

# CF START: A national UK trial to determine whether taking an antibiotic (flucloxacillin) every day predisposes infants with cystic fibrosis (CF) to earlier infection with a bug, *Pseudomonas aeruginosa*, that is resistant to treatment

<b>Submission date</b> 03/10/2016	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 26/10/2016	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 02/07/2025	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Cystic fibrosis is Cystic fibrosis (CF) is an inherited condition which causes the lungs and digestive system to become blocked with mucus. It is caused by a faulty gene, which is responsible for controlling the movement of water and salts in and out of cells. This leads to a buildup of sticky mucus which clogs the lungs, increasing the sufferer's risk of developing airway infections. This study will determine whether taking a daily dose of the antibiotic flucloxacillin, which is prescribed to prevent infection with a type of bug called *Staphylococcus aureus*, leads to infants being more likely to have infections caused by a more resistant bug called *Pseudomonas aeruginosa*. The aim of this study is to find out what the safest and most effective antibiotic approach for infants diagnosed with cystic fibrosis is.

### Who can participate?

Infants under 90 days old who have CF.

### What does the study involve?

Participants are randomly allocated to one of two groups. Infants in the first group are prescribed flucloxacillin to take twice a day as a liquid at a dose of 125mg until they are 36 months old and then twice a day as a liquid at a dose of 250mg until they are 48 months old. Those in the second group are prescribed antibiotics in a targeted manner for symptoms (prescribed specific antibiotics if they need them) if they are found to have bugs in samples taken in the laboratory and if they require a general anaesthesia (being put to sleep for an operation). Participants in both groups are regularly monitored until they are 48 months old to find out how old they are when they first catch the harder to treat bug *Pseudomonas aeruginosa*.

What are the possible benefits and risks of participating?

The result of the study will be of benefit to patients with CF, and contribute to a better understanding of the effect of taking flucloxacillin in a "Prevent and Treat" manner, all of which may lead to benefits for infants and others with CF. There are no notable risks involved with participating.

Where is the study run from?

Alder Hey Children's Hospital and all other cystic fibrosis clinics (UK)

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

August 2016 to July 2028

Who is funding the study?

National Institute for Health Research (UK)

Who is the main contact?

Mrs Claire Soady

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## Contact information

### Type(s)

Public, Scientific, Principal investigator

### Contact name

Mrs Claire Soady

### Contact details

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## Additional identifiers

Clinical Trials Information System (CTIS)

2016-002578-11

Protocol serial number

31531

## Study information

**Scientific Title**

The cystic fibrosis (CF) anti-staphylococcal antibiotic prophylaxis trial (CF START): A randomised registry trial to assess the safety and efficacy of flucloxacillin as a long-term prophylaxis agent for infants with CF

**Acronym**

CF START

**Study objectives**

Use of anti-staphylococcal antibiotic prophylaxis (flucloxacillin) predisposes infants with cystic fibrosis to earlier airway infection with *Pseudomonas aeruginosa* (PsA) compared to infants treated with antibiotics in more targeted manner.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Liverpool Central, 16/09/2016, ref: 16/NW/0629

**Study design**

Randomised; Interventional; Design type: Treatment, Prevention, Drug

**Primary study design**

Interventional

**Study type(s)**

Treatment

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

Cystic fibrosis

**Interventions**

The randomisation sequence is generated by a computer and the infants are allocated one of two treatment strategies in a 1:1 ratio. The randomisation sequence has been generated to ensure equal allocation in clinics and centres depending on the size of those study sites.

“Prevent and Treat”: Infants are prescribed oral flucloxacillin suspension of 125 mg twice a day until 36 months then 250 mg twice a day until 48 months.

“Detect and Treat”: Infants prescribed antibiotics in a targeted manner for cough; asymptomatic growth of pathogens (bugs) from respiratory cultures, and as cover for a procedure requiring a general anaesthesia.

Infants will receive standard CF care for four years and outcomes will be collected on the national CF Registry.

The only additional (and optional) study measure will be a multiple breath washout undertaken between 40-48 months of age.

**Intervention Type**

Other

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

Age at first growth of *Pseudomonas aeruginosa* on a respiratory culture taken as a standard part of CF clinical care and recorded on the national CF Patient Registry

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

1. Lung clearance index measured by multiple breath washout at age 40-48 months
2. Number of courses (and days) of extra antibiotics (oral, intravenous or aerosolised) measured on the CF registry as a routine part of CF care
3. Number (and type) of respiratory cultures taken as a routine part of CF care during the 48 month trial period and recorded on the national CF Patient Registry (is measured using ... at ...)
4. Number of positive respiratory cultures for *Staphylococcus aureus* from samples taken as a routine part of CF care during the 48 month trial period and recorded on the national CF Patient Registry (is measured using ... at ...)
5. Number of positive respiratory cultures for *Pseudomonas aeruginosa* from samples taken as a routine part of CF care during the 48 month trial period and recorded on the national CF Patient Registry
6. Number of positive respiratory cultures for other significant CF pathogens from samples taken as a part of routine CF care during the 48 month trial period and recorded on the national CF Patient Registry
7. Chronic infection rate, as defined by "more than 50% of respiratory cultures are positive for the same pathogen during any 12 month period during the trial" during the 48 month trial period and recorded on the national CF Patient Registry
8. Number of inpatient stays (and number of days) during the 48 month trial period and recorded on the national CF Patient Registry
9. Adverse events occurring during the 48 month trial period and recorded on the national CF Patient Registry
10. Nutritional parameters (weight, height and weight for height percentile) are measured as a part of standard clinical care and recorded on the national CF Patient Registry during the last 8 months of the trial (age 40-48 months)
11. CF Banding (annual cost band allocated to infants in the study each year) is measured using data from the CF Registry

### **Completion date**

30/07/2028

## **Eligibility**

### **Key inclusion criteria**

Current inclusion criteria as of 13/04/2021:

1. A confirmed diagnosis of cystic fibrosis through one of the following three routes:
  - 1.1. Two CF-causing mutations are identifiedOR
  - 1.2. One or no CF- causing mutations identified and a sweat chloride test result greater than 59 mmol/LOR
  - 1.3. Two CFTR mutations (not known CF-causing mutations) and a sweat chloride test result greater than 29 mmol/L
2. Age 90 days or less
3. Consent for inclusion on the national UK CF Registry
4. Consent for inclusion in the CF START trial

**Previous inclusion criteria:**

1. A confirmed diagnosis of cystic fibrosis through one of the following three routes:

1.1. Two CF-causing mutations are identified

OR

1.2. One or no CF-causing mutations identified and a sweat chloride test result greater than 59 mmol/L

OR

1.3. Two CFTR mutations (not known CF-causing mutations) and a sweat chloride test result greater than 29 mmol/L

2. Age 70 days or less

3. Consent for inclusion on the national UK CF Registry

4. Consent for inclusion in the CF START trial

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Sex**

All

**Total final enrolment**

485

**Key exclusion criteria**

1. An inconclusive diagnosis after newborn screening (NBS)\*

2. A condition (non-CF) that, in the opinion of the recruiting investigator will impact on the long-term management and outcome of a participant with CF\*\*

3. Previous growth of PsA from respiratory culture

4. Infants with a history of hypersensitivity to  $\beta$ -lactam antibiotics (e.g. penicillins) or excipients

5. Infants with a history of flucloxacillin associated jaundice/hepatic dysfunction

\*Infants with an inconclusive diagnosis after NBS (termed 'CF Screen Positive Inconclusive Diagnosis (CFSPID)') should not receive standard CF care and should not be recruited into CF START (Munck et al 2015).

The two situations that result in a diagnosis of CFSPID after NBS are

1. Two CFTR mutations recognised, one or both of which are not characterised as CF-causing and the sweat chloride is less than 30 mmol/L

2. The sweat chloride is repeatedly between 30-59 mmol/L and only one or no CFTR mutations are recognised

\*\*Significant non-CF conditions might include chromosomal abnormality (for example, Down syndrome), cerebral palsy, chronic lung disease (oxygen requirement) following pre-term birth and other significant congenital anomalies (for example, severe cardiac disease, tracheo-oesophageal fistula, diaphragmatic hernia).

**Date of first enrolment**

01/11/2016

**Date of final enrolment**

04/05/2023

## Locations

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Alder Hey Children's Hospital**

East Prescott Road

West Derby

Liverpool

United Kingdom

L14 5AB

## Sponsor information

**Organisation**

Alder Hey Children's NHS Foundation Trust

**ROR**

<https://ror.org/00p18zw56>

## Funder(s)

**Funder type**

Government

**Funder Name**

National Institute for Health Research

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

## Results and Publications

**Individual participant data (IPD) sharing plan**

This is a Registry trial. Data will be collected as part of routine clinical care and will remain on the UK Registry after completion of the study. These data will be available on request from the registry steering committee.

**IPD sharing plan summary**

Available on request

**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="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes