Protocol title:

Feasibility of using daily Humidified Nasal High-flow with Oxygen during Sleep and/or Daytime in Hypercapnic COPD patients following recent (< 12 wks.) hospitalization for AECOPD for 90 days

NCT03221387

Date: 10/06/2017

1) Abstract of the study

Humidified Nasal High-flow with Oxygen (HNHF-O2) therapy has been reported to have acute beneficial effects in patients with hypoxemic respiratory failure. HNHF-O2 may be beneficial in patients with COPD and chronic impairments in gas exchange, both hypoxemia as well as hypercapnia. HNHF-O2 may decrease work of breathing, reduce dyspnea, improve airway humidification, and potentially stabilize or reduce carbon dioxide levels. However, there is limited data showing the chronic effects of HNHF-O2 in patients with hypercapnic respiratory failure, specifically those discharged to home following hospitalization for an acute exacerbation. Data that demonstrates that HNHF-O2 is well tolerated, and stabilizes or improves gas exchange long term in patients with COPD is lacking. Similarly, data that demonstrates that this therapeutic regimen is feasible to provide to patients in the home environment are lacking. This is an open-labeled pilot study of thirty patients to determine the safety and feasibility of using the device in the outpatient management of patients with COPD.

2) Protocol Title

Feasibility of using daily Humidified Nasal High-flow with Oxygen during Sleep and/or Daytime in Hypercapnic COPD patients following recent (< 12 wks.) hospitalization for AECOPD for 90 days

3) IRB Review History

Not applicable

4) Investigator

Gerard J. Criner, MD

5) Objectives

To assess the feasibility of using daily home HNHF-O2 during sleep and/or daytime in hypercapnic COPD patients following recent (< 12 weeks) hospitalization for AECOPD for 90 days.

6) Background

Many patients who experience a COPD exacerbation and who have received oxygen in the hospital are candidates for home oxygen use. Long-term oxygen use has been shown to reduce COPD mortality. There are a number of ways by which oxygen can be delivered to patients in the home care setting including nasal prongs, and a variety of mask interfaces. In most patients with COPD oxygen flow rates of 2-4 liters per minute (lpm) are sufficient. A newer approach to oxygen delivery is through a humidified high-flow nasal cannula. While the fraction of inspired oxygen remains the same the flow rate can be increased to up to 60 lpm.[1] The higher flow rate of humidified oxygen has several purported benefits for the COPD patient at home. These include increased patient comfort, less dilution of the oxygen dose by room air, and a slightly increased positive airway pressure that may reduce the work of breathing and allow distal airways to participate in gas exchange (airway recruitment).[2] Additionally, HNHF-O2 leads to washout of the anatomical dead

space of the upper airways.[3] Humidification levels of HNHF-O2 have been shown to improve mucociliary clearance.[4] High flow nasal oxygen has been studied in neonates, children, and adults with the greatest experience being in the neonate and pediatric populations.[5] One of the first studies in the adult COPD patient population by Chatila and colleagues demonstrated that high flow nasal oxygen improved exercise performance and enhanced oxygenation.[6] This study was conducted in ambulatory adult COPD patients; however most of the research since this publication has been directed at COPD patients who have been hospitalized where the goal was avoidance of intubation was the goal of therapy.[1] There have been few studies of the use of high-flow nasal oxygen in adults with COPD in the outpatient setting. Given the potential benefits on exercise tolerance and reduced work of breathing it would be useful to investigate this therapy in this patient population.

7) Setting of the Human Research

Potential subjects will be recruited from the pulmonary care unit located on the 5th floor of the Ambulatory Care Center of Temple University Hospital. Patients will receive HNHF-O2 at home and will be monitored via phone calls and clinic visits throughout the 90 day study period.

8) Resources Available to Conduct the Human Research

Potential subjects will be recruited from the population of patients who are being managed by Temple University pulmonary physicians. Patients are seen at the Temple Lung Center located on the 5th floor of the Ambulatory Care Center on the Health Sciences Campus as well as those who are being seen at the Temple Lung Center at Oaks. Our research staff includes an administrative core that provides regulatory support and coordination of research activities. Importantly, 6.5 FTE research nurse coordinators, and 6 FTE research specialists are readily available to meet the needs of the variety of clinical trials in which we participate complemented by dedicated administrative support that includes a regulatory affairs specialist, grants administration office, QI and IRB regulatory oversight. Most of these individuals have over 15 years of clinical research experience.

The Temple Lung Center outpatient clinic is a newly constructed 14,000 ft^2 facility designed to create an ideal outpatient experience, integrating state of the art pulmonary function, exercise, and physiologic testing with physician visits. It was constructed to provide outpatient care, clinical research and patient and provider education in a state of the art setting. Patient visits, blood draws, lung function and exercise testing all are done in this unicenter of pulmonary research and care. The pulmonary function laboratory has been placed beside our outpatient practice; the waiting room has been designed to accommodate 50 or more persons with additional space to accommodate wheelchairs and/or stackable chairs. All areas are wheelchair accessible. 22 recessed oxygen wall mounts capable of delivering 15 liters per minute of supplemental oxygen are distributed within the waiting area. The Temple Lung Center at Oaks is 5,500 square-foot facility is located in the Oaks Corporate Center on Cresson Boulevard (on Route 422, just 6 miles west of the King of Prussia Mall). The site includes a patient reception/ waiting area and nine private

examination rooms for consultations between Temple physicians and their patients. To facilitate patient evaluation and treatment, full radiological, pulmonary function, and blood-acquisition services are available on-site. The Sleep Center has also opened and is currently seeing patients.

We treat an average of 16,000 outpatients a year; over 50% of these patients carry a diagnosis of advanced lung disease, including COPD, IPF, pulmonary hypertension, and bronchiectasis. We are a major referral center for lung volume reduction surgery.

All physicians, nurses and ancillary staff members will be instructed in the details of this study.

9) Prior Approvals

Not applicable.

10) Study Design

a) Recruitment Methods

Thirty patients hospitalized for acute exacerbation of COPD ≤ the last 12 weeks will be enrolled into the study. Subjects will be recruited from the Temple Lung Center clinical practices in Philadelphia and Oaks, PA.

Potential subjects will be recruited during scheduled office visits to the Temple Lung Center offices in Philadelphia and in Oaks, PA. Many of these patients will be those who have been referred to Temple. We will also contact pulmonology practices in the tri-state area through direct mailings and our monthly research fax blast. The Temple Lung Center also maintains an IRB-approved registry of patients who have agreed to be contacted to discuss participation in clinical research trials.

Describe materials that will be used to recruit subjects. Include copies of these documents with the application. – Not applicable

Subjects will receive compensation in the form of a $25 gift card for each completed visit during their participation in this study.

b) Inclusion and Exclusion Criteria

Consecutive patients ≥ 40 years of age or older who are admitted to the hospital for an acute exacerbation of COPD within the past 12 weeks. Patients will have COPD as the primary diagnosis and have smoked > 10 pack years. Patients should be receiving supplemental oxygen as part of their usual clinical care. Patients must be willing to give informed consent and be willing to participate in measurement of ABGs, brief history and physical examination and answer questionnaires regarding daily use of HNHF-O2 therapy. Women who are pregnant are excluded from this research. Women of childbearing potential will have a urine pregnancy test to ensure that they are not pregnant.

The main exclusion criteria are upper airway or nasal problems that prohibit the use of high flow oxygen and patients with any of the following will be excluded:

current use (≤ 4 weeks of study entry) of any PAP-therapy (e.g., CPAP or NPPV); sleep apnea as follows: STOPBang scores ≥ 5 or STOPBang score ≥ 2 plus BMI > 35 kg/m^2; or Berlin questionnaire scores suggesting high likelihood of sleep apnea with increased risk of sleep-related accident (e.g., occupation as a commercial driver or pilot); or excessive daytime sleepiness (i.e., either of High (>15) score on the Epworth Sleepiness Scale or "fall asleep" accident or "near miss" accident in prior 12 months).

c) Local Number of Subjects

Thirty subjects will be accrued locally for this study.

