Sponsor: COPD Foundation, Inc.

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I. Purpose of the Study & Background

Purpose of the study:

The O_2VERLAP study focuses on a subset of the Chronic Obstructive Pulmonary Disease (i.e. COPD) community that are also living with a diagnosis of Sleep Apnea (i.e. SA); having a diagnosis of both COPD and SA is referred to as Overlap Syndrome (i.e. OS). There are about 300 million people living with COPD globally; of those, OSA affects over 25% of older adults with rates increasing in association with the obesity epidemic. There are approximately 51-75 million individuals living with OS worldwide. This subset of the COPD community is met with increased morbidity and mortality rates compared to either diagnosis alone. The primary treatment for OSA is continuous positive airway pressure (i.e. CPAP, sometimes shortened to PAP). When individuals with OS are adherent to their nighttime CPAP therapies they see significantly improved outcomes, comparable to individuals living with a diagnosis of COPD alone. As a result, the primary aim of this study is to improve CPAP adherence in patients living with OS. The study hopes to do this through a proactive, peer-support based intervention, supplemented by an online curriculum and access to remote CPAP adherence monitoring data and feedback. Peer-coaches will include individuals who are living with COPD and OSA, who are similar to the study population. The COPD Information Line associates will act in this peer-support role through dyadic, telephone-based communication and through secure online chat. The COPD Information Line peer-coaches will be able to provide participants experience-based advice, patient-centered guidance on troubleshooting adherence barriers, as well as patient-centered advice on how to facilitate CPAP adherence. Peer-coaches will also include Respiratory Therapists who will be able to provide coaching from the perspective of a caregiver. Additionally, all peer-based support aims to provide emotional and social support to participants. The Participants will have the ability to chat with their peer coaches online, both in real-time and asynchronously, and will additionally have weekly check ins with their coaches. The curriculum addresses many common CPAP adherence barriers and facilitators. The literature suggests that the combination of peer-support and self-learning can cultivate patient activation and the use of self-management strategies. Ultimately, we expect that this will improve CPAP adherence rates and patient-centered outcomes at 6 weeks and 12 weeks.

Aim #1: Improve adherence to PAP therapy at six weeks in proactive care arm.

Aim #2: Improve patient-centered outcomes (daytime functioning and sleep quality) at six and twelve weeks in proactive care arm.

Background

Chronic Obstructive Pulmonary Disease (COPD) is a group of progressive and debilitating respiratory conditions that affect 15-25 million Americans[1] and over 300 million people worldwide.[2] COPD is the third leading cause of death and the second leading cause of disability in the United States.[3] Each year, COPD results in as many as 800,000 hospital admissions and 1.5 million emergency room visits. Obstructive Sleep Apnea (OSA) is a prevalent chronic medical condition characterized by repeated stops or near stops of breathing during sleep due to collapse of the tissues in the airway.[4] These breathing episodes last 10 seconds or more, and cause repeated sleep disruptions and oxygen desaturations that lead to important health consequences. OSA affects 17% of adults and over 25% of older adults,[5] with rates increasing in association with the obesity epidemic.[6] Sleep apnea aggregates in families,[7] affects all age groups, and disproportionately affects minorities[8] and those from poor neighborhoods.[9] Sleep apnea requires immediate and ongoing therapy because it lowers blood-oxygen levels and disrupts sleep, and is associated with hypertension, myocardial infarction, stroke, atrial

fibrillation, and early mortality and results in an increase of depression, anxiety, cognitive issues, erectile dysfunction, irritability, daytime sleepiness and motor vehicle crashes.[10-17]

Separately, COPD and OSA contribute to the morbidity and mortality of hundreds of thousands of Americans every year. However, when OSA coexists with COPD it is referred to as the Overlap Syndrome (OS).[18] OSA is prevalent in at least 10-15% of patients diagnosed with COPD.[19] While the prevalence rate of OSA is similar in patients with COPD as in the general population, individuals with both of these conditions but who do not use continuous positive airway pressure (CPAP) therapy at night during sleep, have an increased risk of death and more hospitalizations from acute exacerbations, demonstrating the importance of OSA treatment.[20]

It is thought that Overlap Syndrome (OS) is clinically distinct from either condition alone and that patients with OS have a worse prognosis compared with patients with only COPD or OSA for several reasons that have important implications for diagnosis, treatment, and outcome. Studies that have examined the efficacy of PAP therapy for OS have shown that PAP use is associated with improved walking capacity[21] and longer survival in COPD patients who are hypercapnic,[22] and that higher levels of PAP adherence are associated with better outcomes.[20] However, of the ~80% of patients who accept PAP therapy, most patients fall into a partial use pattern of 3-5 hours per night. Adherence with long-term oxygen use has a parallel story; it is beneficial the more it is used but adherence is less than optimal, ranging from 45% to 70%.[23] Thus highlighting the importance of providing this patient population the tools necessary to improve adherence to PAP therapy.

Web-based interventions and remote data telemonitoring are now empirically supported as effective interventions for providing chronic illness care. Web-based interventions helped increase patient activation in a study of patients with multiple comorbidities.[24] In a review of web-based interventions for diabetes management, successful intervention components included goal-setting, personalized coaching, interactive feedback and online peer support.[25] A review of home telemonitoring interventions in patients with heart failure showed that the interventions helped to reduce all- cause mortality and hospitalizations.[26] This literature is evolving relatively quickly. Within the field of sleep medicine, Dr. Stepnowsky has shown that both remote telemonitoring by providers[27] and an interactive web portal accessed and utilized by OSA patients can improve PAP adherence.[28] More recent evidence has shown that simply providing patients with access to their PAP data improves adherence[29] PAP patients have always been able to read limited summary data on their machines, but new technologies now allow patients to view more of their PAP adherence and efficacy data online, along with education about how to understand this information. The O_2VERLAP study's intervention has been developed with this evidence in mind and will therefore include a proactive, patient centered, peer coaching system, an online educational curriculum, which will address common adherence barriers using PAP therapy, as well as adherence facilitators, and lastly the studies proactive care arm will also be provided adherence monitoring data directly to patients.

The study will randomize and enroll 330 participants; half will be randomized to the reactive care arm of the study and the other half to the proactive care arm of the study. The reactive care arm of the study will be given the number of an information line that they can contact to seek advice in PAP therapy adherence and or to seek advice in overlap syndrome health topics. The proactive care arm will be given access to the information line as well, additionally the peer coaches will proactively call the participant, the participant will receive access to an online educational curriculum, the participant will be given access to respiratory therapists who will also act as peer coaches in health topics covered in the curriculum and lastly proactive care arm participants will

have online access to adherence monitoring data to track their progress as they advance through the study program.

II. Criteria for Subject Selection

Number of subjects

The goal is to recruit 330 participants into the study to result in analyzable data of 300 participants (assumes ~10% attrition).

Gender of Subjects

There are no gender-based enrollment restrictions. Subjects of all genders will be recruited to enroll.

Age of Subjects

Subjects recruited for this study will be adults aged 40 and above.

Racial & Ethnic Origin

There are no enrollment restrictions based on race or ethnicity.

Inclusion Criteria

The inclusion criteria are as follows:

1. Age: ≥40 years
2. Primary language: English
3. Diagnosed with both Chronic Obstructive Pulmonary Disease (COPD) and Obstructive Sleep Apnea (OSA)
4. Prescription for positive airway pressure therapy (PAP). There should be no minimum or maximum flow required (i.e., no limitation on PAP modality).
5. Access to the internet viand a PC, tablet, or smart phone to complete all study activities from home or remotely
6. PAP device with wireless modem

Exclusion Criteria

1. Non-English speakers
2. Life expectancy less than or equal to six months

Exclusion criteria includes non-English speakers and those whose life expectancy is less than or equal to six months. The study does not currently have the resources to translate the online curriculum into multiple languages, nor does it have the funds to recruit multi-lingual peer coaches. Additionally, as indicated in the inclusion criteria, access to a computer and internet are necessary for participants to complete the study activities.

Vulnerable Subjects

The study does not seek out the enrollment of any vulnerable populations, should it become questionable that a participant belongs to a vulnerable population the Principal Investigator will assess eligibility on a case by case basis. If the Principal Investigator deems an individual as belonging to a vulnerable population they will be labeled as such in the studies screening log and will be withdrawn from the study. Online recruitment methods will be utilized and research coordinators will speak with each participant after the E-Consent has been signed but before any study activities have been completed by the consented individual. It is on this initial phone call with a consented participant that the study team will be collecting demographic information and the medical history of each participant and be specifically confirming that they do not belong to a vulnerable population.

III. Methods & Procedures

Methods and Procedures

Promotion and Targeted Recruitment

The O_2VERLAP Project Team is coordinating with consultants at several PCORI-funded "patient-powered research networks (PPRNs) including ABOUT PPRN, PRIDEnet PPRN, HealtheHeart Alliance PPRN, and PI Connect PPRN to engage their respective patient communities through study promotion activities. Namely, each consultant will work with their PPRN to distribute study advertisements within their respective communities. We anticipate each PPRN affiliate will be using their respective online, social media communities (where applicable) and email listservs to distribute study advertisements. Facebook offers some relevant targeting options, when posting advertisements, such as: age-specific targeting (i.e. aged 40 and older, per the study's inclusion criteria), gender (i.e. all genders would be included per the studies inclusion criteria), targeting based on healthcare interests and allows for targeting individuals who have visited your page before or subscribe to your Facebook page (i.e. individuals who, at a minimum, have some interest in these communities). So, through targeted advertisements, which will use unique, identifying URL links, we hope to be able to measure the benefit of this distribution strategy and will be able to estimate the effectiveness of each advertisement, within each community. It should be noted that all advertisements will direct potential participants to speak with authorized study staff (i.e. research coordinators listed in the studies delegation of authority log on file with WIRB).

The study will more directly engage the OS population through the COPD Foundation (COPDF) and the American Sleep Apnea Association's (ASAA) robust social media communities, which include: the COPDF Facebook page, the COPDF Twitter account, the Foundation's online community COPD360Social, the ASAA Facebook page and the ASAA Twitter account. Again, whenever possible, advertisements will use a unique URL link, which will aid in tracking the success of various promotions. Other confirmed, targeted, recruitment strategies include: the COPD PPRN and PSCANNER Clinical Data Research Network (CDRN). The COPD PPRN and PSCANNER CDRN will query their respective databases for individuals who meet the study inclusion criteria. These individuals will then be notified of their eligibility. The study's Principal Investigator, Dr. Stepnowsky, is a member of PSCANNER CDRN.

Registration and E-consent Process

After seeing a study advertisement, participants may decide to call the C.O.P.D. Information Line and speak with a trained associate who will then answer any questions that the individual has about the study and participation. Should this satisfy the potential participants interest, they will then be directed to the study portal. Potential participants must register to the portal to be able to view the O2VERLAP Study Consent Form (because this will be an electronic form, we refer to it as the "E-Consent form"). This is necessary for data storage purposes should the potential participant decide to move forward and sign the E-Consent form. Potential participants are encouraged to call the study's research coordinator or the COPD Foundation's Information Line to learn more about the study, should they have questions. The E-Consent form reviews the study background, design, eligibility criteria, potential risks and benefits of the study, the study activities associated with enrollment and the individual study activities associated with each arm. The E-Consent encourages potential participants to discuss participation with family and friends, should they want additional support. One of the last pages of the E-Consent form includes a check list for the participant to review; the list includes confirmation that the participant understands the study design, the low-risk of participating and confirms that the participant comprehends the eligibility criteria.

Should the potential participant decide to move forward and consent to participate, they will digitally sign and date the E-Consent. A copy will be housed in their portal account and available for download. The study team will instruct all consented participants to download a copy of the E-Consent for their personal digital records and paper files should they like to print a copy.

Self-reported Confirmation of Eligibility and Study Team Confirmation of Eligibility

After an individual digitally signs the E-Consent they are then prompted to take a survey, which relies on self-reported confirmation that they meet the studies eligibility criteria. Should an individual respond to a question in a way that indicates that they are not eligible, the study team will be notified by email to schedule a call and confirm that the individual should be excluded from participation. We do anticipate that some individuals will fail to complete this survey which will not affect our ability to screen them successfully. When the E-Consent is signed it triggers an email to the study team to reach out to the newly enrolled individual for their first study phone call; the purpose of this phone call, which is titled the "Confirmation of Eligibility" phone call, is to again confirm that the individual meets the study eligibility criteria. Should the study coordinator confirm that the consented individual is in fact eligible, they will document this in the study portal in the corresponding survey titled "Confirmation of Eligibility" survey and go on to complete additional forms which provide evidence of the participant's eligibility (i.e. Medical History survey and Demographic survey).

Study Screening Log

The study screening log will capture all individuals who E-Consent, as well as document the following scenarios: those that subsequently fail to meet eligibility according to the self-reported confirmation of eligibility survey and those that subsequently fail to meet eligibility on the "The Confirmation of Eligibility" phone call with the study coordinator. The screening log will include documentation of which inclusion or exclusion criteria have not been satisfied.

The study screening log will document reasons for ineligibility where applicable and will therefore provide a metric for reporting this data.

The screening log will also capture all incoming phone calls, from potentially interested study participants who may call the C.O.P.D. Information Line. The screening log will also document any email inquiries received. The screening log will document whether the incoming phone call ultimately lead to an enrollment, a conversation with an ineligible participant or a conversation with a participant who is eligible but declines to E-Consent. The screening log will document why someone is ineligible and will also record the reason why eligible participants decline to E-Consent.

Due to the many, intersecting, workflows and avenues that will be used for recruitment, the screening log will be a working document, housed in a shared file online. The screening log will only be accessible by authorized study personnel listed in the studies delegation of authority log. The log will be updated on a daily basis, in real-time, as screen failures occur, or as soon as the study team has been made aware of screen failures. The screening log will include the following information, to the extent with which it can be collected: date of screen failure, mode of screen failure (I.e. online, phone, email inquiry), information on how the individual heard about the study (I.e. what advertisement or communication topic got their attention and what avenue they received that information – social media platform, affiliated institution, email, support group, COPD PPRN newsletter, conference, etc.), screen failure's first and last name, email when applicable, reason for screen failure (I.e. what eligibility criteria was not met or why the individual does not want to participate), whether the individual would like to be followed up with at a later date, phone number, preferred time to contact and whether the individual would like to be contacted in the future for other research opportunities.

Systematic Effort to Reduce Attrition

After study communications, participants fill out a brief survey in the study portal to indicate their satisfaction level with any given communication, including all modes of communication available. Participants rank the communication from 1 (low) to 10 (high) and are also asked to provide free-text feedback when the communication is ranked at a 7 or lower. The portal has a built-in feedback loop which indicates to study staff when someone is not satisfied with a given communication (i.e. ranked 7 or lower) so that we can readdress a topic or correct areas of inefficiency within our communication procedures, as reported by the participants. We hope that this feedback mechanism will help ensure that we can maintain effective communication with participants and therefore help mitigate a common cause of attrition.

Additionally, there are automated reminders built into the study portal, based on a participant's anticipated timeline for completing study activities. The portal sends participants email notifications that an upcoming study activity is due, if it has not already been completed, and continues to send automated notifications when a study activity is past due. When a participant is at risk of falling behind schedule or has outstanding study activities, this also triggers automated emails to the study team, who will then check-in with a given participant and determine if there are any inhibiting factors that can be addressed.

Lastly, participants will work with their peer-support team (i.e. Information Line peer coach) to complete a 'My Calendar' activity on the platform at the start of their enrollment. The study portal 'My Calendar' application provides participants with an overview of their curriculum-related due dates (i.e. when an upcoming module is due). Each participant can then tailor their schedule and pace for completing study activities based on anticipated due dates. The Information Line peer coaches will complete this activity with participants We hope that collaborative goal-setting with peer coaches and level of communication

occurring between coaches and participants, will decrease the likelihood of attrition and motivate participants to complete activities on time.

Study Design

WEEK ONE

Electronic Data Capture (i.e. EDC) System

The study design is greatly dependent on technology, remote communication and asynchronous online interactions between the research team and study participants, including: remote completion of all study activities, study enrollment processes, health-literacy education, peer-coaching and adherence monitoring. To access the study portal, participants must be able to access the internet and have access to a PC, smart phone, or tablet. It should be noted that the study portal, which is accessed by both the study research team and study participants to complete all study activities, relies on direct entry and is the primary source record for almost all study documentation. Study staff and participants are provided different levels of access to the portal. The study portal is compliant with FDA 21 CFR part 11, HIPAA and industry standards best practices.

DatStat is the company that manages the studies computerized system, which has been validated by the study team to be fully compliant with the aforementioned regulations. The study portal and data is protected by the following security and privacy measures: advanced encryption for data transmission between a participant browser and DatStat's server; at rest data encryption within the DatStat database server; DatStat's physical servers are in a locked cabinet inside of a guarded building and data back-up is encrypted and occurs daily. Per FDA predicate rules standards, the system provides a computer-generated, time-stamped, audit trail, which logs all additions, deletions or alterations to the electronic source records. The audit trail preserves the sequence with which changes to an electronic source document have been made and does not obscure prior entries. All archived records will preserve the original content and meaning of a source accurately. Access to the online system is limited to study participants and authorized research staff who are listed in the IRB-approved study application. Authorized research staff and study participants are trained on how to use the portal, will have a manual and guidelines to reference and an authorized research team member to contact when technical difficulties arise.

HIPAA compliant, study portal trained, DatStat staff, who are also designated by the study team, may enter the system for administrative and technical support related to the management of the computerized system. DatStat does not offer any of the study data, or participant PHI, to third-parties. Additionally, all DatStat staff have completed the following training: HIPAA awareness for Business Associates, from HIPAATraining.com or HIPAA awareness training, from Resource Management Inc., Protecting Human Research Participants, from NIH Office of Extramural Research and 21 CFR Part 11 training, from Computer System Validation.

Portal Registration (i.e. EDC), E-Consent and Confirmation of Eligibility Activities

The potential participant must first register on the study portal, which is where all study activities take place and some online study communications also take place. The registration process includes entering

one's first name, last name, a username and double-entry of a password. The participant will then verify their email using a unique, encrypted URL sent to their registered email address. Once verification of the email address occurs the registered individual will be able to log into the study portal. Upon logging in for the first time, the consent form will appear for the potential participant to review. The consent is presented electronically in the same format as the IRB-approved version. From here forward in this protocol, we will refer to this document as the E-Consent form, since it will be reviewed and signed electronically. Once the individual signs the E-Consent form, a number of activities and communications will then be triggered within the study portal.

As described in the Methods and Procedures section, the most immediate activity following E-Consent signature is the self-reported confirmation of eligibility survey; this activity is assigned to all participants immediately after completing the online consent process. Individuals will be asked to confirm that they satisfy all inclusion and no exclusion criteria. At this point, if they fail to meet eligibility requirements, the research team will be notified and call the individual to confirm. No further study activities will be assigned to this participant, unless the research team discovers that this individual misreported on an eligibility criterion by mistake. However, this would indicate that the E-Consent needs to be reviewed again thoroughly. Note that Appendix A provides the enrollment and randomizations workflows in graphical format.

The research team does a thorough review of the E-Consent form and study obligations by phone when conducting the Confirmation of Eligibility phone call, for example; the eligibility criteria are reviewed again for comprehension, the study obligations are reviewed again for comprehension, the potential risks and benefits of participating are discussed, study compensation is discussed, and study contacts are reviewed. The research team will also provide ample opportunities for the individual to ask questions and will continue the conversation.

Demographic Survey and Medical History

Participants who wish to continue enrollment activities and are also deemed eligible to participate in the study on the Confirmation of Eligibility phone call will then be asked to provide information on their demographics and medical history.

The current PCORI common data model (i.e. PCORI CDM) provides details on the demographic variables that being collected in this study and they are supplemented by a few additional demographic variables which the study team also found to be pertinent.

A survey of the participants Medical History will be taken on the initial phone call. The authorized O_2VERLAP Study team member will go through a list of common comorbidities which are also significant to record, should they be a part of the participants current or past health status. The research team will also ask the individual to report any comorbidities, using the Charlson Comorbidity Index, which are not covered during the questionnaire and this will be recorded as well.

Oxygen prescription, Oxygen Equipment and Self-Report Oxygen Adherence

Participants will be asked whether they are currently prescribed oxygen therapy or not. Individuals that are using oxygen therapy at baseline will be asked to report information about their prescriptions(s), equipment type(s) and self-reported adherence at baseline, 6-weeks and 12-weeks. Individuals will self-report on these prescription(s) online in the study portal. Appendix B provides more details.

