

# Patterns of Adult Food Allergy (PAFA-Stage 2)

<b>Submission date</b> 09/12/2021	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 14/03/2022	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 21/08/2023	<b>Condition category</b> Other	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Many people in the UK suffer from food allergies and intolerances, which cause problems for them when choosing what to eat, buying food, and eating outside the home. Although this is well recognised in children, it affects many adults too. Therefore, the aim of this study is to determine the prevalence of IgE-mediated food allergy in adults aged 18-70 years in a UK-based population. IgE-mediated means that IgE allergy antibodies are a cause of the allergic reaction to a food. The researchers also want to describe the different trajectories of food allergy across the life course, describe adult adverse reactions to foods that are not mediated by IgE and identify potential risk factors for the development of food allergies.

### Who can participate?

Adults aged 18-70 years who have participated in the PAFA-Stage 1 study (<https://www.isrctn.com/ISRCTN72819770>) and have consented to be invited to take part in this study (PAFA-Stage 2).

### What does the study involve?

Participants will be invited to a study centre to complete a questionnaire and have an assessment of IgE-mediated sensitisation to common food and inhalant allergens. This will be done using a skin prick test and serology (a blood test). The blood test will be used to determine IgE-sensitisation to food and inhalant (breathed in) allergens and provide banked samples for later DNA analysis and further immunological analysis to confirm and investigate the causes of allergy and other adverse reactions to food.

### What are the possible benefits and risks of participating?

Participants who report an adverse reaction to food will benefit from a clearer understanding of whether or not they have a food allergy. They may be eligible to take part in the PAFA-Stage 3 study which will involve a more detailed clinical assessment with a medical doctor to confirm whether they have a food allergy or not. Participants who do not have a food allergy but have other types of allergic or associated respiratory disease will also benefit from a clearer understanding of their allergies and associated respiratory diseases such as asthma. The data gathered in this study will contribute to our understanding of the prevalence and trajectory of food allergy which in turn will help with updating current public health policies regarding food allergy including prevention and treatment.

With regards to the risks of participating, during blood collection, slight discomfort is felt and

bruising can occur occasionally. Some people can feel faint whilst blood is being taken. During skin prick testing, in those whose skin reacts to the allergen, a 'wheal' (a small red itchy area) will develop, which is measured and recorded as a positive test. This usually goes away within 10-20 minutes and participants will be offered an antihistamine or steroid cream. There is also a small risk associated with the storage of confidential data and unauthorised disclosure of personal data.

Where is the study run from?

The study is run from GP practices and coordinated by the Universities of Manchester and Southampton with Manchester University NHS Foundation Trust (study sponsor) and the Isle of Wight NHS Trust (UK)

When is the study starting and how long is it expected to run for?

August 2018 to December 2022

Who is funding the study?

Food Standards Agency (UK)

Who is the main contact?

Prof. Clare Mills, [clare.mills@manchester.ac.uk](mailto:clare.mills@manchester.ac.uk)

## Contact information

### Type(s)

Principal investigator

### Contact name

Prof Clare Mills

### ORCID ID

<https://orcid.org/0000-0001-7433-1740>

### Contact details

Division of Infection, Immunity and Respiratory Medicine

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United Kingdom

M13 9PL

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## Additional identifiers

### Integrated Research Application System (IRAS)

295890

### Central Portfolio Management System (CPMS)

50806

# Study information

## Scientific Title

Patterns and prevalence of adult food allergy in a UK population (PAFA-Stage 2)

## Acronym

PAFA-Stage 2

## Study objectives

To determine the prevalence of probable IgE-mediated food allergy in UK adults aged 18-70 years.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Approved 10/11/2021, Yorkshire & The Humber - South Yorkshire Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 1048091; southyorks.rec@hra.nhs.uk), REC ref: 21/YH/0262

