

# To determine the optimum series of investigations to diagnose asthma

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<b>Registration date</b> 03/07/2019	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 25/03/2026	<b>Condition category</b> Respiratory	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Asthma is one of the commonest lung conditions in the UK. Unfortunately, there is no single test to diagnose asthma. Doctors use a range of different breathing tests. It is unclear which one of these is best. As it can be difficult to diagnose asthma, some people may be given long-term treatment they do not need, whilst others are not given treatment that they do need. We want to improve the way asthma is diagnosed, by understanding how to use the routine breathing tests in a better way. We also hope to develop new breathing tests, which may be better to diagnose asthma. The results of this study will be used to help doctors diagnose asthma and get people on the right treatment as soon as possible.

### Who can participate?

#### Patients:

Those with symptoms that could be due to asthma (such as cough, wheeze, breathlessness or chest tightness), aged between 5 and 69 years old. Those who have other lung conditions, are pregnant or have been heavy smokers for a long time are not able to participate.

#### Healthy Volunteers:

Those aged between 5 and 69 years with no known or suspected lung problems. Those who are pregnant or have been heavy smokers for a long time are not able to participate

### What does the study involve?

#### Patients:

There are 4 clinic visits in total over 3 months. There are 2 more optional visits with further lung tests between core visit 1 and 3. Each core visit includes a lung health check, a questionnaire, and some detailed breathing tests (some of these are standard care and some will be new tests). Each visit can take 1- 2 hours. There is also a blood test and allergy test. At the first visit participants will be asked to sign a consent form confirming they are happy to proceed with the study. They will receive a copy of the consent form and information sheet to keep. Participants will be given an inhaler to use to help relieve symptoms (this is a standard inhaler used in routine care for people with asthma). After the second visit participants will start using an asthma preventer inhaler (this is a standard treatment for asthma), at visit 3 and 4 it will be assessed if

the breathing tests and symptoms have improved with this preventer treatment. At the end of the study, the participant and their doctor will receive a report with your test results and a treatment plan.

#### Healthy Volunteers:

There are two visits at the research clinic. At each visit participants will do some routine tests used in asthma diagnosis and also new breathing tests. They will receive a comprehensive assessment of their lung health. This information can be passed onto their GP with their permission for future record.

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

All the tests being used are low risk and are either routinely used by doctors or are used in research clinics around the country. The drugs prescribed are commonly used in asthma and other conditions.

#### Side effects:

Reliever inhaler: Occasionally, people feel shaky or jittery after taking this medication, but this wears off quickly.

Preventer inhaler: Side effects: Occasionally people get a sore throat, hoarse voice or a mouth infection called thrush, this can be avoided by rinsing your mouth with water after taking the medicine.

Breathing tests: all breathing tests are safe and are used routinely by GPs and hospital clinics. Sometimes when you breathe in and out quickly it can make you feel dizzy we perform all lung function measurements with you sitting down.

Mannitol test: this is a safe test and is used in asthma clinics around the world. You might feel short of breath, chest tightness or cough, but these symptoms don't last long. We will give medicine to reverse these symptoms if needed. If you are taking antihistamines we would ask you to stop these for 72 hours before this test.

Blood sample: Occasionally a slight discomfort is felt and bruising can occur where the blood is taken. Some people can feel faint whilst blood is being withdrawn.

Allergy skin prick test: local skin reaction or very rarely systemic reaction that may require antihistamine or anti-inflammatory medication.

Nose swab: It is very rare, but there is a small chance that a nose bleed can occur.

#### Where is the study run from?

Manchester University NHS Foundation Trust (Wythenshawe site)

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

December 2018 to December 2027

#### Who is funding the study?

1. National Institute for Health Research (NIHR) Biomedical Research Centre (BRC)
2. Asthma UK/Innovate

#### Who is the main contact?

1. Dr Clare Murray  
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## Contact information

**Type(s)**

Scientific

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**Additional identifiers****Clinical Trials Information System (CTIS)**

Nil known

**Integrated Research Application System (IRAS)**

243658

**Protocol serial number**

CPMS 40437, IRAS 243658

## Study information

**Scientific Title**

To determine the optimum series of investigations to diagnose asthma

**Acronym**

RADicA

**Study objectives**

To determine the optimum series of investigations to diagnose asthma

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 08/01/19, North West - Greater Manchester East Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ; +44(0)207 104 8009; nrescommittee.northwest-gmeast@nhs.net), ref: 18/NW/0777, IRAS project ID: 243658  
REC reference: 18/NW/0777  
Amendment approval date: 14/03/2019

**Study design**

Observational cohort study

**Primary study design**

Observational

**Study type(s)**

Treatment

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

Asthma

**Interventions**

The Rapid Access Diagnostics for Asthma (RADicA) study will aim to determine the optimum diagnostic pathway for asthma and to determine the optimum series of investigations to predict "steroid-responsive airways disease" based on conventional tests of large airway function and novel tests of small airway function. The study will be a prospective cohort study. Participants with symptoms of asthma (i.e., cough, wheeze, chest tightness and/or breathlessness), not currently taking inhaled corticosteroid treatment will be recruited through primary and secondary care sources. Participants will undergo 4 core visits (2 before and 2 following standard asthma treatment), 1 telephone/text/email contact and up to 2 optional visits.