Remote Adherence Monitoring Set-up Activities

Participants will also be asked to provide information relative to their CPAP device (e.g., serial number, brand, model, DME provider, Sleep Technician or PCP contact information). This information is necessary to coordinate access to the participant's remote adherence monitoring data collected wirelessly via their CPAP device modem. All study participants are required to have a Resmed or Philips Respironics brand CPAP device, with wireless modem, for this reason. More often than not, a patients Durable Medical Equipment (DME) provider is also their CPAP device 'data-steward'; this means that a participant's DME ultimately controls who can and cannot access an individual's CPAP data. Both Resmed and Philips Respironics have online systems for their CPAP device users. DME companies and healthcare providers to login into as necessary for remote data collection, analysis and review. Similarly, to our study portal, these systems can also be accessed using mobile devices. Sleep Apnea patients may use these systems to review their progress with a new Sleep Apnea Mask or coordinate remotely with their sleep doctor to adjust CPAP settings. Chronic care management of diseases like Sleep Apnea are using telemedicine systems more frequently

The study team will have to coordinate with the participant's DME to ensure that their online data profile is appropriately tagged. This will notify the participants data-steward that they are consenting participants in a research study. The specified variables will be represented graphically in the study portal for each participant. The variables will be linked to the study portal using an 'Application Programming Interface' or API. The COPD Foundation research infrastructure, leveraged by the O2verlap study will utilize the Corepoint Health integration engine to facilitate the secure communication and data transmission between the Philips Respironics and ResMed Inc. API's.

As such, both Philips Respironics and Resmed have participated in the development of the data transfer workflow. Data will flow from the ResMed Airview system or Philips Respironics Encore Anywhere online system, through the necessary API's, managed by Corepoint Health integration engine, into the DatStat study platform. After providing the necessary information to either ResMed Inc. or Philips Respironics's data stewards, which is inclusive of proof of a participant's E-Consent, the participant Name, DOB and CPAP device serial number, the data steward will be required to provide the following data variables via the API workflow:

Weekly Updates on Critical Adherence Monitoring Data Variables

1) Total Time Connected (i.e. total time in minutes using a CPAP each evening)
2) Air Leakage (i.e. number of minutes the Sleep Apnea Mask is leaking air beyond a given threshold)
3) Apnea Hypopnea Index (i.e. a record of the number of apneas an individual is experiencing each evening).

These three variables are critical, quantitative indications, of an individual's adherence to CPAP therapy (i.e. the studies primary outcome) and may also provide insight on how to improve adherence. Monitoring these CPAP therapy variables will help both the research participants and authorized research staff to tailor a participant's goal-setting on a weekly basis, acknowledge progress and troubleshoot difficult weeks. The participants randomized to the proactive care arm will review and discuss their data on a weekly basis with a peer-coach to address these topics. Proactive care participants will also be encouraged to call their Peer-coaches during regular business hours via the C.O.P.D. Information Line and will also be encouraged to chat synchronously or asynchronously with Peer-coaches using the study portal.

Baseline Survey Package

All participants will be assigned a baseline survey package. Together the survey's measure a number of important patient-centered outcomes, like daytime sleepiness, daytime functioning, psychosocial factors influencing the survey's included are:

1) Functional Outcomes of Sleep Questionnaire (FOSQ)
2) COPD Assessment Test (CAT)
3) Epworth Sleepiness Scale (ESS)
4) Pittsburgh Sleep Quality Index (PSQI)
5) Patient Reported Outcomes Measures Information Systems Survey (PROMIS)

Randomization

A participant must have completed the following steps in order to move on to randomization. Participant completes the following steps independently [see Appendix A for randomization workflow]:

1) Portal Registration
2) E-Consent Signature
3) Self-reported confirmation of eligibilty survey

Participant and Research Coordinator via First Phone Call:

4) Confirmation of Eligibitliy (i.e. self-report survey and research team confirmation)
5) Medical History
6) Demographic Information collected by research team
7) Self-Report Oxygen Prescriptions and Adherence (if applicable)
8) Participants data-steward provides access to CPAP data
9) Wireless Data Access confirmed by research team
10) ~30-days of baseline CPAP data uploaded to portal (collected retroactively)
11) Baseline Survey Package

Once these steps have been completed the research team will be notified both within the study portal and by email; the notification will indicate that the participant is now ready to be randomized. Envelopes have been made ahead of time and should not be opened ahead of time. The randomization envelope reveals, with equal odds, either the Proactive Care Arm or the Reactive Care Arm. The coordinator will immediately mark the individual as such in their participant profile, within the study portal. See Appendix C for both Respiratory Therapist and Peer Coaching scripts.

Proactive Care Arm

1) The Proactive Care arm of the study is considered the study intervention. If an individual is randomized to the proactive care arm they have access to: Weekly Dyadic Peer Coaching
2) Respiratory Therapist Dyadic Coaching
3) A seven-module online curriculum covering topics on COPD, OSA and Overlap Syndrome
4) Web-based access to adherence data
5) Proactive, dyadic, web-based and telephone support from Peer Coaches to congratulate progress and troubleshoot difficult weeks

Reactive Care Arm

1) Web-based access to adherence data
2) Reactive, dyadic, telephone-based support

Figure 1 below shows a simplified, visual representation of the study design.

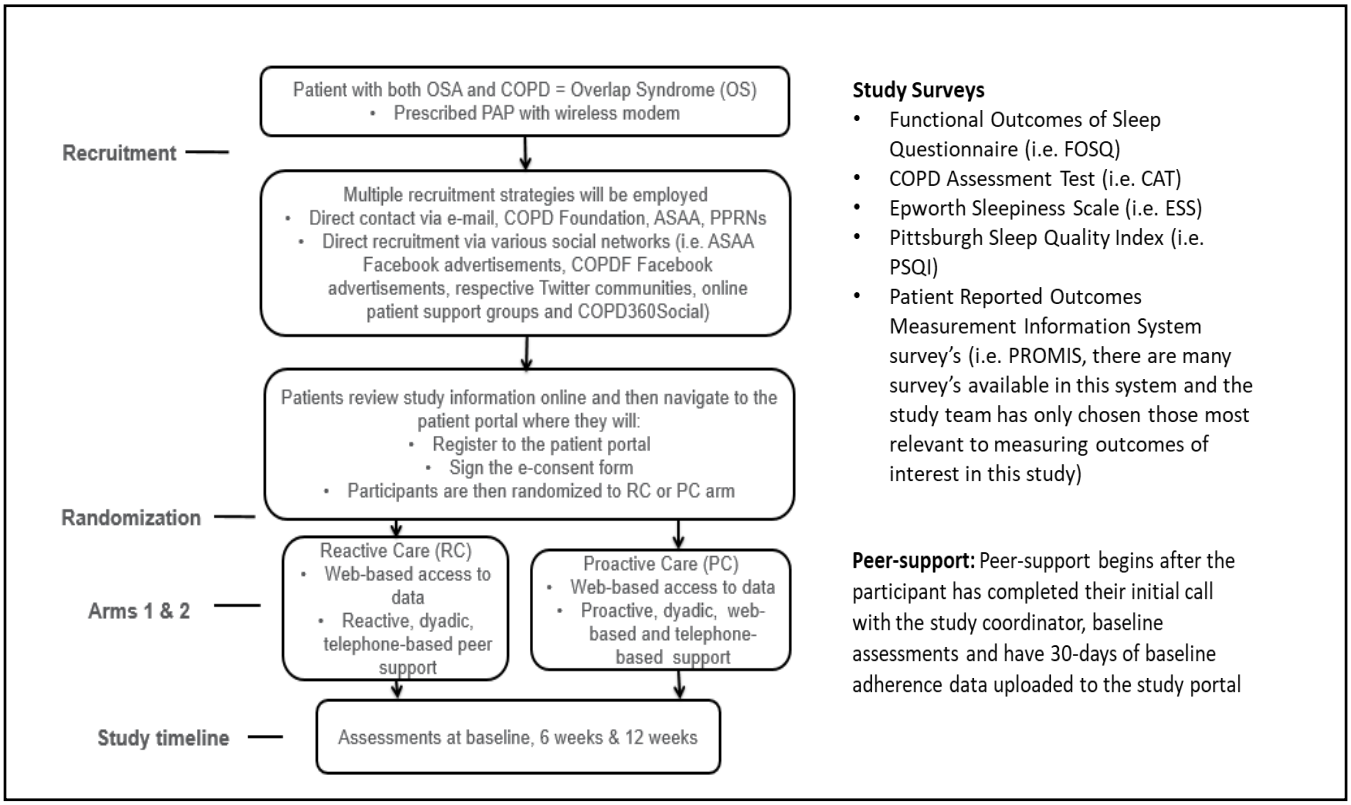

Figure 1.0 Study Design, Study Surveys and Peer Support

Study Activities

Table 1.0 O_2VERLAP Study Activities

Week

Activity	Who's involved?	1	2	3	4	5	6	7	8-15
Portal Registration	Patient	X							
E-Consent	Patient	X							
Self-report eligibility survey	Patient	X							
Confirmation of Eligibility survey	Coordinator	X							
Medical History	Coordinator	X							
Demographic Survey	Coordinator	X							
Patient ID, Email, Phone Number sent to Info Line via salesforce email	Coordinator	X							
Baseline Surveys	Coordinator and Participant	X							
30-days of Baseline CPAP Adherence Data uploaded to portal	Coordinator and ResMed or Philips (PC Arm Only)	X							
Self-report Oxygen Adherence Baseline	Coordinator and Participant (only participants prescribed O_2)	X							
1st Call from Respiratory Therapist Coach; confirm participant can send and receive messages to RT Group; fill out PAP use survey and O_2 use survey, if applicable.	RT Coach and Participant (ALL participants)	X							
1st Message from Peer Coach in portal; confirm participant can send and receive messages; fill out Journal, review and set goals. Fill out My Calendar, review.	Peer Coach (PC Arm Only)	X							
1st call from peer Coach and Module 1 completed together	Peer Coach and Participant (PC Arm Only)		X						
Module 2 Fundamentals of COPD	Participant (PC Arm Only)		X						
Module 3 Fundamentals of Sleep Apnea	Participant (PC Arm Only)			X					

