Official Title:	Impact of ambulatory oxygen delivery method on real-world activity and quality-of-life in patients with interstitial lung disease (ILD) or chronic obstructive pulmonary disease
NCT number:	NCT07512687
Document Type:	Study Protocol with Statistical Plan
Date of the Document:	May 4, 2026

University at Buffalo
The State University of New York

University at Buffalo Institutional Review Board (UBIRB)
Office of Research Compliance | Research Institute on Addictions
1021 Main St. | Buffalo, NY 14203
UB Federalwide Assurance ID#: FWA00008824

APPROVAL OF MODIFICATION

May 6, 2026

Dear Kristopher Clark,

On 5/4/2026**,** the University at Buffalo IRB reviewed the following submission:

Type of Review:	Modification / Update
Title of Study:	Impact of ambulatory oxygen delivery method on real-world activity and quality-of-life with interstitial lung disease (ILD) or chronic obstructive pulmonary disease (COPD)
Investigator:	Kristopher Clark
IRB ID:	MOD00017502
Funding:	K12 scholar award
Grant ID:	None
IND, IDE, or HDE:	None
Documents Reviewed:	• Adverse Event and Safety Questionnaire, Category: Surveys/Questionnaires; • Ambulatory Oxygen ILD COPD Protocol, Category: IRB Protocol; • Consent Form, Category: Consent Form; • COPD Assessment Test (CAT), Category: Surveys/Questionnaires; • End-of-Study Questionnaire, Category: Surveys/Questionnaires; • K-BILD Tool, Category: Surveys/Questionnaires;

The modification materials for the project referenced above were reviewed and approved by the SUNY University at Buffalo IRB (UBIRB) by Full Committee Review. The IRB approved this modification on **5/4/2026.** The expiration date of this study is 2/17/2027. Before 2/17/2027 or within 30 days of study closure, whichever is earlier, you are to submit a continuing review application with required explanations. In order to avoid a lapse in IRB approval, it is recommended that you submit your continuing review at least 30 days for an expedited study and at least 45-60 days for a full board study, prior to the approval end date of the study. You can submit a continuing review application by navigating to the active study in Click IRB and selecting 'Create Modification / CR'. Studies cannot be conducted beyond the expiration date without re-approval by the UBIRB.

In conducting this study, you are required to follow the requirements listed in the Investigator Manual (HRP-103), which can be found by navigating to the IRB Library within the IRB system.

UBIRB approval is given with the understanding that the most recently approved procedures will be followed and the most recently approved consent documents will be used. If modifications are needed, those changes may not be initiated until such modifications have been submitted to the UBIRB for review and have been granted approval.

As principal investigator for this study involving human participants, you have responsibilities to the SUNY University at Buffalo IRB (UBIRB) as follows:

1. Ensuring that no subjects are enrolled prior to the IRB approval date.
2. Ensuring that the study is not conducted beyond the expiration date without re-approval by the UBIRB.
3. Ensuring that the UBIRB is notified of:
    - All reportable information in accordance with the New Information SOP (HRP-024).
    - Project closure/completion by submitting a Continuing Review/Modification submission.
4. Ensuring that the protocol is followed as approved by UBIRB unless a protocol amendment is prospectively approved.
5. Ensuring that changes in research procedures, recruitment or consent processes are not initiated without prior UBIRB review and approval, except where necessary to eliminate apparent immediate hazards to subjects.
6. Ensuring that the study is conducted in compliance with all UBIRB decisions, conditions, and requirements.
7. Bearing responsibility for all actions of the staff and sub-investigators with regard to the protocol.
8. Bearing responsibility for securing any other required approvals before research begins.

If you have any questions, please contact the UBIRB at 716-888-4888 or ub-irb@buffalo.edu. Please include the project title and number in all correspondence with the UBIRB.

Complete Research Protocol (HRP-503)

Table of Contents

Template Instructions

Sections that do not apply:

- *In several sections, the addition of checkboxes for **Not Applicable** have been added to the template as responses.*
    - *If an N/A checkbox is present, select the appropriate justification from the list.*
    - *If an N/A checkbox is not present, or if none of the existing checkboxes apply to your study, you must write in your own justification.*
- *In addition:*
    - *For research where the only study procedures are records/chart review: Sections 6, 21, 22, 24, 25, 26 and 27 do not apply.*
    - *For exempt research: Section 6 may not apply. Section 6.1 will still apply if there is a study intervention.*

Studies with multiple participant groups:

- *If this study involves multiple participant groups (e.g. parents and children), provide information in applicable sections for each participant group. Clearly label responses when they differ. For example:*

Response Example
Intervention Group:
Control Group:

Formatting:

- *Do not remove template instructions or section headings when they do not apply to your study.*

If you are pasting information from other documents using the "Merge Formatting" Paste option will maintain the formatting of the response boxes.

Amendments:

- *When making modifications or revisions to this and other documents, use the **Track Changes** function in Microsoft Word.*
- *Update the version date or number **on Page 3.***

PROTOCOL TITLE:

Include the full protocol title.

Response: Impact of ambulatory oxygen delivery method on real-world activity and quality-of-life in patients with interstitial lung disease (ILD) or chronic obstructive pulmonary disease (COPD)

PRINCIPAL INVESTIGATOR:

Name
Department
Telephone Number
Email Address

Response:

Kristopher Clark, MD

Clinical Assistant Professor

Department of Medicine

Division of Pulmonary, Critical Care and Sleep Medicine

646-621-6773

Kclark4@buffalo.edu

VERSION NUMBER/DATE:

Include the version number and date of this protocol.

Response:

4 – 04/27/26

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
2	02/24/26	Edits were made to address modification requests by the IRB. This includes the additional of abbreviations, statement that devices/equipment used are not investigational, clarified there is no upper age limit for enrollment, clarified the copyright/license permissions for symptom and QOL tools, edited information related to data protection and participant privacy, and added potential risk of skin irritation with device use. The consent form was also modified as per IRB	Yes

		recommendations. The symptom/quality-of-life tools to be used were listed in 12.3.	
3	03/06/26	An additional exclusion criterion was added related to need for participants to have an Oxiwear compatible smartphone. Due to budgeting limitations, we will be unable to provide participants with smartphones. We have removed the CRQ as one of the assessment tools to reduce number of survey participants will complete. The POC has been changed to the Inogen Rove 6 which is an upgraded version of the Inogen One G. We added additional low risk of participant discomfort with answering survey questions and risk of loss of confidentiality of data. The upper age limit was added to section 1.0 and to the Recruitment Flyer and Provider Recruitment Letter. Table 3 in Section 5.0 was updated to include survey tools that will be used. License and agreement specifications in section 13.0 was made more general. The Consent Form was updated to indicate need for compatible smart phone and to include NCATS as a funder of the study. An example key code form has been submitted along with the list of questions asked on the K-BILD.	Yes
4	04/27/26	We have expanded a safety monitoring plan to include adverse and safety event monitoring and reporting, identified an independent data safety monitor, and created new attachments for adverse event screening and for end of study questions. We will utilize a HIPAA-compliant application to communicate participant contact information and oxygen tank use with Health System Services. We have indicated that all wearable devices are FDA cleared. We indicated that electronic research data may be stored on a secure Advarra Cloud server as per UB policy. The consent was modified to include additional information on risks and monitoring. Final versions of all symptoms/quality-of-tools were uploaded.	Yes

FUNDING:

Indicate any funding for this proposal. This should match the Funding Sources page in Click IRB.

Response: K12 career development grant

GRANT APPLICABILITY:

Indicate whether this protocol is funded by a grant (e.g. NIH, foundation grant). For a grant with multiple aims, indicate which aims are covered by this research proposal.

NOTE: This question does not apply to studies funded by a sponsor contract.

Include a copy of the grant proposal with your submission.

Response:

K12 Career Development Grant

RESEARCH REPOSITORY:

Indicate where the research files will be kept, including when the study has been closed. The repository should include, at minimum, copies of IRB correspondence (approval, determination letters) as well as signed consent documents. This documentation should be maintained for 3 years after the study has been closed.

Response:

Electronic files and data will be stored on secure UB Severs

Hardcopy consent forms, quality-of-life and symptom surveys, and other physical documents will be secured in a locked cabinet within a locked office of the Primary Investigator at the following location:

Location: Buffalo General Medical Center

Address: 100 High St, B-814, Buffalo, NY 14203

Department: Medicine

1.0 Study Summary

Study Title	Impact of ambulatory oxygen delivery method on real-world activity and quality-of-life in patients with interstitial lung disease (ILD) or chronic obstructive pulmonary disease (COPD)
Study Design	Prospective, randomized, crossover feasibility pilot clinical trial
Primary Objective	To determine whether ambulatory oxygen therapy (AOT) titrated to patients' submaximal ambulatory oxygen needs impact real-world activity, dyspnea and quality-of-life

Secondary Objective(s)	1. Compare the effect of different AOT delivery devices on patient activity, QOL, and dyspnea 2. Assess whether AOT titrated during a six-minute walk test (6MWT) meets real-world oxygen needs
Research Intervention(s)/ Investigational Agent(s)	AOT delivered by a: • portable oxygen concentrator (POC) (Inogen Rove 6) • compressed gas canisters (D-tanks) No AOT therapy
IND/IDE #	N/A
Study Population	Adults ≥18 to ≤85 years old with stable COPD or fibrotic ILD (fILD) who are ambulatory outside of the home and demonstrate isolated exertional hypoxemia on a 6MWT
Sample Size	24 participants (fILD=12, COPD=12)
Study Duration for individual participants	6-weeks total with sequential 2-week periods with each AOT device (POC, compressed canister) and with no therapy
Study Specific Abbreviations/ Definitions	AOT – ambulatory oxygen therapy CAT – COPD Assessment Test COPD – chronic obstructive pulmonary disease CRO – Clinical Research Office EHR – electronic health record EQ-5D-5L – EuroQol 5-Dimension 5-Level questionnaire FEV1/FVC – forced expiratory volume in 1 second/forced vital capacity fILD – fibrotic interstitial lung disease ICD-10 – International Classification of Diseases 10th Edition IPF – idiopathic pulmonary fibrosis ILD – interstitial lung disease K-BILD – King's Brief Interstitial Lung Disease questionnaire LPM – liters per minute NCATS – National Center for Advancing Translational Science NIH – National Institutes of Health POC – portable oxygen concentrator QOL – quality-of-life SpO_2 – arterial oxygen saturation TLC – total lung capacity US – United States 6MWD – six-minute walk distance 6MWT – six-minute walk test

2.0 Objectives*

2.1 Describe the purpose, specific aims, or objectives of this research.

Response:

The primary objective of this study is to determine whether AOT devices, titrated to maintain adequate arterial oxygen saturation (SpO_2) ≥89% during a submaximal six-minute walk test (6MWT), impact real-world activity, dyspnea, and quality-of-life (QOL) in patients with fibrotic ILD or COPD who have isolated exertional hypoxemia.

Specific Aim 1 – Compare the effect of AOT device (POC or compressed gas canister vs no oxygen therapy) on daily activity, dyspnea, and QOL for patients with fibrotic ILD or COPD with isolated exertional hypoxemia.

Specific Aim 2 – Assess whether AOT titrated during a 6MWT meets real-world exertional oxygen needs.

2.2 State the hypotheses to be tested, if applicable.

NOTE: A hypothesis is a specific, testable prediction about what you expect to happen in your study that corresponds with your above listed objectives.

Response:

We hypothesize that AOT, properly prescribed and used, improves activity, dyspnea, and QOL in patients with fibrotic ILD or COPD who have isolated exertional hypoxemia.

We also hypothesize that AOT devices differentially impact activity and QOL in many patients with fibrotic ILD or COPD due to differences in device size, weight, portability, and how oxygen is delivered.

3.0 Scientific Endpoints*

3.1 Describe the scientific endpoint(s), the main result or occurrence under study.

NOTE: Scientific endpoints are outcomes defined before the study begins to determine whether the objectives of the study have been met and to draw conclusions from the data. Include primary and secondary endpoints. Some example endpoints are: reduction of symptoms, improvement in quality of life, or survival. Your response should ***not*** *be a date.*

Response:

Primary Outcome – Change in physical activity measured by number of steps per day with use of AOT compared to no therapy and between AOT devices.

