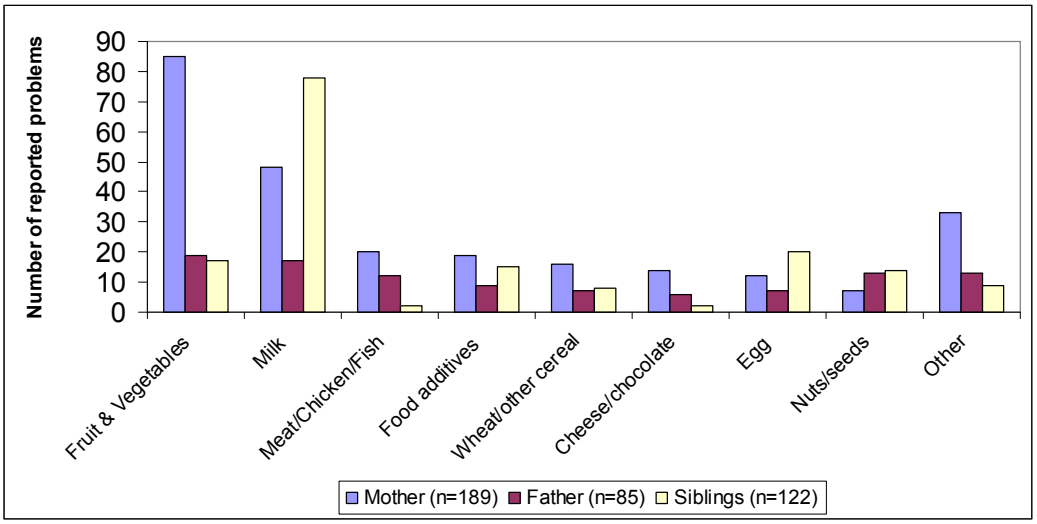
5.2.2 Description of families of the birth cohort

Data were obtained from 969 families of the birth cohort whose babies were born between 1 September 2001 and 31 August 2002.

The age of the pregnant women ranged from 15 – 44 years with a mean age of 27 years and 10 months. Of the 567 pregnant women with other children, 122 (21.5%) reported adverse reactions to food and food ingredients in one or more of their other children. One hundred and eighty nine (19.5%) of the pregnant women and 322 (33.2%) of the families (mother, father, sibling) reported to have a problem related to ingestion of food or food ingredients.

The foods most often reported to cause adverse reactions in the families are summarised in figure 2.

**Figure 2: Foods most often reported to cause adverse reactions in the families of the birth cohort**




The main symptoms relating to adverse reactions to food reported by the pregnant women in the past were diarrhoea, bloating, vomiting, abdominal pain, migraine, urticaria and rashes. Some also reported the foods caused mouth ulcers, wheeze and asthma. The fathers reported vomiting, diarrhoea, throat tightness, urticaria, migraine, abdominal pain and wheeze/asthma. The sibling mainly experienced symptoms such as rashes, vomiting, hyperactivity, diarrhoea, eczema, urticaria, angioedema and wheeze.

5.2.3 Description of the birth cohort infants

500 boys (51.6%) and 469 (48.4%) girls comprised the birth cohort (755 normal and 211 caesarean deliveries). On the day of birth, 733 (75.6%) babies were breast fed, 230 (23.7%) were bottle fed, 4 babies (0.4%) received bottle and breast milk and 1 child was fed parentally (TPN). This rate of breastfeeding on the first day of life (75.6%) is higher than the rate of those who stated that they intend to breast feed the baby when asked at 36 weeks gestation (65.1%).

5.2.4 Maternal dietary intake during pregnancy

Information regarding dietary habits during pregnancy was obtained from 937 (96.7%) pregnant women at 36 weeks gestation using the FFQ.

Eight hundred and thirty four (89%) of the pregnant women followed a normal diet, 67 (7.2%) reported to follow a vegetarian diet and two (0.2%) followed a vegan diet. 28

(3%) pregnant women were on special diet due to medical reasons and six women did not indicate the type of diet they followed.

Five hundred and twenty one women (55.6%) reported they had avoided peanuts during pregnancy. However, 71 (13.6%) of these ate peanuts accidentally and 5 reported that they were uncertain about accidental intake. Therefore in total, 445 (47.5%) women reported complete avoidance of peanuts, another 57 (6.1%) did not exclude peanut but never actually ate any and 360 (38.4%) did eat peanut. It is quite likely that women who reported complete avoidance were actually exposed to traces/hidden nuts.

Twenty four women (2.6%) excluded soya from their diets. A further 46 (4.9%) claimed to have excluded additives from their diets. 190 (19.6%) women avoided some food during pregnancy by own choice. These foods mainly included coffee or caffeine containing drinks, alcohol, cheese, citrus foods and spicy food.

241 (25.7%) pregnant women took a multivitamin, 160 (17.1%) a multi-mineral, 109 (11.6%) calcium, 440 (47%) iron, 3 cod liver oil, 1 fish oil and 6 took evening primrose oil supplementation during pregnancy. Only 130 (13.9%) pregnant women ate ≥ 5 portions of fruit and vegetables per day.

The pregnant women were also asked regarding frequency of food intake of the main allergenic foods during pregnancy as summarised in Table 6.

**Table 6: Reported frequency of food intake during pregnancy (n= 937)**

| | Never N (%) | Moderate N (%) | Frequent N (%) | Uncertain N (%) |
|---|---|---|---|---|
| **Milk** | 2 (0.2) | 97 (10.4) | 381 (88.7) | 7 (0.8) |
| **Wheat** | 1 (0.1) | 75 (8) | 857 (91.5) | 4 (0.4) |
| **White fish** | 107 (11.4) | 782 (83.5) | 44 (46.5) | 4 (0.4) |
| **Shell fish** | 562 (60) | 370 (39.5) | 2 (0.2) | 3 (0.3) |
| **Oily fish** | 500 (53.4) | 425 (45.4) | 9 (1) | 3 (0.3) |
| **Peanut** | 502 (53.6) | 414 (44.2) | 16 (1.7) | 4 (0.4) |

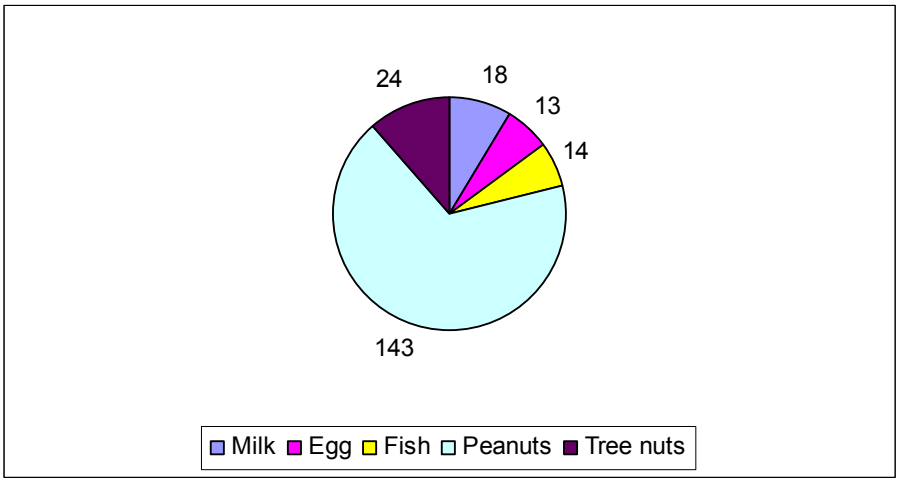
The majority of the pregnant women consumed milk (88.7%) and wheat (91.5%) frequently and white fish moderately (83.5%). In contrast, adding together the categories “never” and “moderate” showed a low intake of shell fish (99.5%), oily fish (98.8%) and peanut (97.8%). With regards to egg intake, the question on egg intake showed a low validity and reliability and although 94% women reported to consume

egg moderately to frequently, this data is not included in table 6 as it is neither valid nor reliable.

5.2.5 Maternal food avoidance during breast feeding

During breast feeding, information was obtained regarding food avoidance (n=927; 95.7%). No information regarding food intake (how often and how much) was obtained at this stage. Six hundred and fourteen mothers (66.2%) breastfed the infant for ≥ 1 week. These mothers were asked regarding any food avoidance during breast feeding. In total, 265/614 (43.1%) mothers reported to avoid one or more foods from their diets. These foods included a wide variety of foods such as the major food allergens, citrus, meat, spicy foods, onion, brassica family, shell fish and strawberries. Of the 265 mothers, 173 avoided some of the main allergenic foods, with 39 avoiding more than one of the main food allergens (figure 3).

**Figure 3: Avoidance of the major allergenic foods during breast feeding (n=173)**




Eighteen (1.9%) mothers avoided milk during breast feeding, but only six mothers managed to completely avoid milk from the infant's diet as 12 children had a formula feed containing cow's milk at some point during the first three months. There were 143 (15.4%) mothers who avoided peanut during breast feeding (101 of these avoided peanut during pregnancy) and 24 (2.6%) avoided tree nuts. Thirteen mothers (1.4%) avoided egg and 14 (1.5%) avoided fish. None avoided wheat or sesame. The reasons given for food avoidance were: following a vegetarian/vegan diet (n=18), advised to avoid certain foods during breast feeding (n=147), dislike of certain foods (n=9), baby's allergy (n=8), mother's own allergy (n=10) and other reasons (n=105) including baby colicky, allergy prevention, fattening foods, high iron content, other child allergic and religious or personal reasons.

