FIRST-line support for Assistance in Breathing in Children (FIRST-ABC): Site Initiation Visit
Agenda

Clinical
- Background
- Trial design
- Patient flow

Research
- Governance
- Support/resources
- Patient flow
- Data collection
- Safety monitoring
## Agenda

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Site Initiation Visit
Background

- Respiratory support is the most common intervention undertaken in paediatric critical care

- Greater adoption of non-invasive respiratory support in all critical care settings

- In neonates and adults, there is RCT evidence to support the early use of non-invasive respiratory support. Limited RCT evidence in the PICU setting
  - Few RCTs, mostly small, disease specific trials
  - No clear evidence of benefit
Clinical dilemma

- Patient comfort
- Risk of complications low
- Need for less intense nursing input

- May not deliver consistent or sufficient distending pressure
- Less than a decade of clinical experience

- 80% do not progress to intubation
- Long history of use

- Patient interface and comfort
- Risk of serious complications
- Need for intensive nursing input

Site Initiation Visit

CPAP

HFNC
FIRST-line support for Assistance in Breathing in Children (FIRST-ABC)

A master protocol of two randomised trials to evaluate the non-inferiority of high flow nasal cannula therapy versus continuous positive airway pressure for non-invasive respiratory support in paediatric critical care
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Research question

In critically ill children assessed by the treating clinician to require non-invasive respiratory support (NRS) [Population]

is the first-line use of high flow nasal cannula (HFNC) [Intervention]

non-inferior to continuous positive airway pressure (CPAP) [Comparator]

in terms of the time to liberation from respiratory support [Outcome]?
Study design

- Master Protocol comprising two pragmatic, multi-centre, parallel groups, non-inferiority RCTs with shared infrastructure, internal pilot and integrated economic evaluation
- 25 UK paediatric critical care units (PICUs & HDUs)
  - England, Wales and Scotland
- 600 in each RCT (1,200 altogether)
- Randomisation - 1:1 to HFNC or CPAP
- Recruitment period
  - Step-up RCT: 30 months
  - Step-down RCT: recruitment finished
Non-inferiority design

- A non-inferiority design was chosen based on previous RCTs and PICS-SG feedback indicating that the potential benefits of HFNC (patient comfort, ease of use) would mean that it would likely be preferred in practice even if not superior to CPAP.
Primary outcome

- Time to liberation from respiratory support
  - defined as the start of a 48-hour period during which the child was free of all forms of respiratory support
Secondary outcomes

- Mortality at PICU/HDU discharge, d60 and d180
- Rate of (re)intubation at 48h
- Duration of PICU/HDU and hospital stay
- Patient comfort, during randomised treatment, assessed using the COMFORT-B score
- Proportion of patients in whom sedation is used during non-invasive respiratory support
- Parental stress, in hospital at the time of consent at 24-48 hours, measured using the Parental Stressor Scale: PICU
- Health-related Quality of Life at six months using age-appropriate PedsQL and CHU9D questionnaires
Economic outcomes

- Total costs at six months
- Quality Adjusted Life Years (QALYs) at six months
- Incremental net monetary benefit
Sample size

- In each RCT, to achieve 90% power with a type I error rate of 2.5% (one-sided) to exclude the prespecified noninferiority margin of HR=0.75 (equating to estimated 16 hours of support, based on pilot study data), 508 events are required.

- Allowing for 5% censoring due to death/transfer and allowing for withdrawal/refusal of deferred consent, and for exclusion due to non-adherence in the per protocol population, we will recruit a total sample size of 600 patients in each RCT.
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Patient flow

Screening

Randomising

HFNC

CPAP

Consenting

Follow-up
Patient flow

- Screening
- Randomising
- HFNC
- CPAP
- Consenting
- Follow-up
Inclusion criteria

- Admitted/Accepted for admission to PICU/HDU
- Age >36 weeks corrected gestational age and <16 years
- Assessed by the treating clinician to require non-invasive respiratory support for an acute illness
Exclusion criteria