## Study design

Observational; Design type: Cross-sectional

## Primary study design

Observational

## Study type(s)

Screening

## Health condition(s) or problem(s) studied

Adult food allergy

## Interventions

PAFA-Stage 2 follows on from PAFA-Stage 1 community survey where people in the general population aged 18-70 years living in Manchester, Southampton or the Isle of Wight were asked if they experienced any adverse reactions to food. In PAFA-Stage 2 the researchers want to find out more about the adverse reactions to foods that PAFA-Stage 1 respondents reported as well as other types of allergies and associated respiratory diseases like asthma. They are using what is called a "case-control" study design which will help them to identify reasons why some people develop food allergies and others do not. This has been used previously to define the prevalence of food allergy in many studies such as the EuroPrevall project and is acknowledged as providing the robust data required by the funder, the Food Standards Agency (FSA), for the development of evidence-based policy for managing food allergies. The methodology has been developed by the study team and their collaborators which includes laboratory scientists, allergists, GPs, dieticians and a gastroenterologist. It has also been scrutinised by experts external to the project team through the Project Steering Committee convened by the FSA which has patient representation from the Anaphylaxis Campaign. The Anaphylaxis Campaign has also provided additional input into the design of patient-facing documents such as the Patient Information Sheet. PAFA-Stage 2 participants will be selected from the PAFA-Stage 1 respondents who agreed to be re-contacted to take part in PAFA-Stage 2, who do not have dementia or are not in

palliative care. Cases will be selected from those with self-reported adverse reactions to foods. Of those who reported no adverse reactions to food and agreed to be contacted for Stage 2, up to two control subjects will be selected per case, selected from the same population area and age-matched where possible. It is estimated that 500 -1,000 eligible participants identified from PAFA-Stage 1 community survey will respond to invitations to be further evaluated in Stage 2. Up to 1,000 age-matched control subjects will also be invited to be evaluated using the same questionnaire and procedures, although precise numbers required to maintain power and confidence in the approach will depend on the response rates. It is anticipated that PAFA-Stage 2 will take between 8-10 months to complete with a further 2 months to analyse data and prepare reports to complete the survey within the project lifetime.

1. Invitation to PAFA-Stage 2 and booking of an allergy assessment visit: Cases and controls will receive a letter from their GP inviting them to take part in PAFA-Stage 2, including a participant information sheet (PIS) describing what is involved in Stage 2. Participants will be invited to contact the research team via either a dedicated phone number or email address to book an appointment. If possible, they will also be provided with a booking system link with the option to book online using either REDCap or an NHS-approved system such as AccuRX. A text message or email reminder will be sent out 1-2 and/or 3-4 weeks after the Stage 2 invitation letter. Those that have not booked their visit after 6 weeks will be contacted directly by phone by the study team. Those who do not have phone or internet access but who wish to participate will be invited to complete the section at the bottom of the invitation letter and return it using an enclosed paid reply envelope; they will then receive an appointment through the post. Those who require the documents in Urdu or Hindi will also have the option to request a study pack in either Urdu or Hindi by completing a section at the end of the invitation letter and returning it using an enclosed paid reply envelope. During the booking process, the study team will establish if there is a potential language barrier for the participant. If a language barrier is identified, participants will be invited to ask a close family member or friend to come with them to their appointment to translate the consent, study procedure, and questionnaire. If no one is available, where possible, a language interpretation service available within primary care will be provided. A text message confirmation of any booked appointments will be sent to participants with a mobile phone number (if provided). This message will include an invitation to reschedule an appointment if necessary.

2. Allergy assessment visit: Each visit is estimated to take a maximum of 55 minutes. During the PAFA-Stage 2 visit, a participant's eligibility to take part in the study will be confirmed, informed regarding reimbursement of reasonable travel expenses and their consent to take part in the allergy assessment recorded. Participants will complete an electronic questionnaire directly using a tablet, have skin prick testing (SPT) to assess sensitisation to common food and inhalant allergen, and (not obligatory) provide a blood sample. The blood samples will be used to (1) isolate plasma/serum for measurement of specific IgE to food and inhalant allergens and for storage for future analysis; and (2) storage of blood cells to allow isolation of DNA for future genetic analysis. Study participants will be given feedback about the test results during the study visit and explain the subsequent follow-up including PAFA-Stage 3 as follows: (a) If a food skin prick test(s) is positive, participants will be invited to take part in the next stage of PAFA (PAFA-Stage 3), which will involve a more detailed clinical assessment with a medical doctor; in this case the GP will be informed. PAFA-Stage 3 is the subject of a separate ethical application. (b) If the food skin prick tests are negative, participants will be told that the research team will wait for the results of the blood test (if one is being done). If the blood tests are positive, the study team will invite the participant to take part in the next stage of PAFA (PAFA-Stage 3) and again inform their GP. If the blood tests are negative, the study team will send this information to the participant's GP together with any advice about what to do next. The participants will be sent a copy of this letter. (c) If the food to which a participant has reported reactions is not on