## 6. Objective II: Establish the lived-in experience of mothers who have avoided peanuts during pregnancy and/or breast feeding

### *6.1 Study Approach*

An experienced qualitative researcher with a social science background was chosen to conduct this part of the research as it was felt that this approach would be less likely to have a bias towards a focus on health issues. A phenomenological approach to the study was taken in order to explore, describe and interpret the lived experiences of mothers who either avoided or ate peanuts during pregnancy/lactation. Phenomenology has its' roots in philosophical theory and focuses on the question 'What is it like to have a certain experience' (11). The researcher used this paradigm to explore 'the meaning of a given situation *to the participant'* (11). The aim of the study was to understand the experiences of individual mothers and again the phenomenological approach is best suited to this.

To facilitate the phenomenological approach to the study, and to focus on individual mothers as the primary unit of analysis, in-depth interviews were conducted on a one-to-one basis. These took place in the mother's homes, although all participants were offered the opportunity to choose an alternative location if preferred. All interviews were audio taped.

### Sampling and selection

The sample was drawn from the birth cohort. The birth cohort was recruited through the antenatal clinics and included all newborn babies born on the Isle of Wight (UK) between September 2001 and August 2002. All expectant mothers were asked to complete a questionnaire regarding any history of allergic disease themselves, the baby's father or any siblings. They completed a food frequency questionnaire at 36 weeks gestation regarding eating habits during pregnancy, which included questions regarding peanut avoidance during pregnancy. The mothers who chose to breastfeed for whatever duration, were also asked regarding avoidance of food during lactation and the reasons for this.

A total of 937 mothers who gave birth during 2001/2002 completed the food frequency questionnaire (88% of target population) and 445 (47%) reported that they successfully avoided peanuts during pregnancy/lactation. A purposive sample frame of 'avoiders' was designed, which reflected the proportion of atopic and non-atopic cases in the total group, whilst ensuring a range of participant types was included according to atopic

history; dietary issues such as types of diet followed (normal, vegetarian, vegan); socio-economic factors; geographical area.
Initially, the study aimed to focus on participants who avoided peanuts during pregnancy/lactation. However, it became apparent during the interviewing process that in order to gain a more robust understanding of the avoidance situation it was necessary to include non-avoiders in the sample. The sample frame was adjusted accordingly, using similar purposive criteria as outlined for the 'avoider' element of the sample.

Data Collection

To facilitate the phenomenological approach to the study, and to focus on individual mothers as the primary unit of analysis, in-depth interviews were conducted on a one-to-one basis. The interviews were conducted between September 2003 to February 2004. These took place in the mothers' homes, although all participants were offered the opportunity to choose an alternative location if preferred. All interviews were audio taped.

Potential research participants were first approached by a letter outlining the nature of the study, along with an explanation of the implications for their involvement. The letter contained a slip and stamped addressed envelope to return should they not wish to be involved. The purposive sample was chosen from those mothers willing to participate. Potential participants were then contacted by telephone, appointments arranged and confirmation letters sent out.

The interviews were unstructured in that there were no predetermined questions asked and the discussion did not evolve in any particular format. However, there were clear research aims, which the researcher needed to keep in mind while conducting the interviews. The researcher tackled this by drawing up an interview schedule which covered the areas which were thought might arise during interview. The researcher then internalised the information on the schedule and this was not taken to the interview. The aim of this process was to refresh the researcher's mind as to the focus of the research, yet conduct free-flowing interviews, which evolved in a conversational style. All interviews started in a similar way, participants were asked why they avoided/did not avoid peanuts. This would entail the participant recalling events of up to two years ago. Most participants recalled the events relating to their decision to avoid or eat peanuts and the interview would develop from the initial recall. The researcher probed where necessary, in particular for influences and effects, as well as

for any improvements, which could have been made to the process of avoidance/non-avoidance. The length of time interviews took ranged from 20 minutes to 1 hour 45 minutes. Field notes and researcher thoughts were noted where necessary immediately after interviews were completed. As themes emerged from the interviews conducted, these were introduced where appropriate in following interviews.

Tapes were anonymously coded and transcribed verbatim. Copies of the full, anonymised transcripts were returned to respondents for their comments as to whether they thought the transcripts represented a record of the discussion as they recalled it. Data collection was an iterative process and took place over a period of 6 months. This period included a break when non-avoiders were recruited to the study. Data collection ceased after 42 interviews had been conducted as it was considered that data saturation had occurred, meaning there were no new emergent themes.

Data analysis was conducted using the principles of content analysis. The transcripts were saved onto NVivo 2 qualitative software package, then open coded and analysis conducted by the researcher to reduce the data down to themes that were relevant to the purposes of the research. Similarities and differences were observed both within individual interviews and across the range of interviews conducted. Patterns and themes were initially identified, then links made between the data and the themes developed. These findings were verified with other members of the project team at regular meetings throughout the research process. In addition all transcripts were sent to mothers who participated to ensure they were satisfied with the content of the interviews.

Ethical Considerations

Ethical approval was obtained from the Isle of Wight, Portsmouth and SE Hampshire Local Research Ethics Committee (Ref 03/03/1469).

## 6.2 Results

### 6.2.1 Participants

The aim was to recruit approximately 50 participants as it was envisaged that this number of participants would be sufficient to reach data saturation. Initially, a total number of 191 potential recruits were approached by letter. Participants were then selected according to the sample frame. The characteristics of the participants are shown in Table 7. A total or 42 participants took part in this study. This represents all

those who consented to take part (22%). The main reason for non-participation was lack of time and inconvenience caused by the time necessary for the interview.

**Table 7. Respondent characteristics**

| Respondent characteristics | Mothers who avoided peanuts | | Mothers who did not avoid peanuts | |
|---|---|---|---|---|
| Number of cases | 25 | | 17 | |
| | Reported family history of atopy | No reported FH of atopy | Reported family history of atopy | No reported FH of atopy |
| Number of cases | 15 | 10 | 9 | 8 |
| Age | | | | |
| Range | 23-36 | 23-35 | 23-42 | 24-39 |
| Mean | 30.91 | 28.83 | 33.66 | 32.33 |
| Maternal education (*n*) | | | | |
| School | 7 | 5 | 3 | 3 |
| Further | 4 | 4 | 5 | 4 |
| Higher | 4 | 1 | 1 | 1 |
| Mean number of children (including child in study) | 1.4 | 1.5 | 2.66 | 2.0 |
| Number of respondents with first children | 4 | 6 | 2 | 2 |

6.2.2 Emergent Themes

Fourteen main themes emerged from the data collected (Table 8). The definition of a main theme was that the topic raised was the subject of more than one interview and/or there was sufficient data generated to explore the topic in more detail. Where quotations are used they are intended to best illustrate the relevant theme.

**Table 8. Main themes**

| |
|---|
| Avoidance tactics |
| Ease of avoidance |
| Continuing avoidance |
| Peanuts or all nuts |
| Danger |
| Sources of information and advice |
| Support for avoidance/non-avoidance |
| Effects of avoidance |
| Labelling |
| Awareness of peanut allergy |
| Family History |
| Improvements to experience |
| Preferred products |
| Value of Skin Prick Tests |

The following section summarises some of the main themes. These themes were chosen as they were considered to best illustrate the foci of the research aims and objectives. In addition they were the most frequent issues raised by the mothers.

<u>Avoidance tactics</u>

A range of participant approaches emerged in relation to peanut avoidance and peanut consumption.

Avoidance tactics ranged from avoiding foods which obviously contained peanut i.e. visible pieces of peanut; avoidance of foods which had peanut listed as an ingredient, to 'total avoidance' of all nuts. The most common model of avoidance was to avoid foods which obviously contained peanuts, these avoiders were less likely to check food

packaging when grocery shopping for nut content than participants who were more active in avoidance (this is discussed in more detail under 'labelling').

Participants' awareness of food ingredients became more acute during pregnancy. This manifested itself in attempts to eat 'simple' foods comprising 'known' ingredients and home made foods where the ingredients were known. When eating out, participants relayed how they would attempt to choose meals containing basic ingredients which participants felt were unlikely to contain peanut. Only in exceptional cases had participants enquired whether there was any 'hidden' peanut content in foods they ordered.

The consistent rationale for non-avoiders appeared to stem from the desire to 'carry on as normal' in relation to diet, in order that the unborn child builds up a resistance to potentially harmful substances:

*'..I suppose it rolls over from a little bit of dirt does you good and I was brought up like that'. (Interview 24; atopic non-avoider)*

Participants who had prior experience of child birth were more inclined to feel that if existing children were healthy and they had not avoided peanuts at that time that adopting a similar approach again made sense. There were instances where mothers had eaten nuts before realising they were pregnant, during the Christmas period for instance. In these cases participants were more likely to continue eating peanuts during pregnancy/lactation, although there were instances of avoidance too.