- Requires immediate intubation and invasive ventilation due to severe hypoxia, acidosis and/or respiratory distress, upper airway obstruction, inability to manage airway secretions or recurrent apnoeas

- Tracheostomy in place

- On home non-invasive ventilation prior to PICU/HDU admission

- Received HFNC/CPAP for >2 hours in the prior 24 hours

- Presence of untreated air-leak (pneumothorax/pneumomediastinum)

- Agreed ‘not for intubation’ or other limitation of critical care treatment plan in place

- Previously recruited to FIRST-ABC

- Midfacial/craniofacial anomalies (unrepaired cleft palate, choanal atresia) or recent craniofacial surgery

- Clinician decision to start other form of non-invasive respiratory support (i.e. not HFNC or CPAP)

SOP 003
Randomisation

- Once eligibility confirmed, child should be randomised as close to starting the treatment as possible
- Dedicated 24/7 phone/web randomisation service
- GCP training not required (study-specific training should be provided - record on Training Log)
- Randomisation Form (*next slide...*)
  - Completed and signed off by trained staff member at time of randomisation
- Whole process takes less than a few minutes
- Research team will receive an auto-generated confirmation email
Confirmation of eligibility

How to randomise

Details required by randomisation service

Confirmation of randomisation

Sign off by trained staff member
Patient flow

- Screening
- Randomising
- HFNC
- CPAP
- Consentening
- Follow-up
Principles

• Although the evidence base to guide practical aspects of non-invasive respiratory support is poor, FIRST-ABC algorithms have been developed based on best evidence and other ongoing RCTs.

• Given that there is variation in when/how non-invasive respiratory support is used, we have adopted a pragmatic approach.

• Algorithms developed using a collaborative approach to facilitate clinical buy-in.
Following randomisation, the child should be started on the randomised treatment as soon as possible.

Once the child stabilises, the treating clinician should start weaning of the treatment when study criteria are met.

The treatment should be stopped when study criteria are met and the patient monitored closely until the child has been off respiratory support for 48 continuous hours.

Switch to the other treatment (e.g. HFNC or CPAP), at the discretion of the treating clinician if child shows signs of respiratory distress or discomfort. The treatment algorithm for the other trial treatment should then be followed.

Escalation to other forms of non-invasive ventilation or invasive ventilation – at the discretion of the treating clinician if the child shows signs of respiratory distress or discomfort.

Site Initiation Visit
Patient flow

- Screening
- Randomising
- HFNC
- CPAP
- Consenting
- Follow-up
HFNC algorithm

START HFNC
Starting flow rate based on patient weight

Monitor clinically for response
If no response
If response, continue until ready to wean

TREATMENT FAILURE
Indicated by one or more of:
- Severe respiratory distress
- FiO2 ≥0.60
- Patient discomfort

SWITCH
To CPAP (see CPAP algorithm)

ESCALATION
To other forms of Non-Invasive AND/OR Invasive Ventilation

Consider WEANING when
FiO2 is ≤0.40 AND respiratory distress is not severe
Change to Weaning flow rate* based on patient weight

Monitor clinically for deterioration
If no deterioration, continue HFNC until ready to stop
If deterioration

WEANING FAILURE
Indicated by one or more of:
- Worse respiratory distress
- FiO2 >0.40

Consider STOPPING when
One or more of:
- FiO2 <0.30
- Mild/no respiratory distress

OFF HFNC for ≥48 hours
Trial treatment complete

Weight (kg) ≤12 13-15 16-30 31-50 >50
Starting flow rate 2 l/min 25-30 l/min 35 l/min 40 l/min 50 l/min
Weaning flow rate 1 l/min 13-15 l/min 18 l/min 20 l/min 25 l/min

Assess COMFORT-B score at least once during first six hours and then at least every six hours.

FIRST-ABC

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SOP 005
HFNC algorithm

- Any approved medical device can be used to deliver HFNC, as per local guidance and usual practice.
- The starting flow rate in the Table is based on best available evidence and is consistent with the ongoing PARIS 2 trial in Australia.