the skin prick testing panel, the study team will arrange for a blood test to this food, if it is available. If these tests are positive, the study team will invite the participant to take part in the next stage of PAFA (PAFA-Stage 3), which will involve a more detailed clinical assessment with a medical doctor. The study team will inform their GP about this. If the blood tests are negative, the study team will send this information to the participant's GP together with any advice about what to do next. The participant will be sent a copy of this letter. (d) If the results are not clear, the participant's case will be discussed with the study doctor and clinical advice will be sent to their GP. The participants will be sent a copy of this letter. Since the PAFA-Stage 2 study visits entail completing a questionnaire and undergoing simple clinical procedures that will take place as far as possible in the community, making use of rooms for research available at GPs or other community spaces close to where participants live. All study visits will be undertaken in a COVID-19 secure manner following the policies in place at the relevant study sites (e.g. GP practices, Manchester University NHS Foundation Trust or the Isle of Wight NHS Trust).

3. Data collection and analysis: All questionnaire responses and allergy assessment results will be gathered together on a secure online research platform called REDCap, allowing for data sharing and analysis of pseudonymised data (personal information such as name and address will not be linked to questionnaire responses). Only those within the study team with permission to view and analyse the data will be granted access using a secure login and password. Interim analysis will be performed on an ongoing basis. The information from the questionnaire will be used to find out whether the symptoms participants experience when they eat a particular food are consistent with an IgE-mediated food allergy. Then using a skin prick test and a blood test the researchers will discover if they have made IgE (a process called sensitisation) to that food. Using answers to the questionnaire and the tests they will identify individuals who may have a probable IgE-mediated food allergy and those with a possible non-IgE-mediated food allergy. Interim analysis will be undertaken as data are uploaded into eLab allowing candidates with probable food allergy to be identified and invited for clinical evaluation (including double-blind placebo-controlled food challenge if appropriate) through PAFA-Stage 3 (which will be described in a separate protocol and ethical submission). The analysis will use classical descriptive statistics. The final analysis will then be performed after the collection of follow-up data from the final participant has been completed, data have been checked and cleaned and database lock has taken place. This will include the case-control analysis to define the risk factors for the development of adult-onset food allergy and confounders. Although the researchers will try to reduce bias it is still likely that other (possibly unobserved) characteristics of those who are willing to be recontacted again for the allergy assessment visit are different from those who do not respond. The researchers will try and take account of this using population weights to account for differences in participants and population as a whole. A repository of data and biological samples will be available in each cohort which can be used for future investigation (e.g. biomarker analysis [serological and/or genetic]), to provide an indication of the extent to which these reactions relate to lactose intolerance and coeliac disease.

### **Intervention Type**

Other

### **Primary outcome(s)**

Probable IgE-mediated food allergy, which is defined as all of:

1. Self-reported symptoms associated with consumption of a particular food which are typical of an IgE-mediated food allergy (see list below) [administered questionnaire]
2. Symptoms onset within 2 hours of contact with food [administered questionnaire]

3. Evidence of sensitization to the same food in the form of a positive skin prick test (SPT;  $\geq 3$  mm wheal) and/or positive serum specific IgE ( $\geq 0.35$  kU/L) and/or positive serum specific IgE to component associated with clinical allergy ( $\geq 0.35$  kU/L) to the same food.

Symptoms considered to be typical of IgE-mediated food allergy include any of the following: itching or tingling in the mouth, lips, ears or throat; swelling of the eyes, lips, or mouth; nettle sting like rash or itchy skin, or red rash; diarrhoea (other than food poisoning); vomiting (other than food poisoning); stomach cramps; hoarseness or swelling of throat; a runny, stuffy nose, or sneezing; red, sore, or running eyes; cough, wheeze, chest tightness, or breathlessness; fainting or dizziness.

Timepoint: December 2022

### **Key secondary outcome(s)**

Probable non-IgE mediated adverse reaction to food, which is defined as all of:

1. Self-reported symptoms associated with consumption of a particular food which are typical of a non-IgE-mediated adverse reaction to food (see below) [administered questionnaire]
2. Symptoms after 2 hours of consumption [administered questionnaire]
3. No evidence of sensitisation to food in the form of a negative skin prick test (SPT;  $< 3$  mm wheal) and/or negative serum specific IgE ( $< 0.35$  kU/L) to the same food.