Self-report Oxygen Adherence 30-days	Coordinator and Participant (only participants prescribed O_2)				X				
6-week surveys +1 week (i.e. FOSQ, CAT, ESS, PSQI, PROMIS surveys)	Participant (PC Arm Only)				X				
Module 4 PAP in Depth I	Participant (PC Arm Only)				X				
Module 5 PAP in Depth II	Participant (PC Arm Only)					X			
Module 6 Oxygen in Depth	Participant (PC Arm Only)						X		
Module 7 Oxygen with your PAP device	Participant (PC Arm Only)							X	
Self-report Oxygen Adherence 12 weeks	Coordinator and Participant (only participants prescribed O_2)								X
12-week (+-1 week) follow-up surveys	Participant (PC Arm Only)								X
Peer Coach Calls	Peer Coach and Participant (PC Arm Only)	X	X	X	X	X	X	X	
RT Coach Calls	RT Coach and Participant (PC Arm Only)	X				X	X		
SAE and AE reporting	ALL study staff members	X	X	X	X	X	X	X	X
Exit Call from coordinator	Coordinator and Participant								X

Peer Coaches

Peer coaches will generally help with the following:

1) The management of a chronic illness
2) Health literacy
3) Emotional Support
4) Social Support
5) Experience-based feedback
6) Goal-setting

C.O.P.D Information Line peer coaches are available to participants Monday through Friday, from 9:00am to 6:00pm ET. If a participant calls the Information Line and does not reach an associate, calls are returned within 24 hours of the last business day. The C.O.P.D. Information Line Peer Coach's availability to the proactive and reactive care arms of the study is the same. There proactive care arm however, will have additional avenues of communicating with the C.O.P.D. Information Line peer coaches (I.e. the chat feature of the study portal) and will also have scheduled calls to check-in with the peer coaches on a weekly basis.

The scheduled calls between proactive care arm participants and peer coaches will be used to discuss progress in the curriculum and weekly CPAP adherence monitoring data. Peer coaches will also reach out to a proactive care arm participant if the portal indicates that they need help, this can happen in a number of ways, such as:

- A participant may indicate in a specific module lesson that they would like to speak with a peer coach
- A participant may choose to send a message to the peer coaches using the chat function within the study portal
- The participant's adherence data may show that they improved their adherence significantly and should be congratulated
- The participant's adherence monitoring data may show that they are adhering at a level below their baseline

Individuals in the reactive care arm will be given the C.O.P.D. Information Line number and told that they can call it whenever they wish, however, they will not have scheduled calls with peer coaches and their study portal data will not trigger peer coaches to call them when they are having a particularly successful or difficult week.

Individuals in the proactive care arm will likely speak with Information Line Coaches at least once a week during their initial seven weeks in the study. Peer-coaches will also be very important in providing emotional and social support to all participants.

Additionally, there will also be certified Respiratory Therapists who are providing peer coaching from the perspective of a caregiver.

All study participants will have a call with a Respiratory Therapist (RT) peer coach at the beginning of the study, to discuss their 30-days of baseline remote adherence monitoring data. This will be an opportunity for the participant to reflect on their current habits and set personal goals for improvement. The RT coaches will ask questions to help determine how well their current Sleep Apnea Mask is fitting them; this will also be an initial step to troubleshoot individually with participants and provide possible solutions to obvious adherence barriers.

The coaches will all be guided and trained on proper interactions with participants, however, no peer-coaches should ever provide the participant with clinical advice. If a coach believes that a participant needs clinical advice they will advise them to contact their preferred healthcare provider.

Quality Tracking and Improvement of Communication Between Peer Coaches and Participants

If a peer coach feels that a participant needs clinical support, should discuss a topic further with a healthcare provider or needs to seek emergency help they will suggest the participant do so. It is required that the peer coaches document any scenario where this occurs. The study portal has a communications tracking survey which peer coaches are required to fill out after each interaction with a participant. The survey captures the mode of communication, date, time and asks the peer coach to provide information on the topics discussed. The survey specifically asks if the coach advised a participant to speak with a healthcare provider or seek medical attention.

The completion of the coach's communication tracking form triggers a similar form in the participants activity list. This provides the participant a chance to rate their interaction on a scale of one to ten, one being not satisfied at all and ten being completely satisfied. It also asks that the participant share what was discussed. If a participant rates their interaction to be a seven or lower we will consider this insufficient and it will immediately trigger the peer coaches to reach back out to the participant. The peer coaches should acknowledge that the participant may not have been satisfied and ask if they can help further. The peer coaches will additionally ask how their communication can be improved upon to apply to future communications.

Data Analysis and Data Monitoring

Accessing the online curriculum, health monitoring data and peer coaching present minimal risk to study participants. Thus, the project was deemed to not need a data-safety monitoring board.

Overarching approach to analyses

Preliminary analyses will begin by examining the distribution of study variables and provide descriptive statistics (e.g., mean, median, standard deviation, quartiles for continuous variable, frequency and percentage for categorical variables) about the study population. Patient characteristics will be compared among study arms by a series of Kruskal-Wallis tests and Chi-square tests (or Fisher's exact tests as appropriate). Variables on which the groups differ initially will be explored as covariates in subsequent analyses. In case of missing data, appropriate data analytic techniques will be used, which may include deletion, imputation, inclusion of an indicator of missing values, or pattern-mixture modeling. The primary analysis will be as intent-to-treat (including all enrolled subjects) and all analyses will be performed using two- sided tests with alpha=0.05. Analyses will be conducted using SAS and R statistical software. Analysis plans to address each hypothesis are as follows:

Study Primary Aim

Our hypothesis is that CPAP adherence at the 6-week time point will be improved in the proactive care group compared to the reactive care group. Random effects model will be used to compare the mean CPAP adherence over 6 months between proactive and reactive care groups. A random intercept will be included in the model to account for the repeated measures of CPAP

adherence over 6 months within each patient. Daily CPAP adherence data will be used for the analyses. Multivariable random effects model will be used to assess the difference in CPAP adherence between the proactive care and the reactive care group with adjustment for potential covariates. Adjustments will be made to correct for baseline imbalances across study groups and to adjust for variables known to influence the outcome. Baseline demographic and other clinically important characteristics will be assessed for imbalance among the study groups using Wilcoxon rank sum test, Chi-square or Fisher's exact test, and their association with the outcome using a simple random effects model. These variables will be included as covariates in the multivariable model if found moderately associated with the outcome or unbalanced ($p<0.15$) across groups. All covariates significant at $p<0.10$ will be kept in the final model.
As a secondary analysis, we will fit a random effects model to assess the difference in CPAP adherence change between two groups. The random effects model is useful for examining longitudinal measures and it will include all available data. An interaction between time and intervention will be included in the model, both random intercept and random slope will be assessed, likelihood ratio test will be used for model comparison. Similarly, multivariable random effects model will be used to assess this association with adjustment for potential covariates.

Study Secondary Aims

Our hypothesis was that the improvement in patient-centered outcomes (daytime functioning and sleep quality) in 6 weeks and 12 weeks will be larger in the proactive care group compared to the reactive group. The change in patient-centered outcomes from baseline to week 6 and week 12 will be compared between the proactive care and the reactive care groups. The difference in change of each outcome will be assessed using analysis of covariance (ANCOVA) with intervention group as a main effect and baseline score as a covariate. Multivariable linear regression analysis will be used to assess the difference in change scores between groups with adjustment for baseline characteristics using similar approaches as described for Hypotheses 1. Baseline variables will be included as covariates in the multivariable linear regression if found moderately associated ($p<0.15$) with the outcome or unbalanced ($p<0.10$) across groups. Only covariates significant at $p<0.10$ will be kept in the final model.

As a secondary analysis, we will also fit a linear random effects model to assess the change from baseline to week 6 by taking into account the correlation of two measurements (baseline and week 6) within each participant as well as using all available data. Long-term maintenance of group effects will be also examined by a linear random effects model to determine whether the change in each outcome (from baseline to 6-week and 12-week follow-up) is different between the study groups.

Study Tertiary Aim

The improvement in the sleep quality and symptoms in 6 weeks and 12 weeks will be larger in the proactive care group compared to the reactive group. The analysis is similar as that listed for the studies secondary aim, please see above.

Potential exploratory analyses

Exploratory analyses are not currently planned, but may be done if warranted.

Addressing heterogeneity of treatment effects (HTE)

To evaluate the HTE, we will assess the interaction between treatment group and several baseline patient characteristics including age, gender, education and socio-economic status. We continue to

think about inclusion of other important sub-groups. If interaction is significant, the treatment effect will be estimated separately for study subgroup.

Data Storage and Confidentiality

Data confidentiality and security are applied at all levels of data acquisition, transfer and storage at the Data Coordination Center (DCC). The Data Coordinating/Data Management System (DCDMS) developed by DatStat meets exacting data management standards of confidentiality, as well as HIPAA requirements [see Appendix D]. Access to the Data Management System (DMS) requires two levels of identification, one to gain access to the secure server and one to gain access to the Registry data management system. Users of the system are assigned job-specific permissions such as data entry, reporting or query resolution. Confidential data collected from the sites are encrypted in transport by the system, as well as at rest, and are only accessible by authorized users of the system.

The server hosting the DMDCS is housed at the Data Coordinating Center and exclusively managed by DatStat personnel. Measures to ensure the security of the data include: restricting access to users with valid IDs and passwords; using a hardware firewall to restrict access to the web server and database; and using the secure sockets layer standard to provide encryption and user authentication. In accordance with DatStat standard operating procedures, system security logs and event logs are monitored daily to detect unauthorized attempts to access the system. DatStat follows internal standard operating procedures and industry standard guidelines for securing data and services running its application. These guidelines and standard operating procedures include securing servers with complex, hard to guess passwords, processes to lock down and secure servers by changing administrator account credentials, managing port security at the firewall level, and restricting logical and physical access to servers to only essential personnel.

All data transferred to DatStat's collocated datacenter are stored, processed, and analyzed within the datacenter. At DatStat's colocation facility, all access to the datacenter is controlled through locked doors which require an escort, and pre-authorization by another internal employee listed on the account. The DatStat office space remains locked after working hours. Access to computer data files is controlled by passwords released only to the personnel who use such files. In addition, data files with personal identifiers are encrypted. Physical access to servers and data backup is restricted to a minimal number of IT professionals. Such access is provided only with strong passwords that regularly expire, minimizing the chance that passwords distributed inadvertently and/or unknowingly could cause inappropriate data access. Access to data stored on the server is available only to designated users who log in with specified usernames and passwords. Users are logged out after a period of time. A listing of the named users with a description of their access privileges is available within the applications.

