Children's Hospital of Philadelphia

Informed Consent/Study Summary Document and HIPAA Authorization Form

Study Title: Pilot Cross-Over Trial of Neurally Adjusted Ventilatory Assist (NAVA) and Coventional Flow Triggered Mechanical Ventilation in Severe Bronchopulmonary Dysplasia (BPD)

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Study Overview:

Your child may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research study, and the risks and possible benefits of participating.

In the sections that follow, the word "we" means the study clinical team and other research staff. If you are a parent or legal guardian who is giving permission for a child, please note that the word "you" refers to your child.

You are being asked to take part in this research study because you have been diagnosed with bronchopulmonary dysplasia (BPD), a form of chronic lung disease that occurs in premature infants, and are receiving support from a mechanical ventilator (a machine that help people breathe when they are not able to breathe enough on their own).

The purpose of this study is to compare your breathing, supplemental oxygen need, and comfort using two different modes on the mechanical ventilator: conventional mechanical ventilation (CMV) and neutrally adjusted ventilatory assist (NAVA). CMV is a standard therapy in this hospital. NAVA is a new therapy in this hospital. NAVA uses a small tube placed in your esophagus to measure the breathing signals in your nerves. The ventilator uses these signals to determine the amount of support you receive with each breath.

If you agree to take part, your active participation will last for 11 days, with 1 day in observation, 5 days in the first ventilation mode and 5 days in the second ventilation mode. After the 11 day study period, we will follow your progress by reviewing your medical record until hospital discharge.

If you take part there will be:

- Medical record review
- Placement of the NAVA catheter in your esophagus
- Use of a skin monitor to measure carbon dioxide levels in the body
- Collection of saliva to measure cortisol levels
- Treatment with CMV and NAVA modes of ventilation

The main risks of this study are associated with the use of the NAVA mode of ventilation. NAVA is not part of routine clinical care at this hospital but is used at other

hospitals to treat infants and children with BPD. The possible risks associated with the use of NAVA include lower oxygen and/or higher carbon dioxide levels in the blood, decreased comfort, greater work of breathing, cardiac arrest, or death. You will not have any direct benefit from participating in this study.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this study if you do not want to. If you take part, you can leave the study at any time. If you do not choose to take part in this study, you can discuss treatment options with your doctor.

Please see below for additional details about the study.

What is the purpose of this research study?

The purpose of this study is to compare your breathing, oxygen need, and comfort during two different modes on the mechanical ventilator: conventional mechanical ventilation (CMV) and neutrally adjusted ventilatory assist (NAVA).

CMV is the name for the common modes used on a mechanical ventilator. To use this mode, the clinician sets all the specific pieces of breathing that will be delivered by the mechanical ventilator to help you breathe. This includes the rate (how many breaths in one minute), how big the breath is (tidal volume), and how long it will take to get a full breath (inspiratory time). When you take a breathe on your own, the ventilator senses this by detecting a change in pressure or flow in the ventilator circuit as you take a breathe in. When the ventilator senses your breath, it gives you extra support based on the settings ordered by your doctor.

NAVA is a different mode on a mechanical ventilator. In this mode, most of the features of the breaths delivered by the ventilator are determined by measuring your own breathing effort with each breath instead of by the settings ordered by your doctor. A NAVA catheter (similar in size and shape to a standard feeding tube) is inserted through your nose and into the stomach. Electrodes on the catheter sense the electrical signals your body uses to move your breathing muscles and determines the size and length of the breath based on these signals. NAVA may sense your breathe before the standard mode (CMV) and begin supporting your breathing sooner.

How many people will take part?

About 25 children will take part in this study.

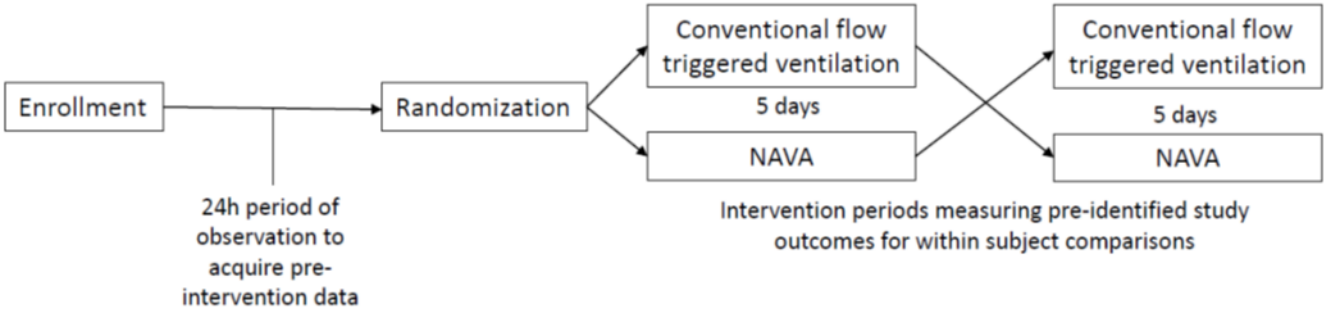
What is the current standard of treatment for this disease?

Children with BPD at CHOP that need help from a mechanical ventilator to breathe receive CMV.

What is involved in the study?

A NAVA catheter, which is similar in size and shape to a standard feeding tube but also has sensors along its length that measure electrical activity in the nearby nerves, will be inserted through your nose and into the stomach. This tube may be used instead of your regular feeding tube at the choice of your doctor. For the first 24 hours after the catheter is placed, we will record baseline information about your breathing. After this first day, a computer will pick at random which ventilation mode you will use for the next 5 days

(either CMV or NAVA). After 5 days on the first ventilator mode, a new NAVA catheter will be placed, and you will be switched to the alternate ventilator mode for 5 days. When on the NAVA mode, your ventilator will be changed to one that works with the NAVA catheter. When on the CMV mode, you will use the standard ventilator prescribed by your doctor. We will monitor your child's breathing, comfort, and tolerability of the two ventilator modes throughout the 11 trial period as shown in the figure below.



How long will you be in this study?

If you agree to take part, your active participation will last for 11 days including 1 day in observation, 5 days using the first ventilator mode and 5 days using the alternate ventilator mode. We will periodically review your medical record until hospital discharge.

What are the study procedures?

Some of the procedures in this study will be repeated several times. Tests that are part of your regular, routine medical care will continue to be performed. The study involves the following tests and procedures.

Medical history:
A study team member will record your medical history important to this study, incuding medications, diagnosis, blood test results, and imaging results.

NAVA catheter placement:
This catheter is placed to sense from your diaphragm when you want to take a breath. This will be placed before the observation period and before starting the second ventilator mode on day 6. This tube may also be used to deliver feedings if prescribed by your doctor.

Transcutaneous carbon dioxide monitor (Tcom):
A transcutaneous monitor is a non-invasive way to measure the amount of carbon dioxide in the blood. Carbon dioxide is a gas produced by the body that is breathed out by the lungs. Measuring the amount that remains in the body helps us determine how well you are breathing and if you are getting enough support from the mechanical ventilator. This machine is routinely used for this purpose in the ICU for care of children.

Salivary cortisol levels:
Saliva will be collected from your mouth with a sterile (clean) cotton swab 3 times per day during each of the 11 days of the trial. We will use the samples to compare corticol levels, a marker of stress in the body, during the different modes of ventilation.

Treatment with CMV and NAVA modes of ventilation:
During the first day of the study a specialized feeding tube will be inserted through your nose and into your stomach. You will be watched for 24 hours while vital signs and the activity of the diaphragm are recorded. Once the observation period ends, a computer will pick at random which mode of ventilation you will begin first (CMV or NAVA). You will be on the first mode of ventilation for 5 days. After the 5 days you will be switched to the second mode of ventilation. Your ventilator settings will be adjusted as needed by your medical team with the help of the study doctors. Data on breathing, oxygen need, and comfort will be recorded through the 11 day.

What will be done with my data and specimens during this study?

During the study, we will collect saliva samples from you. By agreeing to participate in the study, you agree to give these samples to CHOP for research purposes.

Will I receive any results from the tests done as part of this study?

Results that could be important for your clinical care will be shared with you. We will not share other results with you.

What are the risks of this study?

Taking part in a research study involves inconveniences and risks. The main risks of taking part in this study are discussed below.

Risks of NAVA ventilator mode:

The NAVA mode on the ventilator is not used for routine care at CHOP, although it is used at some hospitals to treat childen with lung disease that is similar to yours. Since we do not have clinical experience with this mode of ventilator at this hospital, other than through this research study, we do not yet know how it will affect your breathing. Treatment with NAVA may worsen or improve the amount of amount of extra oxygen you need, the level of carbon dioxide in your blood, and your work of breathing and comfort. Treatment with NAVA may also worsen or improve your vital signs such as heart rate and blood pressure. In the most severe possible case, worsening of vital signs while receiving mechanical ventilation could lead to cardiac arrest or death. The study team and your doctors will closely monitor your breathing and vital signs throughout the trial and make necessary adjustments to your ventilator. This may include stopping the NAVA mode early and returning you to your routine mode of ventilation.

Risks of the NAVA catheter:

The NAVA catheter is similar in size and shape to a feeding tube. It will be inserted through your nose or mouth by your nurse just like a feeding tube. The insertion may cause a gagging sensation or throat irritation. A NAVA catheter will be in place throughout the 11 day trial and will be replaced after the first 6 days. If you receive feedings through a feeding tube placed in your nose or mouth, your doctor may use the NAVA catheter to administer your feedings instead of the standard feeding tube. However, the NAVA catheter may also be placed in addition to your current feeding tube.

Risks with transcutaneous carbon dioxide (CO_2) monitoring:

To measure the CO_2 level in your blood without a blood draw, a non-invasive probe called a transcutaneous CO_2 monitor is placed on your skin. The probe modestly heats the skin and may leave a temporary red mark that resolves after the probe is moved. There is a small chance of burning the skin if the probe is left in place for too long. To help prevent any skin injury, your nurse or respiratory therapist will move the position of the probe several times per day.

Risks of breach of privacy and confidentiality:

As with any study involving collection of data, there is the possibility of breach of confidentiality. Every precaution will be taken to secure you personal information to ensure confidentiality.

Are there any benefits to taking part in this study?

There is no direct benefit to you from taking part in this study. The knowledge gained from this study may help doctors determine the most effective ventilator options for children with sBPD.

Do you need to give your consent in order to participate?

If you decide to participate in this study, you must sign this form. Non-English speakers must sign the short form consent. A copy of this consent form will be given to you to keep as a record.

The consent discussion will be conducted in the NICU in a private setting (e.g. at the bedside, in a private meeting room) where possible, or via telephone or video conference. A study team member will describe the goals and procedures involved in the study. Parents or guardian(s) will be provided the opportunity to ask questions about the study and to discuss the study with their family, friends, and/or other medical professionals. Before any study procedures take place, the consent form must be signed by a legally acceptable surrogate and the investigator-designated research professional obtaining the consent. The consent form will be signed in paper copy form or electronically in REDCap.

What are your responsibilities?

Please consider the study time commitments and responsibilities as a research subject when making your decision about participating in this study.

What happens if you decide not to take part in this study?

Participation in this study is voluntary. You do not have to take part in order to receive care at CHOP.

If you decide not to take part or if you change your mind later there will be no penalties or loss of any benefits to which you are otherwise entitled.

Can you stop your participation in the study early?

You can stop being in the study at any time. You do not have to give a reason.

Can the study doctor take you out of the study early?

The study doctor may take you off of the study if your condition worsens.

What choices do you have other than this study?

There are options for you other than this study including:

- Not participating in this study.
- You may discuss other respiratory support options available to you with your doctor.

What about privacy, authorization for use of Personal Health Information (PHI) and confidentiality?

As part of this research, health information about you will be collected. This will include information from medical records, study procedures, and specimens. Information related to your medical care at CHOP will go in your medical record. This could include physical exams, or tests done in the clinical lab. Medical records are available to CHOP staff. Staff will view your records only when required as part of their job. Staff are required to keep your information private. Information that could identify you will not be shared with anyone - unless you provide your written consent, or it is required or allowed by law. Laboratory test results will appear in your medical record. We will do our best to keep your personal information private and confidential. However, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results of this study may be shown at meetings and published in journals to inform other doctors and health professionals. We will keep your identity private in any publication or presentation.

Several people and organizations may review or receive your identifiable information. They will need this information to conduct the research, to assure the quality of the data, or to analyze the data or samples. These groups include:

- Members of the research team and other authorized staff at CHOP.
- People from agencies and organizations that perform independent accreditation and/or oversight of research; such as the Department of Health and Human Services, Office for Human Research Protections.
- Groups monitoring the safety of this study (Independent safety Monitoring Committee);
- Your samples/data will be shared with an outside laboratory, Salimetrics SalivaLab in Carlsbad, California
- The samples will be analyzed (and stored, if applicable). Your samples/data will be labeled with a study ID number and date/time when they were obtained. The outside laboratories will not know who you are. Private information such as your name, birth date or medical record number will not be shared with them.

By law, CHOP is required to protect your health information. The research staff will only allow access to your health information to the groups listed above. By signing this document, you are authorizing CHOP to use and/or release your health information for this research. Some of the organizations listed above may not be required to protect your information under Federal privacy laws. If permitted by law, they may be allowed to share it with others without your permission.

For subjects age 18 or over, or emancipated minors, identifiable information from this study will be destroyed 10 years from the date of the last treatment; for minors, identifiable information from this study will be destroyed 10 years from reaching the age of 18 or death.

Can you change your mind about the use of personal information?

You may change your mind and withdraw your permission to use and disclose your health information at any time. To take back your permission, it is preferred that you inform the investigator in writing.

Erik Jensen, MD
The Children's Hospital of Philadelphia
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In the letter, state that you changed your mind and do not want any more of your health information collected. The personal information that has been collected already will be used if necessary for the research. No new information will be collected. If you withdraw your permission to use your personal health information, you will be withdrawn from the study.

Financial Information

While you are in this study, the cost of your usual medical care – procedures, medications and doctor visits – will continue to be billed to you or your insurance.

Will there be any additional costs?

There will be no additional costs to you by taking part in this study.

Will you be paid for taking part in this study?

You will not receive any payments for taking part in this study.

Who is funding this research study?

Respiratory Therapy Deprtment and Division of Neonatology at The Children's Hospital of Philadelphia and the American Respiratory Care Foundation are funding this research.

Conflicts of Interest

There are not any individual or institutional conflicts of interest.

What if you have questions about the study?

If you have questions about this study or how your samples/data are going to be used, call the study principle investigator at 215-590-1708. You may also talk to your own doctor if you have questions or concerns.

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia has reviewed and approved this study. The IRB looks at research studies like these and makes sure research subjects' rights and welfare are protected. If you have questions about your rights or if you have a complaint, you can call the IRB Office at 215-590-2830.

What will be done with my data and specimens when this study is over?

Your data and/or saliva samples will not be used for any future research after this study is complete.

Consent to Take Part in this Research Study and Authorization to Use and Disclose Health Information for the Research

The research study and consent form have been explained to you by:

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

By signing this form, you are indicating that you have had your questions answered, you agree to allow your child to take part and you are legally authorized to consent to your child's participation. You are also agreeing to let CHOP use and share the health information that will be collected for this study, as explained above. If you don't agree to the collection, use and sharing of health information, you cannot participate in this study.
NOTE: *A foster parent is not legally authorized to consent for a foster child's participation.*

Name of Child Subject

Both Parents Must Sign this Consent Form

Name of Authorized Representative #1	Relationship to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative #1	Date

Name of Authorized Representative #2	Relationship to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative #2	Date

If the second representative is unavailable, per §46.408(b) / §50.55(e)(2), explain the reason.

Consent to Take Part in this Research Study and Authorization to Disclose Health Information for Research

Name of Subject

Name of Authorized Representative #1	Relation to Subject ☐ Parent ☐ Legal Guardian
Name of Authorized Representative #2	Relation to Subject ☐ Parent ☐ Legal Guardian

If the second representative is unavailable, per §46.408(b) / §50.55(e)(2), explain the reason.

The research study and consent form have been explained to the subject or parent/legal guardian.

By signing this form, you are indicating that you have answered the subject's or parent's/legal guardian's questions, they have agreed to take part in this research study and they are legally authorized to consent to their or their child's participation. They have also agreed to let CHOP use and share their or their child's health information as explained above. If they don't agree to the collection, use and sharing of their or their child's health information, they cannot participate in this study.

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

Witness/Interpreter

By signing this form, you are indicating that:

- The information in the Summary Document as well as any additional information conveyed by the person obtaining consent was presented to the subject in a language preferred by and understandable to the subject or parents/legal guardian's; and
- The subject's or parent's/legal guardian's questions were interpreted and the responses of the person obtaining consent were presented in a language preferred by and understandable to the subject or parent/legal guardian.
- At the conclusion of the consent conference, the subject was asked in a language preferred by and understandable to the subject if s/he understood the information in the Summary Document as well as an additional information conveyed by the person obtaining consent (including responses to the subject's questions) and responded affirmatively.

Name of Witness/Interpreter	Signature of Witness/Interpreter
	Date