We expect few screen failures.

d) Study-Wide Number of Subjects

If this is a multicenter study, indicate the total number of subjects to be accrued across all sites. – Not applicable.

e) Study Timelines

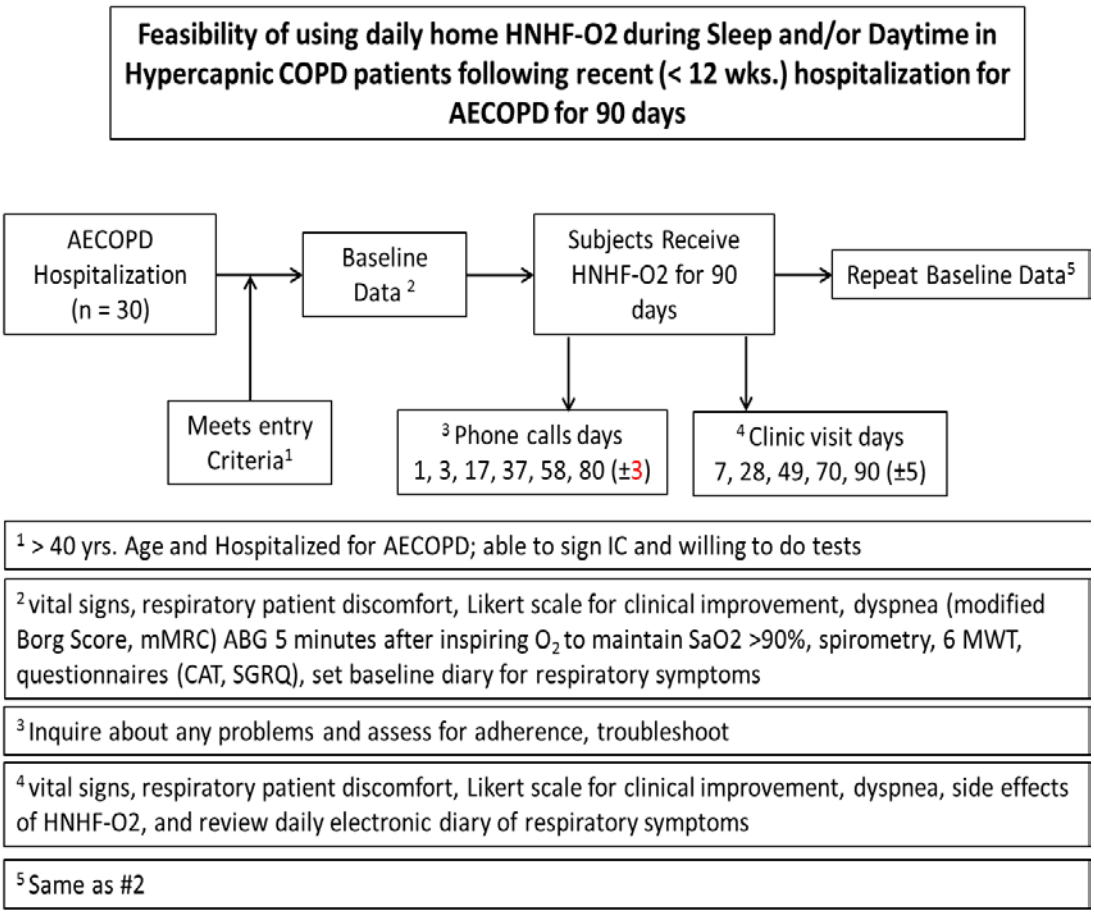
- Subjects will be followed for 90 days with regular telephone follow-up and clinic visits throughout.
- Subjects will be enrolled over a period of 12 months.
- The investigators will complete the data analysis approximately 18 months after the first subject is enrolled.

f) Study Endpoints

The primary endpoints of this study are the feasibility of oxygen therapy by HNHF-O2 at home over a 90-day period in terms of tolerance and hours of use. Descriptive statistics will be used to characterize the patient population in terms of demographic factors and severity of airflow obstruction. Changes in PaO2, PaCO2 and pH across the days will be done by analysis of variance. The effect of baseline PaCO2 on change in PaCO2 with HNHF-O2 therapy will be analyzed as an independent effect on change in PaCO2 levels with HNHF-O2. Changes in respiratory rate, heart rate, blood pressure accessory muscle use will also be assessed by analysis of variance. Patient tolerance and side effects will also be measured across days of use per patient and across days in all patients as group trends. Hours of use per device log and per patient diary will be independently analyzed and compared to one another. The impact on change in exacerbation frequency and severity will be analyzed. Changes in spirometry, 6MWD, GOLD grade and class and BODE scores prior to and after 90 days of HNHF-O2 will be analyzed.

g) Procedures Involved in the Human Research

An overview of the study is provided in the figure below.



Patients who have had a recent COPD exacerbation (<12 weeks since discharge) accompanied with respiratory failure who meet the above inclusion criteria will be considered for participation in the study.

Once informed consent has been obtained patients will be given the opportunity to participate in the sleep substudy until the enrollment goal of ten subjects has been achieved. A separate protocol and consent form has been submitted for this study. The following procedures will be performed as part of the main study:

Test	Visit 1 Screening	Visit 1a Baseline	Visit 2 Clinic Placed on HNHF-O2	Visit 3 Phone Call Day 1	Visit 4 Phone call Day 3 ± 3	Visit 5 Clinic Day 7 ± 5	Visit 6 Phone call Day 17 ± 3	Visit 7 Clinic Day 28 ± 5	Visit 8 Phone call Day 37 ± 3	Visit 9 Clinic Day 49 ± 5	Visit 10 Phone call Day 58 ± 3	Visit 11 Clinic Day 70 ± 5	Visit 12 Phone call Day 80 ± 3	Visit 13 Clinic Day 90 ± 5
Screen	X													
Informed Consent	X													
History & Physical		X				X		X		X		X		X
Pregnancy test for women of childbearing potential		X												
Arterial blood gas◆		X	X											x
Pre- and Post-Bronchodilator Spirometry		X												X
6 minute walk distance		X												X
mMRC Questionnaire		X[2]												
Borg Questionnaire		X[2]	X			X		X		X		X		X
Assess Accessory Muscle use		X	X			X		X		X		X		X
Assess subject comfort		X	X			X		X		X		X		X

Test	Visit 1 Screening	Visit 1a Baseline	Visit 2 Clinic Placed on HNHF-O2	Visit 3 Phone Call Day 1	Visit 4 Phone call Day 3 ± 3	Visit 5 Clinic Day 7 ± 5	Visit 6 Phone call Day 17 ± 3	Visit 7 Clinic Day 28 ± 5	Visit 8 Phone call Day 37 ± 3	Visit 9 Clinic Day 49 ± 5	Visit 10 Phone call Day 58 ± 3	Visit 11 Clinic Day 70 ± 5	Visit 12 Phone call Day 80 ± 3	Visit 13 Clinic Day 90 ± 5
Epworth Sleepiness Scale	X													
Berlin Sleep Questionnaire	X													
STOP-Bang Questionnaire	X													
St. George's Respiratory Questionnaire		X												X
GOLD Category		x												
BODE Index		X												X
Daily Diary	X	X	X			X		X		X		X		X
COPD Activity Test		X												X
Review current medications	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Phone call				X	X		X		X		X		X	
Sleep substudy participants														
Insomnia Severity index		X												
Home sleep study		X[1]				X						X		
Epworth Sleepiness		X[2]				X[2]						X[2]		

Scale														

[1] For those subjects enrolled in the sleep substudy the acquaintance and baseline sleep studies must be completed before beginning HNHF-O2
[2] Questionnaires are done at baseline visit and repeated at home prior to the baseline, day 7, and day 70 sleep studies.
◆ For ABGs, the test will be done on room air after the participant has been off the Airvo device for 20 minutes. If the participant starts to desaturate, then it can be done on 2L of oxygen.

There will be collection of demographic data including age, gender, race, current medications, and comorbid conditions. A patient history of duration of the nature and course of prehospital symptoms, past medical history of smoking, and past use of respiratory medications and nonpharmacological therapy for COPD will be elicited. Historical collection of available clinical data including exacerbation history, reports of chest imaging as well as pulmonary function and/or exercise or cardiac data will be collected.

At baseline, patients will have measurement of vital signs (heart rate, respiratory rate and blood pressure), dyspnea (modified Borg score, mMRC) arterial blood gas after 5 minutes of inspiring supplemental oxygen to keep SaO_2 > 90%, and use of accessory muscles of ventilation. Patients will have spirometry performed pre-and post-bronchodilator administration. Patients will have assessment of their current respiratory health by completing CAT, mMRC and SGRQ questionnaires. A detailed history of their exacerbation frequency and severity will be obtained. Patients will perform a 6-minute walk test. Patients GOLD grade and group will be classified and patients BODE scores will be calculated.

Patients will be queried regarding the presence and magnitude of complaints of cough and sputum production by using a daily electronic diary for a 2-week period of run in. After the 2-week run-in period the patient will be scheduled to return to initiate HFNC with oxygen therapy.

Electronic daily diary of respiratory symptoms.

- Breathlessness (Modified Borg Scale)
- Sputum Quantity, Color, and Consistency
- Peak Flow Measurements
- Presence of Temperature Over 100°F
- Presence of Any Cough, Wheeze, Sore Throat or Nasal Congestion

Patients will be seen in clinic and instructed in the use of HNHF-O2 and its proposed benefits. The necessity of compliance and adherence to the treatment plan will be emphasized.

Following the outpatient clinic visit, patients will be set up at home using an established home vendor for respiratory equipment. Patients will continue to report their daily respiratory symptoms via the electronic diary.

Post placement on optimal dose of HNHF-O2 therapy, subjects will be called the next day to determine if there were any problems.

Patients will report to clinic at baseline and then 7 ± 2, 28 ± 5, 49 ± 5, and 70 ± 5 days for the following assessment:

- Measurements of vital signs (heart rate, respiratory rate and blood pressure)
- Respiratory patient-discomfort and dyspnea assessed using an unmarked 100 mm visual analogic scale from “no discomfort” to “maximal imaginable discomfort”
- Likert scale model indicating marked improvement (+2), slight improvement (+1), no change (0), slight deterioration (-1) and marked deterioration (-2)
- Side effects related to high flow nasal administration: nasal dryness, epistaxis, nasal crusting, eye discomfort, pressure discomfort, increase rhinitis, decreased smell, post nasal drip, hoarseness
- Hours of daily use of HNHF-O2 therapy
- Daily record keeping of daily diary review

At day 90 ± 2 the following will be measured:

- Measurements of vital signs (heart rate, respiratory rate and blood pressure)
- Respiratory patient-discomfort and dyspnea assessed using an unmarked 100 mm visual analogic scale from “no discomfort” to “maximal imaginable discomfort”
- Likert scale model indicating marked improvement (+2), slight improvement (+1), no change (0), slight deterioration (-1) and marked deterioration (-2)
- Side effects related to high flow nasal administration: nasal dryness, epistaxis, nasal crusting, eye discomfort, pressure discomfort, increase rhinitis, decreased smell, post nasal drip, hoarseness
- Hours of daily use of HNHF-O2 therapy
- Daily record keeping of daily diary review
- Arterial blood gas on room air after the participant has been off the Airvo Device for 20 minutes.
- Pre-and post-bronchodilator spirometry

- CAT, SGRQ
- 6 Minute walk test
- GOLD grade and group will be classified
- BODE scores will be calculated.

Application of HNHF-O2 therapy. During HNHF-O2, oxygen will be passed through a heated humidifier (myAIRVO 2, Fisher and Paykel Healthcare) and applied continuously through large-bore binasal prongs, with a gas flow rate of 20-35 liters per minute (or as high as tolerated). Temperature will be adjusted based on patient's comfort and range from 34-37 degrees based on prior experience. The fraction of oxygen in the gas flowing in the system will be adjusted to maintain an SpO2 of 90% or more. High-flow oxygen will be applied at the highest tolerated flow up to 35 lpm at home. Meter time and patient's log of hours of daily use will be measured and compared.

Hypercapnic COPD patients are encouraged to use supplemental oxygen therapy on a continuous basis. The use of the humidified nasal high-flow device in this protocol is not expected to change the total number of hours that the patient receives supplemental oxygen; however it will change the manner in which the oxygen is delivered. Patients will be encouraged to use the device for oxygen delivery as many hours per day as possible.

In order to reduce the risk of contamination and extend the life of the tubing and patient interface it is recommended that the user clean the device at specified intervals. The patient interface should be washed in tap water and reconnected to the heated breathing tube. Thereafter, the device should be run in drying mode. This process takes about 90 minutes to complete and should be performed daily. On a weekly basis the heated breathing tube should be removed along with the patient interface and both washed in warm water with a mild detergent. The outside of the device should be wiped clean with a damp cloth. The inside of the heated breathing tube connection port should be cleaned with a low-lint cloth with mild dishwashing detergent.

The patient has the option to not receive supplemental oxygen during each of these cleaning procedures or to receive supplemental oxygen via a standard nasal cannula.

All supplies necessary for the maintenance of the device will be provided to the subject at no cost to them.

Study procedures:

History and physical exam, vital signs. These are all procedures routinely performed as standard of care.

Lung function testing (spirometry). Pre- and post-bronchodilator testing (spirometry) will be performed according to ATS standards. The bronchodilator

medication (albuterol) opens up the airways and will be used in lung function testing. This medication is often used to treat people with COPD. Spirometry will be performed by experienced study personnel.

Arterial blood gases. Arterial blood gases will be obtained from the radial artery in the wrist by experienced personnel. Blood gases will be obtained on room air after the patient has been off the Airvo device for 20 minutes.

6 minute walk test. Subjects will be asked to walk as far as they can for 6 minutes while receiving supplemental oxygen. Testing will be supervised by experienced study personnel with access to emergency medicine such as sublingual nitroglycerin, aspirin and albuterol.

Dyspnea questionnaires, accessory muscle use, and comfort assessments. The Borg dyspnea questionnaire and mMRC are short questionnaires that can be completed in a minute or two. These questionnaires are included with this submission. Use of accessory muscles requires only subject observation. Subject comfort assessments are also provided with this submission and can be completed in a minute.

During the subject's hospitalization various medications including bronchodilators, corticosteroids, and antibiotics may be administered to manage the COPD exacerbation. These will be prescribed by the subject's physician as standard of care. The subject's usual maintenance medications will be prescribed as clinically indicated as standard of care. Other testing and procedures (such as laboratory testing and radiographic imaging) may be performed. These would also be standard of care.

myAIRVO 2 device. The myAIRVO 2 device is a humidifier with integrated flow generator that delivers high flow warmed and humidified respiratory gases to spontaneously breathing patients through a variety of patient interfaces. It is intended for the treatment of spontaneously breathing patients who would benefit from receiving high flow warmed and humidified respiratory gases. The myAIRVO 2 is for patients in homes and long-term care facilities. The flow may be from 2 – 60 L/min depending on the patient interface. There are few expected side effects of using the myAIRVO 2 device – if the humidification is too low, the subject may experience nasal/throat discomfort or epistaxis.

Optiflow+ nasal cannula. The Optiflow+ nasal cannula is a nasal cannula patient interface for delivery of humidified respiratory gases. There are few expected side effects of using the Optiflow+ nasal cannula – some minor irritation or sensitivity may occur where the cannula sits on the skin.

Telephone calls. Subjects will receive telephone calls on days 1, 3, 17, 37, 58, 80 (after initiation of HNHF-O2) to determine vital status, assess adverse events, compliance with the device, and to answer any questions they may have regarding the study. In addition to the scheduled telephone calls, the subject may receive phone calls from the monitors of the electronic daily diary if the subject fails to report symptoms for three consecutive days.

h) Data and Specimen Banking

Not applicable.

i) Data Management

The primary endpoints of this study are the feasibility of oxygen therapy by HNHF-O2 at home over a 90-day period in terms of tolerance and hours of use. Descriptive statistics will be used to characterize the patient population in terms of demographic factors and severity of airflow obstruction. Changes in PaO_2, $PaCO_2$ and pH across the days will be done by analysis of variance. The effect of baseline $PaCO_2$ on change in $PaCO_2$ with HNHF-O2 therapy will be analyzed as an independent effect on change in $PaCO_2$ levels with HNHF-O2. Changes in respiratory rate, heart rate, blood pressure accessory muscle use will also be assessed by analysis of variance. Patient tolerance and side effects will also be measured across days of use per patient and across days in all patients as group trends. Hours of use per device log and per patient diary will be independently analyzed and compared to one another. The impact on change in exacerbation frequency and severity will be analyzed. Changes in spirometry, 6MWD, GOLD grade and class and BODE scores prior to and after 90 days of HNHF-O2 will be analyzed.

This is a pilot study in which the primary outcome is to determine the feasibility of using high-flow nasal oxygen in patients with COPD who have been recently discharged from the hospital with a COPD exacerbation. As such it is not an efficacy trial and is powered based on the ability to detect safety issues or unforeseen problems. The sample size has been estimated based on the method described by Viechtbauer, et.al.[7]

The safety issue we have identified is the need to withdraw therapy because HNHF-O2 is not tolerated by the subject.

The formula for this calculation is based on the probability of observing at least one of these events:

$P(x > 0) = 1 - (1 - \pi)^n$ where

x = the number of events that occur across the total number of participants

and

π = the probability that the event will occur.

Solving for n yields:

$$n = \frac{\ln(1 - \gamma)}{\ln(1 - \pi)}$$

Where γ = the confidence threshold.

Using a 95% confidence threshold and 15% probability that an event (need to discontinue due to intolerance) occurs the sample size required is:

$n = \frac{\ln(1-0.95)}{\ln(1-0.1)}$ = 28.4 subjects.

The number of subjects has been increased to 36 to accommodate screen failures and dropouts and to provide evaluable data on 30 subjects.

All data will be stored on the REDCap website and on password protected files on password protected computers located on the 7th floor of the Kresge Building. This is an area with access restricted to study personnel.

j) Confidentiality

All data will be stored on the REDCap website. The site is part 11 compliant. All study personnel have been trained in human subjects protections and good clinical practices. Study data will only be accessible to study personnel via password protected websites and computer terminals.

k) Confidentiality

All data will be stored on the REDCap website. The site is part 11 compliant. All study personnel have been trained in human subjects protections and good clinical practices. Study data will only be accessible to study personnel via password protected websites and computer terminals.

l) Provisions to Monitor the Data to Ensure the Safety of subjects

This study utilizes an FDA-approved device for the delivery of warmed humidified gases for a medical indication included in the 510(k) approval letter. As such, and because of the limited enrollment in this trial, there is no need for a data and safety monitoring board. Monitoring of the study will be done by the principal investigator on a routine (monthly) basis in conjunction with the study sponsor and the Director of Research at the Temple Lung Center. All adverse events will be reviewed with particular attention paid to those subjects who discontinued use of the device and those where oxygen therapy needed to be intensified in order to maintain adequate oxygenation.

m) Withdrawal of Subjects

Subjects may discontinue participation in the study at any point and for any reason. This decision will not be held against them in any way. If a subject decides to withdraw, the physician will assess their clinical condition and determine the best course of action for the subject. This may include alternative methods of oxygen administration. Any data that is collected up to the point of subject withdrawal will be retained for analysis.

11) Risks to Subjects

History and physical exam, vital signs. These are all procedures routinely performed as standard of care and are not associated with any adverse effects.