Data presented in manuscript, abstract, poster or other publications will appear de-identified.

Transition from Research Participation

Enrollment into the O_2VERLAP study does not affect the participant's current health plan and only serves to supplement existing prescription for therapy to CPAP by furthering the patients access to health education and peer support. Should a participant decide to withdraw consent it will not affect their healthcare in any way; participants will be reminded of this at the time of consent and throughout their participation in the study.

IV. Risk/Benefit Assessment

Risk Category

Minimal risk: Participation in the O_2VERLAP study presents minimal risk to enrollees. The study does not prescribe or alter any participant health care plans; the educational curriculum, peer coaching and CPAP device adherence monitoring data being provided to participants is meant to proactively supplement standard of care for this population.

Potential Risks Include:

- Survey data: Patients may be uncomfortable answering questions (e.g., age, healthcare utilization) or may be embarrassed by these data. Eligible subjects have the option of not participating. Subjects who enroll will also have the option of prematurely discontinuing the study.

- Confidentiality: There is a small potential risk of a breach of confidentiality, but all appropriate measures will be taken to assure this done not happen. These measures are described below in the "Protection Against Risk" section.

Protection Against Risks

In accordance with HIPPA regulations and Western IRB requirements, all appropriate compliance requirements for data transfer and data use will be met. All reasonable measures will be taken to ensure the privacy and confidentiality for participating subjects. Computerized data are protected with numerous levels of security to prevent unauthorized access to the computerized information, including password-protected files and directories on investigator computers within firewall-protected networks. All data and analysis activities will be performed within the secured computer networks. We require that investigators and staff obtaining access to the data be qualified investigators and staff who are linked to institutions that can be held accountable if violations occur. Access to these data will be restricted to the WIRB approved research staff only. Analytic files will be de-identified of all PHI. All reports/manuscripts will be prepared in such a way that individual patients will not be identifiable. Additional source-specific measures include:

Research subjects can refuse to answer any questions outside of the eligibility criteria/questions critical to analysis or complete aspects of the study they find embarrassing or refuse to complete for any other reason. In previous similar studies, we have found that subjects rarely refuse to complete these study procedures, since they are minimal risk and we collect these data in professional ways.

Potential Benefits to the Subjects

The study participants may benefit from knowledge obtained through peer coaching, CPAP adherence monitoring data being provided to participants via an online portal and they may benefit from the educational curriculum being provided to the proactive care arm participants of the study. The potential knowledge gained is intended to help this patient population improve adherence to their PAP therapies, additionally we anticipate that improved adherence to CPAP therapy will be linked to other improved patient centered health outcomes. However, no benefit will be guaranteed to any participants. We hope that this research will at a minimum provide enough information on the efficacy of the studies proactive care arm program to determine if it is a helpful tool to improve the health outcomes of the OS community.

Importance of the Knowledge to be gained

The O_2VERLAP study will help determine the efficacy of proactive peer coaching in combination with an online educational curriculum to improve the OS populations adherence to CPAP therapy. The OS population has an increased incidence of morbidities and mortality, however when this population uses their CPAP therapy as prescribed these increased risks are lessened to match that of a typical COPD patient. Therefore, this study may help provide a toolset to the OS community to improve their health outcomes.

Alternative to Participation

If an individual chooses not to participate in the O_2VERLAP study they will not affect an individual's regular medical care or health benefits. This language is included in the study consent form and this information will be reiterated to participants at the time of confirmation of eligibility and participants will be reminded of this as they advance through the study program.

V. Subject Identification, Recruitment and Consent/Assent

Method of Subject Identification and Recruitment

Prospective subjects will be recruited through many different avenues, many of which rely on digital communications and social media. This study is in part being conducted using the COPD PPRN technological platform, all prospective subjects will have to enroll in the COPD PPRN to participate in the O_2VERLAP Study. If individuals are already enrolled in COPD PPRN, they will have immediate access to the study pre-screener. If individuals are not enrolled in the COPD PPRN, they will be required to review and sign the COPD PPRN consent form before they will be offered the O_2VERLAP Study eligibility pre-screener. Subjects who do not meet the O_2VERLAP Study eligibility requirements will continue to be enrolled in the COPD PPRN unless they withdraw from the COPD PPRN. O_2VERLAP Study participants will be recruited through the following avenues:

- **COPD Patient-Powered Research Network (COPD PPRN):** Potentially eligible COPD PPRN (WIRB Protocol #20141136) participants will be identified by querying the COPD PPRN database for the study inclusion criteria, namely diagnosis of COPD and OSA. Once a list of patients has been identified, secure emails will be send to those individuals inviting them to visit the study portal and or call the study coordinator to learn more about potentially participating in the O_2VERLAP study. Potential O_2VERLAP participants who go on to register to the study portal and E-Consent, will be contacted within two business days by a study coordinator. The study coordinator will confirm their eligibility and review the consent with them over the phone (please refer to 'Process of Consent' section for more detail). It may be determined that some participants do not meet the eligibility criteria, those individuals will be given a copy of their E-Consent and thanked for their time. The COPD PPRN also has a newsletter which may be utilized to include information about this study.

- **COPD Foundation's COPD360social online community & Facebook page**: COPD360social is the COPD Foundation's online social community that is comprised of over 32,000 patients, caregivers, family members and healthcare professionals. The COPD Foundation also has

their own Facebook page and patient email listserv. These mediums will be used to promote the O_2VERLAP Study through IRB-approved messages and images.

- **ASAA Facebook, Twitter, Email listserv:** As the primary collaborator on this project the American Sleep Apnea Association will post IRB-approved study advertisement, language and images in their social media channels. Additionally, they will attempt to recruit using their patient listserv to send IRB-approved study advertisements, language and images.

- **PCORnet Partners.** The O_2VERLAP project team will be responsible for sending these same study advertisements to O_2VERLAP study partners who are members of PCORnet: (1) PCORnet member organizations already described in the methods section above (PPRNs and the pSCANNER CDRN).

- **Healthcare Providers and Professional Organizations:** This includes organizations that originally were included on the grant submission and serve on the O_2VERLAP Stakeholder Advisory Board, including CHEST, American Association of Respiratory Care (AARC) and the American Thoracic Society (ATS). Further, the COPD Foundation's committees, working groups, and members of the COPD Foundation's pulmonary education program network, which are comprised of healthcare providers, will be notified about the O_2VERLAP Study and provided IRB-approved materials to provide to any interested patients. Additionally, the COPD Foundation's PRAXIS community on COPD360social will be notified of the O_2VERLAP Study through IRB-approved materials.

- **General Public Outreach Approach:** Materials will be developed such as a one-page recruitment sheet for prospective subjects as well as a basic email template that patients can distribute to their communities if they so choose.

Process of Consent

The process of consent will begin electronically through the study portal (i.e. DatStat's HIPAA compliant portal which will also serve as the studies primary source record for most study activities). Potential participants will register to create an account with the study portal. Once the individual has verified their email they will be able to sign into the portal. Upon entering an E-Consent form will be available for participants to review. The E-Consent is written in 5th grade language. WIRB approved study staff will receive secure, automated, email notifications when a new participant signs the E-Consent using their typed signature and date. Given the low risk nature of the study, an E-Consent was deemed acceptable as the initial step in the consent process. After receiving the automated email notification, the study coordinator will call each individual that has E-Consented to confirm their eligibility. The study staff will confirm that the participant understands the risks of participation, obligations of participation and their right to revoke consent at any time. Participants will be given the opportunity to ask questions throughout the conversation and will be encouraged to discuss with family members or caregivers should they like to seek advice outside of the study team. If the participant is confirmed as eligible to participate, shows full comprehension of the study risks and obligations, and would like to continue participating in the study they will begin the pre-randomization study activities, including demographic survey, medical history survey and survey designed to collect information to gain access to their CPAP data. If, however, the individual is not deemed eligible, is unable to comprehend the study risks and

obligations or decides that they are no longer interested in participating in the O_2VERLAP study, they will be logged as a screen failure.

As mentioned above, participants will be reminded throughout that consent process that study participation is entirely voluntary and refusal to participate in the study will involve no penalty or loss of benefits to which the individual is otherwise entitled. They will also be reminded that they may choose to withdraw from the study at any time. In order to keep study documentation accurate and be able to distinguish between consent withdraws and those participants who may become lost to follow up, we will ask that participants call the study coordinator or email the study coordinator to notify them if they would like to withdraw consent or stop participating.

Participants will have access to downloadable copies of their E-Consent in the study portal. All will be encouraged to download a copy for their personal files as well as print a copy for their home health records.

Subject Capacity

Participant capacity will be assessed on the confirmation of eligibility phone call; any individuals who are unable to comprehend the study risks and obligations will be deemed ineligible to participate in the study. Given the remote nature of study participation signature of the E-Consent by a legal authorized representative is not able to be witnessed by study staff and is therefore not an option for this study.

Consent Forms

Throughout the course of this study, per regulatory guidelines, any changes made to the E-Consent language after initial WIRB approval, will be sent to WIRB for review and subsequent approval. An ongoing audit log will be kept to document subsequent WIRB approved changes to the consent form over time.

Documentation of Consent

The electronically signed E-Consent forms will be housed at the COPD Foundation's Data Coordinating Center, DatStat. All E-Consent electronic documents include the participants name, DOB and date of signature. Participants will have access to a downloadable copy of their E-Consent via their portal profile. The study team will encourage all participants to download their E-Consent and print a copy for their home health records.

Costs to the Subject

There are no expected costs associated with participation in this study.

Payment for Participation

Participants will receive compensation in the form of a $25.00 electronic gift card after they are randomized into the study. Participants will receive an additional $25.00 electronic gift card at 6-weeks and again at 12-weeks; participants may be compensated up to $75.00 total for participating in this study.

