

**OBSERVING THE EFFECTS OF SUPPLEMENTAL OXYGEN ON  
PATIENTS WITH PULMONARY FIBROSIS**

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**STUDY PROTOCOL**

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## TECHNICAL ABSTRACT

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*Background:* Pulmonary fibrosis (PF) is a rare, horrific disease. Although nearly every PF patient will be prescribed supplemental oxygen (O<sub>2</sub>), current knowledge of its effects on patients is almost nil. The paucity of data has left an expansive gap in evidence needed by patients and practitioners to make informed decisions about O<sub>2</sub>: no studies have been conducted to examine what patients and prescribers expect PF patients to gain by using O<sub>2</sub>; to determine whether O<sub>2</sub> use creates durable, meaningful improvements in PF patients' daily lives; or to discern whether such putative improvements outweigh patients' perceptions of being "tied to [their] hoses [oxygen cannulas]." Thousands of PF patients are prescribed O<sub>2</sub> despite a globally insufficient understanding of whether or how it affects them.

*Objectives:* To enhance understanding of O<sub>2</sub>—its utility in and adoption by PF patients—by examining how patients perceive it and by determining how perceptions and patient-centered outcome measures change from before to after it is prescribed.

*Methods:* We will collect data before, and for one year after, PF patients are prescribed daily-use supplemental oxygen. This will allow us to compare values for a full-range of outcomes, including dyspnea, quality of life, fatigue, cough, day-to-day functioning and activity space, before and after O<sub>2</sub>. We will use a t test to analyze data for our primary endpoint of change in dyspnea from immediately before to one month after daily-use O<sub>2</sub> is prescribed. Interview data will be analyzed using qualitative methods to derive a conceptual framework for how patients and other relevant stakeholders perceive O<sub>2</sub>.

*Patient Outcomes:* With this study, prescribers and patients will finally know about the effects on PF patients of this universally prescribed therapy, and when PF patients and their practitioners set out to make critical decisions together about O<sub>2</sub>, they can turn to a cache of relevant evidence to inform their choices.

## PUBLIC ABSTRACT

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Pulmonary fibrosis (PF) is a rare condition that causes severe shortness of breath, a nagging dry cough, profound fatigue and early death. Although nearly every PF patient will be prescribed supplemental oxygen (O<sub>2</sub>), we actually know very little about whether or how O<sub>2</sub> might help patients with this horrible disease. For example, we don't know what patients and prescribers expect (or can expect) PF patients to gain by using O<sub>2</sub>; whether O<sub>2</sub> use creates durable, meaningful improvements in PF patients' daily lives; or if such putative improvements outweigh patients' perceptions of being "tied to [their] hoses [oxygen cannulas]." Thousands of PF patients are prescribed O<sub>2</sub> despite a globally insufficient understanding of whether or how it affects them. Our overall objective is to enhance understanding of O<sub>2</sub>—its utility in and adoption by PF patients—by examining perceptions of it and by determining how those perceptions and several things important to patients (like symptoms, quality of life, activity levels) change from before to after O<sub>2</sub> is prescribed. We aim to recruit patients with PF to participate in interviews and/or a one-year study of O<sub>2</sub>. In the one-year study, we will collect data before and for one year after PF patients are prescribed daily-use supplemental oxygen and compare outcomes, including shortness of breath, quality of life, fatigue, cough, and day-to-day functioning before and after O<sub>2</sub>. In addition to this, we will interview O<sub>2</sub> prescribers and primary supporters of PF patients prescribed daily-use O<sub>2</sub> to understand the perceptions of others affected by supplemental O<sub>2</sub>. Without this study, patients and their loved ones will linger uninformed about the effects of this universally prescribed therapy, and when PF patients and their practitioners set out to make critical decisions together about O<sub>2</sub>, they will remain hamstrung by the absence of pertinent data to inform their choices.

## BACKGROUND AND SIGNIFICANCE

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Although understanding of the pathogenesis of PF remains murky, what is clear is that increasing age is a risk factor for PF.[1-3] With the aging United States (U.S.) population, PF will be an expanding health problem for the foreseeable future. Given its estimated U.S. prevalence of around 50 per 100,000 persons,[4] PF may not be a rampant burden on the U.S. health care system right now, but it absolutely and unrelentingly weighs down patients. Patients with PF suffer: they have poor quality of life (QOL);[5-6] their ability to perform physical activities dwindles—their worlds shrink. Many are forced to stop working, and 50% of PF patients face death within three years of being diagnosed.[7]

There are no Federal Drug Administration-approved drugs for PF, and to date, no therapy (medicinal or non-medicinal) has been indisputably proved to benefit PF patients. Nonetheless, a search of websites from U.S. centers with expertise in caring for—and conducting research on—patients with PF shows that supplemental oxygen (O<sub>2</sub>) is a recommended treatment for patients whose peripheral oxygen saturation falls below 89% at rest, with activity or during sleep. Studies to support this recommendation, or studies systematically examining the effects of O<sub>2</sub> on outcomes meaningful to patients with PF, such as those proposed above, do not exist.[8] As a result, prescribers are severely limited in their ability to confidently inform patients about how O<sub>2</sub> will change their lives. In their discussions with PF patients about O<sub>2</sub>, prescribers are forced to draw from the chronic obstructive pulmonary disease (COPD) literature—a cache of data that is surprisingly controversial, quite limited and with dubious applicability to PF patients.[9] And these are discussions that occur daily in clinics where patients with PF receive treatment. Perhaps because of the limited information available, the majority of patients with PF rate themselves as “uninformed” on managing supplemental oxygen;[10] they don’t know what to expect while using it; and there is a paucity of data to substantiate the benefits prescribers hope their PF patients will realize from using supplemental oxygen.