Lung function testing (spirometry). This testing may make subjects feel short of breath. On rare occasions, people feel dizzy or faint. The bronchodilator medication (albuterol) opens up the airways and will be used in lung function testing. This medication is often used to treat people with COPD. Albuterol sometimes increases the heart rate or causes jitteriness or shakiness (tremors), but these effects usually disappear quickly. Spirometry will be performed by experienced study personnel.

6 minute walk test. Subjects will be asked to walk as far as they can for 6 minutes while receiving supplemental oxygen. Subjects may feel short of breath as a result. Rarely, subjects may over-exert themselves and experience chest pain and/or faint. Testing will be supervised by experienced study personnel with access to emergency medicine such as sublingual nitroglycerin, aspirin and albuterol

Arterial blood gases. Arterial blood gases will be obtained from the radial artery in the wrist by experienced personnel. A local anesthetic may be used if necessary. Blood drawing from an artery causes more pain than taking blood from a vein. Bruising can occur. Very rarely, fainting, blood clots, or an infection at the site can occur.

Dyspnea questionnaires, accessory muscle use, and comfort assessments. The Borg dyspnea questionnaire and the CAT, mMRC and SGRQ questionnaires are short questionnaires that can be completed in a minute or two. These questionnaires are included with this submission. Use of accessory muscles requires only subject observation. Subject comfort assessments are also provided with this submission and can be completed in a minute. There are no risks associated with any of these procedures.

myAIRVO device. There are few expected side effects of using the myAIRVO 2 device – if the humidification is too low, the subject may experience nasal/throat discomfort or epistaxis.

12) Potential Benefits to Subjects

Potential benefits of study participation include the subject experiencing a decreased work of breathing. It is also possible that the subject will experience no direct benefit.

13) Privacy and Confidentiality

The study will use or disclose protected health information. A HIPAA authorization form is included with this submission.

14) Compensation for Research-Related Injury

If a subject is injured or becomes ill as a result of this research device or a procedure required to be done only as a part of this research, they should immediately notify the research team who will arrange immediate medical care. There is no commitment by Temple University, Temple University Health System or its subsidiaries, or the study collaborator, Fisher & Paykel Healthcare to provide monetary compensation or free medical care in the event of a study-related injury. All charges will be billed to the subject's insurance carrier.

15) Economic Burden to Subjects

All subjects will need supplemental oxygen as part of their clinical care. The only difference for this research is that the subjects will receive high-flow oxygen. There is no additional charge for this method of oxygen delivery.

16) Consent Process

- We will follow "INVESTIGATOR GUIDANCE: Informed Consent (HRP-802)."

Non-English Speaking Subjects – not applicable. All subjects must be able to speak and read English.

Waiver or Alteration of the Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception) – not applicable**.**

Subjects who are not yet adults (infants, children, teenagers) – Not applicable.

Cognitively Impaired Adults – not applicable.

Adults Unable to Consent – not applicable. All subjects must be able to provide consent. Legally authorized representatives will not be approached.

17) Process to Document Consent in Writing

We will follow "INVESTIGATOR GUIDANCE: Documentation of Informed Consent (HRP-803)."

18) Vulnerable Populations

No vulnerable individuals will be enrolled in this study.

19) Drugs or Devices

The device that will be used for this study is the myAIRVO-2. It and the high-flow nasal prongs will be provided by the manufacturer. The device will be provided to outpatients enrolled in the study. The device manual is submitted with this application.

20) Multi-Site Human Research

Not applicable.

21) Sharing of Results with Subjects

There is no plan to share the results of the study with the subjects at this time.

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6. Chatila W, Nugent T, Vance G, Gaughan J, Criner GJ. The effects of high-flow vs low-flow oxygen on exercise in advanced obstructive airways disease. Chest 2004;126:1108-15.
7. Viechtbauer W, Smits L, Kotz D, et al. A simple formula for the calculation of sample size in pilot studies. J Clin Epidemiol 2015;68:1375-9.