Secondary Outcomes:

- Differences in mean daily SpO_2
- Mean time with SpO_2 <89%
- Total AOT use (time POC was active, number of oxygen canisters used)
- Differences in six-minute walk distances (6MWD)
- Differences in QOL and dyspnea scores

- Correlation between nadir SpO_2 on 6MWT to mean SpO_2 nadir during real-world activities

4.0 Background*

4.1 Provide the scientific or scholarly background, rationale, and significance of the research based on the existing literature and how it will contribute to existing knowledge. Describe any gaps in current knowledge. Include relevant preliminary findings or prior research by the investigator.

Response:

Isolated Exertional Hypoxemia in fILD and COPD: Fibrotic interstitial lung diseases (fILD) consist of a variety of diseases which impair the gas-exchange surface of the lung(1). In chronic obstructive pulmonary disease (COPD), tobacco smoke or other exposures lead to destruction of both airways and lung parenchyma which can impact gas exchange(2). Isolated exertional hypoxemia is common in both diseases(2-6) and is associated with increased mortality, lung function decline, reduced exercise capacity, and impaired QOL(7-11). In the US, guidelines recommend prescribing AOT to patients with ILD or COPD with isolated exertional hypoxemia who are active outside the home; however, recommendations are conditional noting a lack of high-quality evidence(12). Given limited evidence, there is variability in international AOT prescribing guidelines and practices(13-15), highlighting a need for further research on this topic.

Benefits and Limitations of AOT Devices: AOT can be administered via POC, compressed oxygen canisters, or liquid reservoirs (Fig 1)(12,16). Devices vary in cost, size, portability, and how oxygen is administered(1). Which device patients receive is often at the discretion of insurance carriers and local durable medical equipment suppliers. Compressed canisters come in various sizes and provide continuous oxygen flow; however, duration of use is reduced at high flow rates. They are more burdensome than other equipment which may limit mobility. POCs are small and lightweight. They can run indefinitely so long as battery power is maintained. However, POC oxygen delivery is often via demand (pulsed) flow timed to a patient's breath which may not match some patients' breathing patterns. POC settings also do not correlate to continuous flow rates delivered via oxygen canisters. This may lead to inadequate oxygen delivery if patients are not tested on the POC. Liquid oxygen is lightweight, long lasting, and provides higher flow rates with easier portability than canisters or POCs; however, it is difficult to obtain due to increased costs

Fig 1. Examples of oxygen devices (12)

and access issues. While devices perform similarly during 6MWT and other exercise assessments(17,18), we argue that AOT devices differentially impact real-world activity in some patients with ILD and COPD depending on their exertional oxygen needs.

Exertional Desaturation Testing: There are no formal recommendations on exertional oxygen testing. The standard method is a submaximal hall walk test. The 6MWT was designed for distance measuring but has been adapted for oxygen testing(19) and is most often used in AOT research. The reliance on submaximal testing assumes patients with chronic lung disease have limited mobility with most activities performed at submaximal effort. Yet many patients with fILD or COPD have the desire and ability to remain active outside of the home. Some patients may have to frequently perform at greater than submaximal levels of exertion depending on their home environment and activity needs. We previously demonstrated that a significant number of patients with idiopathic pulmonary fibrosis (IPF, the most common fILD) and COPD only demonstrate desaturation with near maximal effort(6). While this suggests that submaximal assessments may not identify oxygen needs in some patients, submaximal testing remains the standard of care. Prior AOT trials have not studied whether submaximal testing accurately identified real-world exertional oxygen needs. The ability to continuously monitor SpO_2 levels longitudinally across a range of real-world activities could inform clinical practice and future AOT trials.

AOT Outcomes and QOL in fILD and COPD: Prior AOT research in fILD and COPD mostly consists of small, single-center studies comparing a specific AOT device to no oxygen during laboratory-based exercise testing. Results suggest that AOT improves exercise time, exercise capacity, and dyspnea(20-27); however, real-world studies have not found consistent or significant benefits of AOT(28-34). Most studies used a 6WMT to identify exertional hypoxemia and provided a single AOT device at fixed settings for all participants regardless of whether the device was able to relieve exertional hypoxemia during the 6MWT. In one study where AOT was titrated to individual needs, it improved QOL measures in fILD(28). Systematic reviews of AOT in ILD have not found sufficient evidence to support or refute its use though only few studies meet inclusion criteria(35,36). In COPD, AOT for isolated exertional hypoxemia has not been shown to improve time to death or first hospitalization, QOL, 6MWT distance (6MWD), dyspnea, or activity(31-34). We suggest that these studies were flawed as a result of 1) not titrating AOT to maintain adequate SpO_2 during submaximal hypoxemia testing; 2) failing to verify whether AOT interventions were sufficient in relieving exertional hypoxemia during real-world activities, and 3) not considering how different AOT devices impact patient activity and outcomes. Therefore, significant opportunities remain for further investigations of AOT use in fILD and COPD.

Wearable Devices in Clinical Trials: Wearable devices can capture data on daily steps, activity level, SpO_2, heart rate, respiratory rate, and other measures across a range of activities. Devices vary by battery life, rechargeability, which parameters are monitored, frequency of data capture, and where they are worn (e.g., wrist,

finger, waist, ear). Direct-to-consumer devices have variable data accuracy especially regarding SpO_2 measurements(37,38) with data collection limited to on-demand or periodic background measures during periods of rest or low activity. Medical grade devices are better able to collect near continuous measurements of SpO_2 and other parameters across a range of patient activities. Real-world studies on AOT have been limited in their use of devices for continuous SpO_2 monitoring, most often utilizing a finger-worn probe for only short durations(39,40). Finger-probes may be more susceptible to motion artifact(41) and patients may be less likely to use them for extended periods compared to devices worn elsewhere. Failure to accurately and longitudinally measure real-world SpO_2 data limits the ability to determine whether prescribed AOT was sufficient in relieving real-world exertional hypoxemia. Newer devices with increased battery life, including ear-worn pulse oximeters FDA-cleared for SpO_2 monitoring during motion, may improve patient compliance and be less susceptible to motion artifact which could allow for improved data collection in AOT trials.

Patient-Reported Issues and Proposed Oxygen Reforms: Patients and caregivers report significant concerns regarding oxygen portability and equipment access(42-46). Professional organizations and advocacy groups(47) support passage of the Congressional Supplemental Oxygen Access Reform (SOAR) Act which aims to revise Medicare reimbursement policies and improve access to oxygen supplies and services(48). Further research on the role of AOT in fILD and COPD, which includes comparisons between different oxygen delivery devices, is essential to further address patient concerns and inform clinical practice and policy decisions.

Significance and Innovation: Prior studies have employed a "one-size-fits-all" approach to AOT. Ours will be the first to compare common methods of AOT delivery which have been titrated to maintain adequate SpO_2 during clinic-based submaximal testing. This study is innovative in being the first study to 1) compare different AOT devices with a control of no oxygen therapy, 2) utilize continuous SpO_2 monitoring via a novel ear-worn device over an extended period of real-world activity, and 3) evaluate if AOT titrated to individual needs during submaximal testing can meet real-world exertional demands. This work will serve as the basis for further grant opportunities (NHLBI K23, R01; PCORI) for conducting larger-scale clinical trials on AOT delivery and oxygen assessments which may include liquid oxygen therapy. Results of this work will address significant gaps in our current understanding of the role of AOT in fILD and COPD and will inform patients, providers, and policymakers on clinical practice and further research needs related to oxygen therapy.

Preliminary Data:

Exertional Oxygen Differences With Higher-Level vs Submaximal Walking(6): We conducted a retrospective review of data from a unique ramped treadmill protocol exercise test in patients with IPF or COPD. Among those who did not desaturate during submaximal testing (IPF=155, COPD=1,130), a significant proportion in both diseases (49% IPF, 25% COPD) demonstrated an oxygen need with near-maximal exertion. It is unknown whether submaximal oxygen

assessments such as a 6MWT can predict real-world exertional oxygen needs or if consideration for routine use of higher-level exercise testing is warranted.

AOT is Common in Low-Income Patients with ILD or COPD(49): We conducted a retrospective review of 2016-2020 administrative claims for Pennsylvania residents with fILD or COPD dually eligible for and receiving Medicaid and Medicare benefits. We found that AOT was common with >60% of patients receiving portable gas canisters and ~15% receiving POCs (Fig 2). This supports a need for further research on how AOT delivery devices impact patient activity and outcomes. Such research could have a significant impact on healthcare costs and resource utilization.

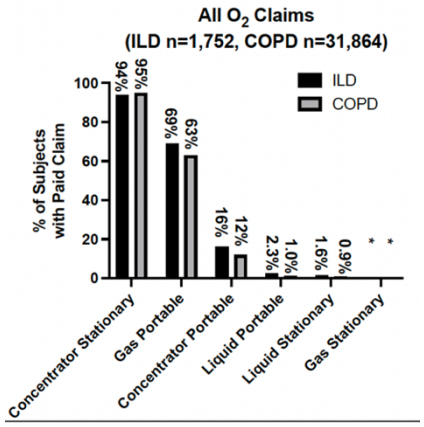

Fig 2. Proportion of claims by oxygen equipment type. Categories with <10 observations are redacted. (49)

4.2 Include complete citations or references.

Response:

1. Clark KP, Degenholtz HB, Lindell KO, Kass DJ. Supplemental oxygen therapy in interstitial lung disease: a narrative review. Ann Am Thorac Soc 2023;20(11):1541-1549.

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13. Saleem F, Hur SA, Cahalan M, Stewart C, Sljivic I, Bhuiyan I, et al. International guideline recommendations and eligibility criteria for home oxygen therapy. Lancet Respiratory Medicine 2023;11(5):402-405.

14. Hardinge M, Annandale J, Bourne S, Cooper B, Evans A, Freeman D, et al. British Thoracic Society Guidelines for home oxygen use in adults. Thorax 2015;70:i1-43.

15. McDonald CF, Serginson J, AlShareef S, Buchan C, Davies H, Miller BR, et al. Thoracic Society of Australia and New Zealand clinical practice guideline on adult home oxygen therapy. Respirology 2024;29(9):765-784.

16. Hardavella G, Karampinis I, Frille A, Sreter K, Rousalova I. Oxygen devices and delivery systems. Breathe (Sheff) 2019;15(3):e108-e116.

17. Khor YH, McDonald CF, Hazard A, Symons K, Westall G, Glaspole I, et al. Portable oxygen concentrators versus oxygen cylinder during walking in interstitial lung disease: A randomized crossover trial. Respirology 2017;22(8):1598-1603.

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supplementation in idiopathic pulmonary fibrosis patients without resting hypoxaemia. Respirology 2017;22(5):957-964.

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31. Holland AE, Hoffman M, Corte TJ, Chambers DC, hepworth G, Ekstrom, MP, et al. Ambulatory oxygen for treatment of exertional hypoxaemia in pulmonary fibrosis (PFOX): a multicentre, randomised, sham-controlled trial. Lancet Respir Med. 2026.

32. McDonald CF, Blyth CM, Lazarus MD, Marschner I, Barter CE. Exertional oxygen of limited benefit in patients with chronic obstructive pulmonary disease and mild hypoxemia. Am J Respir Crit Care Med 1995;152:1616-1619.

33. Nonoyama ML, Brooks D, Guyatt GH, Goldstein RS. Effect of oxygen on health quality of life in patients with chronic obstructive pulmonary disease with transient exertional hypoxemia. Am J Respir Crit Care Med 2007;176(4):343-349.

34. Moore RP, Berlowitz DJ, Denehy L, Pretto JJ, Brazzale DJ, Sharpe K, et al. A randomised trial of domiciliary, ambulatory oxygen in patients with COPD and dyspnoea but without resting hypoxaemia. Thorax 2011;66(1):32-37.

35. Long-Term Oxygen Treatment Trial Research Group, Albert RK, Au DH, Blackford AL, Casaburi R, Cooper JA, Jr., et al. A randomized trial of long-term oxygen for COPD with moderate desaturation. N Engl J Med 2016;375(17):1617-1627.

36. Sharp C, Adamali H, Millar AB. Ambulatory and short-burst oxygen for interstitial lung disease. Cochrane Database Syst Rev 2016;7(7):CD011716.