<table>
<thead>
<tr>
<th>Patient Weight</th>
<th>Starting flow rate</th>
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<tbody>
<tr>
<td>≤12 kg</td>
<td>2 l/min/kg</td>
</tr>
<tr>
<td>13-15 kg</td>
<td>25-30 l/min</td>
</tr>
<tr>
<td>16-30 kg</td>
<td>35 l/min</td>
</tr>
<tr>
<td>31-50 kg</td>
<td>40 l/min</td>
</tr>
<tr>
<td>&gt;50 kg</td>
<td>50 l/min</td>
</tr>
</tbody>
</table>

START HFNC

Starting flow rate based on patient weight (see Table)

SOP 005
HFNC algorithm

<table>
<thead>
<tr>
<th>Patient Weight</th>
<th>Weaning flow rate</th>
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</thead>
<tbody>
<tr>
<td>≤12 kg</td>
<td>1 l/min/kg</td>
</tr>
<tr>
<td>13-15 kg</td>
<td>13-15 l/min</td>
</tr>
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<td>18 l/min</td>
</tr>
<tr>
<td>31-50 kg</td>
<td>20 l/min</td>
</tr>
<tr>
<td>&gt;50 kg</td>
<td>25 l/min</td>
</tr>
</tbody>
</table>

- It is recommended that patients are assessed for readiness to wean at least twice per day (e.g. at ward rounds)

START HFNC

Starting flow rate based on patient weight (see Table)

Monitor clinically for response

If response, continue until ready to wean

Consider WEANING when

FiO2 is ≤0.40 and respiratory distress is not severe

Change to Weaning flow rate based on patient weight (see Table)

Monitor clinically for deterioration

SOP 005
HFNC algorithm

START HFNC
Starting flow rate based on patient weight (see Table)

Monitor clinically for response
If response, continue until ready to wean

Consider WEANING when
FiO2 is ≤0.40 and respiratory distress is not severe
Change to Weaning flow rate based on patient weight (see Table)

If no deterioration, continue HFNC until ready to stop
Monitor clinically for deterioration

Consider STOPPING when
One or more of:
- FiO2 <0.30
- mild/no respiratory distress

HFNC can be stopped when the treating clinician decides that the child does not need any further respiratory support, when the FiO2 and respiratory distress criteria are met.

Standard oxygen therapy <=2 L/min only provides an FiO2 of <0.30
HFNC algorithm

START HFNC
Starting flow rate based on patient weight (see Table)

If response, continue until ready to wean

Consider WEANING when
FiO2 is ≤0.40 and respiratory distress is not severe
Change to Weaning flow rate based on patient weight (see Table)

If no deterioration, continue HFNC until ready to stop

Consider STOPPING when
One or more of:
- FiO2 < 0.30
- mild/no respiratory distress

OFF HFNC for ≥48 hours
Trial treatment complete

[The primary outcome is the time to liberation from any form of respiratory support (for at least 48 hours).]

SOP 005
HFNC algorithm

START HFNC

Starting flow rate based on patient weight (see Table)

Monitor clinically for response

If no response

If response, continue until ready to wean

TREATMENT FAILURE

Indicated by one or more of:

- Severe respiratory distress
- FiO2 ≥0.60*
- Patient discomfort

SWITCH

To CPAP (see CPAP algorithm)

ESCALATION

To other forms of Non-Invasive Ventilation AND/OR Invasive Ventilation

Consider
HFNC algorithm

START HFNC
Starting flow rate based on patient weight *(see Table)*

If response, continue until ready to wean

Monitor clinically for response

Consider WEANING when

- FiO2 is ≤0.40 and respiratory distress is not severe

Change to Weaning flow rate based on patient weight *(see Table)*

Monitor clinically for deterioration

If no deterioration, continue HFNC until ready to stop

Consider STOPPING when

One or more of:
- FiO2 <0.30
- Mild/no respiratory distress

OFF HFNC for ≥48 hours

Trial treatment complete

WEANING FAILURE
Indicated by one or more:
- Respiratory distress worse
- FiO2 >0.40

SOP 005
HFNC algorithm

START HFNC
Starting flow rate based on patient weight (see Table)

If response, continue until ready to wean
Monitor clinically for response

Consider WEANING when
FiO2 is \( \leq 0.40 \) and respiratory distress is not severe
Change to Weaning flow rate based on patient weight (see Table)

If no deterioration, continue HFNC until ready to stop
Monitor clinically for deterioration

Consider STOPPING when
One or more of:
- FiO2 <0.30
- mild/no respiratory distress

OFF HFNC for \( \geq 48 \) hours
Trial treatment complete

WEANING FAILURE
Indicated by one or more:
- Respiratory distress worse
- FiO2 >0.40

Consider

ESCALATION
To other forms of Non-Invasive Ventilation AND/OR Invasive Ventilation

Consider

SWITCH
To CPAP (see CPAP algorithm)

Back to Starting flow rate

Trial treatment complete

SOP 005

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HFNC algorithm

START HFNC
Starting flow rate based on patient weight (see Table)

If response, continue until ready to wean

Monitor clinically for response

Consider WEANING when
FiO2 is ≤0.40 and respiratory distress is not severe

Change to Weaning flow rate based on patient weight (see Table)

Monitor clinically for deterioration

If no deterioration, continue HFNC until ready to stop

Consider STOPPING when
One or more of:
- FiO2 <0.30
- mild/no respiratory distress

OFF HFNC for ≥48 hours

Trial treatment complete

If clinically worse restart HFNC and consider

Back to Starting flow rate

Back to weaning flow rate

Trial treatment complete
Patient flow

- Screening
  - Randomising
    - HFNC
    - CPAP
  - Consenting
CPAP algorithm

CONTINUOUS POSITIVE AIRWAY PRESSURE

START CPAP
Starting pressure: 7-8 cm H₂O

Monitor clinically for response

If no response

TREATMENT FAILURE
Indicated by one or more of:
- Severe respiratory distress
  - FiO₂ ≤ 0.60*
- Patient discomfort

If response, continue until ready to wean

Consider WEANING when
FiO₂ is ≤ 0.40 AND
respiratory distress is not severe
Change to 5 cm H₂O pressure

Monitor clinically for deterioration

If no deterioration, continue CPAP until ready to stop

If deterioration

Consider STOPPING when
One or more of:
- FiO₂ < 0.30
- Mild/no respiratory distress

OFF CPAP for ≥ 48 hours
Trial treatment complete

If clinically worse, restart CPAP and consider

SWITCH
To HFNC (see HFNC algorithm)

ESCALATION
To other forms of Non-Invasive AND/OR Invasive Ventilation

WEANING FAILURE
Indicated by one or more of:
- Worse respiratory distress
  - FiO₂ > 0.40

Back to 7-8 cm H₂O

Back to 5 cm H₂O

Assess COMFORT-B score at least once during first 6 hours and then at least every 6 hours.

SOP 006
CPAP algorithm

- Any approved medical device can be used to deliver CPAP, as per local guidance and usual practice.
- The starting pressure is based on best available evidence, mainly from physiological studies in PICU.
Once the child shows signs of improvement, the treating clinician will usually decide to start weaning CPAP.

Clinicians will still be able to start weaning at their discretion, as long as the study criteria are met.

Weaning CPAP during the trial involves reducing the pressure from 7-8 to 5 cm H$_2$O.
CPAP algorithm

START CPAP
Starting pressure 7-8 cm H₂O

Monitor clinically for response

If response, continue until ready to wean

START WEANING when
FiO₂ is 0.30 to 0.40 and respiratory distress is not severe
Change to 5 cm H₂O

Monitor clinically for deterioration

If no deterioration, continue CPAP until ready to stop

Consider STOPPING when
One or more of:
- FiO₂ <0.30
- mild/no respiratory distress