*'I think with Rosie being the third one, before I found out I was pregnant, I think I had eaten some peanuts, and probably because it was the third one I thought I've done it now, not that I ate loads but just the odd ones aren't going to make a lot of difference I suppose' (Interview 29; atopic non-avoider).*

Craving peanuts during pregnancy was an issue for some participants, whether they had intended to avoid peanuts or otherwise (this is discussed in more detail under 'Ease of Avoidance').

Family history

A family history of atopy was an important theme in relation to the avoidance and non-avoidance question. Although there were participants with atopic and non-atopic backgrounds, who were both avoiders and non-avoiders, avoiders showed a stronger propensity to have a family history of food allergy and were more likely to have witnessed a severe food allergic reaction.

Participants with a family history of food allergy tended to be accustomed to the process entailed in food avoidance, even if the food was not peanut. The concept of peanut avoidance represented an extension of their existing behaviour patterns.

*'We read the ingredients on most of our shopping anyway because we have to avoid milk products, so I have to read through everything' (Interview 11; atopic avoider with food allergic child)*

Non-avoider participants appeared to be as informed about peanut allergy as avoiders but were less likely to have had personal experience of food allergy or the associated reactions.

There was a perception amongst non-avoiders in particular, that food allergy was a 'separate' issue from asthma, hay fever, and other non-food-related allergies. Even in cases where there was an awareness of a potential link between peanut consumption and asthma, there was some difficulty in visualising the link. In some cases this resulted in a somewhat fatalistic approach towards avoidance: If a child was genetically programmed to develop asthma then nothing could be done to prevent this.

*'Well I just assumed that if you ate peanuts your child was more likely to have skin complaints or asthma, but asthma runs in the family anyway, so the chances of her getting it were high.' (Interview 33; atopic non-avoider)*

Danger

The perception of the peanut as 'dangerous' was widespread among participants. The perceived danger was two-fold: Firstly, avoiders believed eating peanuts during pregnancy/lactation could be a cause of atopy, in particular peanut allergy. Secondly,

and more prevalent across both avoiders and non-avoiders, that once the child was born, peanuts represented a choking hazard.

Avoiders comprised more first time mothers than non-avoiders. In relation to the perceived risk of peanut allergy a 'better safe than sorry' approach was common amongst avoiders. There appeared to be a received belief that avoiding peanuts during pregnancy/lactation would have a preventative effect in relation to the child developing a peanut allergy. This is supported by participants' descriptions of messages received via written information and verbal advice (this is explored in more detail under 'sources of information and advice'). Once the child had been born the concern remained as to if, or when, to introduce peanuts to the growing child. Amongst avoiders this concern was most commonly two fold as outlined earlier. Non-avoiders concerns focussed predominantly upon the dangers associated with peanuts and choking.

*'The first time he had anything with nuts on, he was quite tiny, at the finger food stage, he had a burger bap with nuts on it. It was just a co-incidence that on the way home he got a fever and was ill and of course I panicked, oh my God it was that tiny little seed that was on the bap'. (Interview 13; non-atopic avoider)*

Non-avoiders tended to be more concerned about the danger of their young child choking on peanuts rather than the danger of peanut allergy. Again, participants who had successfully given birth to children in the past and not avoided peanuts yet whose children had experienced no ill effects, tended to be less concerned about the dangers of peanut consumption than first time mothers.

*'I have seen people absolutely panic if they have gone anywhere near a peanut and I just couldn't be bothered. If something terrible had happened with my first one then I probably would be more cautious but there isn't and she has had things like that and she has been alright that I haven't worried too much really'. (Interview 24; atopic non-avoider with one previous child)*

Continuing avoidance

There were a range of views expressed about when peanut should be introduced into a child's diet. As discussed, amongst non-avoiders the focus was primarily avoidance of choking. For avoiders there was some concern that if peanuts were to be introduced to their child's diet this should be at the 'right' time. The ages suggested by participants

for peanut introduction ranged from 'the first year' to 'not under the age of seven'. The most commonly suggested age to introduce peanuts to the child's diet was three years old. Some participants had already introduced peanut to their children at the time of interview, this was predominantly in the form of peanut butter and to a lesser degree, foods such as biscuits and cereals.

*'… chocolate spread because that does have a trace of peanut, biscuits… we just tried her on all our normal things and luckily she didn't have any allergies (Interview 39; atopic non-avoider).*

There were participants who felt that peanuts were not a particularly 'good' food and they had no intention of deliberately feeding their children peanuts. Vegetarians however, tended to view peanuts as a valuable source of protein.

Participants in the study placed considerable emphasis on the outcome of the skin prick tests for allergies, which were conducted as part of the wider study. Where participants' children had been skin prick tested and shown a negative reaction there was a perception that the children were therefore not allergic to peanut and as a result mothers felt less concerned about peanut being given to their child without their knowledge. There were also mothers whose concern about peanut was such that they wanted to be responsible for introducing peanut to their child, in case the child either choked or had an allergic reaction. In exceptional instances, participants felt they were overly concerned with their child's food intake with the result that they were cautious about allowing the children into any environment where they might eat something with peanut content. This was particularly the case with participants who had a family history of peanut allergy or other food allergy.

*'Yes, I sat at the table watching her. It was terrible and for about an hour after I was watching where she was and what she was doing and things, it was scary. Then I thought this is a bit silly really, because if it is going to happen it's going to happen quick. It does with me, within a few minutes I know if I have got problems. I thought that was quite funny, I amused myself doing that because I was so worried.' (Interview 8; atopic avoider participant with food allergy to pineapple, blackcurrant and avocado)*

Sources of information and advice

Participants 'general knowledge' relating to peanut avoidance was comprised of information from medical sources, parenting magazines and books, and to a lesser degree friends and family, television, newspapers and the internet.

Participants reported that their main source of written information was medical, primarily information packs provided by the hospital or given to them by the midwife or health visitor. Midwives and health visitors tended to be the main source of verbal advice, GP's were more likely to be a source of advice when respondents had specific concerns or queries. Where participants had experienced a previous pregnancy, they were less likely to have received as much in the way of written or verbal advice as first time mothers.

On the whole, there appeared to be a 'blanket approach' towards peanut avoidance advice from all sources. The underlying message was it was safer to avoid peanuts whether an atopic family history exists or not. However, participants' understanding of this advice and their ensuing behaviour ranged from: Avoidance of all suggested foods to avoid, including peanuts; avoidance of all suggested foods to avoid, except peanuts (as this was perceived as an issue for those with an existing food allergy); a reduction in the intake of the suggested foods to avoid; 'avoidance' of foods suggested if not liked or usually eaten; to a continuation of the usual diet, irrespective of all food avoidance advice. Guidance in relation to lactation and food avoidance appeared to be very limited; the main focus of peanut avoidance was during pregnancy. There were two instances where participants had eaten peanuts during pregnancy and avoided peanuts during lactation, as this was their understanding of the advice given.

Avoiders were comprised of two main types: The 'advice followers' who tended to follow the medical advice given and whether atopic or non-atopic avoided all the recommended foods. The 'careful eaters' who had tended to seek out further information from pregnancy books and magazines for example, and who felt they had made an informed decision to avoid peanuts.

Non-avoiders were comprised of three main types: Participants who 'carried on eating as normal' to ensure a balanced diet; participants who felt 'I've done this before and everything was okay' and participants whose understanding of peanut avoidance was 'It doesn't relate to me as I don't have a food allergy'.

As well as medical sources of information and advice, magazines such as Practical Parenting, Mother and Baby and pregnancy books such as those by Dr Miriam Stoppard and What to Expect, formed the major source of information for participants. The perceived benefit of the magazines was the up to date information.

*'They (magazines) tend to keep you a bit more up to date than the doctors seem to, by the time the doctor finds out you have had the magazine and read it two months beforehand.' (Interview 42; atopic non-avoider)*

These magazines appeared to have a propensity to be a little negative in their coverage of current health related issues including peanut avoidance and peanut allergy in children. Where mothers had experienced a number of pregnancies, they tended to refer to the original copy of the book if necessary, which would not necessarily have up-to-date avoidance information, this appeared to be another factor associated with existing mothers being less likely to avoid peanuts than first time mothers.

Family and friends did not appear to act as a significant source of information for participants: The exceptions to this were participants with peanut allergic family members or friends.

Support for avoidance/non-avoidance

Participants were generally happy with the level of medical support available. On the whole participants tended not to have sought out such support but felt it was available if required. Where participants had received medical support, it was primarily via midwives, as well as health visitors, GPs and specialists such as the allergy centre. There were a few instances where it was felt health visitors were too prescriptive with their advice to avoid peanuts. Generally, midwives were seen as a good source of support with a relaxed approach.

Participants reported that midwives would tend to advise on avoidance and then try to ensure participants ate as healthy a diet as possible given their avoidance choices and physical well being during pregnancy.

*'I think the biggest thing was to get me to eat, they weren't worried about what I ate at all ….if I fancied it I ate it' (Interview 24; non-atopic non-avoider participant who experienced severe sickness throughout pregnancy)*

Where avoiders had family members with peanut allergy, they had sought support from the local allergy centre. Usually, although not always, participants with partners and husbands had discussed peanut avoidance with them. As outlined, friends were a source of support for some, particularly for first time mothers. However, peers going through a similar experience were rarely mentioned as a source of support. Participants tended to see the decision to avoid or otherwise as a very 'personal' decision from whichever perspective they were coming to it.