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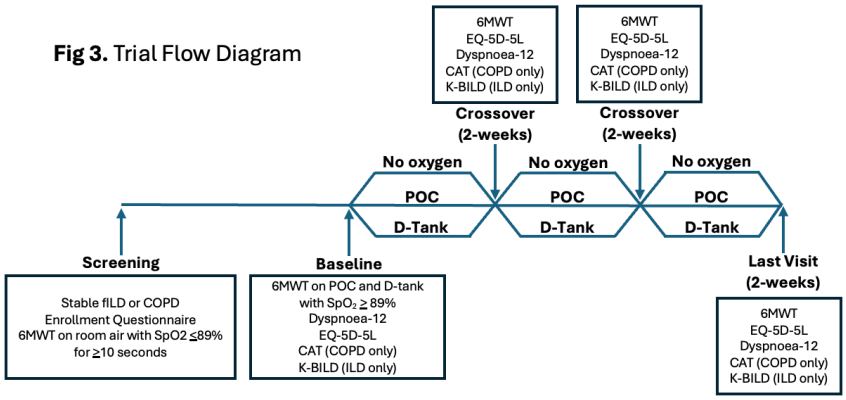
5.0 Study Design*

5.1 Describe and explain the study design (e.g. case-control, cross-sectional, ethnographic, experimental, interventional, longitudinal, observational).

Response:

We will pilot a prospective, randomized, crossover clinical trial evaluating the effect of AOT devices compared to no AOT on real-world activity, dyspnea, and QOL in patients with fILD or COPD who have isolated exertional hypoxemia (Fig 3). Participants will be randomized to sequences of 2-week periods of 1) no AOT therapy or AOT delivered via 2) POC (Inogen Rove 6) or 3) portable compressed canisters (D-tanks). A screening 6MWT will be completed on no oxygen to determine eligibility followed by repeated 6MWT on both devices to titrate oxygen therapy. 6MWT will be repeated at the end of each 2-week arm. Participants will be instructed to use POC setting and compressed canister flow rate at levels that maintained SpO_2 ≥89% during the 6MWT.

Fig 3. Trial Flow Diagram



QOL and dyspnea surveys will be completed at baseline and every 2-weeks. Multiple self-administered symptom and QOL tools validated for use in ILD and/or COPD will be used. The King's Brief Interstitial Lung Disease (K-BILD) questionnaire is a 15-question tool assessing health-related QOL measures over the preceding 2-weeks in participants with ILD(50,51). The COPD Assessment Test (CAT) is a 10-question tool assessing the impact of COPD on wellbeing and daily life(52,53). The Dyspnoea-12 is a 12-question tool evaluating breathing symptoms and their impact on well-being(54,55). The EuroQol 5-Dimension 5-Level (EQ-5D-5L) is a general (e.g., not disease-specific) QOL assessment tool with questions across a range of QOL domains and have been studied for use in ILD and COPD(41,57). All participants will complete the Dysponea-12 and EQ-5D-5L. The K-BILD will only be administered to participants with ILD and the CAT will only be administered to those with COPD.

Activity level including daily steps will be measured by ActiGraph LEAP, a wrist-worn activity monitor which has been extensively used in prior clinical trials for remote patient activity monitoring(58-61). Data collected includes step count, energy expenditure, total movement, activity level, heart rate, heart rate variability, cardiac rhythm, and respiratory rate. SpO_2 will be measured with Oxiwear, a rechargeable ear-worn pulse oximeter FDA cleared for SpO_2 monitoring during motion(62). Subjects will be asked to wear devices during waking hours. A subgroup of subjects (fILD=3, COPD=3) will wear a Nonin WristOx2 finger-worn oxygen probe (used in most prior AOT studies) for 2 consecutive days during each 2-week period to corroborate Oxiwear SpO_2 data(29,40,41,63).

6.0 Study Intervention/Investigational Agent

6.1 Describe the study intervention and/or investigational agent (e.g., drug, device) that is being evaluated.

Response:

All participants will complete sequential 2-week arms using one of two AOT devices or no AOT during normal activities of daily living. Participants will be randomized in the order in which they will be AOT. AOT will be provided through two devices:

- Inogen Rove 6 POC (Figure 1) – Provides oxygen via demand pulsed flow (bolus delivery timed with patient's breaths) at settings ranging from 1 to 6. Each setting has a fixed amount of oxygen which can be delivered per minute. Higher settings provide larger oxygen boluses. The amount delivered each breath also depends on a person's respiratory rate. The device is battery powered and rechargeable. The battery can last over 6 hours on a setting of 1 with lower battery life at higher settings. It weighs 4.8 pounds. The POC stores data on device use, distribution of flow settings, device state (off, power up, active use), and battery capacity. Inogen has provided POCs for use in prior clinical trials(41,64).
- Portable compressed oxygen D-tank canisters (Figure 2) – Provides oxygen at a continuous flow rate. Each tank holds approximately 404-425 liters of oxygen. When empty, tanks weight approximately 8 pounds. Duration of tank use will be dependent on required flow rate. Higher flow rates will result in faster depletion.

Wearable devices for real-world measures include:

- Oxiwear (Figure 3) – A novel, ear-worn pulse oximeter FDA-cleared for SpO_2 monitoring during motion and across skin tones. Oxiwear provides continuous SpO_2 and heart rate measurements for up to 12 hours of continuous use. It is battery-powered and can be recharged in 30 minutes. The device will sync to an app on a participant's smartphone. The app will upload data to Oxiwear 's cloud-based interface. Oxiwear will provides an alert (device vibration, smartphone notification) when SpO_2 levels fall below a set threshold though for the purposes of this trial participants will be asked to not manually check their SpO_2 or self-titrate their AOT.
- ActiGraph LEAP (Figure 4) – An FDA-cleared wristworn device with accelerometer and other data sensors which has been used extensively in prior research for monitoring patient activity. With continuous monitoring, the device battery can last up to 4 days. The battery is rechargeable. Up to 21 days of data can be stored on the device. Subjects are blinded to all data recordings. Data is downloaded directly off the device to computers via ActiGraph ActiLife software interface. The ActiGraph LEAP collects the following data: step count, non-sedentary time, energy expenditure, activity level, gait speed, heart rate, heart rate variability, skin temperature, respiratory rate, and cardiac rhythm.

- Nonin WristOx2 (Figure 5) – An FDA-cleared finger-worn pulse oximeter directly connected to a wrist-worn recording and storage device which provides continuous SpO_2 and heart rate monitoring for up to 72 hours. The device is not rechargeable and requires 2 AAA batteries. Data can be blinded to the patient. Data is downloaded directly off the device to a computer via Nonin WristOx2 software interface.

None of the oxygen equipment or wearable devices are investigational.

Figure 1.

www.inogen.com

Figure 2.

www.emstuff.com

Figure 3.

www.oxiwear.com

Figure 4.

https://ametris.com/actigraph-leap

Figure 5.

www.nonin.com

6.3 Drug/Device Handling: If the research involves drugs or device, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.

- *If the control of the drugs or devices used in this protocol will be accomplished by following an established, approved organizational SOP (e.g., Research Pharmacy SOP for the Control of Investigational Drugs, etc.), please reference that SOP in this section.*

Response:

POCs and all wearable devices will be stored in a locked office within the UB Clinical Research Office (CRO) located at 875 Ellicott St, 6th Floor, Buffalo, NY 14203. We will also store a select number of D-tanks for use during the in-office 6MWT to be provided to participants for transport home when they have been assigned to the D-tank arm of the study. D-tanks will be stored safely and as per UB requirements for the storage of oxygen canisters. Both POC and D-tanks will be provided to participants for 2-week periods. Wearable devices (Oxiwear, ActiGraph LEAP, Nonin WristOx2) will be provided for the full 6-week study. At the completion of each 2-week arm, participants will return to the CRO where the POC and D-tank will be returned and at which time data will be extracted from the POC, ActiGraph LEAP, and Nonin WristOx2. All equipment and devices will be cleaned and reset to baseline conditions as per manufacturer recommendations before being provided to a new participant.

6.4 If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

- *Identify the holder of the IND/IDE/Abbreviated IDE.*
- *Explain procedures followed to comply with sponsor requirements for FDA regulated research for the following:*

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

Response:

N/A

7.0 Local Number of Subjects

7.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed locally.

Response:

24 participants will be enrolled (12 with fILD and 12 with COPD).

7.2 If applicable, indicate how many subjects you expect to screen to reach your target sample (i.e. your screen failure rate).

Response:

We anticipate screening no more than 100 participants for this pilot study.

7.3 Justify the feasibility of recruiting the proposed number of eligible subjects within the anticipated recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?

Response:

This is a pilot study. Information from this pilot study will be used to derive informed power calculations associated with future work and thus sample size and estimates of screening and recruitment are primarily based on accurate assessment of study parameters and published recommendations(65,66).

In 2024, the UBMD pulmonary specialty clinic saw approximately 250 patients with an ILD diagnosis including 17 with idiopathic pulmonary fibrosis (IPF), >100 with sarcoidosis, and ~100 with other forms of ILD. COPD is one of the most common chronic lung diseases in the US with the number of UBMD pulmonary clinic patients with COPD far exceeding those with ILD. We do not anticipate having difficulty meeting our recruitment goals. To maximize recruitment efforts, we will also provide recruitment flyers and letters to pulmonary providers with General Physicians PC who may refer additional patients for consideration in joining this clinical trial. We may also recruit participants who are members of the Buffalo Research Registry or UB ILD

Research Registry who have diagnoses of fILD or COPD. These participants will be recruited via letter. As part of their registry enrollment, they have consented to being contacted about potential research opportunities.

8.0 Inclusion and Exclusion Criteria*

*8.1 Describe the criteria that define who will be **included** in your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

- Adults 18 to 85 years old with pulmonologist-diagnosed fibrotic ILD or COPD able to provide informed consent
  - fILD will include idiopathic pulmonary fibrosis, sarcoidosis, or other ILD with fibrotic changes on lung imaging (reticulations, honeycombing, traction bronchiectasis)
  - COPD subjects will have fixed airway obstruction on spirometry of <70%-predicted value as per Global Initiative for Obstructive Lung Disease diagnostic criteria(66)
- Self-report as being ambulatory outside of home without use of an assistive device (e.g., cane, walker)
- Stable lung disease on stable medical therapy for preceding 3 months
- Isolated exertional hypoxemia (SpO_2 <89% for ≥10 seconds) on a 6MWT conducted while breathing room air
- Able to maintain SpO_2 ≥89% for the full duration of a 6MWT while using the POC and portable oxygen canister used in this pilot study at a POC setting no higher than 6 and at oxygen flow rate via D-tank canister at no more than 6 liters per minute (LPM)

*8.2 Describe the criteria that define who will be **excluded** from your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

- Subjects <18 years old or >85 years as ILD and COPD are rare in children and older adults >85 are more likely to have comorbidities which may limit their activity inside or outside of their home
- Subjects with mixed ILD and COPD diagnoses
- Resting hypoxemia (SpO_2 <89%) on room air
- Emergency room visit or hospital admission in 3 months prior to recruitment
- Change in medical therapy in 3 months prior to recruitment
- Need for assistive devices (cane, walker, etc) for ambulation

- Pregnant
- Current smoker or residing with a current smoker
- Currently engaged in a pulmonary rehabilitation program
- Participants without a smartphone compatible with the Oxiwear app (necessary to collect Oxiwear oxygen saturation data) or those with a compatible smartphone device but without home wife or cellular service plan allowing for Oxiwear data uploading

8.3 Indicate specifically whether you will include any of the following special populations in your study using the checkboxes below.

NOTE: Members of special populations may not be targeted for enrollment in your study unless you indicate this in your inclusion criteria.

Response:

☐ Adults unable to consent

☐ Individuals who are not yet adults (infants, children, teenagers)

☐ Pregnant women

☐ Prisoners

N/A – We will not include any of these special populations

8.4 Indicate whether you will include non-English speaking individuals in your study. ***Provide justification if you will exclude non-English speaking individuals.***

In order to meet one of the primary ethical principles of equitable selection of subjects, non-English speaking individuals may ***not*** *be routinely excluded from research as a matter of convenience.*

In cases where the research is of therapeutic intent or is designed to investigate areas that would necessarily require certain populations who may not speak English, the researcher is required to make efforts to recruit and include non-English speaking individuals. However, there are studies in which it would be reasonable to limit subjects to those who speak English. Some examples include pilot studies, small unfunded studies with validated instruments not available in other languages, studies with numerous questionnaires, and some non-therapeutic studies which offer no direct benefit.

Response:

Due to current limitations with funding that would be needed to provide translation and interpretation services, non-English speakers will be excluded from this pilot study.

9.0 Vulnerable Populations*

If the research involves special populations that are considered vulnerable, ***describe the safeguards included to protect their rights and welfare.***

NOTE: You should refer to the appropriate checklists, referenced below, to ensure you have provided adequate detail regarding safeguards and protections. You do not, however, need to provide these checklists to the IRB.

9.1 For research that involves ***pregnant women,*** *safeguards include:*
NOTE CHECKLIST: Pregnant Women (HRP-412)

Response:

☒ **N/A**: This research does not involve pregnant women.