SOP 006
CPAP algorithm

**START CPAP**
Starting pressure 7-8 cm H₂O

Monitor clinically for response

*If no response*

*If response, continue until ready to wean*

**TREATMENT FAILURE**
Indicated by One or more:
- Severe respiratory distress
- FiO₂ ≥0.60*
- Patient discomfort

**Consider**

**SWITCH**
To HFNC (see HFNC algorithm)

**ESCALATION**
To other forms of Non-Invasive Ventilation AND/OR Invasive Ventilation
CPAP algorithm

START CPAP
Starting pressure 7-8 cm H₂O

If response, continue until ready to wean

Monitor clinically for response

Consider WEANING when
FiO₂ ≤0.40 and respiratory distress is not severe

Change to 5 cm H₂O

If no deterioration, continue CPAP until ready to stop

Monitor clinically for deterioration

Consider STOPPING when
One or more of:
- FiO₂ < 0.30
- mild/no respiratory distress

OFF CPAP for ≥48 hours

Trial treatment complete

Consider WEANING FAILURE
Indicated by one or more:
- Respiratory distress worse
- FiO₂ > 0.40

If deterioration

SWITCH
To HFNC (see HFNC algorithm)

To other forms of Non-Invasive Ventilation AND/OR Invasive Ventilation

ESCALATION

OFF CPAP for ≥48 hours

Trial treatment complete

Back to 7-8 cm H₂O

SOP 006
Once CPAP has been stopped - if the child deteriorates and requires some form of support within 48 hours, the clinical team can choose to either go back to CPAP at 5 cm or 7-8 cm based on clinical assessment until they are finally off all forms of respiratory support for 48 hours.

SOP 006
Online training

- An online training package, primarily focused on the treatment algorithms, will be available to sites.
- Less than 30 minutes to complete.
- Aimed at clinical staff delivering HFNC/CPAP.
  - Encourage as many clinical staff as possible to complete the training to facilitate adherence to the protocol.
- Compatible with most modern internet browsers (as well as mobile phones/tablets).
- Certificate available upon completion.

Link to access the training: [http://tiny.cc/firstabc](http://tiny.cc/firstabc)
Participating sites

Addenbrookes' Hospital
Alder Hey Children’s Hospital
Birmingham Women and Children’s Hospital
Bristol Royal Hospital for Children
Chelsea and Westminster Hospital
Evelina London Children’s Hospital
Great North Children’s Hospital
Great Ormond Street Hospital
Hull Royal Infirmary
John Radcliffe Hospital
James Cook University Hospital
King’s College Hospital
Southampton Children’s Hospital
Leicester Royal Infirmary and Glenfield Hospital
Luton and Dunstable University Hospital
Royal Blackburn Teaching Hospital

Site Initiation Visit

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Agenda

**Clinical**
- Background
- Trial design
- Patient flow

**Research**
- Governance
- Support/resources
- Patient flow
- Data collection
- Safety monitoring
Governance - Central

• Sponsor:
Great Ormond Street Hospital for Children
NHS Foundation Trust

• Clinical Trials Unit:
ICNARC CTU
Governance - Central

- Ethics: East of England - Cambridge South REC (Ref: 19/EE/0185)
  - Favourable ethical opinion - 26 July 2019

- HRA/HCRW Approval (IRAS number: 260536)
  - Approval - 26 July 2019

- NIHR CPMS ID: 42112

- ISRCTN Registry ID: ISRCTN60048867
Governance - Local

- Local confirmation of capacity and capability
  - Local site document packs sent

- Site responsibilities/activation
  - Signed Clinical Trial Site Agreement
  - Delegation Log and Staff Contacts Form

- All needed prior to site activation
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ICNARC CTU

Email: firstabc@icnarc.org

Tel: 020 7269 9277

Web: icnarc.org/Our-Research/Studies/FIRST-ABC
Support/resources

- Site Initiation Visits
- Site teleconferences
- Routine Monitoring Visits
- Newsletters
- Posters
- HFNC/CPAP prompts

...let us know if you have any other ideas!
Local resources

- Direct research costs from the grant
  - Quarterly infrastructure payments:
    - Participation in step-up RCT: £250 per quarter
  - Per patient payments:
    - £150 per eligible patient recruited

- Invoices submitted to ICNARC quarterly
  - Must include a PO number requested beforehand
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Patient flow

- Screening
  - Randomising
  - HFNC
  - CPAP
  - Consenting
  - Follow-up
Electronic Screening and Enrolment Log

- Excel spreadsheet
- Record all admissions to the unit
Electronic Screening and Enrolment Log

<table>
<thead>
<tr>
<th>Section A: Child details</th>
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<tbody>
<tr>
<td>Hospital number / local identifier</td>
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- Screening Outcomes:

- Randomised (Section B)
- Not randomised - Met ≥1 exclusion criteria (Section C)
- Eligible not randomised (Section D)
- Not randomised - Eligibility unknown

Site Initiation Visit
## Electronic Screening and Enrolment Log

### Section B:

<table>
<thead>
<tr>
<th>Trial Number</th>
<th>Requires immediate intubation and invasive ventilation</th>
<th>Clinician decision to start other form of non-invasive respiratory support (i.e. not HFNC or CPAP)</th>
<th>Tracheostomy in place</th>
<th>Received HFNC/CPAP for &gt;2 hours in the prior 24 hours</th>
<th>On home NIV prior to unit admission</th>
<th>Presence of untreated air-leak (pneumothorax/pneumomediastinum)</th>
<th>Mid/cranio-facial anomalies (unrepaired cleft palate, choanal atresia) or recent craniofacial surgery</th>
<th>Agreed ‘not for intubation’ or other limitation of critical care in place</th>
<th>Previously recruited to FIRST-ABC (step-up or step-down)</th>
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<tr>
<td>19001</td>
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### Site Initiation Visit
### Section D:

<table>
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<tr>
<th>Reason not randomised</th>
<th>Comments</th>
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</table>

- Select reason and explain in Comments section

#### Clinical decision

- Parental decision
- Missed/identified too late
- Lack of HFNC/CPAP devices
- Other (state in Comments)

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**Site Initiation Visit**

**SOP 003**
Screening and Enrolment Log

• Submit regularly to ICNARC CTU
  – e.g. fortnightly
  – email to firstabc@icnarc.org

• Do not submit any identifiable information
# Screening Tool (optional)

**Screening Tool**

<table>
<thead>
<tr>
<th>Hospital number</th>
<th>Hospital Acceptance to PICU/HRU? (Y/N)</th>
<th>Age &gt;36 weeks corrected gestational age and &lt;16 years? (Y/N)</th>
<th>Requires non-invasive respiratory support...</th>
<th>...within 72 hours post extubation? (Y/N)</th>
<th>Eligibility confirmed by Name of staff</th>
<th>If randomised Trial Number</th>
<th>If not randomised Provide reason</th>
</tr>
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**First ABC Screening Tool**

**Exclusion criteria**

- Requires immediate intubation and invasive ventilation due to severe hypoxia, acidosis and/or respiratory distress.
- Upper airway obstruction, inability to manage airway secretions or recurrent apnoeas.
- Tracheotomy in place.
- Received HFOV/CPAP for >2 hours in the prior 24 hours.
- On home non-invasive ventilation prior to critical care unit admission.
- Presence of uncorrected air leak (pneumothorax/pneumomediastinum).
- Midfacial/craniofacial anomalies (unipalatal cleft palate, choanal atresia) or recent craniofacial surgery.
- Agreed 'not for intubation' or other limitation of critical care treatment plan in place.
- Previously recruited to FIRST-ABC

**Unsure if a patient is eligible? Contact**

- Your Principal Investigator or research team for assistance.
- ICNARC CICU: 02072699277 (in office hours) or 02072699290 (emergency; out of office hours).
- For non-urgent queries, email: firstabc@icnarc.org

*FIRST-ABC Screening Tool v1.0, 24 May 2019*
Patient flow

- Screening
- Randomising
- HFNC
- CPAP
- Consentting
- Follow-up
Co-enrolment

- Observational studies
  - Permitted

- Interventional studies
  - Agreement to be sought
    - Agreement confirmed between: BESS, INHALE, OXY-PICU
  - Ongoing/upcoming trials?
  - Record on CRF
Patient flow

- Screening
- Randomising
- HFNC
- CPAP
- Consenting
- Follow-up
Patient flow

Screening

Randomising

HFNC

CPAP

Consenting

Follow-up
Deferred consent (i)

- Due to the emergency and time-sensitive nature of the clinical situation, FIRST-ABC will use a research without prior consent model.

- Model devised in line with the CONseNt methods in paediatric Emergency and urgent Care Trials (CONNECT) study guidance.
  - Developed by Dr Kerry Woolfall and colleagues.

- Used in previous paediatric critical care trials.
  - FiSh, Oxy-PICU, Fever & FIRST-ABC Pilot Studies.
Deferred consent (ii)

- Previous research shows that many parents are unfamiliar with research without prior consent but
- Parents supported its use in the FIRST-ABC Pilot Study (and other trials aimed at improving treatments for critically ill children)

- Parents gave deferred consent in the FIRST-ABC Pilot Study because...
  - they wanted to help other children in the future (100%)
  - they felt that studies like FIRST-ABC are important (95%)
Procedure

- Child confirmed eligible

- Randomisation

- When appropriate, once child has stabilised - but usually 24-48 hours after randomisation

- Approach parent/legal guardian for informed consent

- Upon recovery, approach child for assent (if appropriate)
Timing of approach

- Check timing is appropriate
  - Parents happy to be approached once child is stable and after initial stress
  - Consult nursing staff about child’s condition and their views on how parents are coping
  - Ask nursing staff to introduce you and ask parents if convenient time to discuss research

- Bereaved - may not be appropriate in hospital

- Every parent is different, should gauge case by case
Procedure

- Provide information
- Allow time to read information sheet
- Invite/encourage questions
- Confirm decision
Explaining the study (i)

- Information should be clear, concise and not medicalised

- Explain:
  - why we are doing FIRST-ABC
  - why consent cannot be sought in emergency situations
  - Explain respiratory support and CPAP/HFNC in simple, easy to understand terms

- Allow time to think about the study, discuss with friends/family and ask questions
Documents

- Parent/Legal Guardian Information Sheet
- Parent/Legal Guardian Consent Form (and associated postal or bereaved versions)
- Parent/Legal Guardian Information Leaflet
- Age-appropriate Patient Information Sheets
- Assent Form
Consent options

- Continued participation (e.g. treatment)
- Access to medical notes for data collection
- Experiences and reactions questionnaire in-hospital
- Questionnaire follow-up at six months
- Sharing of anonymised data
- Contact about future research participation

- If parent/guardian declines, clarify which aspects they are declining
  - e.g. they may be willing to allow access to medical notes for data collection but may not want to receive the follow-up questionnaire at six months
FIRST-line support for Assistance in Breathing in Children

Consent Form - Parent or Legal Guardian
Version 1.2, 17 January 2020

To be completed by the Researcher:
Hospital name: 
Trial Number: 
Child’s full name: 

To be completed by the Parent or Legal Guardian:
Once you have read and understood each statement – if you agree, please write your initials in each box

1. I confirm that I have read and understood the Participant Information Sheet (version 1.2, dated 27/11/2019) for the above research study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. 

2. I understand that participation is voluntary, and that I am free to withdraw consent at any time, without giving any reason and without my child’s medical care or legal rights being affected.

3. I agree to for my child to continue to take part in this study.

4. I understand that relevant sections of my child’s medical records and data collected during the study (including name, date of birth, postcode and NHS number), held by the NHS or by NHS Digital, may be looked at by individuals from the NHS Trust, the Intensive Care National Audit & Research Centre (ICNARC), NHS Digital or regulatory authorities where it is relevant to my participation in this research. I give permission for these individuals to have access to my child’s records.

5. I agree to complete a questionnaire about my experiences and reactions to being in the intensive care or high dependency unit.

6. I understand that ICNARC will send me a questionnaire to find out how my child is doing in six months time.

7. I understand that the information collected in the study will be used to support other research in the future, and may be shared anonymously with other researchers.

8. I would like to be contacted about any future related studies.

Your signature: ___________________________ Date: ___________________________
Your full name (PRINT): ___________________________
Researcher signature: ___________________________ Date: ___________________________
Researcher full name (PRINT): ___________________________

Once signed please turn over and complete

Consent Form (Parent or Legal Guardian) v1.2, 17 January 2020
Parental Stressor Scale

- If in agreement, parents invited to complete questionnaire at/around the time of consent

- Option to go through the questionnaire with the parent or leave with them and collect later

- If there are questions the parent does not wish to answer, those questions can be left blank

- Data entered onto the eCRF
Refusal/Withdrawal of consent

- All data occurring up to time of refusal/withdrawal retained, unless parent/legal guardian requests otherwise

- Total vs. partial - may withdraw from different parts, clarify which

- Choice of whether to continue on or switch from the randomised treatment will be made by the treating clinician
When to approach - bereaved

- In hospital
  - It is at the discretion of site staff to determine if appropriate for each family
  - Obtain information from colleagues and bereavement counsellors
  - Establish the most appropriate research team member to notify parents of involvement in research study
  - Follow in hospital consenting procedures
When to approach - bereaved

- By post
  - Post first consent package four weeks after randomisation
    - Personalised covering letter and copy of PIS and consent form

  - If no response after four weeks, send second follow-up consent package
Assent

- To be obtained prior to hospital discharge if condition allows (e.g. regain capacity)

- Follow parent consenting procedures

- Involve parents when discussing study with patient

- If likely to regain capacity after hospital discharge, provide parents with age-appropriate information sheet
Responsible staff

- Principal Investigator (PI)
- GCP trained research staff (on Delegation Log)
Follow-up

• Centrally conducted questionnaire follow-up at six months post-randomisation

• Measures
  – Pediatric Quality of Life Inventory (PedsQL)
  – Child Health Utility (CHU9D)
  – Health services/resource use questionnaire

• Option to receive questionnaire by email or post
  – Telephone follow-up if no response

• Survival confirmation with sites ahead of questionnaire being sent and then again at end of study
  – Access to NHS Spine?
Site Initiation Visit

Agenda

Clinical
- Background
- Trial design
- Patient flow

Research
- Governance
- Support/resources
- Patient flow
- Data collection
- Safety monitoring
Case Report Forms

- Randomisation Form
- Parental Stressor Scale
- Case Report Form
- FIRST-ABC/PICANet Condensed Report Form
- SAE Reporting Form
e-CRF

- Secure web-based data entry system:
  - [https://ctu.icnarc.org/macro/](https://ctu.icnarc.org/macro/)
  - Full audit trail - all changes to data are recorded against a named user

- Email [firstabc@icnarc.org](mailto:firstabc@icnarc.org) to set-up an account
  - Individual must be listed on Delegation Log

- Data should be entered promptly
Agenda

Clinical
- Background
- Trial design
- Patient flow

Research
- Governance
- Support/resources
- Patient flow
- Data collection
- Safety monitoring
Safety monitoring

- From randomisation until the time of liberation from all forms of respiratory support for 48 hours

- Adverse Events (AEs)
  - Specified and unspecified

- Serious Adverse Events (SAEs)
  - Report on SAE Reporting Form
  - ICNARC CTU must be informed within 24 hours of the site team becoming aware of the event
Timeline from here

- FIRST-ABC opened to recruitment on 6 August 2019
  - First patient - Great Ormond Street Hospital
  - 22 sites currently open

- Today - SIV

- Between now and opening -
  - Commence training with your local staff
  - Receive access to online training
  - Obtain local approvals and sign contract
  - Send Delegation Log/Research Staff Contacts Form
  - Set-up access to Randomisation System and eCRF

- ...commence screening/recruitment!

Site Initiation Visit