

# Born early, breathe easy

<b>Submission date</b> 08/01/2016	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 12/02/2016	<b>Overall study status</b> Completed	<input checked="" type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 06/03/2024	<b>Condition category</b> Neonatal Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

This project looks at whether some babies born early can have long-term breathing problems as they go through childhood which have not yet been detected. Research on very premature babies has shown that their lungs may not work as well as babies born at, or earlier to, their due date. Work already done by the researchers of this project has also shown that some moderately premature babies are at risk of having breathing problems as they grow up. The next step of this research is to invite some families to participate in a study to look at possible reasons why children born early may have breathing problems. The researchers want to know whether there are differences in the structure and function of the airways in the children born prematurely compared to those born on time. If prematurely born children are different, they may benefit from closer follow-up and possibly some treatment to improve their breathing.

### Who can participate?

Children (and families) aged between 7-12 who were born prematurely (at 34 weeks gestation or less)

### What does the study involve

First of all, each child does some breathing tests (at home, if possible) and both them and their parents are asked to fill in some questionnaires about their daily life. A sample of saliva (spit) is also collected. The aim of the visit is to assess how many children have lower than expected results on the breathing test. Children with a lower than expected result are asked to take part in the next stage. For this stage, each child and their parents visit the laboratory on two occasions to have more detailed breathing tests before and after exercising on a stationary bicycle. After the first visit, each child is given an inhaler to use twice a day for 12 weeks. The type of inhaler they are given is allocated randomly and could be one containing fluticasone propionate, a fluticasone propionate/salmeterol xinafoate combination or a placebo (dummy inhaler). Any response to the inhaler treatment will be seen at the second visit. Finally, some children are invited to have a MRI scan of their lungs to look at how well they are working.

### What are the benefits and risks?

The researchers aim to show that children born early have limitations in their lung function which may cause breathing problems. If so, they will be able to find out if treating with medicine is successful in easing the symptoms. Children born preterm have generally been ignored, however the evidence from this study may indicate to healthcare policy makers that closer

follow-up is required in these children; secondly, it may indicate that treatment should be considered an option in all children born preterm, (extremely or moderately) with reduced lung function. In the future, this surveillance and treatment may reduce the burden on NHS resources in terms of GP and hospital visits. As with all medicines, there are some small risks of side effects. However these are rare and often mild.

Where is the study run from?  
Children's Hospital for Wales (UK)

When is study starting and how long is it expected to run for?  
March 2015 to December 2019

Who is the main contact  
Mr John Lowe

**Study website**  
[www.rhino-health.org](http://www.rhino-health.org)

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**EudraCT/CTIS number**

2015-003712-20

**IRAS number****ClinicalTrials.gov number****Secondary identifying numbers**

2015-003712-20

## Study information

**Scientific Title**

Respiratory Health Outcomes in Neonates - A randomised, double blind, double-dummy placebo-controlled trial of inhaled treatment to establish the mechanisms of prematurity-associated airway obstruction and inflammation

**Acronym**

RHINO

**Study objectives**

The overall aim is to establish the underlying mechanisms of chronic airway obstruction observed in symptomatic children who are born preterm and to establish if there are different phenotypes of this condition that do or do not respond to standard inhaled therapy.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

South West - Central Bristol Research Ethics Committee, 26/11/2015, ref: 15/SW/0289

**Study design**

Single-centre, randomised, double blind, placebo controlled trial

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Community

**Study type(s)**

Other

**Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet

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

Prematurity-associated respiratory disease

**Interventions**

Random assignment to using one of the three following metered-dose inhalers

1. Fluticasone propionate
2. Fluticasone propionate/salmeterol xinafoate combination
3. Placebo

**Intervention Type**

Drug

**Phase**

Phase IV

**Drug/device/biological/vaccine name(s)**

1. Fluticasone propionate
2. Salmeterol xinafoate

**Primary outcome measure**

The primary outcome will be the difference in pre and post treatment percent predicted FEV1 after 12 weeks of therapy between the active and placebo groups

**Secondary outcome measures**

1. Differences in measures of obstructive airway disease (pulmonary function tests)
2. Differences in response to exercise challenge between treatment groups.
3. Differences in biomarkers of airway inflammation between treatment groups
4. Differences in respiratory and neurological symptoms (questionnaire)
5. MRI parameters: apparent diffusion coefficient (ADC) between 3 comparison groups (preterm, FEV1  $\leq$ 85% at baseline; preterm control, FEV1  $\pm$ 1 standard deviation from normal; and term

control, FEV1  $\pm$ 1 standard deviation from normal).

6. Pre- and- post treatment differences in objectively measured physical activity

7. Adverse events

All outcomes to be measured after 12 weeks of therapy between the active and placebo groups

**Overall study start date**

12/03/2015

**Completion date**

30/06/2020

## **Eligibility**

**Key inclusion criteria**

1. Children aged 7-12 at the time of screening
2. Born at a gestational age  $\leq$ 34 weeks (NB. Approximately n=50 term controls will also be invited)
3. Resident in the south Wales area whom, in the opinion of the Investigator, are possible to follow up
4. Fully informed proxy consent from parents/guardians and assent from child where possible

**Participant type(s)**

Patient

**Age group**

Child

**Lower age limit**

7 Years

**Upper age limit**

12 Years

**Sex**

Both

**Target number of participants**

200 Randomised from approximately 1000 screened

**Total final enrolment**

53

**Key exclusion criteria**

1. Respiratory tract infection within the last three 3 weeks (will be asked to consider participating at a later date)
2. Congenital abnormalities
3. In the opinion of the Investigator have:
  - 3.1. Severe cardiopulmonary defects, or
  - 3.2. Neuromuscular disease, or

3.3. Severe neurodevelopmental impairment  
Which prohibit the possibility of compliance with the study protocol

**Date of first enrolment**

01/05/2016

**Date of final enrolment**

31/12/2019

## **Locations**

**Countries of recruitment**

United Kingdom

Wales

**Study participating centre**

**Children's Hospital of Wales**

Heath Park

Cardiff

United Kingdom

CF144XN

## **Sponsor information**

**Organisation**

Cardiff University

**Sponsor details**

30-36 Newport Road

Cardiff

Wales

United Kingdom

Cardiff CF24 0DE

**Sponsor type**

University/education

**Website**

<http://www.cardiff.ac.uk/racdv/resgov/contactus/index.html>

**ROR**

<https://ror.org/03kk7td41>

# Funder(s)

## Funder type

Government

## Funder Name

Medical Research Council

## Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

## Funding Body Type

Government organisation

## Funding Body Subtype

National government

## Location

United Kingdom

# Results and Publications

## Publication and dissemination plan

We will publish the results in scientific journals. However we will also make our findings available on the study website in a format accessible to our participants and the wider community. we have a parent representative to support us with this dissemination.

## Intention to publish date

15/12/2021

## Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date

## IPD sharing plan summary

Data sharing statement to be made available at a later date

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	version 10	13/12/2021	10/01/2022	Yes	No
<a href="#">Protocol file</a>		16/10/2018	22/08/2022	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Statistical Analysis Plan</a>	Trial Protocol and Statistical Analysis Plan		06/03/2024	No	No