*'It's like all these things you take your information home and go and make your own decision'. (Interview 6; atopic avoider)*

Ease of avoidance

For participants who remained impartial to peanuts throughout their pregnancy peanut avoidance was perceived as being quite straightforward. However, cravings for peanuts presented a real difficulty for some participants.

*'If someone says you have to avoid something you sometimes just eat it anyway. Because of having a food allergy and you know how bad the reaction can be, you don't do it, no matter how bad the craving is' (Interview 8; atopic avoider).*

Some participants described how pregnancy seemed to bring on a craving for peanuts, even though they were not usually interested in eating peanuts. There were limited instances where mothers had intended to avoid peanuts but they lapsed during pregnancy due to such cravings.

One participant gave in to this craving seven months into pregnancy and ate a single packet of peanuts but then did not eat peanuts again throughout pregnancy/lactation. Another atopic non-avoider reported that she ate 'a bowl full' of peanuts every night and always carried some peanuts in her handbag. Some avoiders described how they experienced peanut cravings during pregnancy and how they had to eat 'a snickers bar' or 'a bag of peanut M & M's' directly after giving birth. These participants were

unsure if the cravings were as a result of their pregnancy or brought on because they knew they were not supposed to eat peanuts.

Participants who were accustomed to avoiding peanuts due to an existing allergy or in relation to other young children, made no changes in relation to grocery shopping and neither did non-avoiders on the whole, although most made an effort to 'cut down' on their peanut/nut intake. Participants who were not keen on eating peanuts and didn't crave peanuts experienced few changes in this respect. Participants who normally bought peanuts and peanut products had to find replacement foods. This was reported as initially taking more time than their usual shop, and in some instances may have involved spending slightly more money, however it did not appear to be an area of concern. All participants, without exception, were avoiding or reducing some elements in their diets and these changes seemed to be easily integrated into their grocery shopping and food preparation routines. Participants appeared to be quite habitual in relation to grocery shopping and diet and would tend to purchase similar foods each time they shopped.

Despite avoiders' best intentions, the physical, psychological and emotional experience of pregnancy occasionally overrode the decision to follow a strict peanut avoidance diet. There were two cases where participants had experienced problems in keeping food down during their pregnancies. And two further instances where participants were hospitalised for prolonged periods during their pregnancies. In these situations consuming any types of food, was considered to be better than consuming nothing. The hospital diets did however exclude peanut.

Labelling

There were non-avoider participants who claimed they never checked packaging for peanut content. However, on the whole non-avoiders had an awareness of foods with 'obvious' peanut content as outlined earlier. Similarly, avoiders most commonly either avoided 'obvious' peanuts but didn't check packaging for peanut content or would avoid products which obviously contained peanuts and would also check the front picture on the packet for signs of peanut content. There were a few more fastidious avoiders who would check the front of the packet initially, followed by the list of ingredients if they were unsure about peanut content. The 'may contain' labelling appeared to be a bit of misnomer, as participants who were determined to avoid peanuts would tend to check the ingredients list if they had any doubt about peanut content; those participants

wishing to avoid peanuts where possible either assumed there was no peanut content unless it was obvious, or again would check the ingredients list. It was suggested that a 'tick box' approach in relation to nut content might be clearer than the existing labelling.

*'I wouldn't actually give them a meal that had actually got nuts in the ingredients on the meal, but if it said this product may contain nuts then yes I would give it to them, because I think to a certain extent they just write it on there to cover themselves a lot of the time'. (Interview 31; non-atopic avoider)*

Peanuts or all nuts

There was a lack of clarity among participants about which nuts should be avoided and why. All avoiders reported that they avoided all nuts to a certain degree not just peanuts. In some cases this was because the participant did not tend to eat other nuts anyway. Even amongst non-avoider participants there was an awareness that too many nuts, particularly peanuts, may not be a good thing. Predominantly the reason for avoiding all nuts rather than solely peanuts, was an uncertainty about which nuts could be harmful.

*'Some of the books I read specified peanuts and some specified all nuts to avoid. I just swept the board and said like all nuts in my head and then I didn't have to worry about things then. I found that easier just to sort of ignore nuts as best I could.' (Interview 36; non-atopic avoider)*

In addition, there was also a lack of clarity amongst participants about why peanuts should be avoided. There were three participants who were avoiding peanuts because they had peanut allergic children. They each had varying degrees of understanding about the link between avoidance and allergy and all felt they should know more. Other avoiders, both with atopic and non-atopic family histories, gave a range of explanations in relation to peanut avoidance, all inferring that avoidance was necessary to prevent the possibility of the child becoming allergic to peanut.

Finally, there was a lack of clarity about how peanut allergy could occur. There were participants who did not know, or could not recall, the reasons for peanut avoidance. A limited number of participants were content to know that there was a requirement to

avoid peanuts if medical sources said so, and not require all the facts explaining why. On the whole however, participants felt there should be clearer explanations about the risks involved and the possible outcomes of eating peanuts during pregnancy/lactation.

*'I think you like to think you are doing the right thing… I mean they say don't eat pate and they can give you very good reasons why not, and certain things like don't eat raw eggs because it contains such and such. But when they say don't eat peanuts or avoid them and you say why, well there is a very slight possibility that it may be related to allergies in children but that's not proved. You have to think it's not proved, it's hard to avoid something when you are not sure if it's any benefit or not, so it would be nice to know that there was a bit more grounding for avoiding really.' (Interview 4; atopic avoider)*

## 7. Objective III: Establish peanut sensitisation and clinical reactions at 1, 2 & 3 year of age

### 7.1 Study Approach

At the age of one year, all the birth cohort infants were invited to be reviewed at a clinic for a medical examination guided by a detailed questionnaire. All infants were approached to undergo skin prick testing to a standard battery of food allergens which included peanuts. Skin prick tests were conducted with commercial extracts of standard food and aeroallergens (Soluprick SQ allergens-ALK Allergologisk Laboratorium A/S, Horsholm, Denmark). The wheal was measured after transfer to paper from the skin with translucent tape. Measurement was undertaken in standard fashion, measuring the largest wheal diameter and the diameter orthogonal to it. The mean wheal diameter was calculated. Results were expressed as positive if mean diameter was 3mm or more in the presence of a negative control and a positive histamine reaction after 15 minutes.

Infants were invited for a food challenge if they had never previously knowingly eaten a large amount of the food to which they had a positive skin prick test or if they had a previous adverse reaction to foods regardless of their skin prick test result. Food challenges were conducted with all foods except peanuts and sesame as it is considered that infants should not be exposed to these foods in the first two years of life (12). Therefore peanut challenges were only conducted at 3 years of age. We aimed to perform all challenges after 6 weeks of exclusion diet, but each challenge and reported symptoms were assessed individually to ensure it was a true negative food challenge rather than the child outgrowing the FHS.

Challenges were performed following an algorithm. Procedures for both one-day and one-week challenges have been described by us elsewhere (13).

All eligible infants underwent open challenges and only those with a positive reaction were invited to participate in a double-blind, placebo-controlled food challenge (DBPCFC). Those with a history of immediate symptoms were invited to the hospital to undergo the challenge procedure. Challenges were performed at home when the history indicated delayed development of symptoms and negative SPT. Some of these home challenges started at hospital and were continued at home. Reactions during a home challenge were reported by parents on a food and symptom diary. We ensured

that following a negative challenge all children consumed a normal portion of the suspected food. Children with one-day challenges consumed a normal portion on the day of challenges. Children with one-week challenges consumed normal portions for one week. In addition all children were contacted 4-6 weeks after the negative challenges to find out whether they were eating the food regularly without any reaction.

## 7.2 Results

### 7.2.1 Sensitisation data at 1,2 and 3 years of age

Although we approached all children for skin testing a proportion did not consent and as a result the test was carried out on 763, 675 and 643 children at 1, 2, and 3 years of age respectively. Overall 20 children had a positive skin prick test to peanuts at either 1, 2 or 3 years of ages. This information is presented in table 9.