## PURPOSE

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The innovative research defined in this protocol challenges the current confines of medical practice—one patient, one place, one time—by studying multiple patients, from around the country, at multiple time points. This will be accomplished by using methods that cut across the data spectrum, from individual perceptions to patient-reported outcome measures (PROs) to assessments of functionality (using cutting edge medical geography technology). The proposed project will be the first-ever, broad-based, critical examination in the PF population of O<sub>2</sub> (a therapy that patients view as frightening, burdensome and as a “milestone” in their loss of independence[11]).

This research proposes partnering with patients to define a new standard of knowledge around supplemental oxygen’s effects on patients with PF. The interstitial lung disease (ILD) field should not be satisfied with depending entirely on the COPD literature, or with making clinical decisions about O<sub>2</sub> therapy in PF patients, based on assumptions that have been formulated on extrapolations of limited data from patients with a different disease. This study calls for the systematic collection and analysis of data from PF patients across the country, to more fully elucidate the effects of O<sub>2</sub> on patients’ lives. These data will reveal the benefits of—or call attention to misconceptions about—O<sub>2</sub> therapy for PF patients. As a consequence, the ILD field will gain confidence that current conceptions and prescribing practices around O<sub>2</sub> are correct, or that thinking and practices need to be substantially modified to improve patients’ lives. For

example, we hypothesize that O<sub>2</sub> will improve activity space (i.e., expand a patient's world by allowing them to do more and go more places), but perhaps we will find the opposite is true: because of the burdens it imposes (delivery devices are heavy and may not hold enough oxygen to allow patients to stray too far from home), O<sub>2</sub> could shrink patients' worlds even more. If this were the case, then we would need to investigate further to identify mutable factors and decipher how to change them to maximize benefits of O<sub>2</sub> therapy.

The contributions of this research will advance the care of patients with PF by arming patients and prescribers with the capability to engage in thoughtful discussions, and make informed decisions, about O<sub>2</sub> therapy—discussions and decisions that are patient-focused and data-driven, not based on expert opinion or inferences drawn largely from research in COPD. It is anticipated that these contributions will launch a patient-centered treatment approach in PF by exposing patients' needs, preferences, expectations and tolerances regarding supplemental oxygen. The contributions will likely enhance patient satisfaction by empowering them with knowledge about supplemental oxygen, by strengthening their voice when it comes to their healthcare decisions, and by increasing their sense of control over their disease. We expect this work will reassure PF patients that the need for O<sub>2</sub> therapy does not equate to a giant step down the horrible path to death. Finally, the results of this study will drive the formulation of additional testable hypotheses about supplemental oxygen in PF, and they will be useful in planning future studies aimed at enhancing health and reducing the weight of PF on patients' lives.

## AIMS AND HYPOTHESES

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**Aim 1:** **To determine the effects of O<sub>2</sub> on outcomes meaningful to PF patients.**

*Hypothesis 1.1:* *Compared with just prior to starting supplemental oxygen, after one month of use, dyspnea, QOL, fatigue, cough, day-to-day functioning and activity space will be better.*

*Hypothesis 1.2:* *Compared with just prior to starting using O<sub>2</sub>, the outcomes in hypothesis 1.1 will remain better after 9-12 months.*

**Aim 2:** **To identify primary supporters' and prescribers' expectations and perceptions of O<sub>2</sub>, and for patients, their expectations and perceptions of O<sub>2</sub> before and after it is prescribed.**

*Hypothesis 2.1:* *Before being prescribed supplemental oxygen, patients will perceive it only negatively.*

*Hypothesis 2.2:* *Within one month of O<sub>2</sub> being prescribed, fears about it will lessen, but patients will still perceive it as overwhelmingly burdensome and in a negative light.*

*Hypothesis 2.3:* *After nine months of using O<sub>2</sub>, patients will have learned to live much better with it and accept that it is beneficial overall.*

## DESIGN, METHODOLOGY, AND ANALYSIS

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### I. General overview

Four groups of subjects will participate in this study:

1) 300 patients with PF not yet on daily-use supplemental oxygen

\* Of these 300, the first 40 participants who are interested, in addition to having study data collected, will participate in telephone interviews at baseline and

three additional time points. The remaining 260 will only have study data collected and not participate in telephone interviews.

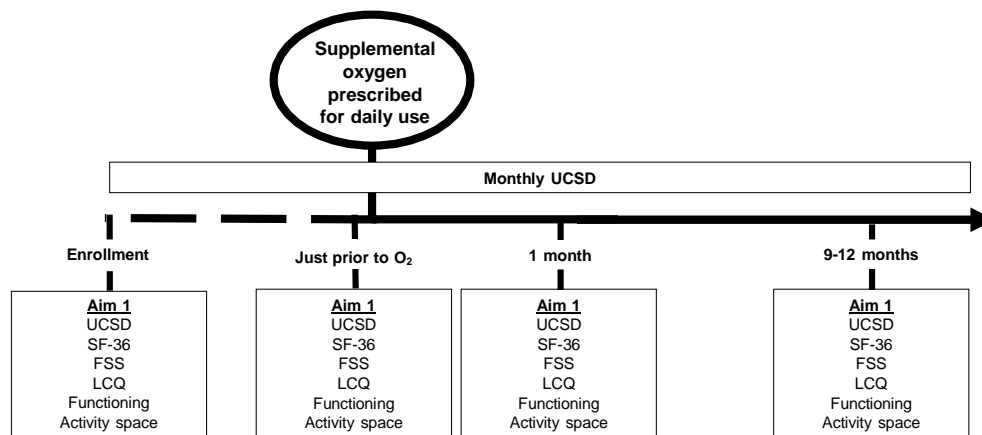
- 2) 20 patients with PF who using supplemental oxygen during the day
- 3) 20 primary supporters/caregivers of patients with PF
- 4) 20 oxygen prescribers

## II. Aim 1: To determine the effects of O<sub>2</sub> on outcomes meaningful to PF patients.

### A. Design for Aim 1

For this aim, we will conduct a pre-/post- longitudinal study in 300 patients who have not yet been prescribed supplemental oxygen for use on a daily basis. Please see Figure 1. After carefully considering a number of options, we decided that having each subject serve as his/her own comparator (control) is the most appropriate and efficient way to conduct this study. We will collect primary data at four time points: T<sub>0</sub>) at enrollment; T<sub>1</sub>) just before supplemental oxygen is started; T<sub>2</sub>) after one month ( $\pm$ one week); and T<sub>3</sub>) after 9-12 months of daily supplemental oxygen use. Between these time points, we will also collect monthly response data for the University of California San Diego Shortness of Breath Questionnaire (UCSD). Doing so gives us the opportunity to plot rich trajectories for dyspnea (primary endpoint) and to detect subtleties that a less frequent data collection schedule for this outcome might miss. These monthly data will be used in exploratory analyses. In another exploratory analysis, we will also compare questionnaire scores from 20 subjects already on daily-use supplemental oxygen at the time of study enrollment (these 20 subjects will participate in a single telephone interview as well; please see Aim 2 below for details) with 20 age- and gener-matched subjects not on daily use supplemental oxygen at time of enrollment.

**Figure 1.** Schematic of longitudinal study design



UCSD=University of California San Diego Shortness of Breath Questionnaire; SF-36=Short-form 36-item instrument; FSS=Fatigue Severity Scale; LCQ=Leicester Cough Questionnaire

### B. Outcome Measures for Aim 1

1. The University of California San Diego Shortness of Breath Questionnaire (UCSD)[12]: A 24-item dyspnea questionnaire that asks respondents to rate themselves from 0 (“Not at all”) to 5 (“Maximally or unable to do because of breathlessness”) in two areas: 1) how short of breath they are while performing

- various activities (21 items); and 2) how much shortness of breath itself, fear of hurting themselves by overexerting, and fear of shortness of breath limit them in their daily lives (3 items). Scores range from 0 to 120, with higher scores indicating greater dyspnea. The Principal Investigator (PI) has published a paper on the UCSD that includes data for the following: 1) data to support the validity of the UCSD as an instrument capable of assessing dyspnea over time in patients with PF; and 2) an estimate for the change in UCSD score that constitutes a minimum important difference (MID) in patients with PF: range 5-11 with a point estimate of 8.[13] The UCSD takes 5 minutes to complete.
2. The Short Form 36-Item Instrument (SF-36)[14]: A generic health-related QOL (HRQL) questionnaire with eight domains which comprise two component summaries (physical and mental). Each domain and component is scored from 0-100, with higher scores connoting greater HRQL. The PI has used the SF-36 extensively and published a paper that includes MID estimates for the SF-36 and data to support the validity of the SF-36 as an instrument capable of assessing HRQL over time in patients with PF.[15] The SF-36 is the most popular HRQL instrument ever used and takes 15 minutes to complete.
  3. The Fatigue Severity Scale (FSS): A 9-item questionnaire, scored from 9-63, with higher scores indicating more severe fatigue. The FSS takes less than five minutes to complete.
  4. The Leicester (pronounced Lester) Cough Questionnaire (LCQ)[16]: A 19-item questionnaire that taps the physical, psychological and social aspects of cough. Scores range from 7-63, with higher scores indicating better cough-related QOL. The LCQ takes five minutes to complete.
  5. Actigraph GT3X+ Tri-Axis Actigraph Monitor: A small, lightweight (19 grams), plastic accelerometer (about the size of a matchbox) affixed to an elastic band and comfortably worn around the waist. The device continuously records data which can be downloaded onto a computer via a USB cable. It will be used to measure physical activity—including the physical activity level (PAL, defined by the total daily energy expenditure divided by whole-night sleeping energy expenditure) and step counts per day. (see “Device Specifications” submission for HS-2790)
  6. iGotU GT-600 GPS data-logger from MobileAction Technologies: A lightweight GPS unit that is small and easily worn on a lanyard around the participant’s neck. It has good reliability and spatial accuracy, even in urban settings.[17] The GPS data-loggers will be used to track the movement patterns of participants over the course of a typical week and develop measures of “activity space”. Activity space is often defined as the local areas within which people move or travel in the course of their daily activities[18] and can be used to examine whether people’s mobility changes during the course of medical treatment. Recent research suggests that collecting GPS data on people’s movements is more accurate than travel diaries or semi-structured interviews which ask participants to recall their activities and movements throughout the study period.[19-20] Data from the GPS loggers will be imported into ArcGIS mapping software and used to create secondary outcome measures which examine the extent of a participant’s activity space and how this changes over time.[21-23] We



will ask subjects to keep a trip/travel diary, so we can understand where trips outside the home were taken. (see “Device Specifications” submission for HS-2790)

### C. Methodology for Aim 1

After a patient’s PF diagnosis is confirmed and his/her physician agrees to the patient delaying the start of daily-use O<sub>2</sub> for 7-10 days if/when it is prescribed (so that we may collect data just prior to the subject starting daily-use supplemental oxygen), the participant may be enrolled in the study if he/she wishes to participate and fulfills all remaining inclusion criteria.

At the time of enrollment, patient-participants will be assigned a unique study identifier and will undergo time point T<sub>0</sub> data collection. Once enrolled, subjects will complete the UCSD (24 items, 10 minutes to complete) every month either via a secure study portal or via paper-and-pen format.

#### 1. T<sub>0</sub> data collection in detail

- a. Complete questionnaires (UCSD, SF-36, FSS and LCQ).

**Most subjects will complete these questionnaires electronically via a secure study portal, but paper forms are available to subjects without access to a computer or to those who—for whatever reason—prefer paper over electronic format.** The electronic versions will be administered with the assistance of the Colorado Clinical and Translational Research Institute’s (CCTSI) Behavioral Medicine Core Lab (located at National Jewish Health), and housed on the CCTSI’s HIPAA-compliant RedCap server.

- b. After receiving them via mail/express delivery, wear both accelerometer (Actigraph) and GPS data-logger (iGotU) for 23 hours per day for seven consecutive days.

Besides the Actigraph and iGotU, the packet will contain detailed instructions on how to use/wear the devices, replacement batteries, when and how to return the devices and contact information for study personnel in case subjects have any questions. When data collection is complete, subjects will mail the accelerometer and GPS units back to study personnel via a pre-addressed, postage-paid envelope.

2. T<sub>1</sub> data collection in detail: after time point T<sub>0</sub>, the next larger data collection will occur when it is imminent that daily-use supplemental oxygen will be prescribed (i.e., time point T<sub>1</sub>). Research coordinators will keep in close contact with patients and keep tabs on when they have routine follow-up clinic visits with their physicians. We will rely on subjects to inform us when their physicians wish to prescribe daily-use supplemental oxygen, but research coordinators will call subjects after each follow-up clinic visit to inquire about their oxygen status and whether daily-use supplemental oxygen has been recommended or prescribed. As detailed above, when oxygen prescription is imminent, subjects will wait one week before starting it, so that we can collect time point T<sub>1</sub> data. The details of this procedure will be outlined in a

Patient/Doctor Study Packet for the patient-subject to bring with him/her to his/her doctor visits. The packet will serve as a reminder to both the patient-subject and his/her physician/oxygen prescriber of the study's requirements/procedures. Study subjects will obtain a signed document from their physician to ensure they are comfortable with the patient-subject waiting a week before starting supplemental oxygen. The physician/oxygen prescriber will be able to contact study personnel if he/she has any questions.

- a. Complete questionnaires (UCSD, SF-36, FSS and LCQ).
  - b. After receiving them via mail/express delivery, wear both accelerometer (Actigraph) and GPS data-logger (iGotU) for 23 hours per day for seven consecutive days. Will also keep a Travel/trip log.
3. T<sub>2</sub> data collection in detail: this will occur after a subject has been on daily-use supplemental oxygen for one month.
    - a. Complete questionnaires (UCSD, SF-36, FSS and LCQ).
    - b. After receiving them via mail/express delivery, wear both accelerometer (Actigraph) and GPS data-logger (iGotU) for 23 hours per day for seven consecutive days. Will also keep a Travel/trip log.
  4. T<sub>3</sub> data collection in detail: this will occur after a subject has been on daily-use supplemental oxygen for 9-12 months.
    - a. Complete questionnaires (UCSD, SF-36, FSS and LCQ).
    - b. After receiving them via mail/express delivery, wear both accelerometer (Actigraph) and GPS data-logger (iGotU) for 23 hours per day for seven consecutive days. Will also keep a Travel/trip log.

#### D. Data analysis for Aim 1

1. Primary and secondary endpoints: the analytic methods we will use to test the working hypothesis that supplemental oxygen improves dyspnea (according to UCSD scores) and complete this aim include paired t tests for the primary and secondary endpoints (all other questionnaire measures).
2. GPS data: we will use the standard deviational ellipse (both one and two standard deviations) as measures of activity space from data gathered from the GPS units.
3. Potential influence of demographic variables: to examine whether demographics (e.g., age, gender, ethnic/racial group or socioeconomic status) modify outcomes, we will conduct separate univariate analyses with the cohort stratified on each of these demographic variables.

4. Exploratory analyses on longitudinal data: because we are collecting longitudinal data, in certain exploratory analyses, we will also use longitudinal analytic methods—mixed-effects models will be the workhorse in these exploratory analyses—to compare the various outcomes across multiple time points while controlling for potentially influential variables. The benefits of mixed-effects models are that the model structure is very flexible and allows incorporation of time-varying covariates (meaning adjustments can be made for changes in disease severity over time), all available data can be used (thus avoiding imputation or case-wise deletion for missing values), and these models can account for the within-subject correlation inherent in repeated measures data.
5. Exploratory analysis comparing questionnaire scores from the 20 subjects already on daily-use supplemental oxygen at the time of study enrollment with 20 age- and gener-matched subjects not on daily use supplemental oxygen at time of enrollment. For this analysis, we will use unpaired t tests.

### **III. Aim 2: To identify primary supporters' and prescribers' expectations and perceptions of O<sub>2</sub>, and for patients, their expectations and perceptions of O<sub>2</sub> before and after it is prescribed.**

#### **A. Design for Aim 2**

For this aim, we will conduct semi-structured phone interviews with four sub-groups of participants: 1) patient-participants who have been on daily-use O<sub>2</sub> therapy for greater than one year; 2) primary supporters of PF patients who have been on daily-use O<sub>2</sub> therapy for greater than one year; 3) prescribers of supplemental oxygen; and 4) 40 of the 300 longitudinal study patient-participants who are not currently (at time of enrollment) prescribed daily-use O<sub>2</sub> therapy. Note: Group 4 will participate in telephone interviews at T<sub>0</sub>, T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub>. Each semi-structured phone interview will last approximately 30 minutes and will be audio recorded and transcribed verbatim.

#### **B. Methodology for Aim 2**

1. The 20 PF patient-participants who have been on daily-use supplemental oxygen for greater than one year will participate in a one-time individual phone interview to capture their perceptions of supplemental oxygen.
2. The 20 primary supporters will also be asked to participate in a one-time phone interview to capture their perceptions of supplemental oxygen. We want to know how they perceive supplemental oxygen affecting their patient loved-one, how the patient's being on supplemental oxygen affects them and how having supplemental oxygen in the home affects the dynamics of the household.
3. The 20 oxygen prescribers will also be asked to participate in a one-time phone interview to capture their perceptions of supplemental oxygen—how/when they prescribe it, how they expect patients to benefit from it, and how they monitor their patient's status after it is prescribed.

4. To capture perceptions from PF patients before and after they are prescribed daily-use supplemental oxygen, we will conduct four interviews with 40 subjects who are not on daily-use supplemental oxygen at the time of enrollment in the longitudinal study. These four interviews will take place at the following time points: T<sub>0</sub>) at enrollment, T<sub>1</sub>) just before going on daily-use supplemental oxygen, T<sub>2</sub>) after having used supplemental oxygen on a daily basis for one month and T<sub>3</sub>) after having used supplemental oxygen on a daily basis for 9-12 months.

#### C. Outcome Measures for Aim 2

Please see “Interview Guides” submission for HS-2790.

#### D. Data analysis for Aim 2

The goal of the qualitative analysis of the semi-structured interviews is to capture the words participants use, their perceptions of supplemental oxygen, the hurdles it creates, and the barriers to its use, and for PF patients in the longitudinal study, how these perceptions change over time. Consistent with qualitative methodology, analysis is planned as a continuous process beginning with initial interviews and continuing throughout and beyond the data generation period. Data will be coded following a process of initial review, with labeling of data by content, process, or impressions of the person coding. A contracted qualitative data expert and a research assistant will independently code 10% of the data, and then meet to discuss codes, establish inter-coder reliability, and create an initial master code list. Before coding the remaining data, the qualitative data expert will debrief the rest of the research team to get their input on the initial master code list. Once consensus is reached as to the precision and completeness of the master list, the research assistant will then code the remaining data using this code list, consulting with the qualitative data expert when questions arise. Following initial coding, the qualitative data expert will examine the data for categories, domains, or themes. Codes are analyzed into categories and broad classifications of cultural meaning called domains. Transcripts will be analyzed for themes and patterns. The degree of consensus about particular topics discussed across subjects and over time within the same subject will also be noted. After this coding is completed, the qualitative data expert will organize codes into categories that reflect symbolic domains of meaning, relational patterns within domains, and finally overarching themes. Relationships within domains are usually structured according to "organizing principles," such as inclusion, symbol, sequence, function, partwhole, or others. Using this analysis, an analytic summary of each interview will be written. In the summaries and resulting publications, the research team will use research participants' own words and narratives to preserve the tone and emotion of their experiences and increase the theoretical depth of the final description of the effects of supplemental oxygen on PF patients' lives. Narratives, as a specific kind of speech act in the interview settings, will be indexed in the coding process, and a narrative analysis will ensue. These narratives will be analyzed for substantive and conceptual meaning along with interview discourse. Comparisons across subjects and over time within subject will add detail and depth to the dimensions of the effects of supplemental oxygen.

The software package ATLAS.ti will be used to analyze the qualitative data. This software will allow us to read through the text, identify meaningful segments of text, assign a codeword to that text, and define the codeword (for reliability and concept

clarity) within the software program. Codes or higher-level super-codes can be linked within the program to record relationships among the emerging concepts. As a theory-building qualitative package, ATLAS.ti will be used to code the data, to help the investigators record memos and insights about the data, and to build and test theories. The collaboration among the research team, will entail biweekly meetings, with review of the analysis to date and discussion of findings as they are assembled, and considering their implications.

The synthesis stage of data analysis involves triangulating the findings from interviews, as well as demographic information, exploring comparisons across different methods and samples, and revisiting the literature to compare findings to other investigations. The trustworthiness of study findings will be heightened through attention to the credibility, transferability, dependability, and confirmability of the data. Methods to enhance trustworthiness include prolonged engagement, persistent observation, an audit trail, and triangulation. Triangulation is the most effective way to ensure reliability and validity of ethnographic data by obtaining comparable, confirmatory data from multiple sources from different points in time, and through the use of multiple methods. Triangulation will involve meetings of the research team to engage in reflexive team analysis, including reviewing the range of data, examining contradictory data, and considering the possibility of symbolic meaning or social desirability underlying apparent discrepancies. Memos kept throughout the fieldwork experience will document decisions about sampling, categorization, and the like.

## DATA MANAGEMENT AND SECURITY

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### A. Databases

We will have three databases for this study: 1) Microsoft Excel database to store accelerometer and GPS data; 2) Microsoft Excel database to store the key to the unique study identifiers and 3) RedCap database to house questionnaire data.

The Excel databases will be password-protected and kept on a password-protected computer in a locked office at NJH. The key to the unique identifiers will exist in a separate database in a password-protected file on a password-protected computer in a locked office at NJH. The passwords to both file will be known only to the PI and research coordinator(s). The RedCap database will be password-protected, securely housed on CCTSI's HIPAA-compliant RedCap server and will be accessible only to the PI and research coordinator(s).

### B. Unique Identifiers

Upon enrollment, each study participant will be assigned a unique identifier. Every document (electronic or paper) and/or device will be labeled with or attached this unique identifier, with the exception of the study consent forms. Study consent forms will be stored separately in a locked filing cabinet in a locked office on the main National Jewish Health (NJH) campus.

### C. Interview Data

Interviews will be conducted in a private office at NJH. Last names will not be used during the interview. The interviews will be audio-recorded and the audio files of the interviews will be uploaded to a secure website [www.ibackup.com](http://www.ibackup.com). The recordings will be transcribed verbatim by a professional medical transcriptionist. The transcripts will then be uploaded back on to the same secured website where the PI or research coordinator(s) can access the files. The password to the website will be known only to the PI or research coordinator(s).

#### D. Travel/Trip Log

Information from patient-participants' travel/trip log will be stored on a password-protected electronic file on a password-protected computer in a locked office at NJH. Any hard-copies will be scanned and stored electronically on a password-protected computer and then destroyed through secured document disposal.

## DETERMINING ELIGIBILITY

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### A. Inclusion Criteria

\*All study participants must be 18 years of age or older.

#### 1. Patient-Participants

(Using daily O<sub>2</sub> therapy at time of enrollment)

- Diagnosis of PF
- Able to read and speak English
- Has been on daily-use supplemental oxygen for more than one year

(Not using daily O<sub>2</sub> therapy at time of enrollment)

- Diagnosis of PF
- Able to read, speak and write in English
- Has not been prescribed daily-use supplemental oxygen
- Forced vital capacity <75% and diffusing capacity <65% of predicted values
- Subject's physician allows the subject to abstain from daily-use supplemental oxygen for 7-10 days after prescription to allow data for collection

#### 2. Primary Supporters

- Self-report status of providing care or support to a person living with pulmonary fibrosis who has used supplemental oxygen for more than one year
- Able to speak English

#### 3. O<sub>2</sub> Prescribers

- Self-report status of being a prescriber of daily-use supplemental oxygen to PF patients
- Able to speak English

### B. Exclusion Criteria

\*Study participants cannot be under 18 years of age.

### 1. Patient-Participants

(Using daily O<sub>2</sub> therapy at time of enrollment)

- No diagnosis of PF
- Cannot read or speak English
- Has not been on daily-use supplemental oxygen for more than one year

(Not using daily O<sub>2</sub> therapy at time of enrollment)

- No diagnosis of PF
- Cannot read, speak or write in English
- Has been prescribed daily-use supplemental oxygen
- Forced vital capacity >75% and diffusing capacity >65% of predicted values
- Subject's physician will not allow the subject to abstain from daily-use supplemental oxygen for one week after prescription to allow for data collection

### 2. Primary Supporters

- Does not self-report status of providing care or support to a person living with PF who has used supplemental oxygen for more than one year
- Cannot speak English

### 3. O<sub>2</sub> Prescribers

- Does not self-report status of being a prescriber of daily-use supplemental oxygen to PF patients
- Cannot speak English

## C. Determining Eligibility

1. The PI will determine the eligibility of all potential patient-participants once the appropriate medical records have been obtained for each subject.
2. Any study personnel may determine the eligibility of primary supporters or supplemental oxygen prescribers.

## RECRUITMENT AND ENROLLMENT

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### A. Recruitment

#### 1. The P<sub>3</sub>FContact Registry:

Potential patient-participants who sign up for the P<sub>3</sub>F Contact Registry and are seemingly eligible for the study will be contacted by study personnel. Patients will need to provide Authorization to release protected health information so study personnel can collect the necessary data to determine eligibility. (see "HIP-024 Instruction Guide submission for HS-2790.) If the potential patient-participant is eligible and interested in the study, he/she will be consented and enrolled in the study.

Primary supporters of PF patients can also sign up for the P<sub>3</sub>F Contact Registry. It is assumed anyone who fits the criteria to sign up for the Registry will be eligible for this study, so they will be contacted by study personnel and informed of the study. If the primary supporter is interested in the study, he/she may begin the enrollment process.

2. Internet advertising and newsletters:

The study will be advertised on the Internet and in a monthly newsletter sent to PF patients (see the next section “Advertising” for more detail). If potential participants are interested in the study, they can contact study personnel to find out if they are eligible for the study. Patients will need to provide Authorization to release protected health information so study personnel can collect the necessary data to determine eligibility. Once eligibility has been determined for any potential participant, the enrollment process can begin.

3. Flyers

Flyers will be posted in clinics around the country. A letter to physicians asking for support of the P<sub>3</sub>F and the study will be sent out along with flyers. Again, contact information for study personnel will be provided on the flyers and interested persons can inquire about their eligibility. Patients will need to provide Authorization to release protected health information so study personnel can collect the necessary data to determine eligibility. Once eligibility has been determined for any potential participant, the enrollment process can begin.

4. Phone calls

Phone calls will be made to supplemental oxygen prescribers around the country. If they are interested in learning about the study, the study will be prescribed to them using protocol language. If they are interested in participating in the study, they will be enrolled. (see “Telephone Script for Prescribers” submission for HS-2790).

5. Word of mouth

People may hear about the study through word-of-mouth. In fact, this is hoped for, especially for the primary supporters and supplemental oxygen prescribers. If a patient-participant wants to invite their primary supporters and/or doctor to participate in the study, he/she may feel free to do so. They can also tell their friends about the study (patients may participate in online support groups or have online friendships with other patients across the country, and the sharing of information between patients may be a great way to spread word about the study).

B. Enrollment

Enrollment will entail consenting eligible and willing participants and assigning each participant a unique identifier. Once a unique identifier has been assigned to a study



participant, the appropriate data collection process for that particular participant can begin.

## ADVERTISING

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We will advertise for this study on the P<sub>3</sub>F website ([www.pfresearch.org](http://www.pfresearch.org)), on the websites of patient advocacy groups including the PFF and the Coalition for Pulmonary Fibrosis, and on [clinicaltrials.gov](http://clinicaltrials.gov) and the Clinical Trial Listing on the NJH website. The study will also be advertised in the PFF monthly newsletter. (see “Web/Newsletter Advertisement” submission for HS-2790)

We will send letters requesting support to ILD physicians across the country. We will include flyers to be posted in their waiting and examination rooms. (see “Flyer Advertisement” and “Letter to Prescriber” submission for HS-2790)

## CONSENT PROCESS

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We will be performing consent over the telephone; therefore, we will mail or make available the consents to potential subjects (excluding prescribers and primary supporters/caregivers) so they can review the form before undergoing the consent process. The study personnel who is obtaining consent will be in a private office at NJH, and she will ensure that the potential subject is in a private, quiet place where the consent process can be performed appropriately. Study personnel will consent subjects by going through the consent with the potential subject line-by-line, section-by-section. Potential subjects will have as much time as they need to consider study participation. Subjects will be asked throughout the consent process if they have any questions. They will also be asked to repeat back certain details of the consent and authorization. Finally, they will be asked if they understood everything in the consent form and if not, to please ask any questions.

For prescribers and primary supporters/caregivers, verbal consent will be obtained over the phone. Telephone scripts for this consent process will be used to obtain consent (see HS# 2790 submissions “Telephone Script for Prescribers” and “Telephone Script for Primary Supporters”).

The research coordinator(s) and assistant(s) will primarily consent study subjects. Since the investigators are not likely to always be in the room while this conversation happens (over the phone), they will not be available during the discussion to answer questions. However, if a potential subject has a question for one of the investigators, they can consent at a different time with either of the study investigators. They will also be given the contact information for the PI and asked to contact the PI with any questions should they wish to do so before completing the consent process.

## RESEARCH PROCEDURES

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Subjects will be recruited from across the U.S. It is anticipated that, for the majority of subjects, questionnaires will be completed online through a study portal that maintains subject confidentiality. For subjects who cannot—or wish not to—use the Internet to complete questionnaires, study personnel will mail questionnaires to subjects who will be asked to return

them to study personnel at NJH via pre-addressed, postage-paid envelopes. (see “Questionnaires” submission for HS-2790)

Accelerometers and GPS data-loggers will be mailed to subjects. Study personnel will contact subjects via telephone to help them get acquainted with the devices and put them on for data collection. Mailed packages will contain the devices, replacement batteries, and return envelopes/packaging (pre-addressed, postage-paid).