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Appendices

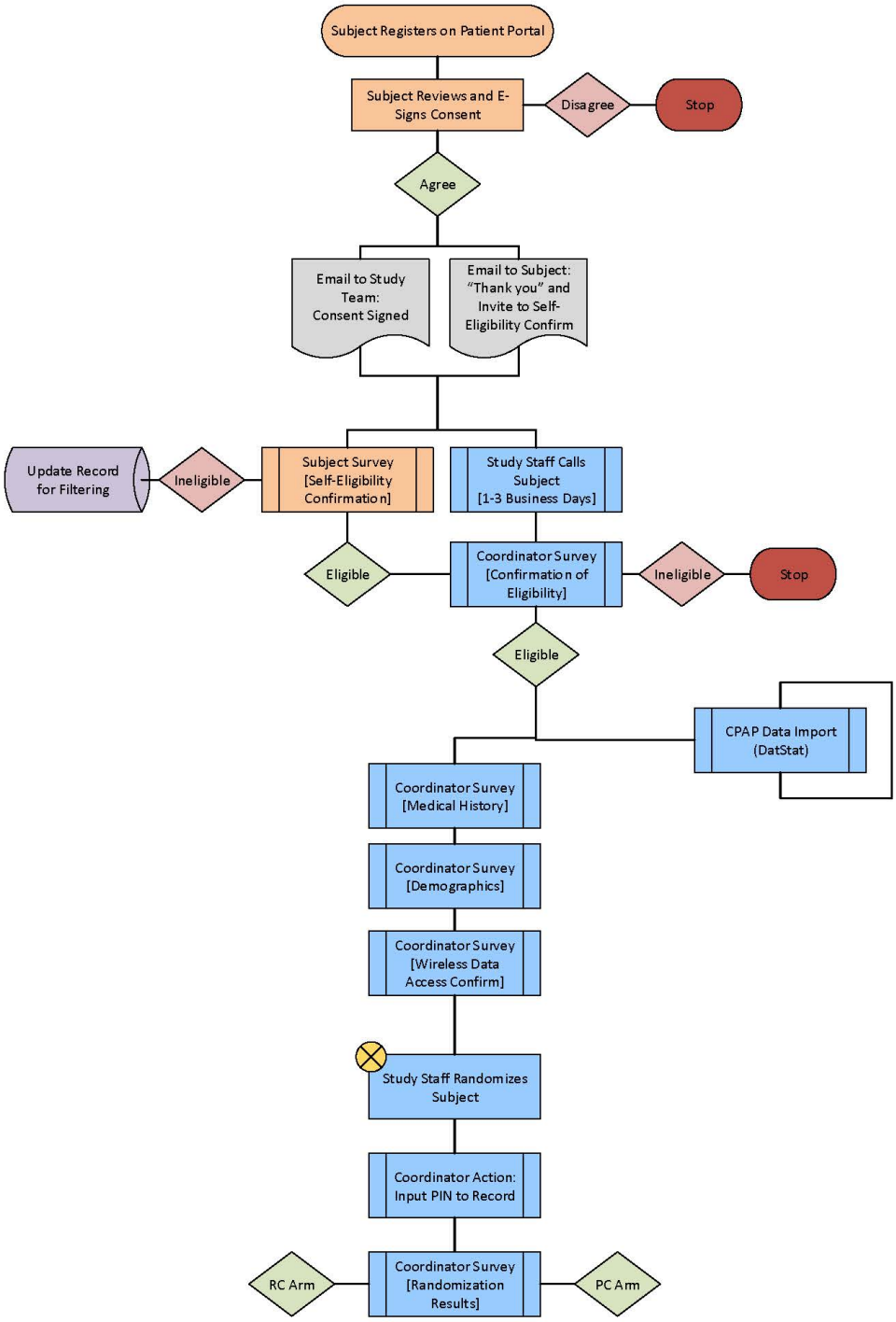
Appendix A: O_2VERLAP Enrollment and Randomization Coach Workflow

Appendix B: Oxygen Adherence Monitoring

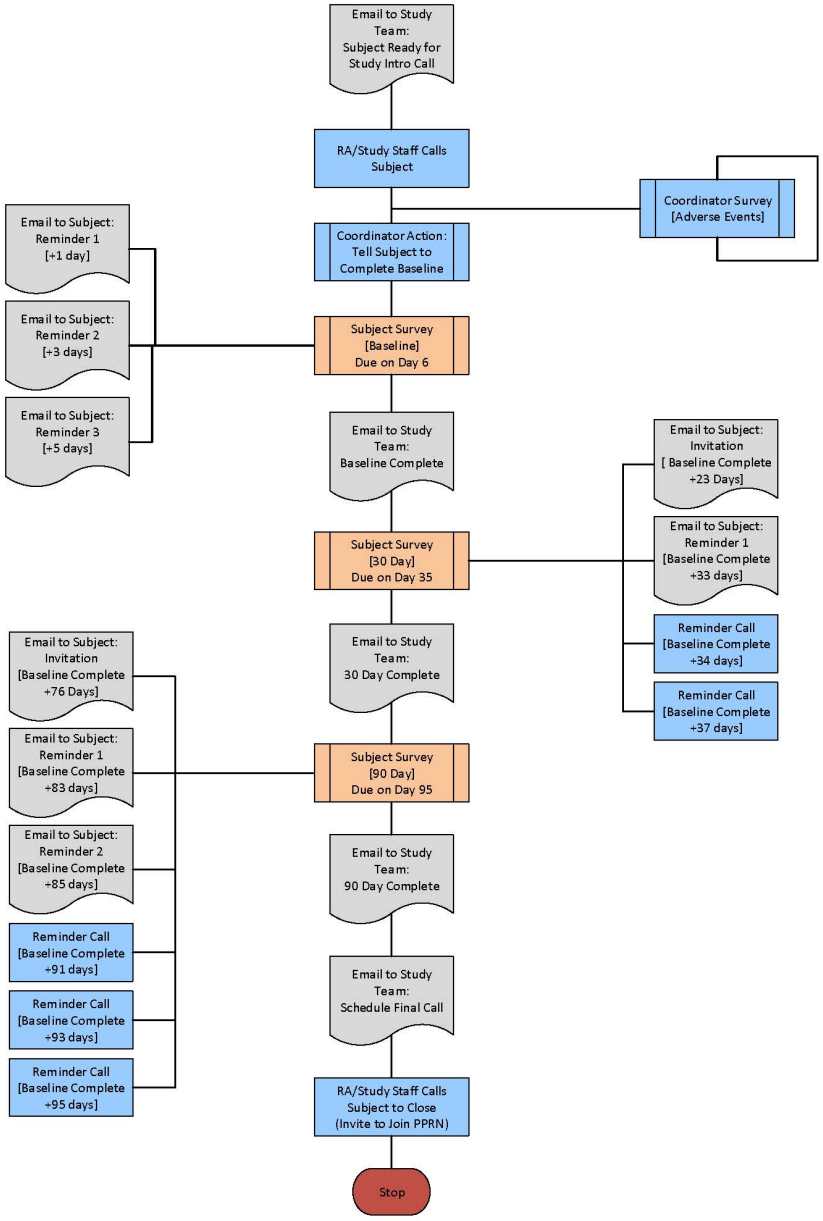
Appendix C: Respiratory Therapist Scripts and Peer Coach Scripts

Appendix D: DatStat Security and Compliance

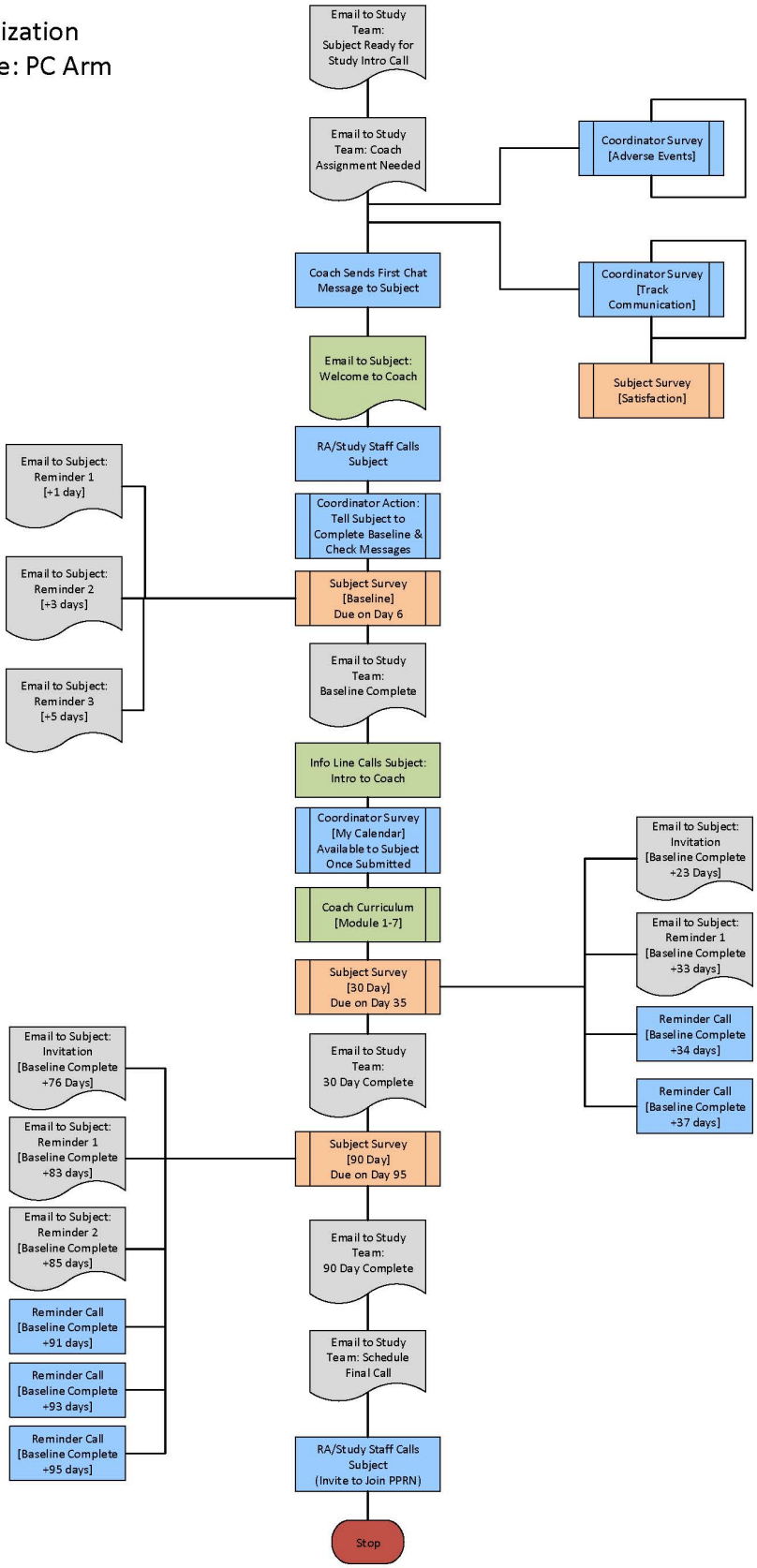
Enrollment Workflow



Randomization
Outcome: RC Arm



Randomization
Outcome: PC Arm



Appendix B: Oxygen Adherence Monitoring

This subset of the studies participants (i.e. oxygen users) will be asked to answer the following questions at Baseline. Subsequent reporting on oxygen adherence at 30-day, 60-day and 90-day follow-ups is very similar but will also require updates on changes to the ongoing oxygen prescriptions listed in the system and adding any new oxygen prescriptions.

1. **Baseline Assessment:**
    a. Oxygen Equipment (multiple-choice which allows multiple selections)
        i. stationary concentrator
        ii. portable concentrators
        iii. oxygen tanks
        iv. home fill system with tanks
        v. liquid oxygen reservoir with portable system
        vi. other [include text box with unlimited word count]
        vii. Would you like to provide any additional information or explanations relating to your oxygen equipment which were not covered? [include text box with unlimited word count]
        viii. Please indicate at what point during the day you use each of the above selected Oxygen Equipment. Please list each selected item above and give a brief description of the time of day or activity which requires use of this equipment. [include text box with unlimited word count]

    b. Additionally, for any item chosen above there should then appear a multiple-choice selection, allowing multiple selections, which asks a participant to indicate at what time of day they use this equipment.

        Example

        "Portable Concentrator" selected

        What time of day do you typically use this equipment?
        i. Morning
        ii. Afternoon
        iii. Evening
        iv. During Sleep

        What activities do you use this equipment during?
        i. I use this while sitting in place.
        ii. I use this when walking long distances only (i.e. to walk a dog, to run errands, to go to the grocery store, to enjoy an afternoon outside).
        iii. I use this when walking long or short distances (i.e. to walk a dog, to run errands, to go to the grocery store, to enjoy an afternoon outside, or to simply go to the bathroom, or while you stand to make lunch, or to go upstairs)
        iv. I use this when exercising only.
        v. I use this during sleep.

    c. [for each equipment listed above, it should have a corresponding "Oxygen prescription" survey]

"[insert relevant equipment name AND there should also be an option for "other" to report on additional equipment not classified above] Oxygen Prescription"

i. dose
ii. duration of use
iii. date of original prescription
iv. other [include text box with unlimited word count]
v. Would you like to provide any additional information or explanations relating to this oxygen prescription which were not covered? [include text box with unlimited word count]

d. Typical adherence in last 7-days (self-assessment of percentage of time they complied with oxygen prescription; this section should autopopulaate sections based on the type of equipment the participant reported using in the above question. For example, stationary concentrator should have its own section, home fill systems with tanks should have its own section)
[the response option should show Sunday-Saturday, with each having a corresponding text box that only allows numeric values that are two-digits long- this should show a total at the bottom of the page indicating the total amount of time the participant is self-reporting as using oxygen that week]

Please report your use of your [populate type of Equipment being reported based on initial Oxygen Equipment question AND provide an "other" option]. Please report your use of this equipment at rest, as well as when you are using your oxygen moving around. Please also include the number of hours this equipment is used while you are sleeping.

i. Sunday: [Answer: text box allowing only two-digit numeric values]
ii. Monday: [Answer: text box allowing only two-digit numeric values]
iii. Tuesday: [Answer: text box allowing only two-digit numeric values]
iv. Wednesday: [Answer: text box allowing only two-digit numeric values]
v. Thursday: [Answer: text box allowing only two-digit numeric values]
vi. Friday: [Answer: text box allowing only two-digit numeric values]
vii. Saturday: [Answer: text box allowing only two-digit numeric values]

TOTAL HOURS: [values should add up and be divided by 168 hours in a week, and then multiplied by 100 to give percentage] e.g. if someone reports only using all oxygen equipment for a total of 24 hours this week, we would have (24/168)*100=14.28%.

Now, please report the total number of hours you used oxygen during sleep ONLY (on average) while sleeping: [Answer: text box allowing only two-digit numeric values]

Additionally, please provide any comments or explanations of oxygen use for the week which have not yet been covered; for example, did anything prevent you from using your oxygen? Have you run into any other difficulties using your oxygen as prescribed? Did you find that your oxygen was particularly useful during a given activity? Is there anything else you would like to share about your use of oxygen this week? [include text box with unlimited word count to allow participants to provide additional insights to their adherence patterns for the week being self-reported]

2. Subsequent 30-day, 60-day and 90-day assessments:

a. The participant should be asked “Have any of your oxygen prescriptions changed since you last reported your weekly oxygen use?”
    i. “Yes, one or more of my oxygen prescriptions have changed.”
    ii. “No, my oxygen prescriptions are the same as they were when I volunteered to participate in this research.”.

If the answer is NO then the participant should be required to fill out items 1b, 1c and 1d listed above.

However, if a participant indicates “Yes..” one or more prescriptions has changed then the answer should populate based on their initial selection in item 1a. above; they should be able to select from their currently identified prescriptions.

Please indicate the type of update required:
i. I need to update this oxygen prescription.
ii. I no longer use this oxygen prescription.
iii. I would like to add a new oxygen prescription.

If they choose i. or iii, the corresponding items 1b, 1c and 1d for that prescription should appear to be updated along with all other, current, prescriptions previously reported in item 1a.

If they choose ii. the portal should show their current list of other, current, prescriptions previously reported in item 1a. They should be asked to self-report on the current oxygen prescriptions by filling out items 1b, 1c and 1d for each oxygen prescription. It should also indicate that [insert old equipment and prescription] has been removed and ask the participant to enter the date which this prescription was discontinued.

Appendix C: Respiratory Therapist Scripts and Peer Coach Scripts

Respiratory Therapist Scripts

PAP Questions:

These questions should be asked each time a Respiratory Therapist coach interacts with a participant.

After each interaction you should fill out a communications tracking form to document the conversation. When you complete your communications tracking form in the study portal, the participant will then be triggered to fill out a communication satisfaction survey; they will be asked to rate the conversation from 1-10 (i.e. 1 being not satisfied at all and 10 being completely satisfied) and will also be prompted to provide feedback. Should a participant rate any study communication less than seven, the team will be prompted to reach back out to that participant to reconcile any miscommunications or perceived inefficiencies.

"Hi, my name is _____, I am one of the Respiratory Therapists which will be acting as a Peer Coach during the study. I should first say that any advice that is given throughout the study does not replace regular visits with your healthcare providers, in fact, depending on your questions we may recommend you continue a conversation or topic with your healthcare provider so that you can receive clinical support."

"Do you have any questions about that?" [Answer questions, clarify.]

"Let's get started reviewing some of your current PAP device settings and habits. I am going to ask you some general questions about how you currently use your PAP device. There are no right or wrong answers! We want to help as much as possible. Ok, let's get started."

1) Are you wearing your PAP device?*
   1a. If so is it every night? How many hours?*
2) Do you experience leaking, skin irritation, nasal or mouth dryness, or pressure sores from your mask?
   2a. If so what do you do about it?
3) How are you cleaning and disinfecting your PAP unit and associated tubing?
4) How do you clean and disinfect?
   4a. How often is it done?
5) When was last time each of the following were replaced:
   5a. Mask
   5b. PAP tubing
   5c. Filters
   5d. If not within 6 months, why not?
6) Have you experienced daytime sleepiness even though you are using your PAP?
7) Have you been told that you still snore while wearing the PAP?

Oxygen Questions:

The following questions should be asked during every communication with a participant who is currently prescribed oxygen.

“Alright, now let’s review your current use of oxygen. Please remember there are no right or wrong answers! We are here to help.”

1) Are you wearing your oxygen with the PAP?*
   1a. If so is it every night? How many hours?*
2) How often do clean and disinfect your oxygen humidifier (if you use one)
3) How often do you change your oxygen cannula?
4) If you are not wearing your oxygen as directed by your physician, why not?
5) Have you noticed that you are experiencing any changes in your ease of breathing?*

Baseline Data review:

“Thank you! Now, let’s review your baseline data [navigate to baseline data, ensure participant is also viewing baseline data]. As you can see, we have uploaded your last 30-days of CPAP data. We have included three variables, the ‘total time connected’ each evening which reflects the total amount of time your CPAP device was worn on a given night, your ‘Apnea Hypopnea Index’ as it was recorded each evening and we also have ‘total leakage’ or the amount of air leaking from your mask each evening, recorded as well. Let’s take a closer look at each and discuss what these might mean for you and let’s set goals for improvement where we can! [review each variable individually] [set goals relating to improving total time connected]”

“I know we can reach these goals together! If you would like to speak with one of the RT Coaches you can reach us by using the chat function in the portal [navigate to chat function and instruct participant to send a message to the RT group]. Ok, now I’ll say hello back! Great. If you need to reach us you can message online at any time.”

“Do you have any questions? [Answer all questions]”

“Lastly, I just want to reiterate that we are here to help. You have no reason to feel insecure with us, we are your friends. But, if you have any clinical emergencies please always remember to seek help from your healthcare providers or call 911.”

“Now I am going to fill out a communication form to record what we have discussed today. You will also receive a communication form to fill out.”

“Thank you for your time! The next scheduled RT coach calls will be when you complete Modules 5 & 6, so we may not call you for a little while. But, remember you can use the chat function to reach us anytime! I look forward to speaking with you soon.”

Post-question Script:

“Thank you for taking the time to speak with me and share some of your current therapy habits. Now that we have discussed your currently uses of therapy, I am curious what you would like to see change? How would you like to improve your life, your therapy use? Some example would be to increase the use of your CPAP device or

Resource to disinfecting and common mark problems, as well as solutions:

http://www.aarc.org/wp-content/uploads/2014/04/pap_adherence.pdf

Peer Coach Scripts

Peer Coach Scripts

1) First Call: Portal Functions, When to call you Peer Coaches?, Journal entry, Module 1 Introductions, My Calendar
2) Voicemail
3) Check in's (i.e. changes in medications, prescriptions, travel plans, adverse events)
4) AE form
5) Outgoing call

Initial Call:

"Welcome to the O_2VERLAP Study…my name is {INSERT PEER HEALTH COACH NAME}. How are you today?"