9.2 For research that involves ***neonates of uncertain viability or non-viable neonates,*** *safeguards include:*
NOTE CHECKLISTS: Non-Viable Neonates (HRP-413), or Neonates of Uncertain Viability (HRP-414)

Response:

☒ **N/A:** This research does not involve non-viable neonates or neonates of uncertain viability.

9.3 For research that involves ***prisoners****, safeguards include:*
NOTE CHECKLIST: Prisoners (HRP-415)

Response:

☒ **N/A:** This research does not involve prisoners.

9.4 For research that involves ***persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children")****, safeguards include:*
NOTE CHECKLIST: Children (HRP-416)

Response:

☒ **N/A:** This research does not involve persons who have not attained the legal age for consent to treatments or procedures ("children").

9.5 For research that involves ***cognitively impaired adults****, safeguards include:*
NOTE CHECKLIST: Cognitively Impaired Adults (HRP-417)

Response:

☒ **N/A:** This research does not involve cognitively impaired adults.

9.6 Consider if other specifically targeted populations such as students, employees of a specific firm, or educationally or economically disadvantaged persons are vulnerable. ***Provide information regarding their safeguards and protections, including safeguards to eliminate coercion or undue influence.***

Response:

Our target population is adults with diagnosed fILD or COPD who live in the greater Buffalo, NY area. It is possible that participants may be economically or educationally disadvantaged. It is also possible the participants may be students or employees of UB or UBMD. None of these populations are specifically targeted for this study. Eligible participants will undergo an informed consent process and will be given sufficient time to consider the risks and benefits of study enrollment before deciding whether or not to enroll. Participants will be informed that they may drop out of the study at any time.

10.0 Eligibility Screening*

10.1 Describe ***screening procedures*** *for determining subjects' eligibility. Screening refers to determining if prospective participants meet inclusion and exclusion criteria.*

Include all relevant screening documents with your submission (e.g. screening protocol, script, questionnaire).

Response:

We anticipate that the majority of participants who enroll in this study will be UBMD patients and identified by their primary care physician or UBMD pulmonologist.

To maximize our recruitment efforts, we will screen medical record data within the UBMD electronic health record (EHR) to identify patients with oxygen prescription orders with diagnoses of fILD or COPD utilizing International Disease Classification 10th Edition (ICD-10) diagnoses codes. fILD codes include those for IPF, sarcoidosis, connective tissue disease associated ILD (e.g., rheumatoid arthritis, scleroderma, dermatomyositis), hypersensitivity pneumonitis, and other pulmonary fibrosis diagnoses. We will also screen the Buffalo Research Registry and the UB ILD Research Registry for potentially eligible participants. ICD-10 codes that may be used for screening include:

- COPD - *ICD10: J40, J41, J41.0, J41.1, J41.8, J42, J43.0, J43.1, J43.2, J43.9, J44.0, J44.1, J44.9, J47.0, J47.1, J47.9, J89.2, J89.3*
- fILD – D86.0, D86.2, D86.9, J67.2, J67.9, *J84.1, J84.10, J84.11, J84.111, J84.112, J84.113, J84.114, J84.115, J84.116, J84.117, J84.17, J84.170, J84.178, M05.10, M33.21, M34.81, M33.11, M35.02*

We will review most recent pulmonary function test data including spirometry to ensure findings consistent with underlying diagnosis. COPD participants must have forced expiratory volume in one second / forced vital capacity (FEV1/FVC) < 70%-predicted as per internationally recognized diagnostic criteria(56). fILD

participants must have total lung capacity (TLC) <80%-predicted indicative of a restrictive lung disease.

We will review most recent CT imaging or radiology reports, when available, to determine presence of fibrotic changes (reticulations, honeycombing, traction bronchiectasis) for participants identified as having fILD, and absence of such findings for those identified as having COPD.

☐ **N/A:** There is no screening as part of this protocol.

11.0 Recruitment Methods

☐ **N/A:** This is a records review only, and subjects will not be recruited. NOTE: If you select this option, please make sure that all records review procedures and inclusion/exclusion screening are adequately described in other sections.

11.1 Describe when, where, and how potential subjects will be recruited.

NOTE: Recruitment refers to how you are identifying potential participants and introducing them to the study. Include specific methods you will use (e.g. searching charts for specific ICD code numbers, Research Participant Groups, posted advertisements, etc.).

Response:

Participants will be recruited from UBMD pulmonary and primary care clinics, General Physicians PC pulmonary clinics, the Buffalo Research Registry, and the UB ILD Research Registry. For UBMD clinics, participants may be identified and referred by their treating provider or contacted via recruitment letter (Attachment A) if identified as potentially eligible for the trial based off EHR screening criteria.

Participants with General Physicians PC will be identified and referred by their treating pulmonologist at General Physicians PC.

The Buffalo Research Registry, hosted by the Clinical and Translational Science Institute, serves to connect researchers and community members. Community volunteers who joined the registry have agreed to be contacted about research opportunities. The registry will be screened to identify potential members who may be eligible to join this pilot study. The ILD Research Registry is hosted by the UB Jacobs School of Medicine and Biomedical Sciences. The registry maintains diagnosis and other medical data on patients with ILD living in Western New York. Participants in the registry have agreed to be contacted about research opportunities related to their ILD. Participants enrolled in these registries who are identified as being potentially eligible for this study will be contacted via a patient recruitment letter (Attachment A).

Recruitment flyers (Attachment B) will be displayed in UBMD primary care and pulmonary clinics. A provider recruitment letter (Attachment C) with recruitment flyers will be distributed to General Physician PC pulmonary clinics. All recruitment letters and fliers will include information on the pilot study, its

purpose, inclusion/exclusion criteria, and information on how to enroll in the study. Copies of the informed consent form will also be provided.

Participants who wish to have more time to review the consent form and consider joining the study will be given additional time. A follow-up phone will be placed within 48 hours (Attachment D).

11.2 Describe how you will protect the privacy interests of prospective subjects during the recruitment process.

NOTE: Privacy refers to an individual's right to control access to him or herself.

Response:

All study participants will be assigned a unique study number and all data collected for this study will be associated with this number rather than participant identifying information. The participant identification key will be stored in a separate password-protected secure file with access limited to the Primary Investigators. All electronic participant data will be stored on an encrypted Advarra cloud server in a password protected database file or in password-protected folders on encrypted servers as per UB policy. Advarra Cloud meets stringent security and compliance standards, including SOC2, the Health Insurance Portability and Accountability Act (HIPAA), 21 CFR Part 11, and NIST 800-53. It provides scalable, encrypted storage with continuous data backup and disaster recovery capabilities. It also ensures high availability and data redundancy, minimizing the risk of data loss and supporting uninterrupted trial operations. System access is restricted to authorized personnel only, with multi-factor authentication and end-to-end encryption in place to safeguard sensitive participant information. Regular security audits and vulnerability assessments are conducted to maintain the integrity and confidentiality of the data.

All study visits will be conducted in the CRO. A private office will be used to review consent form, complete questionnaires and surveys, obtain vital signs, set up equipment and devices, retrieve equipment and device data, and collect vital signs. All 6MWT will be done in a hallway within the CRO. Every effort will be made to maintain participant privacy during the 6MWT.

SpO_2 data obtained from Oxiwear will be uploaded to their HIPAA-compliant cloud server. No identifying information is required to use Oxiwear or upload data. All participants will be assisted in setting up the Oxiwear app on their smartphone during their initial study visit. They will be given a unique identifier for use in the app only (different from their name or their unique study number) which further protects their privacy. After completion of the study, participants will be assisted in removing the Oxiwear app and data from their smartphone.

Data stored on the ActiGraph LEAP, Nonin WristOx2, and Inogen Rove 6 POC will be manually retrieved by the research team every 2-weeks during study visits. No patient identifying information is stored on these devices. Device data will be transferred to a smartphone and/or laptop device used by the primary researchers. The smartphone and/or laptop will be encrypted and password-protected as per

UB policy. Extracted data will be stored in Advarra cloud server or password-protected files on secure servers as per UB policy with access limited to the research team. Device data will be deleted and devices restored to factory/baseline settings as per manufacturer recommendations prior to being used by a new participant.

11.3 Identify any materials that will be used to recruit subjects.

NOTE: Examples include scripts for telephone calls, in person announcements / presentations, email invitations.

For advertisements, include the final copy of printed advertisements with your submission. When advertisements are taped for broadcast, attach the final audio/video tape. NOTE: You may submit the wording of the advertisement prior to taping to ensure there will be no IRB-required revisions, provided the IRB also reviews and approves the final version.

Response:

Attachment A – Participant Recruitment Letter

Attachment B – Recruitment Flyer

Attachment C – Provider Recruitment Letter

Attachment D – Participant Recruitment Phone Call Guide

12.0 Procedures Involved*

*12.1 Provide a description of **all research procedures or activities** being performed and when they are performed once a subject is screened and determined to be eligible. Provide as much detail as possible.*

NOTE: This should serve as a blueprint for your study and include enough detail so that another investigator could pick up your protocol and replicate the research. For studies that have multiple or complex visits or procedures, consider the addition of a schedule of events table in in your response.

Response:

People who meet general inclusion/exclusion criteria and who are interested in joining the study will be contacted by the Primary Investigator or Research Coordinator and scheduled for an in-person screening session. If possible, the informed consent will be completed prior to this visit over the phone with participant mailing the completing form or bringing it to the screening visit. Otherwise, the informed consent will be reviewed at the screening visit. Once the informed consent is signed by the participant, they will be asked to complete an Enrollment Questionnaire (Attachment E) to provide further information on their potential eligibility (smoking history, activity level, medical history) and information on their treatment providers in order to obtain medical record data needed to confirm eligibility. All consented participants will undergo a screening 6MWT on room air. To continue in the study, participants must demonstrate isolated exertional hypoxemia (SpO_2 <89% for ≥10 seconds) during the screening

6MWT. Participants without isolated exertional hypoxemia will not be eligible to continue in the study.

Eligible participants will then complete a full baseline visit, preferably on the same day but no more than14 days from signing the consent (to allow time for medical record review). Baseline vital sign data (heart rate, respiratory rate, blood pressure, resting SpO_2) along with weight and height collected. Participants will then complete additional 6MWTs using both the POC and D-tank canister in order to titrate POC setting and D-tank flow rate to maintain $SpO_2 \geq 89\%$ for the duration of a 6MWT. Participants must be able to maintain $SpO_2 \geq 89\%$ for the duration of a 6MWT on both the POC (up to a max setting of 6) and the D-tank (up to a max flow rate of 6 LPM). Participants who are unable to maintain $SpO_2 \geq 89\%$ on either device up to these settings will not be eligible to continue in the study and will be referred back to their treating provider for further oxygen eligibility testing or treatment. Participants will rest for 30 minutes between 6MWTs. Participants will complete baseline QOL and system assessment tools. All participants will complete the Dyspnoea-12 and EQ-ED-5L. ILD participants will also complete the K-BILD while COPD participants will complete the CAT.

Participants will be randomized to 2-week sequential periods utilizing 1) no oxygen therapy, 2) POC oxygen delivery at setting established during 6MWT, and 3) D-tank oxygen delivery at flow rate established during 6MWT.

All participants will be given an Oxiwear ear-worn saturation probe and an ActiGraph LEAP wrist-worn activity monitor. They will be educated on the use of these devices. They will be assisted with setting up the Oxiwear app and connecting the device to their smartphone and educated on how to do daily data uploads. Participants without a compatible smartphone or without a cellular plan or home wifi needed to upload Oxiwear data will be excluded from the study. Participants who do not have a compatible smartphone or who have a compatible smartphone but do not have a cellular data plan or high wifi needed to upload the Oxiwear data will be excluded from the study. Randomly selected participants (fILD=3, COPD=3) will also be given a Nonin WristOx2 with instruction to use this in conjunction with the Oxiwear and ActiGraph LEAP during pre-assigned 2 consecutive day periods during each 2-week arm in order to corroborate Oxiwear SpO_2 data. Participants will be instructed to use their AOT delivery device and wearable devices every day while awake during routine activities inside and outside of the home. They will be instructed to charge their devices/equipment every night or more often as needed.

Participants will be informed that Oxiwear will send a vibration and a smartphone alert a low SpO_2 is detected. Participants will be asked to ignore these notifications and to avoid self-monitoring their SpO_2 or self-titrating their AOT device.

Participants will be educated on the use of the POC and D-tank. They will be instructed to not titrate device setting or flow rate during the study.

Participants will be scheduled for return visits every 14 days. At each return visit, they will complete a 6MWT using whichever device (or no oxygen therapy during

the 2-week arm without oxygen) provided during that 2-week period. They will be asked whether they were alerted to low oxygen levels and whether they self-monitored their SpO_2 or adjusted their AOT device. All participants will complete new Dyspnoea-12 and EQ-5D-5L surveys at each follow-up. fILD participants will also complete new K-BILD surveys and COPD participants will complete new CAT forms. Vital signs, height, and weight will be re-measured. Data will be extracted from the Inogen POC, Oxiwear, ActiGraph LEAP and Nonin WristOx2 (if applicable). Participants will be provided with new equipment as indicated by the randomization schedule. At each follow-up visits, participants will be screened for any adverse or safety events (Attachment G).

Participant may receive a phone call in between follow-up visits. The purpose of the phone call is to remind them to use equipment and devices, ask if they are having any issues with equipment or devices, screen for adverse or safety events, and help troubleshoot issues (see Attachment F, Attachment G).

At study completion, participants will complete an End of Study Questionnaire asking them which intervention they felt best improved their activity, symptoms, and quality-of-life and which device (POC or oxygen tank) they would prefer to use (Attachment H).

All equipment including POC, Oxiwear, ActiGraph LEAP, and Nonin WristOx2 will be cleaned and reset to baseline settings as per manufacturer recommendations prior to being given to a new study participant.

12.2 Describe what data will be collected.

NOTE: For studies with multiple data collection points or long-term follow up, consider the addition of a schedule or table in your response.

Response:

- Demographic data (gender, race/ethnicity, age)
- Past medical history
- Current medications
- Most recent pulmonary function testing results
- Most recent chest imaging and reports (chest x-ray or CT chest scan)
- Vital signs (heart rate, resting SpO_2, respiratory rate) at baseline and every 2-weeks
- Height and weight at baseline and every 2-weeks
- 6MWT data which includes SpO_2, heart rate, blood pressure at end of test, 6MWD, and a numerical value of perceived dyspnea and fatigue as scored by the modified BORG scale (ranges from 0 to 10). 6MWT will be completed at baseline (on no oxygen and on POC and D-tank) and every 2-weeks

- Quality-of-life and symptom surveys at baseline and every 2 weeks (Dypsnoea-12, and EQ-5D-5L for all participants; K-BILD for fILD participants; CAT for COPD participants).
- Oxiwear sensor data which includes continuous SpO_2 and heart rate data
- Actigraph LEAP sensor data which includes activity level, motion, total steps, heart rate, heart rate variability, cardiac rhythm, and respiratory rate
- Nonin WristOx data which includes SpO_2 and heart rate
- POC device information which includes duration of device use, flow setting distribution, user breathing trend, device state distribution (normal state, flow change, power-up, shut down, error), and oxygen concentration trend
- D-tank utilization data including number of tanks used/refilled

12.3 List any instruments or measurement tools used to collect data (e.g. questionnaire, interview guide, validated instrument, data collection form).

Include copies of these documents with your submission.

Response:

Attachment E – Enrollment Questionnaire

Attachment F – Participant Follow-up Phone Call Guide

Attachment G – Adverse Event and Safety Monitoring Questionnaire

Attachment H – End-of-Study Questionnaire

Dyspnoea-12 Tool

King's Brief Interstitial Lung Disease (K-BILD) Questionnaire

COPD Assessment Test (CAT)

EuroQol 5-Dimension 5-Level (EQ-5D-5L) Quality of Life Tool

Example Key Code

12.4 Describe any source records that will be used to collect data about subjects (e.g. school records, electronic medical records).

Response:

Data on eligibility will be reviewed within the UBMD medical record for participants recruited from UBMD clinics. Demographic and medical history data will be reported by participants on the Enrollment Questionnaire. Participants will provide consent for release of health information at time of consent in this pilot study allowing research team members to obtain and review outside records (primary care and/or pulmonology notes, pulmonary function test results, imaging

reports, prior oxygen testing) related to their fILD or COPD diagnosis to confirm eligibility.

*12.5 Indicate whether or not **individual** subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings will be shared with subjects or others (e.g., the subject's primary care physician) and if so, describe how these will be shared.*

Response:

Participants will only be told the Inogen POC setting and D-tank flow rate that maintained their SpO_2 on the 6MWT as they will be instructed to use the equipment at these settings/flow rates during their real-world activity for this pilot study. No other individual results will be shared with participants or their providers.

*12.6 Indicate whether or not **study** results will be shared with subjects or others, and if so, describe how these will be shared.*

Response:

No study results will be shared with participants outside of those made public through presentations or eventual manuscript publication.

13.0 Study Timelines*

13.1 Describe the anticipated duration needed to enroll all study subjects.

Response:

Screening and recruitment for this study is expected to begin in March 2026. Prior to enrolling participants, we will ensure all necessary contracts and agreements are in place for use of oxygen delivery devices and wearable devices as required by UB. Wearable devices will be purchased once research funds are made available. We obtain necessary licenses/copyright permissions for the use of the symptom and QOL tools that will be used in this study. This study will be registered with ClinicalTrials.gov prior to enrolling the first participant.

We are targeting recruitment of 24 participants. Each participant will complete 6-weeks in this study. We anticipate enrolling and initiating the first participant by May 1, 2026. We are targeting running up to 5 participants concurrently. To avoid the confounder of Western New York's winter weather on activity outside of the home, we will suspend real-world data collection between November 1 and March 31 (e.g., real-world activity will only be monitoring between April 1 and October 31). We anticipate completing the data collection for all 24 participants by 10/31/27.

13.2 Describe the duration of an individual subject's participation in the study. Include length of study visits, and overall study follow-up time.

Response:

Each participant will be in the study for a total of 6-weeks from time of baseline 6MWT (maximum of 8 weeks from time of screening assessment).

All potentially eligible participants who provide informed consent will first undergo a screening visit during which they will complete the Enrollment Questionnaire and a 6MWT on room air to determine their eligibility with continuing in the study. The screening session is expected to last no more than 1 hour.

For participants eligible to continue in the study, additional baseline measures will be obtained, preferably on the same day as the screening visit or within 14 days in cases where further review of outside medical records is necessary to confirm eligibility. Baseline testing includes completion of repeated 6MWTs on the POC and D-tank to titrate oxygen delivery, vital sign measurements, height/weight measurements, and completion of the symptom and QOL tools. Completion of baseline assessments is expected to last no more than 3 hours.

Participants will then complete randomly assigned 2-week periods with either no oxygen therapy or oxygen delivered by POC or D-tank during their normal real-world activity with monitoring of their activity, clinical measures, and SpO_2. Every 14 days, participants will return to the CRO to complete updated symptom and QOL tools, repeat a 6MWT, have updated vital signs/height/weight measured, and allow for data extraction from devices and equipment. They will then be provided with updated equipment for the next study arm as indicated by the randomization schedule. Each follow-up visit is expected to last no more than 2 hours.

Total study participation time will be no more than 8 weeks with no more than 10 total hours spent with in-person visits.

13.3 Describe the estimated duration for the investigators to complete this study (i.e. all data is collected and all analyses have been completed).

Response:

We anticipate that from time of IRB approval and availability of research funds to completion of data collection, analysis and publication will be about 2 years.

14.0 Setting

14.1 Describe all facilities/sites where you will be conducting research procedures. Include a description of the security and privacy of the facilities (e.g. locked facility, limited access, privacy barriers). Facility, department, and type of room are relevant. Do not abbreviate facility names.

NOTE: Examples of acceptable response may be: "A classroom setting in the Department of Psychology equipped with a computer with relevant survey administration software," "The angiogram suite at Buffalo General Medical Center, a fully accredited tertiary care institution within New York State with badge access," or, "Community Center meeting hall."

Response:

Participants will come to the Clinical Research Office (CRO) located within the UB Clinical and Translational Research Center for all in-person study visits. A

private room will be used for the participant to meet with the Primary Investigator or Research Coordinator to complete the informed consent process and Enrollment Questionnaire. If eligible to continue after the screening 6MWT, participants will also complete QOL and symptom monitoring tools and have vital signs, height and weight measured. Participants will complete all 6MWT within a dedicated space at the CRO. Access to the CRO is restricted to authorized personnel with badge access.

14.2 For research conducted outside of UB and its affiliates, describe:

- *Site-specific regulations or customs affecting the research*
- *Local scientific and ethical review structure*

NOTE: This question is referring to UB affiliated research taking place outside UB, i.e. research conducted in the community, school-based research, international research, etc. It is not referring to multi-site research. UB affiliated institutions include Kaleida Health, ECMC, and Roswell Park Cancer Institute.

Response:

☒ **N/A:** This study is not conducted outside of UB or its affiliates.

15.0 Community-Based Participatory Research

15.1 Describe involvement of the community in the design and conduct of the research.

NOTE: Community-Based Participatory Research (CBPR) is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

Response:

☒ **N/A:** This study does not utilize CBPR.

15.2 Describe the composition and involvement of a community advisory board.

Response:

☒ **N/A:** This study does not have a community advisory board.

16.0 Resources and Qualifications

*16.1 Describe the qualifications (e.g., education, training, experience, expertise, or certifications) of the Principal Investigator **and** staff to perform the research. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research.*

NOTE: If you specify a person by name, a change to that person will require prior approval by the IRB. If you specify a person by role (e.g., coordinator, research assistant, co-investigator, or pharmacist), a change to that person will not usually require prior approval by the IRB, provided that the person meets the qualifications described to fulfill their roles.

Response:

All study team members have expertise in their field as it relates to this study and have completed necessary training regarding humans subject research.

Kristopher Clark, MD, is the ***Primary Investigator*** for this study. Dr. Clark is a Clinical Assistant Professor in the UB Jacobs School of Medicine Department of Medicine's Division of Pulmonary, Critical Care and Sleep Medicine. Dr. Clark has >2 years of clinical experience as an attending physician at UB caring for patients with ILD. He completed his fellowship training at the University of Pittsburgh where he had ILD clinical and research mentorship from Dr. Daniel J. Kass, Director of the UPMC Dorothy P. and Richard P. Simmons Center for Interstitial Lung Disease. Dr. Clark's prior research experience has focused on supplemental oxygen assessments, oxygen policies, and cost factors in ILD and COPD. He is the PI for the UB ILD Research Registry and the site PI for the industry-sponsored MOMENTOUS Study (*IMpact Of an ecg ai ModEl oN The diagnosis Of pUlmonary hypertenSion)* which uses an artificial intelligence approach to identify the diagnosis of pulmonary hypertension in ILD. He leads the UB monthly ILD multidisciplinary conference and is actively developing a dedicated multidisciplinary specialty ILD center at UB.

Sanjay Sethi, MD, is the Director of the UB Clinical and Translational Science Institute (CTSI), Director of the UB Clinical Research Office (CRO), and Tenured Professor and Division Chief of the UB Jacobs School of Medicine Department of Medicine's Division of Pulmonary, Critical Care and Sleep Medicine. Dr. Sethi has extensive experience in conducting clinical and translational research primarily as it relates to COPD including clinical and randomized trial design and implementation.

Daniel J. Kass, MD, is an Associate Professor at the University of Pittsburgh School of Medicine, Department of Medicines, Division of Pulmonary, Allergy, Critical Care and Sleep Medicine. Dr. Kass also serves as the Director of the UPMC Dorothy P. and Richard P. Simmons Center for Interstitial Lung Disease. Dr. Kass has a volunteer Adjunct position with the UB Jacobs School of Medicine in the Division of Pulmonary, Critical Care and Sleep Medicine. Dr. Kass is an expert in ILD patient care and is an NIH-funded researcher in ILD focusing on fibroblast biology in IPF and systemic sclerosis. He also has extensive experience in NIH-funded clinical trials in ILD and expertise in ILD oxygen assessments and

patient care. Dr. Kass has a pending UB adjunct appointment in process. He will assist in study design, conceptual implementation, and in the interpretation and analysis results in addition to providing direct mentorship to Dr. Clark.

Lora Cavuoto, PhD, is a Professor in the Department of Industrial and Systems Engineering and Director of the Surgery Human Factors and Ergonomics Laboratory in the Department of Surgery. She specializes in ergonomics and biomechanics. She has published in the areas of occupational safety and has specific expertise in the use of wearable technology to impact health including in data extraction and signal processing.

Gregory Wilding, PhD, is a Professor and Chair of the UB School of Public Health and Health Professions, Department of Biostatistics; Director of the UB Office of Clinical Trial Development and Implementation (OCTDI); and Director of the UB Biostatistics, Epidemiology, and Research Design (BERD) Core. He has extensive experience in designing and implementing clinical and randomized trials and in comparative and qualitative data analyses.

Catherine Wrona is a **Research Coordinator** for this study. She has 8 years of clinical research experience and 21 years of basic research experience. As the Research Coordinator, she will support patient recruitment, obtain consent, and assist with data entry, and provide mentoring and training to the Primary Investigator regarding the role of a Research Coordinator in clinical trials.

Maja Tankoska-Jakimovski, MD, is a **Research Coordinator** for this study. Dr. Tankoska has nearly three years of research experience and is currently working at the UB Clinical Research Office. As the Research Coordinator, she will support patient recruitment, obtain consent, and assist with data entry, and provide mentoring and training to the Primary Investigator regarding the role of a Research Coordinator in clinical trials.

Graduate Student (TBD) – Dr. Cavuoto will identify a graduate student who will assist with data extraction, signal processing, and data analysis from wearable devices.

Research Assistant (TBD) – Dr. Wilding will identify a Research Assistant from within the OCTDI who will assist in implementation and data analysis for this study.

Describe other resources available to conduct the research.

16.2 Describe the time and effort that the Principal Investigator and research staff will devote to conducting and completing the research.

NOTE: Examples include the percentage of Full Time Equivalents (FTE), hours per week. The question will elicit whether there are appropriate resources to conduct the research.

Response:

Dr. Clark will devote 75% of his time to this research.

Co-investigators, research coordinators, graduate student (TBD), and research assistant (TBD) will dedicate no more than 10% of their time to this research.

16.3 Describe the availability of medical or psychological resources that subjects might need as a result of anticipated consequences of the human research, if applicable.

NOTE: One example includes: on-call availability of a counselor or psychologist for a study that screens subjects for depression.

Response:

Participants found to have resting hypoxemia (SpO_2 <89% breathing room air) or who are unable to maintain ambulatory SpO_2 ≥89% during a 6MWT despite POC setting of 6 or D-tank flow rate of 6 LPM will be referred back to their treating pulmonologist and/or primary care physician for further oxygen testing and evaluation. Participants who experience an adverse event or report any other issue requiring medical care will be receive care from their treating provider and healthcare team.

The Primary Investigator, who is a board-certified practicing pulmonary and critical care physician, will be on call for the duration of this study to triage calls from participants for any concern related to this study. Both primary mentors for this study (Dr. Sethi and Dr. Kass) are also board-certified practicing pulmonologists who will be available for further consultation with the Primary Investigator as needed to assist in triaging participant concerns.

16.4 Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

Response:

All study team members will complete training on humans subject research, maintaining confidentiality, securing patient data, eligibility criteria, and the informed written consent process.

Prior to enrolling participants, all necessary UB-approved contracts, licenses, and agreements will be in place with non-UB study partners (Health Systems Services, Inogen, wearable device manufacturers) which will outline the study process, role of the study partner and study partner's responsibility and actions needed to maintain participant safety and confidentiality.

17.0 Other Approvals

17.1 Describe any approvals that will be obtained prior to commencing the research (e.g., school, external site, funding agency, laboratory, radiation safety, or biosafety).

Response: The funding agency National Institute of Health (NIH)/National Center for Advancing Translational Science (NCATS) approval and appointment will be obtained before commencing this research.

☐ **N/A:** This study does not require any other approvals.

18.0 Provisions to Protect the Privacy Interests of Subjects

18.1 Describe how you will protect subjects' privacy interests during the course of this research.

NOTE: Privacy refers to an individual's right to control access to him or herself. Privacy applies to the person. Confidentiality refers to how data collected about individuals for the research will be protected by the researcher from release. Confidentiality applies to the data.

Examples of appropriate responses include: "participant only meets with a study coordinator in a classroom setting where no one can overhear", or "the participant is reminded that they are free to refuse to answer any questions that they do not feel comfortable answering."

Response:

In-person study visits (screening, baseline measures, and follow-up visits) will be completed in a private room in the CRO. Participants will be required to complete a 6MWT in a hallway within the CRO. All efforts will be made to ensure privacy during the 6WMT.

Health Systems Services, who will provide participants with the D-tanks used in this study, will be required to know the name and address of study participants in order to make deliveries and refills for the oxygen canisters. Participants will consent to this disclosure as part of the informed consent process. An agreement will be in place between UB and Health System Services indicating the responsibility of Health System Services in maintaining participant confidentiality and protecting participant data. Health System Services will provide members of the research team with access to a secure, HIPAA-compliant web-based application ClickUp. This application will allow members of the research team to provide Health System Services with the contact information for participants to assist with delivery of oxygen tanks during this arm of the study. Health System Services will use this software to record participants' oxygen tank usage to the research team.

18.2 Indicate how the research team is permitted to access any sources of information about the subjects.

NOTE: Examples of appropriate responses include: school permission for review of records, consent of the subject, HIPAA waiver. This question ***does apply*** *to records reviews.*

Response:

A HIPAA Waiver will be completed allowing access to UBMD medical records for the purpose of screening for eligible participants seen by UBMD pulmonologists or primary care physicians.

As part of the consent process, participants will provide a signed HIPAA authorization allowing the research team to obtain medical records (progress notes, pulmonary function testing, chest imaging and reports, prior oxygen assessments) from their treating providers in order to confirm their eligibility.

Oxiwear data will be accessed via remote login to Oxiwear's HIPAA-compliant cloud server where data can be downloaded for further management and analysis.

Data from other wearable devices and from the Inogen POC will be manually extracted from the devices/equipment during in-person study visits.

Only the Primary Investigator or other authorized study team members will have access to the above data.

19.0 Data Management and Analysis*

19.1 Describe the data analysis plan, including any statistical procedures. This section applies to both quantitative and qualitative analysis.

Response:

Accelerometry, heart rate, activity, SpO_2, respiratory rate, and other biometric data will be extracted from the wearable devices throughout the study period. Data will first be filtered to remove noise and identify any potential outliers. Then data will be segmented based on the time periods of the study. Data on 6MWT results and vital signs during each study visit will be manually recorded by the Primary Investigator or Research Coordinators into an electronic data base. Participants will complete QOL and symptom tools manually (e.g., pen and paper) during baseline and each follow-up visit with results subsequently recorded into the electronic database.

Specific Aim 1 – Compare the effect of AOT delivery (POC vs compressed oxygen canister vs no oxygen therapy) on daily activity, QOL, and symptoms for patients with fILD or COPD.

Outcomes: Our primary outcome is change in steps per day between AOT devices and compared to no therapy. Secondary outcomes include differences in mean daily SpO_2; mean time with SpO_2 <89%; total AOT use (time POC was active, number of D-tanks used); differences in 6MWD; and differences in QOL and symptom scores.

Analysis: Analyses will be according to intention-to-treat principles where participants are analyzed according to the sequence they are randomly assigned. To describe the observed variability in outcomes and estimate differences between experimental conditions, similar analytic approaches will be used for all assessments, namely mixed linear models. Outcomes will be fit as a function of fixed effects representing condition, period, a condition by period interaction, and a random participant effect. Once a model is fit, specific linear contrasts based on the estimated model parameters will be constructed and used to test equality of marginal means corresponding to condition done in conjunction with a two-sided 0.05 nominal significance level. Point estimates and corresponding 95% confidence intervals to quantify condition differences will be provided.

***Specific Aim 2 – Assess whether AOT titrated during a 6MWT meets real-world exertional* oxygen needs**

Outcomes: We will correlate nadir SpO_2 on 6MWT to mean SpO_2 nadir during real-world activities and determine if AOT device settings/flow rates which

relieve exertional hypoxemia during 6MWT were sufficient in relieving exertional hypoxemia during real-world activities.

Analysis: Correlation coefficients will be estimated and mixed linear models will be used to assess associations.

19.2 If applicable, provide a power analysis.

NOTE: This may not apply to certain types of studies, including chart/records reviews, survey studies, or observational studies. This question is asked to elicit whether the investigator has an adequate sample size to achieve the study objectives and justify a conclusion.

Response:

As this is a pilot study on the feasibility of our study design and to collect preliminary data to support a larger clinical trial, a power analysis was not performed. We will target the enrollment 24 participants (fILD=12, COPD=12) who will complete the study. Information from this pilot study will be used to derive informed power calculations associated with future work and thus sample size is primarily based on accurate assessment of study parameters and follows published recommendations(57,58).

19.3 Describe any procedures that will be used for quality control of collected data.

Response:

The research team will ensure that all manually collected data fields are completed appropriately.

20.0 Confidentiality*

A. Confidentiality of Study Data

*Describe the local procedures for maintenance of confidentiality of **study data and any records that will be reviewed for data collection**.*

*20.1 A. Where and how will all data and records be stored? Include information about: password protection, encryption, physical controls, authorization of access, and separation of identifiers and data, as applicable. Include physical (e.g. paper) **and** electronic files.*

Response:

All study participants will be assigned a unique study number at time of consent prior to completing any screening or baseline measures. All data collected will be associated with the study number and stored on a secure Advarra Cloud server or secure, password-protected servers as per UB policy with access limited to members of the research team. A separate file (key code) associating participant names and study numbers will be stored in a separate password-protected file on a secure UB server with access limited to the Primary Investigator.

No personal identifying information will be used to associate any wearable device or AOT equipment data to participants. When an identifier is required, a random user name (different from participant's name and from study number) will be assigned. Data will be manually extracted directly from the Nonin WristOx2, ActiGraph LEAP, and Inogen POC by the Primary Investigator or Research Coordinator during in-person study visits and will be stored in a password protected, secure UB server with access limited to the research team. Data collected from the Oxiwear ear-worn pulse oximeter will be updated to the Oxiwear cloud-based HIPAA-compliant interface by participants via use of a smartphone app. Participants will be assisted in setting up the app and no personal identifying information will be associated with this data.

Data collected via hard copy documents will be stored in a locked cabinet in the locked office of the Primary Investigator (Buffalo General Medical Center, 100 High Street, Room B-814, Buffalo, NY 14203).

For Oxiwear, data will be downloaded from the company's HIPAA compliant cloud-based server. Data from other wearable devices and from the Inogen POC will be manually extracted directly from the device by a member of the research team.

Health Systems Services will provide the Primary Investigator with and research team with electronic access to a HIPAA-compliant web-based application ClickUp to track participant usage of oxygen tanks.

All electronic study data will be stored in a password-protected, encrypted folder or secure server as per UB policy. Access to all study data will be limited to the research team.

20.2 A. How long will the data be stored?

Response:

Electronic, de-identified data will be stored indefinitely. Hard copy files will be stored for at least 3 years before being destroyed.

20.3 A. Who will have access to the data?

Response:

Only members of the study team will have access to the data.

20.4 A. Who is responsible for receipt or transmission of the data?

Response:

The Primary Investigator and other assigned study team members will be responsible for receipt and transmission of data.

20.5 A. How will the data be transported?

Response:

Hard copy files will be transported by the Primary Investigator or research team member from the CRO to the secured office at Buffalo General Medical Center. Most other files will be stored on secure UB servers.

B. Confidentiality of Study Specimens

*Describe the local procedures for maintenance of confidentiality of **study specimens**.*

☒ **N/A:** No specimens will be collected or analyzed in this research. *(Skip to Section 21.0)*

20.6 B. Where and how will all specimens be stored? Include information about: physical controls, authorization of access, and labeling of specimens, as applicable.

Response:

N/A

20.7 B. How long will the specimens be stored?

Response:

N/A

20.8 B. Who will have access to the specimens?

Response:

N/A

20.9 B. Who is responsible for receipt or transmission of the specimens?

Response:

N/A

20.10 B. How will the specimens be transported?

Response:

N/A

21.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

NOTE: Minimal risk studies may be required to monitor subject safety if the research procedures include procedures that present unique risks to subjects that require monitoring. Some examples include: exercising to exertion, or instruments that elicit suicidality or substance abuse behavior. In such cases, N/A is not an acceptable response.

21.1 Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

Response:

Adverse and safety event data will be reviewed quarterly by an independent Data Safety Monitor. The independent Data Safety Monitor for this study will be Carla Fredericks, MD, a board-certified pulmonologist with UBMD who has experience with clinical trials and data safety monitoring.

Safety analyses will include summaries of participant-reported adverse and safety events. Participants will be screened for adverse or safety events every 2-weeks during in-person visits and during between-visit phone calls. Any event determined to be serious or unanticipated will be reported to the University at Buffalo Institutional Review Board as per university policy. Participants who experience an adverse event will receive necessary medical care from their local healthcare team.