Travel/trip log templates will also be provided for participants. These can be filled out either electronically or by hand. Participants can print out electronic copies of the log and send this back with their study devices. (see “Travel/trip Log Template” submission for HS-2790)

Telephone interviews will be conducted via the P<sub>3</sub>F’s toll-free number (1-855-609-0010). Study personnel will call from a private, quiet office and place the subject on speaker phone. A handheld, digital audio recorder will be used to record the conversation.

## RISKS AND BENEFITS

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### A. Risks

The likelihood and severity of the potential risks associated with participating in this research are at most minimal. Subjects will be inconvenienced with respect to the time needed to collect data. Loss of confidentiality is a concern in all research. Some of the items on the questionnaires may make subjects uncomfortable by provoking certain emotions, but our experience using these questionnaires in other projects suggests this will not be the case.

Risks associated with using the study devices are minimal. At most, it might be burdensome for participants to remember to wear the devices for the required duration of use. Also, there is some risk of loss of confidentiality of data, particularly with using the GPS device (in the sense that if a patient stays mostly at home, PHI such as the participant's address might be associated with the data on the GPS device). Of course, we will adhere strictly to appropriate research practices and maintain confidential any potentially identifying information.

When applicable: the risks associated with abstaining from using oxygen for a week are minimal. To ensure this, we are asking the health care providers of each participant who will abstain from using oxygen for a week to approve this action (i.e. we will not ask a participant to abstain from using oxygen if they absolutely require it at the point of prescription/advisement). Patients who acutely or profoundly decompensate, and are put on supplemental oxygen because of that decompensation, will not be asked to wait one week before starting to use supplemental oxygen.

### B. Benefits

The Hawthorne Effect suggests that subjects who know they are in a study may change their behavior. Thus, PF patients who are wearing an accelerometer and GPS unit may change their behavior (i.e., become more physically active), because they know someone will be looking at their data. Of course, this will not be advertised to potential subjects; we view this as an occult potential benefit.

Many patients feel like they are contributing to advancing understanding of PF by participating in research studies. We suspect (and hope) that many of the people who participate in our project will feel the same way.

Participation in this study contributes to advancing our understanding of a serious and fatal disease that affects not only PF patients but also their families, and every person with whom they have a relationship. The benefits of generating data that can be used to improve patient/prescriber communication, partnership and planning around the issue of supplemental oxygen are considered great to society.

### C. Risk/Benefit Analysis

The risks of the study are minimal and the benefit to society is great. Potential subjects do not have to participate in the study if they feel the risks are too great. Finally, while there are no guaranteed direct benefits to study subjects, they still might gain a sense of satisfaction in knowing they contributed to the greater good of medicine and patient care for pulmonary fibrosis.

## COMPENSATION

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For the patient-participants in the longitudinal study, they will receive a gift card of \$25 after each telephone interview (4 time points). Patient-participants will not initially be told about the gift card in order to try not to coerce their decision to participate in the interviews. For instance, we will not advertise about the gift card or tell potential subjects up front if they have inquiries about the study. Patient-participants will be paid after each telephone interview (timing depends on the disease progression/supplemental oxygen requirements of each patient-subject).

## MONITORING AND QUALITY ASSURANCE

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Questionnaire data will be collected by RedCap and stored on a secure server. When filling out the questionnaires, patients will have the option to skip items that make them feel uncomfortable or distressed in any way.

In order to ensure confidentiality of data, all devices that will be mailed to and from participants' residencies will be assigned a number using an NJH asset tag. This will help to keep track of each device. Also, the packages sent to and from the participant's house will be trackable and insured. Data from the devices will be uploaded to a password protected computer that is kept in a locked office. Once data has been uploaded to the secure computer, the device will be cleared of all data contents and ready for use by the next participant.

Finally, all data collected will not contain participants' names but rather their unique identifier.

Should any unanticipated problems arise throughout the duration of the study the PI will be responsible for evaluating and reporting such problems. It will also be the PI's responsibility to terminate study conduct or individual subject's participation should either event be necessitated.

## DISSEMINATION OF RESULTS

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We plan to post study results on the P<sub>3</sub>F website. These will be posts on all the data collected, including de-identified transcripts of the phone interviews. This will hopefully inspire others in the PF community to reflect on their own feelings about supplemental oxygen and share their thoughts or opinions on the website's forum. Study results may also be available through project collaborators, such as the Pulmonary Fibrosis Foundation's (PFF) website and newsletter, the Coalition for Pulmonary Fibrosis's website or the National Home Oxygen Patients Association's website.

The PI and one patient team member will present results at international meetings, including those of the American Thoracic Society (ATS) and the American College of Chest Physicians (ACCP). We will take advantage of the fact that recently, both the ATS and ACCP have committed to including patients in presentations at their yearly meetings. In addition, the PI and one patient team member will present results at the PFF-sponsored Pulmonary Fibrosis Summit in 2013.

Publications in respiratory and quality of life journals will reach clinicians and others interested in the quality of life of PF patients.

Emails to PF support group leaders across the country will also serve to notify and spread study results to relevant stakeholders.

Grand Rounds presentations will be given by the team (including patients) at the University of Colorado Anschutz Campus, NJH, and Kaiser Permanente.

## PROJECT CONTRIBUTORS

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Please see "Project Contributors" submission for HS-2790 for an extensive summary of project contributors for this study.

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