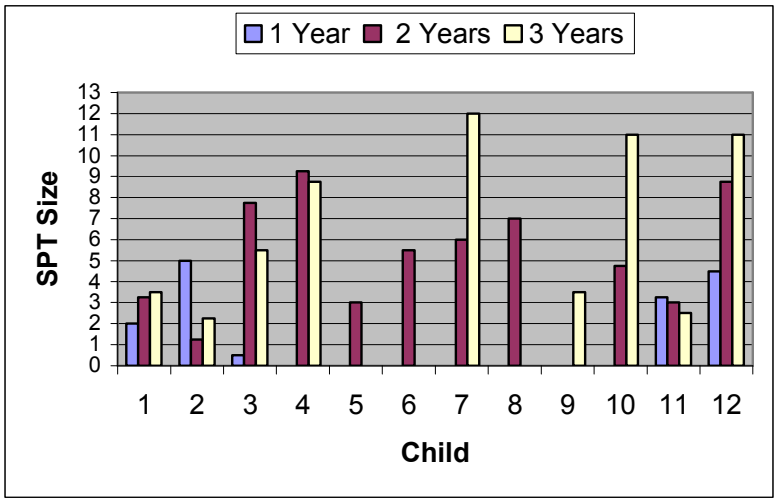
**Table 9: Skin Prick test results to peanuts at 1, 2 and 3 years of age**

| Study No | SPT 1 yr mm (n=763) | SPT 2 yr mm (n=675) | SPT 3 yr mm (n=643) |
|---|---|---|---|
| 3 | 2.00 | 3.25 | 3.5 |
| 67 | 5.00 | 1.25 | 2.25 |
| 71 | <0.5 | 7.75 | 5.5 |
| 82 | 1.75 | Not done | 4.25 |
| 117 | 0 | 9.25 | 8.75 |
| 137 | Not done | 9.5 | 7.75 |
| 160 | 0 | 3.0 | 0 |
| 232 | Missing | Missing | 6.0 |
| 242 | Not done | Missing | 10.5 |
| 341 | Not done | 4.25 | 0 |
| 444 | 0 | 5.5 | 0 |
| 448 | 0 | 6.0 | 12.0 |
| 613 | 0 | 7.0 | 0 |
| 647 | 0 | 0 | 3.5 |
| 652 | 0 | 4.75 | 11.0 |
| 667 | 0 | 5.5 | Not done |
| 758 | 3.25 | 3.0 | 2.5 |
| 804 | 0 | Not done | 4.0 |
| 818 | 0 | Not done | 5.5 |
| 972 | 4.5 | 8.75 | 11.0 |

Three children were sensitised at 1 year of age and 13 children were sensitised at 2 and 3 years of age. Therefore the rates of sensitisation at 1, 2 and 3 years of age were 0.4% (95%CI 0.08-1.1), 1.9% (95%CI 1.03-3.27) and 2.0% (95%CI 1.08-3.43)

respectively. Twelve children had the skin tests at 1, 2 and 3 years of age. Figure 4 demonstrates the changes in the skin test data for each of these 12 children.

**Figure 4: Trend in peanut SPT data among those who were tested at 1, 2 and 3 years of age**




There was a significant change between year one and two. Of these twelve children, 8 had a negative skin prick test data at 1 but were positive at 2. The reverse was observed with another 2 children.

7.2.1 Clinical allergy to peanuts at 3 years of age

Ten children underwent peanut challenges as shown in table 10. Three children were not challenged due to a clinical reaction coupled with the size of their skin prick test (case no.: 242,448, 972; SPT size: 10.5, 12.0 and 11.0mm respectively). Additionally two children (case no.: 341, 818) were eating peanuts without any adverse reaction.

**Table 10. The outcomes of peanut challenges conducted at 3 years of age.**

| Study No | Type of Challenge | Outcome | Total Dose | Reaction |
|---|---|---|---|---|
| 3 | Open | Negative | 10 grams | None |
| 67 | Open | Negative | 8 grams | None |
| 71 | Open | Positive | 500 mg | Erythema and hives |
| 160 | Open | Negative | 10 grams | None |
| 444 | Open | Negative | 10 grams | None |
| 613 | Open | Negative | 6.5 grams | None |
| 647 | Open | Positive | 1.5 grams | Hives |
| 652 | Open | Positive | ½ peanut | Urticaria |
| 758 | Open | Negative | 8 grams | None |
| 804 | Open | Negative | 8 grams | None |

Based on the challenge outcome coupled with clinical history and SPT information, the rate of clinical allergy to peanut at 3 years of age is 0.67% (6 out of 891 who were followed up at 3 years of age).

## 8. Objective IV: Explore associations between dietary exposures of mothers to peanuts and peanut sensitisation and clinical reactions of their children

### 8.1 Study approach

The information from the FFQ and the standardised follow up form completed at 3,6 and 9 months provided the data on maternal dietary exposures which were then looked at in relation to the infants' SPT and challenge data as shown below.

### 8.2 Results

#### 8.2.1 Maternal dietary intake during pregnancy and infant's sensitisation to food allergens

At one year

Information on maternal dietary intake during pregnancy and infant sensitisation to foods was available on 91% (882/969) of the birth cohort. At one year only a small number of children were sensitised to food allergens and statistical inferences could not be made. Only 2 children were sensitised to milk, 3 to peanut and 2 to fish at the age of one year. Additionally, 14 children were sensitised to egg, 2 to sesame and 1 child was also sensitised to corn, potato and rice, but we did not have valid and reliable information on frequency of intake of these foods by the mother. In this small number of children, food intake during pregnancy did not appear to influence the development of sensitisation to food allergens (table 11). Interestingly, for peanut and fish maternal consumption of those infants sensitised to these foods, fell within the lower range of intake, and for those sensitised to milk and wheat maternal consumption fell within a higher range.

**Table 11: Maternal dietary intake during pregnancy and infant's sensitisation to food allergens at one year**

| **SPT** | **Maternal reported rate of food consumption during pregnancy** | | | | |
|---|---|---|---|---|---|
| **Milk** | **Never N (%)** | **Moderate N (%)** | **Frequently N (%)** | **Uncertain N (%)** | **Total** |
| **Positive** | 0 | 0 | 1(50.0) | 1(50.0) | **2** |
| **Negative** | 1(0.1) | 77(10.3) | 668(89.1) | 4(0.5) | **750** |
| **Peanut** | | | | | |
| **Positive** | 1(33.3) | 2(66.7) | 0 | 0 | **3** |
| **Negative** | 406(54.4) | 322(43.1) | 15(2.0) | 4(0.5) | **747** |
| **Fish** | | | | | |
| **Positive** | 0 | 2(100.0) | 0 | 0 | **2** |
| **Negative** | 86(11.5) | 622(82.9) | 38(5.1) | 4(0.5) | **750** |

At two years

Information on maternal dietary intake during pregnancy and sensitisation to foods was available for 87% (843/969) of the birth cohort at two years. At the age of two years, 5 children were sensitised to milk, 1 to wheat, 13 to peanut and 3 to fish. Additionally, 14 children were sensitised to egg and 5 to sesame but we did not have information on frequency of intake of these foods by the mother. As with the one year data, in this small number of children, food intake during pregnancy did not appear to influence the development of sensitisation to food allergens (table 12).

**Table 12: Maternal dietary intake during pregnancy and infant's sensitisation to food allergens at two years**

| **SPT** | **Maternal reported rate of food consumption during pregnancy** | | | | |
|---|---|---|---|---|---|
| **Milk** | **Never N (%)** | **Moderate N (%)** | **Frequently N (%)** | **Uncertain N (%)** | **Total** |
| **Positive** | 1(20.0) | 0 | 3(60.0) | 1(20.0) | **5** |
| **Negative** | 0 | 59(9.1) | 585(90.7) | 1(0.2) | **645** |
| **Wheat** | | | | | |
| **Positive** | 0 | 0 | 1(100.0) | 0 | **1** |
| **Negative** | 0 | 48(7.4) | 598(92.3) | 2(0.3) | **648** |
| **Peanut** | | | | | |
| **Positive** | 7(53.8) | 5(38.5) | 1(7.7) | 0 | **13** |
| **Negative** | 353(55.5) | 270(42.5) | 10(1.6) | 3(0.5) | **636** |
| **Fish** | | | | | |
| **Positive** | 0 | 2(66.7) | 1(33.3) | 0 | **3** |
| **Negative** | 77(11.9) | 536(83.1) | 30(4.7) | 2(0.3) | **645** |

8.2.2 Maternal dietary intake during pregnancy and infant's food hypersensitivity

At one year

FHS was diagnosed in 39 children by one year. This was based on OFC (n=35) and a clear history and/or positive SPT (n=4). The results of the children with FHS based on OFC with relation to reported food intake of the mother during pregnancy is summarised in table 13. Of the 39 children, 22 suffered from milk FHS, 4 from wheat hypersensitivity (one child suffered from wheat and milk hypersensitivity). Additionally 14 children suffered from FHS to foods for which we did not have any information on maternal dietary consumption such as egg, corn and salicylates. In this small number of children, frequency of food intake during pregnancy did not appear to influence the development FHS. Interestingly for milk and wheat hypersensitivity maternal consumption of these foods fell within the higher range of intake as with sensitisation.

**Table 13: Maternal dietary intake during pregnancy and infant's FHS at one year**

| FHS | Maternal reported rate of food consumption during pregnancy | | | | |
|---|---|---|---|---|---|
| **Milk** | **Never N (%)** | **Moderate N (%)** | **Frequently N (%)** | **Uncertain N (%)** | **Total** |
| **Positive** | 1(4.5) | 0 | 18(81.8) | 3(13.6) | **22** |
| **Negative** | 1(0.1) | 97(10.6) | 813(88.9) | 3(0.3) | **914** |
| **Wheat** | | | | | |
| **Positive** | 0 | 0 | 4(100.0) | 0 | **4** |
| **Negative** | 1(0.1) | 75(8.0) | 853(91.4) | 4(0.4) | **933** |

At two years

An even smaller number of children underwent food challenges at the age of two years as food challenges were not performed in the case of accidental exposure with symptoms or an increase in SPT size. FHS diagnosed by OFC at age two was defined as all children with a positive OFC at one year who had not outgrown their FHS or those with newly diagnosed FHS with a positive OFC at age two. This data is summarised in table 14.

**Table 14: Maternal dietary intake during pregnancy and infant's FHS at two years**

| FHS | Maternal reported rate of food consumption during pregnancy | | | | |
|---|---|---|---|---|---|
| **Milk** | **Never N (%)** | **Moderate N (%)** | **Frequently N (%)** | **Uncertain N (%)** | **Total** |
| **Positive** | 1(10.0) | 2(20.0) | 6(60.0) | 1(10.0) | **10** |
| **Negative** | 1(0.1) | 95(10.2) | 825(88.9) | 7(0.8) | **928** |
| **Wheat** | | | | | |
| **Positive** | 0 | 0 | 3(100.0) | 0 | **3** |
| **Negative** | 1(0.1) | 75(80.3) | 854(91.4) | 4(0.4) | **934** |

Of the 10 children with positive OFC to milk, 1 mother never ate milk or milk containing foods during pregnancy, 2 mothers had a moderate milk intake, 6 mothers frequently ate milk and 1 was uncertain. Of the 3 children with positive OFC to wheat, all 3 mothers frequently ate wheat and wheat containing foods.

8.2.3 The role of other maternal dietary intake related factors during pregnancy

Intake of maternal fatty acid intake and fruit and vegetable intake were also investigated. There was no association between fatty acid intake and infant sensitisation or FHS. The fruit and vegetable intake showed that there was no statistical significant difference between sensitisation to foods and recommended fruit and vegetable (5 portions or more per day) intake. However, recommended fruit and vegetable intake, significantly reduced the rate of FHS as diagnosed by OFC (table 15) and DBPCFC (not presented) at age one and two. This data therefore suggest that fruit and vegetable intake may affect the development of FHS although this needs to be confirmed by future studies.

**Table 15: Fruit and vegetable intake and the development of FHS at one and two years**

| | Adequate intake N (%) | Insufficient intake N (%) | p-value ($\chi$2 test) |
|---|---|---|---|
| **Positive SPT to any food 1 yr** | 2 (13.3) | 15 (86.7) | 0.75 |
| **Positive SPT to any food 2 yrs** | 6 (24) | 19 (76) | 0.25 |
| **FHS based on OFC 1 yr** | 12 (30.8) | 27 (69.2) | 0.001* |
| **FHS based on OFC 2 yrs** | 6 (27.2) | 16/22 (72.8%) | 0.01* |

* Statistically significant

8.2.4 Maternal food avoidance during breast feeding and infant's sensitisation to food allergens

The relationship between maternal food avoidance during breast and infants sensitisation to foods and FHS is summarised in tables 16 and 17.

**Table 16: Maternal food avoidance during breast feeding and infant's sensitisation to food allergens at one year**

| Food | Avoiders (infants with positive SPT) | Non- avoiders (infants with positive SPT) |
|---|---|---|
| **Milk** | 0 | 2 |
| **Egg** | 0 | 14 |
| **Fish** | 0 | 2 |
| **Peanut** | 1 | 2 |
| **Any food** | 5 | 12 |

**Table 17: Maternal food avoidance during breast feeding and infant's sensitisation to food allergens at two years**

| Food | Avoiders (infants with positive SPT) | Non- avoiders (infants with positive SPT) |
|---|---|---|
| **Milk** | 0 | 5 |
| **Egg** | 0 | 14 |
| **Fish** | 0 | 3 |
| **Peanut** | 2 | 10 |
| **Any food** | 9 | 15 |

Of the children sensitised to milk, egg and fish at one and two years, none of the mothers avoided the particular food during breast feeding. Three children were sensitised to peanut at age one, 1 mother avoided peanuts and 2 did not. At the age of two, 13 children were sensitised to peanut, 2 mothers avoided peanut and 10 did not avoid peanut. We did not have any data on peanut consumption from one of the mothers.

Of the 17 children sensitised to any food allergen at age one, 12 mothers did not avoid any foods and 5 mothers did avoid some foods during breast feeding. Of the 24

children sensitised to any food allergen at age two, 15 mothers did not avoid any foods and 9 did.

8.2.5 Maternal food avoidance during breast feeding and infant's food hypersensitivity

**At one year**

Of the six mothers who avoided milk during breast feeding, none of their children developed milk hypersensitivity and of the 921 mothers who did not, 22 children developed milk hypersensitivity based on OFC. For egg, none of the avoider's children developed egg hypersensitivity and 17 of the non-avoiders did. 17 of the avoiders' children developed FHS and 22 of the infants born to those mothers who did not avoid foods during pregnancy developed FHS. This information is summarised in table. 18.

**Table 18: Maternal food avoidance during breast feeding and infant's FHS based on OFC at one year**

| Food | Avoiders infant's with FHS | Non-avoiders infant's with FHS | p-value ($\chi$2 test) |
|---|---|---|---|
| **Milk** | 0 | 22 | 1.0 |
| **Egg** | 0 | 17 | 1.0 |
| **Any food** | 17 | 22 | 0.55 |

Of the children with FHS to milk and egg none of the mothers avoided the particular food during breast feeding. None of the mothers avoided wheat and sesame and we could therefore not look at the relationship between wheat avoidance and development of FHS.

**At two years**

Of the six mothers who avoided milk during breast feeding, none of their children developed milk hypersensitivity and of the 921 mothers who did not, 10 children developed milk hypersensitivity. Also for egg and fish, none of the avoider's children developed egg or fish hypersensitivity and 12 (egg) and 1 (fish) of the non-avoiders did. Seven of the infants born to those mothers who avoided any foods during breast feeding developed FHS and 15 infants of those who did not avoid foods during pregnancy. This information is summarised in table 19

**Table 19: Maternal food avoidance during breast feeding and infant's FHS based on OFC at two years**

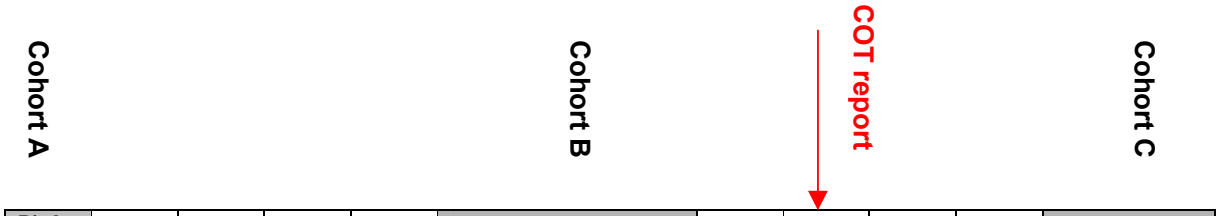
| Food | Avoiders infant's with FHS | Non-avoiders infant's with FHS | p-value ($\chi$2 test) |
|---|---|---|---|
| **Milk** | 0 | 10 | 1.0 |
| **Egg** | 0 | 12 | 1.0 |
| **Fish** | 0 | 1 | 1.0 |
| **Any food** | 7 | 15 | 0.90 |

Of the children with FHS to milk, egg and fish none of the mothers avoided the particular food during breast feeding. None of the mothers avoided wheat and sesame and we could therefore not look at the relationship between wheat avoidance and development of FHS.

## 9. Objective V: Compare the peanut sensitisation rates and clinical reactions to peanuts using the three sequential birth cohorts

### 9.1 Study approach

In order to meet this objective three whole population birth cohorts were compared. Two of these cohorts (cohort A and B) were born prior to the publication of the COT report and the third cohort (cohort C) was the birth cohort described in 5.1.1. These are schematically shown below.




| Birth cohort | | | | | FAB study birth cohort | | | | | | | FAIR study birth cohort | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1989 | 1990 | 1991 | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 |

### 9.2 Results

Cohort A comprised of children born in 1989. 981 children were skin prick tested at 4 years of age and 11 (1.1%) were sensitised to peanuts. Further details on this 11 children extracted through their notes is shown below in table 20.

**Table 20: Details of children sensitised to peanuts in cohort A:**

| Study No | SPT size mm At 4 years | Symptoms on clinical examination at 4 years | Peanut status |
|---|---|---|---|
| 381 | 3.00 | Asthma<br>Eczema<br>Rhinitis | No reported problems |
| 393 | 4.00 | Eczema | No reported problems |
| 521 | 10.00 | Eczema | No reported problems |
| 761 | 4.00 | Eczema | No reported problems |
| 924 | 6.00 | None | Reported 2-5 episodes of urticaria due to egg, peanut and cashew nut |
| 956 | 3.50 | Did not attend | No reported problems |
| 1022 | 3.00 | Did not attend | No reported problems |
| 1274 | 3.00 | Did not attend | No reported problems |
| 1319 | 3.00 | Eczema | No reported problems |
| 1364 | 4.00 | Did not attend | No reported problems |
| 1027 | 3.00 | Eczema | No reported problems |

When these children were 5 an attempt was made to contact them and the following in formation was available below:

| Study No | Peanut Status |
|---|---|
| 381 | Ate roasted peanuts with no reaction |
| 393 | Ate peanut butter with no reaction |
| 521 | Never eaten peanut |
| 761 | Ate peanut mixed in foods with no reaction |
| 924 | Never eaten peanut |
| 956 | Ate raw peanut, peanut butter, peanut mixed in foods with no reaction |
| 1022 | Ate raw and roasted peanuts, peanut butter, peanut mixed in foods with no reaction |
| 1274 | Ate roasted peanuts but spat out immediately |
| 1319 | Ate peanut butter with a reaction |
| 1364 | Ate peanut butter with a reaction |
| 1027 | Ate peanut butter with no reaction |

These children did not undergo any food challenges and the follow up data at 5 years of age suggests that the great majority were only sensitised to peanuts most of whom had a relatively small SPT size. The only two likely allergic children (study no. 521 and 924) with SPT sizes of 10 and 6mm respectively (i.e. above the suggested 95% predictivity) had never consumed peanuts.

Cohort B included children who were born between 1994 to 1996 and at three years of age 1246 of this cohort were skin prick tested to peanuts. Forty-one (3.3%) children had a positive SPT to peanuts as shown in table 21.

**Table 21: Details of children sensitised to peanuts in cohort B**

| Study No | SPT size mm | Peanut status |
|---|---|---|
| 23 | 7.00 | Peanut challenge – negative |
| 42 | 13.50 | Reaction at home |
| 102 | 12.50 | Reaction at home |
| 204 | 3.25 | Peanut challenge – positive |
| 231.1 | 5.00 | Reaction at home |
| 275.1 | 10.50 | Reaction at home |
| 278 | 3.25 | Peanut challenge – negative |
| 337 | 3.00 | Peanut challenge – negative |
| 356 | 5.50 | Peanut challenge – positive |
| 393 | 5.50 | Peanut challenge – negative |
| 401 | 4.25 | Reaction at home |
| 506 | 7.50 | Eaten peanut safely |
| 666 | 8.50 | Reaction at home |
| 709 | 3.25 | Peanut challenge – negative |
| 765 | 7.00 | Peanut challenge – positive |
| 874 | 6.00 | Refused challenge |
| 1013 | 3.50 | Eaten peanut safely |
| 1036 | 3.50 | Eaten peanut safely |
| 1205 | 3.00 | Peanut challenge – negative |
| 1423 | 8.00 | Peanut challenge – negative |
| 1596 | 8.00 | Peanut challenge – negative |
| 1690 | 5.50 | Peanut challenge – negative |
| 1784 | 3.00 | Peanut challenge – negative |
| 1816 | 9.00 | Peanut challenge – positive |
| 1817 | 9.25 | Reaction at home |
| 1841 | 3.00 | Peanut challenge – positive |
| 1873 | 3.50 | Peanut challenge – negative |
| 1905 | 7.50 | Peanut challenge – positive |
| 1921 | 9.25 | Reaction at home |
| 1955 | 5.00 | Peanut challenge – negative |
| 1969 | 13.50 | Reaction at home |
| 2060 | 12.00 | Reaction at home |
| 2097 | 9.00 | Peanut challenge – positive |
| 2101 | 9.00 | Peanut challenge – positive |
| 2222 | 3.00 | Peanut challenge – negative |
| 2242 | 3.75 | Peanut challenge – negative |
| 2340 | 3.25 | Peanut challenge – negative |
| 2482 | 7.75 | Refused challenge |
| 2679 | 3.50 | Peanut challenge – negative |
| 2725 | 6.25 | Eaten peanut safely |
| 2751 | 3.00 | Eaten peanut safely |

Of the 41 children who had a positive SPT response to peanut in cohort B, 10 children reported a convincing clinical reaction to peanut occurring at home, with a range of symptoms including angioedema, urticaria, wheezing, rhinorrhoea, and vomiting and

abdominal discomfort. A diagnosis of peanut allergy was accepted in these children, and oral challenges were not performed. Five children had eaten peanuts without any adverse effects and hence did not undergo the challenge procedure. Of the remaining 26 children, 24 had an oral challenge to peanut, and 8 challenge results were considered positive. Overall 18 (1.5%) of children in cohort B were considered to have symptomatic allergy to peanuts. There was a direct relationship between the likelihood of a positive reaction to peanut and skin test wheal size. The median SPT sizes for those who did or did not clinically react to peanut were 9.0 and 3.25mm, respectively ($p \leq 0.001$, Mann-Whitney U test).

With regards to cohort C, 13 children were sensitised at 3 years of age as described in section 7.2.1. Therefore the rate of sensitisation at 3 years of age for this cohort was 2.0%.

Comparing the rates of sensitisation to peanuts in the three cohorts using the Chi-squared test for trend the following result is obtained.

**Contingency table analysis**

| | | | |
|---|---|---|---|
| Observed | 11 | 970 | **981** |
| % of row | 1.12% | 98.88% | |
| | | | |
| Observed | 41 | 1205 | **1246** |
| % of row | 3.29% | 96.71% | |
| | | | |
| Observed | 13 | 630 | **643** |
| % of row | 2.02% | 97.98% | |
| | | | |
| **Total** | **65** | **2805** | **2870** |
| | 2.26% | 97.74% | |

TOTAL number of cells = 6
Test of equivalence of incidence rates over time:
Chi-square = 11.9, DF = 2, p = 0.0026
(Fisher-Freeman-Halton exact p = 0.0023)

Decomposition of trend components:
Chi-square for linear trend ($M^2$) = 2.66, DF = 1, p = 0.1031
Chi-square for non-linear trend = 9.23, DF = 1, p = 0.0024

There is evidence of a significant change sensitisation rate over time (p = 0.0026), the majority of the association being explained by the non-linear component of trend (p= 0.0024).

With regards to changes in the clinical allergy comparing cohorts B and C (where this information is available), there was no significant change in the rate of peanut allergy between the cohorts ($p=0.146$, Fishers Exact Test).

## 10. Discussion

In total, 969 families were recruited to the birth cohort used for this project. Adverse reactions to food were reported by 33.2% of the families. The foods most often reported to cause problems by the mothers were fruit and vegetables, milk and food additives; fruit and vegetables, milk and nuts by the fathers and milk, egg and fruit and vegetables by the siblings.

The birth cohort study sample consisted of 500 boys and 469 girls. During pregnancy 89% of mothers followed a normal diet and 47.5% avoided peanuts during pregnancy. The majority of pregnant women had consumed milk (88.7%) and wheat (91.5%) containing foods ≥ 4 times per week and between 53.4 and 60.0% of mothers never ate oily fish or shell fish. 46.5% mothers ate white fish frequently i.e. ≥ 4 times per week.

Maternal food intake during pregnancy and infant's sensitisation to foods or FHS at one or two years of age could not be statistically assessed as very few children developed FHS and became sensitised to foods.

In this small sample subset, maternal dietary intake during pregnancy did not appear to influence the development of sensitisation to food allergens or FHS. This study is unique as it is an observational study investigating the role of maternal food intake during pregnancy, by means of a validated FFQ, in a non-selective population and the development of sensitisation to foods and FHS.

Previously conducted observational studies looking at maternal intake during pregnancy have focused mainly on peanut consumption (14;15) in the development of allergic disease in the infant. Hourihane et al (14) found that in utero exposure to peanut can trigger sensitisation, in particular where there is a family history of atopy. In contrast, Lack and colleagues (15) determined that in utero sensitisation of the foetus to peanuts did not seem to be a factor in the development of peanut allergy. Unfortunately, both studies are guilty of recall bias and the questionnaires used to determine this information is not discussed and it is not clear whether these questionnaires were validated.

Previous intervention studies in this area included three studies that looked at maternal dietary manipulation and the development of atopy in high risk families. One study

found that maternal avoidance of milk and egg from 28 weeks of pregnancy, increased the prevalence of egg allergy up to the age of five years (16). Another study found that maternal of intake of egg during the last trimester did not affect IgE production (17) and the third study found that egg avoidance from 20 weeks gestation reduced the prevalence of atopy (18). It is known that neonates have low serum IgE levels, and the IgG in the newborn's serum is essentially of maternal origin (19).
In addition, two of the studies, clearly indicated that maternal food consumption affected IgG production (17;18). This indicates that maternal food consumption during pregnancy affects IgG production and raised the question whether food intake during pregnancy may affect the development of FHS.

As this was not the case in our study, it could perhaps be explained by the fact that we studied a non-selective group of children rather than a high risk subgroup. It is known that there is a maternal effect in the development of allergic disease in the infant and that infants born to mothers suffering from atopic disease are more at risk of becoming allergic.

Fruit and vegetable intake (≥ 5 portions per day) were significantly associated with reduced FHS at age one (based on OFC) and age one and two. This confirms the data by Stazi et al (20) which indicated that low maternal intake of fruit (less than three portions per week) was associated with a positive SPT to six allergens, of which milk was the only food allergen, and eczema. Some studies have looked at the effect of anti-oxidants on the development of epithelial cells of the human lung and it is also suggested that reduced maternal dietary antioxidant intake during pregnancy might be associated with the impaired lung development that is associated with wheeze, asthma, and reduced lung function later in life (21). The possible mechanisms for the role of fruit and vegetables in the development of FHS are still unclear.