Symptoms typical of non-IgE mediated adverse reaction to food include any of the following: difficulty swallowing; regurgitating stomach contents (stomach contents raising back to the oesophagus or mouth); reflux/ heartburn/indigestion; fainting or dizziness; headaches; stomach cramps; diarrhoea (other than food poisoning); vomiting (other than food poisoning); constipation; other digestive problems (e.g. bloating, wind)

Timepoint: December 2022

### **Completion date**

31/12/2022

## **Eligibility**

### **Key inclusion criteria**

1. All must be respondents to the PAFA-Stage 1 community survey and consent to be invited to take part in PAFA-Stage 2
2. Cases will be identified as participants who responded to the PAFA-Stage 1 and indicated they have a self-reported adverse reaction to food which is consistent with it being a possible food allergy
3. Controls will be identified as participants who responded to the PAFA-Stage 1 and indicated they do not have a self-reported adverse reaction to food
4. Both cases and controls will be capable of giving informed consent

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

70 years

**Sex**

All

**Key exclusion criteria**

Adults who have dementia, Alzheimer's disease, or are receiving palliative care

**Date of first enrolment**

01/12/2021

**Date of final enrolment**

04/08/2023

## **Locations**

**Countries of recruitment**

United Kingdom

Netherlands

**Study participating centre**

**Manchester Royal Infirmary**

Cobbett House

Manchester Royal Infirmary

Oxford Road

Manchester

United Kingdom

M13 9WL

**Study participating centre**

**St Mary's Hospital**

Parkhurst Road

Newport

United Kingdom

PO30 5TG

**Study participating centre**

**NIHR CRN: Greater Manchester**  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**  
**Bowland Medical Practice**  
52 Bowland Road  
Baguley  
Manchester  
United Kingdom  
M23 1JX

**Study participating centre**  
**Bodey Medical Centre**  
28 Ladybarn Lane  
Fallowfield  
Manchester  
United Kingdom  
M14 6WP

**Study participating centre**  
**Barlow Medical Centre**  
Barlow Medical Centre  
828 Wilmslow Road  
Didsbury  
Manchester  
United Kingdom  
M20 2RN

**Study participating centre**  
**St Johns Medical Centre**  
Altrincham Health & Wellbeing Ctr  
31-33 Market Street  
Altrincham  
United Kingdom  
WA14 1PF

**Study participating centre**  
**Moss Side Health Centre**  
Monton Street

Manchester  
United Kingdom  
M14 4GP

**Study participating centre**

**Tower House Surgery**

Tower House  
Rink Road  
Ryde  
United Kingdom  
PO33 1LP

**Study participating centre**

**St Francis Practice Ltd**

Pilgrims Close  
Chandlers Ford  
Eastleigh  
United Kingdom  
SO53 4ST

**Study participating centre**

**Old Fire Station Surgery**

68a Portsmouth Road  
Weston  
Southampton  
United Kingdom  
SO19 9AN

**Study participating centre**

**The University of Manchester School of Biological Sciences**

Manchester Institute of Biotechnology  
131, Princess Street  
Manchester  
United Kingdom  
M1 7DN

**Study participating centre**

**The University of Southampton**

Paediatric Allergy and Respiratory Medicine  
Tremona Road  
Southampton

United Kingdom  
SO16 6YD

**Study participating centre**  
**Amsterdam University Medical Centre (AMC)**  
Department of Experimental Immunology  
K0-134 Meibergdreef 9  
Amsterdam  
Netherlands  
1105 AZ

## Sponsor information

**Organisation**  
Manchester University NHS Foundation Trust

**ROR**  
<https://ror.org/00he80998>

## Funder(s)

**Funder type**  
Government

**Funder Name**  
Food Standards Agency; Grant Codes: FS101174

**Alternative Name(s)**  
The Food Standards Agency, FSA

**Funding Body Type**  
Private sector organisation

**Funding Body Subtype**  
Other non-profit organizations

**Location**  
United Kingdom

## Results and Publications

## Individual participant data (IPD) sharing plan

A fully anonymised dataset will be made available by the Food Standards Agency (planned timeline: by 31/12/2022) to be accessed through the Government website. Publication will be pursued as per the open government policy of the Food Standards Agency in conjunction with their Information Governance risk assessment (previous FSA-funded allergy studies have had some data published openly: <https://data.food.gov.uk/catalog/datasets?search=allergy#results>).

## IPD sharing plan summary

Stored in publicly available repository

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes