Imperial College London

BACH♭

TRIAL

BREATHING ASSISTANCE IN CHILDREN WITH BRONCHIOLITIS

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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NIHR | National Institute for Health and Care Research

Coordinating Centre / Trial Management team

- Trial coordinated by Imperial Clinical Trials Unit

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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 BRONCHIOLTIS

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

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BREATHING ASSISTANCE IN CHILDREN WITH BRONCHIOLITIS

Severe bronchiolitis

Severe respiratory distress
- RR >70/min
- Grunting
- Severe retractions

AND/OR

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

24/7 screening of infants aged <12 months with acute bronchiolitis in paediatric emergency, assessment units and inpatient wards

NOT SEVERE BRONCHIOLITIS

SEVERE BRONCHIOLITIS

One or more of:
- Severe respiratory distress
- Recurrent short apnoeas (<3 per hour, <10 sec each)

Exclusion criteria met?

Yes → Exclude

No

RANDOMISE (N=584)

CPAP (N=292)   HFNC (N=292)

Trial flow

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BACH b TRIAL
BREATHING ASSISTANCE IN CHILDREN WITH BRONCHIOLITIS

24/7 screening of infants aged <12 months with acute bronchiolitis in paediatric emergency, assessment units and inpatient wards

NOT SEVERE BRONCHIOLITIS

Trial of low-flow oxygen up to 2 L/min

RESPONSE

NO RESPONSE

BACHb Trial

MODERATE BRONCHIOLITIS

One or more of:
- Persistent hypoxaemia
- Moderate respiratory distress

Exclusion criteria met?

Exclude

Yes

No

RANDOMISE
(N=924)

HSO
(N=462)

HFNC
(N=462)

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

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>**

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 > 6 weeks age group

Randomising in Sealed Envelope

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

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

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**

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

Questions