In terms of breast feeding, 52% of mothers who breast fed avoided certain foods from their diets for a variety of reasons. 1.9% mothers avoided milk during breast feeding, 15.4% mothers avoided peanut (101 of these avoided peanut during pregnancy) and 2.6% avoided tree nuts. None avoided wheat or sesame, 1.4% avoided egg and 1.5% avoided fish.

Food allergens such as milk, egg, wheat and peanut, have long been known to be detectable in breast milk. It is however uncertain whether this might lead to sensitisation or tolerance of these foods in the breast fed infant, or what variables affect

these two possible outcomes. Our data suggests that maternal food avoidance during breast feeding led to fewer children who became sensitised or developed FHS to that particular food compared with those whose mothers did not. This data were however statistically insignificant due to the small numbers who became sensitised and developed FHS. No intervention studies in unselected populations have been performed as yet, primarily because a very large population will be needed to show a significant effect of the intervention.

A number of randomised controlled trials in high-risk infants have investigated the effect of different dietary allergy prevention programmes during breast feeding or pregnancy and breast feeding. In agreement with our data, these studies found that avoidance of milk, egg, fish, peanuts and soya for 3 months (22) or the full duration of breast feeding (23) reduced the prevalence of eczema (22), allergic disorders and wheeze and nocturnal cough at eight years (24) modification and/or house dust mite reduction. In addition, Arshad et al (25), found reduced sensitisation to food allergens at 12 months.

Three quarters of mothers (75.6%) attempted breastfeeding on the day the infant was born, but this was reduced to any breastfeeding of 35.2% at 3 months, 23.1% at 6 months and 9.7% at 9 months. The main reasons given for discontinuation of breastfeeding was too little milk, hungry baby or discomfort/pain during feeding.

A variety of formulas were used during the first year of life, starting with whey based, and followed by casein-based and follow-on formulas. Reasons for choosing a formula were mainly own preference, advised to by health professional or family member, or formula given in hospital. The main reasons for changing formulas were hungry babies and advice by a health professional.

In this group of children, breastfeeding duration did not seem to affect the prevalence of FHS at all. Numerous studies have attempted to examine the role of breast-feeding in the development of allergy. Differences in methodology and inevitable flaws in design make these studies difficult to compare, and no single definitive study has yet been published. Methodological differences include whether a study is prospective or retrospective, interventional versus observational or self-selective versus randomised studies. Design flaws in previous studies include small sample size, lack of randomisation, short breast feeding duration and definition of “exclusive” breast feeding. Definition of the clinical outcomes studies and the age at which the study participants were evaluated also differed greatly.

In summary the work carried out to address the first and fourth objective showed that maternal dietary intake during pregnancy, omega-3 fatty acid intake, and breast feeding duration did not appear to influence the development of sensitisation to food allergens or FHS. . Fruit and vegetable intake (≥ 5 portions per day) during pregnancy were however significantly associated with reduced FHS at age one (based on OFC) and age one and two. In addition, food avoidance during breast feeding showed that fewer children whose mothers avoided a food, became sensitised or developed FHS to that particular food compared with those who did not.

The second objective was to explore the lived-in experience of mothers who had avoided peanuts during pregnancy and/or breast feeding

The main findings revealed the importance of clarity with regard to the peanut avoidance issue. Important factors informing participants' decisions in relation to peanut avoidance included participants understanding of information and advice in relation to peanut allergy; a family history of atopy or otherwise; personal experience of food allergic reactions; prior experience of child birth; and individual sense of what constitutes a 'good' diet. Sources of information and advice for participants were primarily medical, parenting books and magazines and to a lesser degree, friends, family, television, newspaper articles and the Internet. Support for avoidance/non-avoidance was felt to be available from health professionals should it be required, primarily via midwives as well as health visitors and GP's. Avoiding peanuts during pregnancy/lactation did not pose too many difficulties to mothers who did not crave peanuts; for those who did, avoidance proved to be more of a struggle. Additionally, participants who experienced complications during pregnancy were not always able to maintain a strict avoidance diet. The impact of avoidance on mothers' everyday lives comprised an increased awareness of dietary intake, changes in diet leading to changes in shopping, cooking and eating out habits. Some participants felt that the requirement to avoid peanuts actually made them crave peanuts during pregnancy. There were concerns about introducing peanuts to a child's diet that created pressures for participants.

Provision and dissemination of information and advice was an important influencing factor in participants' decision to avoid peanuts or otherwise. Variations were identified in information and advice provision, dissemination, and respondents' understanding of it. The study revealed that there was a requirement for clear, consistent factual advice and information about the real risks associated with peanut consumption during

pregnancy/lactation and peanut allergy in the developing child, and specifically to whom these risks apply.

The 'blanket approach', which appears to have been taken towards provision of information and advice about peanut avoidance, caused confusion among participants. Participants with both atopic and non-atopic family histories felt they needed to be clear about the possible risks entailed in relation to their particular situation.

Participants with personal experience of, or direct involvement with, food allergy, tended to have more awareness of peanut allergy than participants who had no such experience or involvement. As potential mothers would be approaching their pregnancy with differing levels of awareness and understanding in relation to peanut allergy, it would seem that information and advice needs to be pitched so that it is comprehensible and clear to all.

The decision to avoid peanuts or otherwise appeared to be very much an individual decision. In order for participants to make as informed a decision as possible, important advice and information needed to be imparted as soon into the pregnancy as possible.

There was a perception that information available for pregnant women can be biased towards the negative i.e. what to avoid, and that a more balanced approach with positive advice outlining foods which are good to eat, would be helpful.

The study revealed, that it was important that any information regarding potential risks of peanut consumption during pregnancy/lactation should be relayed to participants who have existing children: It appears there was a tendency for both health workers and participants themselves, to be of the opinion that 'they've done it all before'. As a result, it seems that these participants may not have been aware of up to date medical advice regarding food avoidance.

Clarification also appeared to be required regarding which foods should be avoided i.e. peanuts or all nuts and some guidance about which foods are likely to contain these substances.

To aid the avoidance process, both for mothers avoiding peanuts during pregnancy/lactation and for those with peanut allergy, clear standardised labelling of

products outlining whether the product contains nuts or not would be useful. With regard to shopping for food, avoiders most commonly avoided foods which contained 'obvious' peanuts or which showed a picture with peanuts on the packet. More fastidious avoiders would check the ingredients if they were uncertain about peanut content. The 'may contain' labelling was a bit of a misnomer for both avoider 'types' as neither group felt it was a valuable source of guidance but rather a 'get out clause'.

In relation to continuing avoidance and introducing peanuts to a child's diet, again there appeared to be a requirement for clear, consistent information and advice about whether avoidance should continue during lactation and at what stage in the child's development peanuts can be introduced to the diet.

This study highlighted the maternal experience of peanut avoidance during pregnancy/lactation and identified key factors, which need to be considered when issuing advice, or designing intervention studies which focus on avoidance.

The limitations of the work undertaken to address this objective primarily related to its' qualitative and exploratory nature. As such the study findings cannot be directly replicated nor used for generalisation purposes. As the participants in the study were not necessarily aware of the CMO advice which was issued on peanut avoidance, the findings cannot reflect directly on this advice, but rather on the ways in which it was disseminated to pregnant and lactating mothers. Qualitative research relies on the researcher to act as the 'research instrument' through which the research framework is structured and findings emerge. In this instance, the researcher had a social research background and therefore the research study has been achieved through this particular prism of experience.

Our third objective was to establish peanut sensitisation and clinical reactions at 1, 2 & 3 year of age. Three children were sensitised at 1 year of age and 13 children were sensitised at 2 and 3 years of age. Therefore the rates of sensitisation at 1, 2 and 3 years of age were 0.4% (95%CI 0.08-1.1), 1.9% (95%CI 1.03-3.27) and 2.0% (95%CI 1.08-3.43) respectively. There was a significant change between year one and two. In a cross sectional study of slightly older children in Southampton and Manchester, Hourihane et al have recently (FSA annual meeting November 2005) reported a prevalence of peanut sensitisation of 30/1072 = 2.8% (95%CIs 1.8-3.7). Although the rate of sensitisation in their study appears to be slightly higher, the difference is not statistically significant (p=0.34).

Finally we explored whether there have been any changes over time in terms of both the sensitisation to peanuts as well as clinical allergy to peanuts. Our data suggested that there was a significant non-linear trend with regards to peanut sensitisation with a decrease being observed between the two cohorts born in 1994-1996 and 2001-2002. The rate of clinical allergy to peanuts comparing the cohort remained the same. As the numbers of those sensitised and those who were symptomatic were actually relatively small, it is difficult to draw any inferences in terms of the impact of the COT report. Nevertheless our data suggests that although the rate of clinical allergy has remained unchanged there is some evidence that the rate of sensitisation has decreased over time.

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**Appendices**

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| Appendix 1 | Recruitment questionnaire |
| Appendix 2 | Food frequency questionnaire |
| Appendix 3 | Three month questionnaires |
| Appendix 4 | Six month questionnaire |
| Appendix 5 | Nine month questionnaire |