The wearable devices used in this study will collect data related to our study outcomes and are not being used to monitor for adverse events. We expect to see variations in vital sign and activity parameters during the course of this study including periods of exertional desaturation. These results may vary based on participants' ILD/COPD disease severity, level of physical activity, and with use of different oxygen devices which differ on weight and portability. However, it is possible that wearable devices incidentally record clinical abnormalities unrelated to this study such as sustained brady or tachyarrhythmias ($\geq$15 minutes) which require further evaluation to determine if the finding is real and clinically significant. These will be recorded as adverse events and participants and their treating providers will be notified of such findings so that the issue can be further investigated by the treating provider. This approach is in line with prior clinical trials on ambulatory oxygen use which did not identify vital sign or activity outcomes as adverse or safety events(31,35).

Participants who develop resting hypoxemia during the study will no longer be eligible to continue in the study and will be referred to their treating provider for oxygen testing and prescription. Data collected up until time of ineligibility will still be analyzed.

Oxiwear does not have the ability to blind SpO_2 results from participants. If Oxiwear detects low oxygen saturations (threshold adjustable but no lower than 87%), it will alert the participant with a vibration from the device and with an alert to their smartphone. Participants will be asked to not self-monitor their SpO_2 through the Oxiwear app or other oxygen monitoring devices during this study, and to not self-titrate their POC or D-tank. Some Oxiwear alerts may be due to poor signal quality and therefore not reflective of true hypoxemia. Participants will be advised to stop activity for at least 5 minutes should they receive Oxiwear alerts for $\geq$5 consecutive minutes as episodes of true exertional hypoxemia are expected to be transient and to recover with brief cessation of activity. If low saturation alerts continue despite 5 at least 5 minutes of rest then participants will

be recommended to seek medical treatment and the event will be recorded as an adverse event.

21.2 Describe what data are reviewed, including safety data, untoward events, and efficacy data.

Response:

We will follow the ICH Guideline for Good Clinical Practice E6(R3) in identifying adverse events as "any unfavourable medical occurrence in a trial participant administered the investigational product"(69). Safety analyses will include summaries of participant-reported adverse and safety events. An Adverse Event and Safety Monitoring Questionnaire (Attachment G) will completed a member of the research team to screen participants for adverse or safety events during each in-person visit (every 2-weeks) and during between-visit phone calls. Participants will be asked "have you had any problems with or changes in your health since we last saw you?" In addition, we will screen for and ask participants about the following adverse events of special interest which are adapted from those used in prior AOT trials(31,35).

- Burns related to oxygen use
- Skin irritation or injury from wearable device use
- Development of resting hypoxemia
- Exacerbation of underlying ILD or COPD
- Nosebleed or dry nose
- Musculoskeletal injury from tripping or falling while using AOT
- Emergency room visit or hospital admission

Participants who report receiving Oxiwear alerts of low oxygen saturations that do not resolve after at least 5 minutes of rest will have the event recorded as an adverse event.

We will also collect any adverse or safety reports from the participant's treating provider including a report of hospitalization, death, or other concerns. Participants may also contact the Primary Investigator or designee at any time during the research period to report an adverse or safety event. The Primary Investigator or designee will be on call to take such reports and triage participant concerns throughout the study.

Serious adverse events will be immediately reported to the Data Safety Monitor and Primary Investigator as well as the University at Buffalo IRB. Serious adverse events will be any adverse event that:

- Results in death
- Is immediately life threatening
- Results in persistent or significant disability/incapacity

Adverse Events will be graded 1 to 5 as defined below:

- Grade I (mild) – An event that is transient and may require only minimal treatment or therapeutic intervention. This event generally does not interfere with usual activities of daily living.
- Grade 2 (moderate) – An event that is usually alleviated by additional specific therapeutic intervention. The event interferes with usual activities of daily living, causing discomfort but poses no significant or permanent risk of harm to the subject.
- Grade 3 (severe) – An event that requires intensive therapeutic intervention. The event interrupts usual activities of daily living, or significantly affects the clinical status of the subject.
- Grade 4 (life threatening) – An event and/or its immediate sequalae that is associated with an imminent risk of death or with physical or mental disabilities that affect or limit the ability of the subject to perform activities of daily living (eating, ambulation, toileting, etc).
- Grade 5 (fatal) – Death (loss of life) as a result of an event.

Data collected from wearable devices and from portable oxygen equipment will be reviewed quarterly by the research team as part of an ongoing efficacy analysis.

21.3 Describe any safety endpoints.

Response:

We do not foresee the need for any safety endpoints; however, the Data Safety Monitor will halt the study if they deem it to be necessary. Participants who experience an adverse event will receive necessary medical care from their local healthcare team.

21.4 Describe how the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).

Response:

An Adverse Event and Safety Monitoring Questionnaire (Attachment G) will be used to screen participants every 2-weeks during in-person visits and during between-visit phone calls.

The participant's treating provider may report concerns for Adverse or Safety Events to the Primary Investigator at any time.

Participants may contact the Primary Investigator or designee at any time to report an Adverse or Safety Event. The Primary Investigator or designee will be on call to triage and record such concerns during the duration of this study.

Resting and ambulatory saturation data will be collected by direct observation of 6MWT by research staff and by manual or data download from wearable devices.

21.5 Describe the frequency of safety data collection.

Response:

Participants will be screened for adverse or safety events every 2-weeks during in-person visits and during between-visit phone calls. Participants may also self-report any events by contacting the Primary Investigator who will be on-call for this study. Treating providers may report events at any time.

Data for 6MWT will be collected at the time of the test (screening, baseline, every 2 weeks). Clinical data from wearable will be collected every 2 weeks and reviewed quarterly. Data from Oxiwear can be viewed remotely after participants upload the data, therefore can be collected more frequently based on when participants upload data.

21.6 Describe who will review the safety data.

Response:

The results of safety data will be reviewed by the Data Safety Monitor as well as the Primary Investigator and other members of the research team.

21.7 Describe the frequency or periodicity of review of cumulative safety data.

Response:

Cumulative safety data will be reviewed quarterly.

21.8 Describe the statistical tests for analyzing the safety data to determine whether harm is occurring.

Response:

N/A

21.9 Describe any conditions that trigger an immediate suspension of the research.

Response:

We do not foresee any condition which will trigger an immediate suspension of the research; however, the Data Safety Monitor will halt the study if they deem it to be necessary.

22.0 Withdrawal of Subjects*

☐ **N/A:** This study is not enrolling subjects. This section does not apply.

*22.1 Describe **anticipated** circumstances under which subjects may be withdrawn from the research without their consent.*

Response:

Participants who consent for the study may be subsequently withdrawn if they do not meet further study inclusion/exclusion criteria the during 6MWT testing or if subsequent review of medical data indicates that the participant does not meet study inclusion/exclusion criteria. Participants who developing resting hypoxemia during the course of the study no longer be eligible to continue but will have their

data remain in the study for analysis. Participants who lose access to an Oxiwear-compatible smartphone device or means of uploading Oxiwear data from their smartphone will be unable to continue in the study.

22.2 Describe any procedures for orderly termination.

NOTE: Examples may include return of study drug, exit interview with clinician. Include whether additional follow up is recommended for safety reasons for physical or emotional health.

Response:

Upon the completion of the study period, final wearable device and AOT equipment data will be collected, all devices/equipment provided to participants will be returned at which time the participant's involvement in this study will cease.

Participant who wish to withdrawal early from the study will be asked to notify the Primary Investigator in writing. The Primary Investigator will advise the participant to stop using the study devices/equipment and arrangements will be made for the prompt return of all devices and equipment to the Primary Investigator.

22.3 Describe procedures that will be followed when subjects withdraw from the research, including retention of already collected data, and partial withdrawal from procedures with continued data collection, as applicable.

Response:

If a participant opts to withdrawal from participation in the study, collection of data from wearable devices and AOT equipment will cease. Any data collected during the study up until the time the participant notifies the Primary Investigator in writing of their desire to withdrawal from the study will be still be maintained and used for final analyses. This includes data that remains on study devices that were collected prior to the participant's notification of withdrawal but which had not yet been extracted by the research team. Participants who withdrawal from the study will return all study devices and equipment to the Primary Investigator.

23.0 Risks to Subjects*

23.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to their participation in the research. Consider physical, psychological, social, legal, and economic risks. Include a description of the probability, magnitude, duration, and reversibility of the risks.

NOTE: Breach of confidentiality is always a risk for identifiable subject data.

Response:

We anticipant that participants will experience periods of exertional dyspnea especially during the 2-week arm in which no ambulatory oxygen will be provided. The literature and clinical experience indicate that episodes of

exertional hypoxemia are most often transient events of short duration which self-limit patient activity, and that oxygen levels rapidly recover after cessation of activity; therefore it is unlikely that such episodes occurring over the duration of this study will cause any short- or long-term adverse consequences(59). Due to lack of high-quality data on whether AOT provides any meaningful benefit to patients with exertional hypoxemia, current US recommendations for AOT are conditional and, outside of the US, AOT is not as commonly prescribed. Prior studies of AOT use did not report any adverse or safety event related to desaturation episodes(31,35). This pilot study is designed specifically to see if our experimental approach can allow for larger, multi-site clinical trials that can exam the ability of AOT to meet exertional oxygen demands with real-world activity and how symptoms, activity, and QOL are affected.

Use of AOT and wearable devices may impede participants' mobility and dexterity which could lead to a risk of fall or other injury. This risk is anticipated to be low with the use of the lightweight portable AOT equipment in this study along with wearable devices that will be used predominantly on the ear and wrist. Participants will be educated on proper device and equipment use including on the risk of falls and how to minimize this.

There may be a risk of skin irritation with use of wearable devices. This risk is expected to be low with the devices used in this study. Participants will be instructed to remove devices during periods of rest to allow any irritation to resolve. Alternatively, they will be instructed to alternate devices between ears/wrists/fingers.

There is an increased risk of fires and burns when using supplemental oxygen therapy. Participants who are current smokers or reside with current smokers will be excluded. Participants will be educated on this risk and advised to not use AOT near open flames including when cooking on gas stoves.

Use of oxygen therapy may lead to dry nose and potentially nosebleeds. This risk is expected to be low with duration of oxygen use in this study. Nosebleeds are most likely to be minor and resolve with removal of oxygen and holding pressure over the bridge of the nose for several minutes.

Some survey questions about symptoms or participants' well-being may involve sensitive issues and/or participants may be uncomfortable or embarrassed answering these questions. This risk is expected to be low as the survey tools used in this study are commonly used in research and clinical practice.

There is a risk of loss of confidentiality of study data. This risk is expected to be low.

23.2 Describe procedures performed to lessen the probability or magnitude of risks, including procedures being performed to monitor subjects for safety.

Response:

All participants enrolled in this study will be required to demonstrate isolated exertional hypoxemia. Participants will be educated on symptoms associated with

exertional hypoxemia and advised that such episodes are expected to be brief and resolve with a few moments of rest or stopping activity.

Participants will be educated about the risk of injury from use of wearable devices and oxygen equipment, as well as risk of dry nose/nosebleed. They will be educated on proper use of devices and equipment to minimize these risks. They will be advised to remove oxygen equipment and hold pressure over the bridge of the nose for several minutes in case of nosebleed.

Any participant who is a current smoker or lives with a current smoker will be excluded from this study. Participants will be counseled on the fire risk associated with supplemental oxygen use and provided with instructions to keep oxygen equipment away from fires and other open flames.

Participants will be informed that they may decline to complete surveys related to symptoms and quality-of-life. They will be encouraged to discuss any concerns related to symptoms and quality-of-life with their treating provider.

This risk of loss of confidentiality of study data will be minimized by the measures in place for maintaining confidentiality as noted in Section 20.

Participants will have in-person follow-up visits every 2-weeks at which time vital signs will be measured. Phone calls will also be made to participants in between study visits. These communications will allow for ongoing evaluation of any safety issues or other participant concerns.

The Primary Investigator and Research Coordinators will be available to triage any other concerns participants may have related to this study throughout the duration of the study.

*23.3 If applicable, indicate **which procedures** may have risks to the subjects that are currently unforeseeable.*

Response:

N/A

23.4 If applicable, indicate which research procedures may have risks to an embryo or fetus should the subject be or become pregnant.

Response:

N/A

23.5 If applicable, describe risks to others who are not subjects.

Response:

As noted, oxygen therapy carries a risk of fire and burns. Any participant who is a current smoker or lives with a current smoker will be excluded from this study. Participants will be counseled on the fire risk associated with supplemental oxygen use and provided with instructions to keep oxygen equipment away from fires and other open flames.

24.0 Potential Benefits to Subjects*

24.1 Describe the potential benefits that individual subjects may experience by taking part in the research. Include the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit.

*NOTE: Compensation **cannot** be stated as a benefit.*

Response:

There is no direct benefit for individual participants from participating in this study though participants may experience improvement in dyspnea, activity, or quality-of-life during the period of using AOT therapy for this study as these are the primary measures being studied. Participants will know the POC setting and oxygen canister flow rate which maintained their SpO_2 during a 6MWT. This information may be used by them to discuss ongoing AOT with their treating provider after completion of this study.

The potential benefits of this study exceed the minimal risk to participants.

25.0 Compensation for Research-Related Injury

☐ **N/A:** The research procedures for this study do not present risk of research related injury (e.g. survey studies, records review studies). This section does not apply.

*25.1 **If the research procedures carry a risk of research related injury,** describe the available compensation to subjects in the event that such injury should occur.*

Response:

We anticipate risk of injury to be minimal; however, should participants be injured they will receive necessary medical care from their local healthcare team. There is no plan for compensation for research-related injuries.

25.2 Provide a copy of contract language, if any, relevant to compensation for research related injury.

*NOTE: If the contract is not yet approved at the time of this submission, submit the current version here. If the contract is later approved with **different language regarding research related injury**, you must modify your response here and submit an amendment to the IRB for review and approval.*

Response:

N/A

26.0 Economic Burden to Subjects

26.1 Describe any costs that subjects may be responsible for because of participation in the research.

NOTE: Some examples include transportation or parking.

Response:

Participants will be responsible for transportation and parking costs associated with attending the study visits. As use of the Oxiwear device requires data upload to a cloud-based server, participants may also be responsible for associated data fees from their cellular carrier or internet-service provider. Participants will be responsible for the additional home electrical cost associated with charging the devices and equipment used in this study, though such costs are expected to be minimal and not add significantly to their standard electrical bill.

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

27.0 Compensation for Participation

27.1 Describe the amount and timing of any compensation to subjects, including monetary, course credit, or gift card compensation.

Response:

Participants who consent to this study will be provided with $50 gift cards for time spent during each study visit: $50 for completing the screening Enrollment Questionnaire and 6MWT, $50 for completing the baseline 6MWTs and QOL and dyspnea surveys, and $50 for each follow-up visit after study weeks 2, 4 and 6. The maximum amount that any participant can receive is $250 for completion of the entire study. Participants will be informed that they may drop out of the study at any time.

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

☐ **N/A:** There is no compensation for participation. This section does not apply.

28.0 Consent Process

28.1 Indicate whether you will be obtaining consent.

NOTE: This does not refer to consent documentation, but rather whether you will be obtaining permission from subjects to participate in a research study.
Consent documentation is addressed in Section 29.0.

☒ ***Yes*** *(If yes, Provide responses to each question in this Section)*
☐ ***No*** *(If no, Skip to Section 29.0)*

28.2 Describe where the consent process will take place. Include steps to maximize subjects' privacy.

Response:

Participants who meet basic inclusion/exclusion criteria will be invited to attend a screening visit at which time the informed consent process will take place within

a private room in the CRO. If possible, the consent form will be completed prior to this visit via phone call.

28.3 Describe how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study.

NOTE: It is always a requirement that a prospective subject is given sufficient time to have their questions answered and consider their participation. See "SOP: Informed Consent Process for Research (HRP-090)" Sections 5.5 and 5.6.

Response:

Participants who are invited to join the study based off of screening of UBMD medical records or from eligibility determined from review of data from the Buffalo Research Registry or UB ILD Research Registry will be provided with a copy of the informed consent to review before the screening visit. Participants referred from their UBMD or General Physicians PC pulmonologists will be given a copy of the informed consent to review prior to their initial visit or at their initial study visit.

All participants will be provided with sufficient time to review the informed consent and ask any questions from the Primary Investigator. Should a participant wish to have further time to consider joining the study, a follow-up phone call and/or follow-up visit will be scheduled within 48 hours.

28.4 Describe any process to ensure ongoing consent, defined as a subject's willingness to continue participation for the duration of the research study.

Response:

Participants who wish to withdrawal their consent for participating in this study will be asked to submit this in writing to the Primary Investigator. Otherwise, continued involvement in the study by attending study visits and utilizing study equipment and devices will imply the participant's ongoing consent to participate.

28.5 Indicate whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." Pay particular attention to Sections 5.4-5.9. If not, or if there are any exceptions or additional details to what is covered in the SOP, describe:

- *The role of the individuals listed in the application who are involved in the consent process*
- *The time that will be devoted to the consent discussion*
- *Steps that will be taken to minimize the possibility of coercion or undue influence*
- *Steps that will be taken to ensure the subjects' understanding*

Response:

☒ We have reviewed and will be following "SOP: Informed Consent Process for Research (HRP-090)."

Non-English Speaking Subjects

☒ **N/A:** This study will not enroll Non-English speaking subjects. *(Skip to Section 28.8)*

28.6 Indicate which language(s) other than English are likely to be spoken/understood by your prospective study population or their legally authorized representatives.

NOTE: The response to this Section should correspond with your response to Section 8.4 of this protocol.

Response:

N/A

28.7 If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language, how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study, and any process to ensure ongoing consent. Indicate the language that will be used by those obtaining consent.

NOTE: Guidance is provided on "SOP: Informed Consent Process for Research (HRP-090)."

Response:

N/A

Cognitively Impaired Adults

☒ **N/A**: This study will not enroll cognitively impaired adults. *(Skip to Section 28.9)*

28.8 Describe the process to determine whether an individual is capable of consent.

Response:

N/A

Adults Unable to Consent

☒ **N/A**: This study will not enroll adults unable to consent. (*Skip to Section 28.13)*

When a person is not capable of consent due to cognitive impairment, a legally authorized representative should be used to provide consent (Sections 28.9 and 28.10) ***and, where possible, assent of the individual should also be solicited*** *(Sections 28.11 and 28.12).*

28.9 Describe how you will identify a Legally Authorized Representative (LAR). Indicate that you have reviewed the "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" for research in New York State.

NOTE: Examples of acceptable response includes: verifying the electronic medical record to determine if an LAR is recorded.

Response:

N/A

☐ We have reviewed and will be following "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."

28.10 ***For research conducted outside of New York State****, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the research. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

N/A

28.11 Describe the process for ***assent of the adults****:*

- *Indicate whether assent will be obtained from all, some, or none of the subjects.* ***If some, indicate which adults will be required to assent and which will not.***

Response:

N/A

- ***If assent will not be obtained from some or all subjects, provide an explanation of why not.***

Response:

N/A

28.12 Describe whether ***assent of the adult*** *subjects will be documented and the process to document assent.*

NOTE: The IRB allows the person obtaining assent to document assent on the consent document using the "Template Consent Document (HRP-502)" Signature Block for Assent of Adults who are Legally Unable to Consent.

Response:

N/A

Subjects who are not yet Adults (Infants, Children, and Teenagers)

☒ **N/A**: This study will not enroll subjects who are not yet adults. *(Skip to Section 29.0)*

*28.13 Describe the criteria that will be used to determine **whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research** under the applicable law of the jurisdiction in which the research will be conducted **(e.g., individuals under the age of 18 years)**. For research conducted in NYS, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children."*

NOTE: Examples of acceptable responses include: verification via electronic medical record, driver's license or state-issued ID, screening questionnaire.

Response:

N/A

*28.14**For research conducted outside of New York State**, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

N/A

28.15 Describe whether parental permission will be obtained from:

Response:

☐ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

☐ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

☐ Parent permission will not be obtained. A waiver of parent permission is being requested.

NOTE: The requirement for parent permission is a protocol-specific determination made by the IRB based on the risk level of the research. For guidance, review the "CHECKLIST: Children (HRP-416)."

*28.16Describe whether permission will be obtained from individuals **other than parents**, and if so, who will be allowed to provide permission. Describe your procedure for determining an individual's authority to consent to the child's general medical care.*

Response:

N/A

*28.17 Indicate whether assent will be obtained from all, some, or none of the **children**. If assent will be obtained from some children, indicate which children will be required to assent.*

Response:

N/A

28.18 When assent of children is obtained, describe how it will be documented.

Response:

N/A

29.0 Waiver or Alteration of Consent Process

Consent will not be obtained, required information will not be disclosed, or the research involves deception.

☒ **N/A:** A waiver or alteration of consent is not being requested.

29.1 If the research involves a waiver or alteration of the consent process, please review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure that you have provided sufficient information for the IRB to make the determination that a waiver or alteration can be granted.

NOTE: For records review studies, the first set of criteria on the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" applies.

Response:

N/A

29.2 If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations. Provide any additional information necessary here:

Response:

N/A

30.0 Process to Document Consent

☒ **N/A:** A Waiver of Consent is being requested.
(Skip to Section 31.0)

30.1 Indicate whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not or if there are any exceptions, describe whether and how consent of the subject will be obtained including whether or not it will be documented in writing.

NOTE: If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent. This is sometimes referred to as 'verbal consent.' Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information.

If you will document consent in writing, attach a consent document with your submission. You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)". If you will obtain consent, but not document consent in writing, attach the script of the information to be provided orally or in writing (i.e. consent script or Information Sheet).

Response:

☒ We will be following "SOP: Written Documentation of Consent" (HRP-091).

31.0 Multi-Site Research (Multisite/Multicenter Only)*

☒ **N/A:** This study is not an investigator-initiated multi-site study. This section does not apply.

31.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed across all sites.

Response:

N/A

*31.2 If this is a multi-site study **where you are the lead investigator**, describe the processes to ensure communication among sites, such as the following.*

- *All sites have the most current version of the IRB documents, including the protocol, consent document, and HIPAA authorization.*
- *All required approvals have been obtained at each site (including approval by the site's IRB of record).*

- *All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.*
- *All engaged participating sites will safeguard data as required by local information security policies.*
- *All local site investigators conduct the study appropriately in accordance with applicable federal regulations and local laws.*
- *All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.*

Response:

N/A

31.3 Describe the method for communicating to engaged participating sites.

- *Problems (inclusive of reportable events)*
- *Interim results*
- *Study closure*

Response:

N/A

*31.4 If this is a multicenter study **where you are a participating site/investigator**, describe the local procedures for maintenance of confidentiality.*

- *Where and how data or specimens will be stored locally?*
- *How long the data or specimens will be stored locally?*
- *Who will have access to the data or specimens locally?*
- *Who is responsible for receipt or transmission of the data or specimens locally?*
- *How data and specimens will be transported locally?*

Response:

N/A

31.5 If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods. Local recruitment methods are described elsewhere in the protocol.

- *Describe when, where, and how potential subjects will be recruited.*
- *Describe the methods that will be used to identify potential subjects.*
- *Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final*

audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)

Response:

N/A

32.0 Banking Data or Specimens for Future Use*

☐ **N/A:** This study is not banking data or specimens for future use or research outside the scope of the present protocol. This section does not apply.

*32.1 If data or specimens will be banked (stored) for **future use, that is, use or research outside of the scope of the present protocol**, describe where the data/specimens will be stored, how long they will be stored, how the data/specimens will be accessed, and who will have access to the data/specimens.*

NOTE: Your response here must be consistent with your response at the "What happens if I say yes, I want to be in this research?" Section of the Template Consent Document (HRP-502).

NOTE: If the UBIRB has approved this study to bank data and/or specimens for potential future use outside the scope of this research study, any future use or disclosure of the data that is not described within the approved study must be submitted for review to the UBIRB.

Response:

Demographic, clinical, biometric (from wearable devices), and AOT equipment data will be stored on secure UB servers in password-protected files. Oxiwear data will first be uploaded to Oxiwear cloud-based storage platform by participants via Oxiwear's smartphone app. Members of the research team will download data from the cloud-based platform. No participant-identifying information will be associated with this data. Data will be stored indefinitely and may be used by the future studies related to AOT use in fILD and COPD.

32.2 List the data to be stored or associated with each specimen.

Response:

Data for each participant will be stored associated with a unique study number.

32.3 Describe the procedures to release banked data or specimens for future uses, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

Response:

The use of banked data by anyone other than the Primary Investigator and co-investigators must be approved by the Primary Investigator. Requests must be submitted to the Primary Investigator in writing and approval will be considered on a case-by-case basis.