At Core Visit 1, following written informed consent (and assent where applicable), the participant will be thoroughly evaluated (structured clinical history and examination) following a proforma. Participants in whom asthma is deemed low probability AND in whom an alternative diagnosis is suspected (e.g. pneumonia) would be withdrawn from the study and would be

evaluated further in collaboration with their GP or if appropriate due to clinical urgency and/or severity direct referral to a general respiratory clinic would be arranged. All other participants will continue in the study. Those continuing will complete the following tests:

1. Skin prick test (if the patient is on antihistamines, this test will be deferred to a future visit and medication withheld as indicated)
2. Blood test (offered to all participants - can be completed at any baseline visit. However as these are not safety bloods, if declined the participant can still continue in the study)
3. Pregnancy test - if applicable
4. Nasopharyngeal swabs
5. FeNO
6. VOCs
7. IOS (pre-salbutamol)
8. PExA (pre-salbutamol)
9. MBW (pre-salbutamol)
10. Spirometry (pre-salbutamol)
11. Administration of inhaled salbutamol for bronchodilator reversibility testing
12. IOS (post-salbutamol)
13. Spirometry (post-salbutamol)

Following the visit all patients in the study will be issued with an inhaled short acting bronchodilator to use as required in case they become symptomatic between visits. Participants will receive an electronic peak flow and be asked to record twice-daily PEF measurements for 2-weeks.

All participants will attend Core Visit 2. This visit will occur between core visit 1 and entering the treatment period phase providing there is a gap of  $\geq 24$ hrs from completing bronchodilator reversibility challenge (done in core visit 1), and/or  $\geq 48$ hrs between methacholine challenge visit (optional visit 1) and/or bronchoscopy visit (optional visit 2). The procedures conducted at core visit 2 are:

1. Symptoms (ACQ)
2. Collection of PEF measurements (if not completed 2 weeks this can be collected at next visit)
3. IOS (pre-mannitol)
4. PExA (pre-mannitol)
5. MBW (pre-mannitol)
6. Spirometry (pre-mannitol)
7. Mannitol provocation challenge
8. IOS (post-mannitol)
9. Sputum will be collected where expectoration is voluntarily achieved at any point during the visit, note we would most likely expect sputum during/following the mannitol challenge
10. Participants will be instructed to commence their treatment with a standard steroid inhaler once they have completed their last baseline visit (baseline visits include: core visit 1, core visit 2, optional visit 1, optional visit 2) and 2 weeks PEF monitoring.

There will be two optional visits offered to eligible participants, these visits can occur at any point between core visit 1 and starting treatment phase, providing there is a gap of  $\geq 24$ hrs from completing bronchodilator reversibility challenge (done in core visit 1), or  $\geq 48$ hrs between challenge tests and/or bronchoscopy.

Optional visit 1: Methacholine challenge. The running order for the procedures conducted at this visit is as follows:

1. Symptoms (ACQ)
2. IOS (pre-methacholine)
3. Spirometry (pre-methacholine)

4. Methacholine provocation challenge

5. IOS (post-methacholine)

Optional visit 2: Bronchoscopy visit (offered on upto 20 adult participants). The running order for the procedures conducted at this visit is as follows:

1. Consent

2. Bronchoscopy

At the end of the baseline visits and on completion of 2 weeks of PEF monitoring, participants will start the treatment phase with a standard first line asthma treatment (a steroid inhaler 'Flixotide accuhaler' will be prescribed in all patients to be used morning and evening. Also a reliever inhaler 'Ventolin accuhaler' will be prescribed to be used as required for symptom control).

Core visit 3 will occur 1-2 weeks after participant is commenced on steroid inhaler. It is an early response visit. The procedures conducted at this visit are:

1. Symptoms (ACQ)

2. Clinical examination

3. Check adherence

4. Blood test (in adults, also offered in children  $\geq 12$  yrs. However as these are not safety bloods, if declined the participant can still continue in the study)

5. FeNO

6. VOCs

7. IOS

8. PExA

9. MBW

10. Spirometry

11. Participants will receive a repeat supply of inhalers

Core visit 4 will occur 6-8 weeks after participant is first commenced on steroid inhaler. The procedures conducted at this visit are:

1. Symptoms (ACQ)

2. Clinical examination

3. Nasopharyngeal swabs

4. Blood test (in adults, also offered in children  $\geq 12$  yrs. However as these are not safety bloods, if declined the participant can still continue in the study)

5. FeNO

6. VOCs

7. PExA

8. MBW

9. IOS (pre Mannitol provocation)

10. Spirometry (pre Mannitol provocation)

11. Mannitol provocation

12. IOS (post Mannitol provocation)

13. Spirometry (post Mannitol provocation)

14. GP letter

In addition to the study described we will also recruit age and gender matched healthy controls who will attend 2 visits. This will enable data collection for 'normal' ranges in some of the novel lung function tests where data is lacking. At visit 1, healthy volunteers will be asked to conduct the following:

1. Informed consent

2. Demographics/Clinical history

3. Symptoms

4. Clinical Examination
5. Skin prick test (if the patient is on antihistamines, this test will be deferred to visit 2 and medication withheld as indicated)
6. Blood test (offered to all participants - can be completed at any visit. However as these are not safety bloods, if declined the participant can still continue in the study)
7. Pregnancy test - if applicable
8. Nasopharyngeal swabs
9. FeNO
10. VOCs
11. IOS (pre-salbutamol)
12. PExA (pre-salbutamol)
13. MBW (pre-salbutamol)
14. Spirometry (pre-salbutamol)
15. Administration of inhaled salbutamol for bronchodilator reversibility testing
16. IOS (post-salbutamol)
17. Spirometry (post-salbutamol)

At visit 2 (between 1 and 12 weeks later) , healthy volunteers will be asked to conduct the following:

1. Symptoms
2. Clinical examination
3. FeNO
4. VOCs
5. IOS
6. PExA
7. MBW
8. Spirometry

### **Intervention Type**

Other

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

Large airway function measured using:

1. Spirometry (FEV1, FVC, MEF25-75) at visits 1, 3, 4.
2. BDR ( $\Delta$  FEV1 or FVC following 400mcg inhaled Salbutamol) at visit 1.
3. FeNO (NO ppb) at visits 1-4.
4. PEFv (variability measured twice daily over 2 weeks)
5. BHRmann (mannitol PD15) at optional visit 1.
6. BHRmeth (Methacholine PD20) at visits 2, 4.

Small airway function measured using:

1. IOS (Rrs5Hz, Rrs20Hz, R5-20, Xrs5Hz, Xrs 20Hz, X5-20) at visits 1-4.
2. MBW (LCI, Scond, Sacin) at visits 1-4.

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

1. Asthma symptoms measured using Asthma Control Questionnaire (ACQ-5) at visits 1-4.
2. Experimental biomarkers of small airway inflammation measured using:
  - 2.1 PExA at visits 1-4.
  - 2.2 VOC at visits 1-4.
3. Blood tests including: Blood eosinophil count, cell culture, immune cell count, measures of immune cell activation (Mbd2, CCL17, CCR4) YKL-40 (CHI3L1), AMCase (CHIA), Chitotriosidase (CHIT1) at visits 1, 3, 4.
4. Sputum eosinophil at visits 2, 4.

**Completion date**

31/12/2027

## Eligibility

**Key inclusion criteria**

1. Males and females  $\geq 5$  years and  $<70$  years
2. Clinical suspicion of asthma from GP or referring health care professional
3. One or more symptom in keeping with asthma (i.e., cough, wheeze, chest tightness and breathlessness)
4. Capable of giving informed consent or where under 16 years attends with parent or legal guardian.
5. Participants must be able to communicate well in English

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

5 years

**Upper age limit**

70 years

**Sex**

All

**Total final enrolment**

140

**Key exclusion criteria**

1. Pregnant women
2. Current ICS (used within previous 2 weeks) or oral steroid treatment (within the previous 4 weeks)
3. Former/Current smokers if  $> 10$  pack year smoking history
4. Other relevant comorbidities (e.g., other lung disease; CF, COPD, ILD or bronchiectasis)
5. Recent antibiotic treatment within previous 2 weeks (these participants may be able to enter the study at a later date)

**Date of first enrolment**

03/12/2018

**Date of final enrolment**

30/06/2027

# Locations

## Countries of recruitment

United Kingdom

England

## Study participating centre

**Manchester University NHS Foundation Trust**

Cobbett House

Oxford Road

Manchester

England

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# Sponsor information

## Organisation

Manchester University NHS Foundation Trust

## ROR

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

# Funder(s)

## Funder type

Government

## Funder Name

Asthma UK; Grant Codes: AUK-PG-2018-406

# Results and Publications

## Individual participant data (IPD) sharing plan

The authors will consider all reasonable requests for deidentified data, following approval by the study sponsors. Proposals should be directed to [research.sponsor@mft.nhs.uk](mailto:research.sponsor@mft.nhs.uk). To gain access, data requestors will need to sign a data access agreement.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		05/09/2024	19/09/2024	Yes	No
<a href="#">Results article</a>	Asthma diagnosis: a comparison of established diagnostic guidelines in adults with respiratory symptoms	05/09/2024	20/09/2024	Yes	No
<a href="#">Protocol article</a>		26/10/2024	28/10/2024	Yes	No
<a href="#">HRA research summary</a>			26/07/2023	No	No
<a href="#">Other publications</a>	What do patients think about home-based testing for better asthma diagnosis? Insights from a qualitative study	23/03/2026	25/03/2026	Yes	No
<a href="#">Protocol file</a>	version V2	14/03/2019	03/07/2019	No	No
<a href="#">Protocol file</a>	version 8.1	22/02/2023	12/06/2023	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes