

Imperial College
London



BREATHING ASSISTANCE IN CHILDREN WITH BRONCHIOLITIS

BACH^b Trial
Randomisation
User Training v1.0
October 2023

Randomisation User Training

Sponsor: Imperial College London

Sponsor Ref: 22HH7629

Funder: NIHR

Funder Ref: NIHR152262

CPMS ID: 57649

Chief Investigator: Dr P Ramnarayan

Study Coordination Centre: Imperial Clinical Trials Unit

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ISRCTN reference: ISRCTN52937119

FUNDED BY

NIHR | National Institute for
Health and Care Research

Coordinating Centre / Trial Management team

- Trial coordinated by Imperial Clinical Trials Unit
- Chief Investigator: Dr. Padmanabhan Ramnarayan (Ram)
- Trial Manager: Richard Cleaver
- Nurse Educator: Katy Bridges
- Trial Monitor: Yu-Chieh Chiu
 - Email: bachbstudy@imperial.ac.uk Tel: 07999 044627
 - Address: Room 503, 5th Floor, Medical School Building,
Imperial College London, St Mary's Campus, Norfolk Place,
London, W2 1PG

Introduction to BACHb

Design

- Two Stratum Multi-centre Randomised Clinical Trial of respiratory support in infants with acute bronchiolitis
- Interventional non-CTIMP

Aim

- To evaluate the clinical and cost-effectiveness of the use of HFNC separately in two distinct populations of infants with bronchiolitis (moderate and severe bronchiolitis).

Interventions

- Moderate stratum: Humidified Standard Oxygen (HSO) or High Flow Nasal Cannula (HFNC)
- Severe stratum: Continuous Positive Airway Pressure (CPAP) or High Flow Nasal Cannula (HFNC)

Population

- Hospitalised infants aged up to 12 months with a clinical diagnosis of acute bronchiolitis.
- 1508 participants over a 30 month period from 01/SEP/2023 to 31/MAR/2026
 - 924 in Moderate stratum
 - 584 in Severe stratum

Sites

- 50 hospitals across the UK – Emergency departments, Paediatric Assessment Units and general paediatric wards

Sponsor and Funder

- Imperial College London will be sponsor – Ref: 22HH7629
- Funded by the National Institute for Health and Care Research (NIHR) – Ref: NIHR152262

HRA Approval

- Reviewed by Yorkshire & The Humber - South Yorkshire Research Ethics Committee
- HRA approval granted on 21/AUG/2023
- ISRCTN registered (ISRCTN52937119)

Research questions

MODERATE BRONCHIOLITIS

In hospitalised infants with bronchiolitis not responding to low-flow nasal cannula oxygen, is the use of HFNC superior to HSO in reducing time to hospital discharge?

SEVERE BRONCHIOLITIS

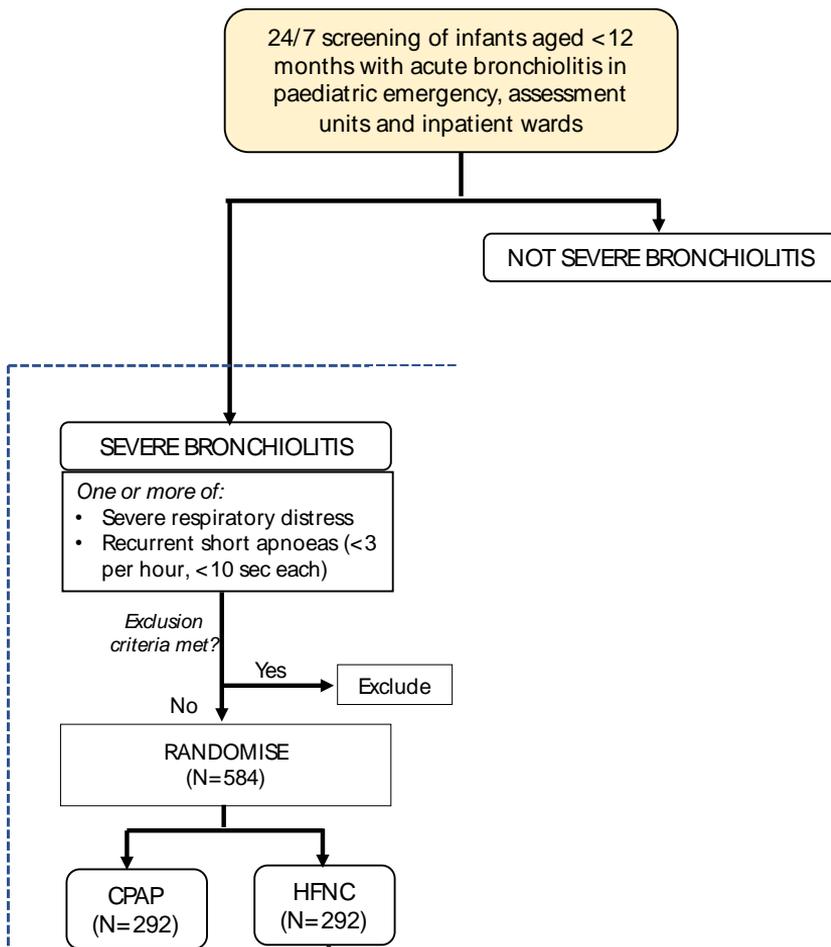
In hospitalised infants with bronchiolitis and severe respiratory distress, is the use of HFNC superior to CPAP in reducing time to hospital discharge?

Trial flow

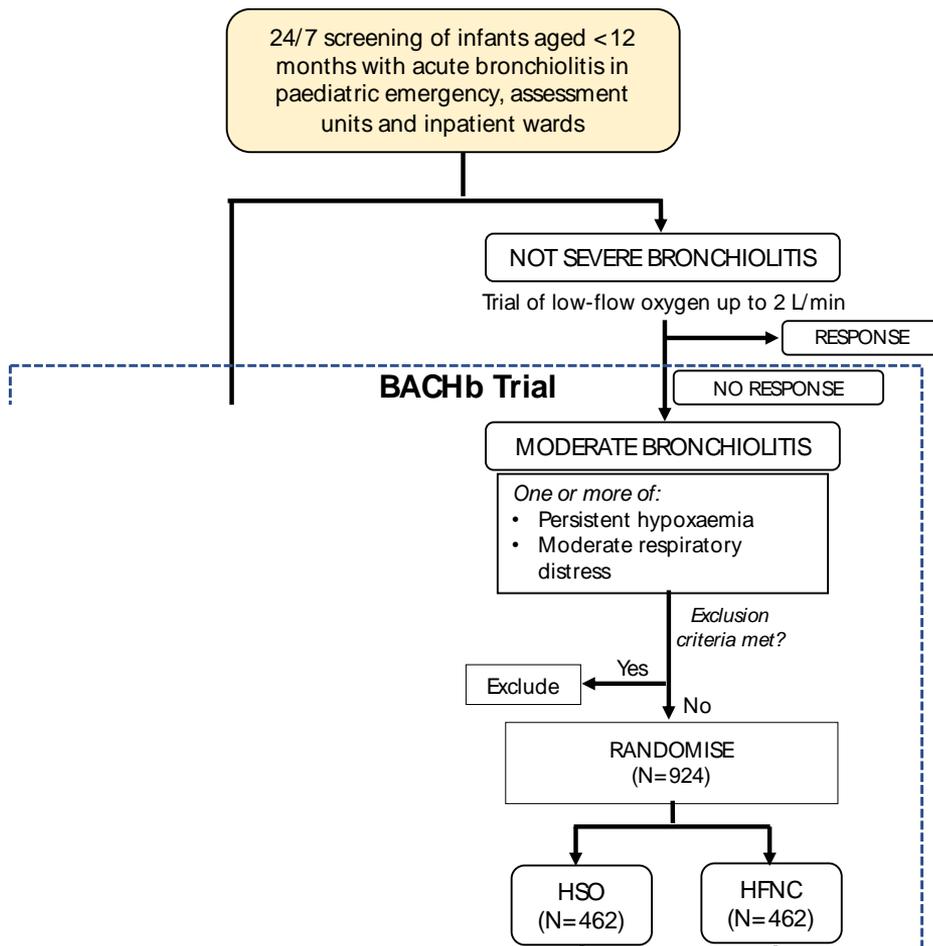
**Severe
bronchiolitis**
Severe respiratory
distress

- RR >70/min
- Grunting
- Severe retractions

AND/OR
Recurrent short apnoeas
(>3/hr, lasting <10 sec)



Trial flow



Moderate bronchiolitis

SpO₂ <90% in up to 2 L/min nasal cannula

AND/OR

Moderate respiratory distress

- RR 55-70/min
- Moderate retractions

Inclusion criteria

1) Hospitalised infant aged <12 months with a clinical diagnosis of acute bronchiolitis
AND

2) Clinically assessed at least twice 15 minutes apart to have EITHER:

a) Severe respiratory distress and/or recurrent short apnoeas
[SEVERE BRONCHIOLITIS stratum] OR

b) Lack of response to LFNC oxygen up to 2 L/min, as indicated by persistent hypoxaemia and/or moderate respiratory distress
[MODERATE BRONCHIOLITIS stratum]

Exclusion criteria

Clinical decision that patient needs immediate I&V

Prolonged apnoeas (>10 sec needing stimulation)

Ongoing active air leak

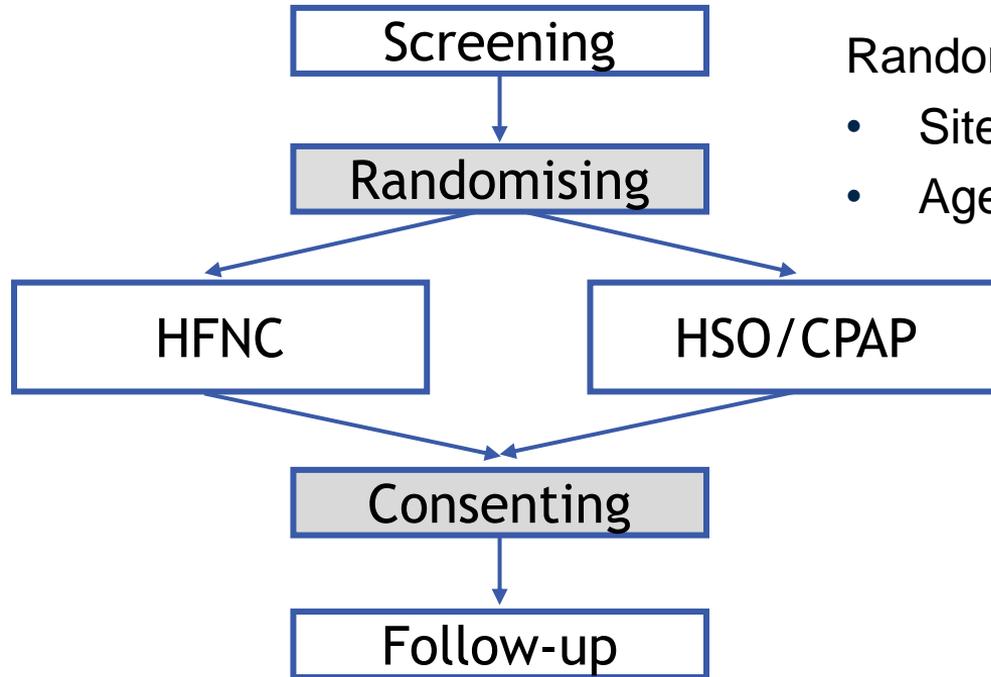
Received HSO, HFNC or CPAP for >2 hrs in past 24 hrs

On home ventilation prior to hospital admission

Tracheostomy in place

Choanal atresia/stenosis, midfacial anomalies or recent craniofacial surgery

Previously recruited to BACHb trial in the last 90 days



Randomisation stratified by

- Site
- Age <6 weeks, >/=6 weeks

Good Clinical Practice (GCP)

- International, ethical and scientific quality standard to which all research involving human participants is conducted
- Comprised of 13 core principles & applies to all clinical investigations that could affect safety and well-being of human participants, providing international assurance that:
 - Data and reported results of clinical investigations are credible and accurate
 - Rights, safety and confidentiality of participants in clinical research are respected and protected
- You are encouraged to obtain GCP certification, such as that available through NIHR:
<https://www.nihr.ac.uk/health-and-care-professionals/learning-and-support/good-clinical-practice.htm>

Principles of Good Clinical Practice (GCP)

1. Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).
2. Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
3. The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.
4. The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
5. Clinical trials should be scientifically sound, and described in a clear, detailed protocol.
6. A trial should be conducted in compliance with the protocol that has received prior Institutional Review Board (IRB)/ Independent Ethics Committee (IEC) approval/favourable opinion.

Principles of Good Clinical Practice (GCP)

7. The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.
8. Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task.
9. Freely given informed consent should be obtained from every subject prior to clinical trial participation.
10. All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
11. The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).
12. Investigational products should be manufactured, handled, and stored in accordance with applicable [Good Manufacturing Practice\(GMP\)](#). They should be used in accordance with the approved protocol.
13. Systems with procedures that assure the quality of every aspect of the trial should be implemented.

Randomisation

- Randomisation performed soon after confirming eligibility and as close as possible to anticipated start of randomised treatment
- Eligible infants enrolled into either ‘severe’ stratum or ‘moderate’ stratum based on inclusion criteria
- Once randomised to moderate stratum, infants cannot be randomised to severe stratum and vice versa
- Infants with moderate bronchiolitis missed during screening who then deteriorate and later fulfil criteria for severe bronchiolitis – **can only be randomised** to severe stratum if they have **not** received any of the trial treatments (HSO or HFNC)
- Randomisation performed using a web-based system in Sealed Envelope
- Record each randomisation on screening/randomisation log and print randomisation form

Randomisation Users – Access to Sealed Envelope

- Sealed Envelope is a browser-based randomisation system accessed via the link <https://www.sealedenvelope.com/access/> with email address and password to log-in
- **Please sign the combined training log / access request form** to complete your training and request a user account
 - ❖ Completing this training and signing training log means randomisation only users do not then need to be on Delegation Log, complete full GCP training, complete OpenClinica training, or provide CV for BACHb
- Site trial team will submit the log to Trial Management at bachbstudy@imperial.ac.uk for us to set-up your Sealed Envelope account
- You will receive confirmation of your user account and log-in details by email

Randomising in Sealed Envelope

1. Log-in using your email address and password
2. Select the BACHb Trial from the list and **click** the button to **Access with <Your Role> at <Your Site>**

Access

Please log in

To log in you must enter your registered email address and password.

Email address:
BACHbstudy@imperial.ac.uk

Password:
●●●●●●●●

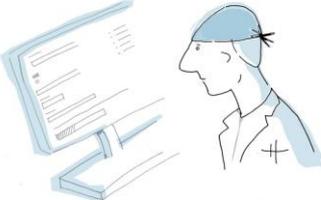
Log in

[Forgot your password?](#)

Programs and data held on this server are PRIVATE PROPERTY. Unauthorised access is prohibited and is contrary to the Computer Misuse Act 1990, which may result in criminal offences and a claim for damages. Users are reminded to keep their log in details confidential and never to share them with any other person. Users must contact Sealed Envelope Ltd immediately if they become aware of any suspicious activity.

2023-10-17 10:05:44+00:00

Access version 7.5.3



Access TRIALS MY ACCOUNT LOG OUT - BACHB TRIAL (ID 21326) sealed envelope

Trials

These are the trial applications you have access to. Some of these applications may exist in different environments, and you should take care to pick the correct one. **Live systems** are for real use in your study. The **test environment** is for testing applications – please don't enter real data in this environment.

Your last log in was 17 Oct 2023 10:06 (today)

Test

The test environment is for your user acceptance testing. Do not enter real data!

BACHb TEST

ID: bachb

Breathing Assistance in Children with bronchiolitis

Access with role: Investigator at 01: Site 01

ON Disable notifications for this role

Randomising in Sealed Envelope

3. Select **Randomise** from the menu bar in the top left
4. **Enter Participant Details** – Month and Year of Birth, whether patient has moderate or severe bronchiolitis and whether patient is in the $<$ or \geq 6 weeks age group

This is a test system for your user acceptance testing. Do not enter real data!

BACHb TRIALS HELP MY ACCOUNT LOG OUT - BACHb TRIAL (ID 21326 - INVESTIGATOR AT ST MARY'S HOSPITAL, IMPERIAL COLLEGE HEALTHCARE NHS TRUST) sealed envelope

Randomise Randomisations Queries

BACHb
Breathing Assistance in Children with bronchiolitis

Enter dummy data only into this test system. Do not enter real participant data here.

Release candidate 1.0.0-RC6, CRF revision 58

This is a release candidate for your system. Once you have completed your acceptance tests against this version and you are happy that it behaves correctly [contact us](#) and we will send you a form for signature that authorises us to make this version of your system live.
There is documentation on the system release process [available here](#).

This is a test system for your user acceptance testing. Do not enter real data!

BACHb TRIALS HELP MY ACCOUNT LOG OUT - BACHb TRIAL (ID 21326 - INVESTIGATOR AT ST MARY'S HOSPITAL, IMPERIAL COLLEGE HEALTHCARE NHS TRUST) sealed envelope

Randomise Randomisations Queries

Randomisation

Participant details

Participant ID
Automatically generated

Month and Year of birth *
Aug/2023

Does the child have moderate bronchiolitis or severe bronchiolitis?*

- MODERATE BRONCHIOLITIS: infants who have not responded to LFNC oxygen up to 2 L/min, as indicated by persistent hypoxaemia and/or moderate respiratory distress (respiratory rate 55-70/min and moderate chest recession).
- SEVERE BRONCHIOLITIS: infants with severe respiratory distress (respiratory rate >70/min, or grunting, or marked chest recession) and/or recurrent short apnoeas

Moderate
 Severe
[reset]

Age group *
 <6 weeks old
 ≥6 weeks old
[reset]

Inclusion criteria

Randomising in Sealed Envelope

5. Complete the **Inclusion and Exclusion Criteria**

6. Click the **Randomise** button at the bottom of the page

Inclusion criteria

Hospitalised infant aged <12 months with a clinical diagnosis of acute bronchiolitis? *

Yes

No

[reset]

Lack of response to LFNC oxygen up to 2 L/min, as indicated by persistent hypoxaemia (SpO2 <90%, or <92% if age < 6 weeks or if underlying health problems present)

No ▾

Lack of response to LFNC oxygen up to 2 L/min, as indicated by moderate respiratory distress (respiratory rate 55-70/min and/or moderate chest recession)

Yes ▾

Exclusion criteria

Clinical decision that patient needs immediate intubation and ventilation for life-threatening hypoxaemia, shock or decreased conscious level. *

Yes

No

[reset]

Prolonged apnoeas (>10 seconds needing stimulation) *

Yes

No

[reset]

Ongoing active air leak (pneumothorax, pneumomediastinum) *

Yes

No

[reset]

On home ventilation prior to hospital admission *

Yes

No

[reset]

Tracheostomy in place *

Yes

No

[reset]

Choanal atresia/stenosis, midfacial anomalies or recent craniofacial surgery *

Yes

No

[reset]

Previously recruited to the BACHb trial in the last 90 days *

Yes

No

[reset]

Randomise

Randomising in Sealed Envelope

7. Review the information entered on the Review and Sign page
8. If correct, enter your password at end of page and click **Confirm** button
***If incorrect use the “Back” link below the Investigator’s Declaration box to return and edit details**

This is a test system for your user acceptance testing. Do not enter real data!

BACHb TRIALS HELP MY ACCOUNT LOG OUT BACHb TRIAL (ID 21326 - INVESTIGATOR AT ST MARY'S HOSPITAL, IMPERIAL COLLEGE HEALTHCARE NHS TRUST) sealed envelope

Randomise Randomisations Queries

Review and sign

This form has not yet been saved. Please complete the declaration below to save the form.

Randomisation

Participant details

Participant ID
-
Automatically generated

Month and Year of birth
Aug/2023

Does the child have moderate bronchiolitis or severe bronchiolitis?
Moderate

Age group
≥6 weeks old

Inclusion criteria

Hospitalised infant aged <12 months with a clinical diagnosis of acute bronchiolitis?
Yes

On home ventilation prior to hospital admission
No

Tracheostomy in place
No

Choanal atresia/stenosis, midfacial anomalies or recent craniofacial surgery
No

Previously recruited to the BACHb trial in the last 90 days
No

Investigator's declaration

By entering my password below I declare that the information presented in this form accurately reflects the medical records, including the results of tests and evaluations performed on the dates specified.

Name
BACHb Trial (ID 21326 - Investigator at St Mary's Hospital, Imperial College Healthcare NHS Trust)

Date
17 Oct 2023 10:22 (UTC)

Password*
●●●●●●●●

Confirm

Back

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Randomising in Sealed Envelope

7. You should receive a **Success** pop-up box confirming randomisation and intervention
8. Click **OK** to clear the pop-up and view the Randomisation confirmation form
9. **Print** the form page and **save / file** locally for retrieval by the site trial team

This is a test system for your user acceptance testing. Do not enter real data!

BACHb TRIALS HELP MY ACCOUNT LOG OUT - BACHb TRIAL ID 21326 - INVESTIGATOR AT ST MARY'S HOSPITAL, IMPERIAL COLLEGE HEALTHCARE NHS TRUST sealed envelope

Randomise Randomisations Queries

Participant ID 01-M-0018 | 01: St Mary's Hospital, Imperial College Healthcare NHS Trust, United Kingdom

Return to participant Visit: Randomisation Create a query

Randomisation

The participant was successfully randomised.

Randomised to **1) High flow nasal cannula (HFNC)** on 17 Oct 2023 11:23 (BST)

Edit

Participant details

Participant ID
01-M-0018
Automatically generated

Month and Year of birth
Aug/2023

Does the child have moderate bronchiolitis or severe bronchiolitis?
Moderate

Age group
4-5 years old

Success
Randomised to **1) High flow nasal cannula (HFNC)** on 17 Oct 2023 11:23 (BST)

OK

This is a test system for your user acceptance testing. Do not enter real data!

BACHb TRIALS HELP MY ACCOUNT LOG OUT - BACHb TRIAL ID 21326 - INVESTIGATOR AT ST MARY'S HOSPITAL, IMPERIAL COLLEGE HEALTHCARE NHS TRUST sealed envelope

Randomise Randomisations Queries

Participant ID 01-M-0018 | 01: St Mary's Hospital, Imperial College Healthcare NHS Trust, United Kingdom

Return to participant Visit: Randomisation Create a query

Randomisation

The participant was successfully randomised.

Randomised to **1) High flow nasal cannula (HFNC)** on 17 Oct 2023 11:23 (BST)

Edit

This form was created at 17 Oct 2023 10:23 (UTC) by BACHb Trial ID 21326 - Investigator at St Mary's Hospital, Imperial College Healthcare NHS Trust

Participant details

Participant ID
01-M-0018
Automatically generated

Month and Year of birth
Aug/2023

Does the child have moderate bronchiolitis or severe bronchiolitis?
Moderate

Age group
4-5 years old

Imperial College
London

Questions