"As a reminder, this call may be monitored and/or recorded for quality and training purposes."

"I look forward to being your peer health coach today." [insert personal statement which relates Peer Coach experiences to that of participant i.e. COPD diagnosis, appreciation for peer help, past clinical experience if any, reason for volunteering etc.]

"Would you please tell me a little bit about yourself and your motivations for joining this study?"

"The purpose of the COPD Foundation's Information Line is to provide information and referrals to educate, empower, and engage the COPD community in order to improve their lives with COPD."

"As we begin exploring the online study portal, please remember that throughout this process we are here to help you along the way. When you begin the online study courses, you will be reviewing information about COPD and obstructive sleep apnea. You may already know some of the information being presented to you, but some information may be new. Regardless of whether information is new or old, you may call a Peer Health Coach anytime Monday through Friday from 9am to 6pm Eastern to ask questions and get answers!"

"Alright, let's log into the portal and explore some of the basic functions you may use to communicate with our Peer Health Coaches."

[Assist participant login if necessary, instruct on what URL to visit, how to change password etc. , however participant should be logged in at this point already because they will have been on the phone with a CRC just before connecting to speak with a peer coach– COPDF will add troubleshooting steps here once portal is finalized]

[COPDF to add instructions on how to chat with peer Coach via portal here]

"Now, let's test it out together. Please send me a message saying 'hello' and I'll reply!"

“Great! This online chat function is another way you may communicate with a Peer Health Coach. We will not see these messages automatically, but our Team will check the portal daily and should get back to you within 24 hours. However, please remember you may also call us Monday through Friday from 9am to 6pm Eastern. The chat function is great for questions you may have if you are reviewing materials outside of business hours or if you prefer not to chat on the telephone, but we encourage you to please call in and speak with someone anytime you have a question.”

“Alright, now, let’s fill out a Journal entry together! I’ll help you get there, let me know if you have any questions [Instructions on how to navigate to Journal]. Ok, so, we hope you’ll fill this journal out as often as possible. It would be helpful for you to fill it out daily so we can check in to see how you are feeling. The Journal will always ask you for the date and time. Please fill that out [wait a moment]. Great! Now, let’s move on to the symptoms check-in, please review what the symptoms for a Green, Yellow and Red Day are… which type of day are you having? If you are having a Green Day, great! You may sometimes have a yellow or red day; on yellow days please take the actions written to the right of the yellow day, please also be sure to report this to your healthcare provider at your next visit! It’s important to let your provider know how you’re feeling, it could be the onset of a cold or an exacerbation. If you are having a Red day, please call 911 immediately. Seek help. The study team is here for peer-support, but we cannot be relied on when you need clinical help. If you are having a red day, always call 911 and seek help! ”

“Do you have any questions?” [Answer questions]

“Alright, now let’s fill out the remaining questions in the Journal. We would like you to rate your quality of life, activity level, stress, mood, sleep satisfaction, confidence leaving the home and ‘How are you breathing today?’. We ask that you rate these from one to ten, one being that you are not satisfied at all and ten means that you are completely satisfied. Ok, please fill these out. Let me know when you are done! [Pause to allow for completion.] Great! Ok, now let’s hit submit.”

“The portal is going to log all of your responses to the Journal, so you will be able to look at your progress over time! Let’s look at that now… [Navigate participant to the graphs showing their Journal history. Confirm that the participant is also viewing the Journal entry graphs.] Alright, now that you can see the results, which of these are most important to you? What do you hope to see improve over time? [goal setting]”

“Anytime we speak with you we will ask you the following four things:”

1) Have you had any adverse events since we last spoke?
2) Have you had any changes in your oxygen prescription since we last spoke? Have you had any changes in your PAP prescription since we last spoke?
3) Do you have any travel plans, even for just a short weekend road trip?
4) How are you doing today? We want to help, if we can.

“Do you have any questions about when to call a Peer Health Coach or how to get into contact with a Peer Health Coach?”

"Thank you for your time today and we encourage you to get started on your coursework at your earliest convenience."

Voicemail Script:

"Hello, this is {INSERT PEER HEALTH COACH NAME} and I'm calling from the COPD Foundation's Information Line for [first name only, of participant]. This call is regarding the O_2VERLAP study. Please feel free to contact us for more information toll-free at 866-316-2673. We are available Monday through Friday from 9am to 9pm Eastern (except holidays)."

Adverse Event, Questions to ask on each call:

1) Have you had any adverse events since we last spoke?
2) Have you had any changes in your oxygen prescription since we last spoke? Have you had any changes in your PAP prescription since we last spoke?
3) Do you have any travel plans, even for just a short weekend road trip?
4) How are you doing today? We want to help, if we can.

Outgoing Call:

"Hello, this is {INSERT PEER HEALTH COACH NAME} and I'm calling from the COPD Foundation's Information Line regarding the O_2VERLAP Study. May I speak with {INSERT PATIENT NAME}?"

"As a reminder, this call may be monitored and/or recorded for quality and training purposes."

My Calendar:

"Alright, now that we have gotten that squared away lets go to your dashboard to view your My Calendar application. Enter the date you started Module 1 Lesson 1. Once you do this you should see seven square which represent each curriculum module. The date which that Module should be completed by, or the due date, will be directly under the square. This is great to reference as you are trying to determine how to budget time for the week. We hope you will find this helpful!"

Journal:

"Alright, now, lets navigate to our journal. You will notice that the top of the screen asks you to enter the date and time, please [participants name] enter your name and date. After that point you are ready to report how well you feel on a given day as it relates to your Quality of Life, Activity Level, Stress, Mood, Sleep Satisfaction, Confidence leaving the home and How are you breathing today. Over time, your responses to these items will be logged in a graph displayed in your Insights section of the dashboard.

Do you see your entry in the insights section now? [Pause for respons….]

Excellent!

Do you have any questions?"

Appendix D: DatStat Security and Compliance

Data Transmission and Storage

Our servers, databases, and web presences employ multiple forms of security features, while our securityprotocols are designed to protect both the data itself, as well as the participants involved in data collection efforts.

Data Transmission

DatStat secure servers are registered with site certificates provided by AddTrust that provide for advanced encryption over the wire. As each user moves through the survey form, his/her responses are encrypted while in-transit between the browser and DatStat's server using SSL (Secure Sockets Layer) and40, 56, 128 or 256-bit Public Key Encryption. For those customers hosting on their own premises, we recommend using https, which requires a secure certificate.

Data Storage & At Rest Encryption

All servers used for data collection are highly fault-tolerant and equipped with redundant, hot-pluggable power supplies, redundant network interfaces, and hot-swappable RAID disk storage. All primary serversare plugged into a monitored, uninterruptible power supply (UPS). All customer web applications and servers are hosted in servers running Windows Server 2008 R2 or later.

Each customer is allocated an individual database (no comingling customer data) on our database serversto store collected data. Data is encrypted while at rest within our database infrastructure using native encryption enabled and managed within the database server.

Server Protection

Physical security

DatStat servers are stored in a locked server cabinet/rack, which are housed in a state-of-the-art, well- ventilated data center. Physical access to servers and data backup is restricted to a minimal number of ITprofessionals. The facility is secured by guards who monitor all access to the building and will notify DatStat personnel of any building compromise or intrusion.

Logical security

Servers are protected from remote attacks through use of dedicated hardware firewalls (WatchGuard), with auditing enabled at the recommended settings. WatchGuard LiveSecurity keeps IT staff advised of allknown security alerts. Firewalls closely monitor traffic to block suspicious packets from access to all systems.

Security patches are applied to DatStat servers on a timely and ongoing basis. Logs are created by the web servers to increase accountability and are essential in investigating incidents after the fact. The following are logged: failed and successful logins, attempts to access files/ directories without authority,successful and failed attempts to access sensitive data.

Data Backup

Database backups are conducted by DatStat on a daily basis. Backups are encrypted using 256-bit AES encryption and streamed over on a private network to a secure offsite location. Secure, online restorationis available at any time for all available backups from this location. Daily backups are maintained for a week, weekly backups are maintained for a month, and monthly backups are maintained for a year.

Data Access

Access to data stored on the server is available only to designated users who log in with specified usernames and passwords. Users are logged out after a period of time. A listing of the named users witha description of their access privileges is available within the applications.

Software features

DatStat provides all the necessary functionality to create fully HIPAA Compliant forms and systems. Access is tightly controlled and limited to authorized individuals using the following safeguards:

- Roles and privileges defined by data owners
- Stringent password requirements, such as minimum length, change and reuse frequency,encryption, uniqueness, and expiration.
- User names that are unique, tied to an individual, and never deleted (to prevent reuse)
- Automatic log off and lockouts, with email notification to system administrator/security staff
- Limited and controlled delete capabilities for authorized users only

DatStat products are developed and backed by a complete software engineering team, including softwarearchitects, software engineers, and support/QA engineers. Their work is guided by more than 20 standardoperating procedures and supervised by our highly experienced Chief Product Officer. Biographical information for our executive team members can be found at http://www.datstat.com/leadership and resumes for key staff are available upon request.

DatStat provides regular updates (maintenance releases and new versions) to customers as part of theirannual license fee).

Standard Operating Procedures (SOPs)

DatStat employs a variety of Standard Operating Procedures in the areas of HR, IT, Support, Consulting,and Engineering to ensure customer security and patient privacy. At all times and notwithstanding any termination or expiration of contract, DatStat will hold information in strict confidence and will not disclose PHI or other confidential information to any third party.

The following SOPs are in place at DatStat to ensure staff compliance with HIPAA regulations as well as business continuity in the event of a disaster or other emergency.

Personnel Clearance

DatStat requires all employees to pass a criminal background check and to sign the *DatStat Inc. Employment, Confidential Information, and Information Assignment Agreement*. These steps must be completed before the start of employment.

Limited DatStat staff, including your DatStat project manager and qualified technical staff, may have access to the collected data. This access is based only on your permission and is performed in accordancewith DatStat SOPs by DatStat employees who have completed proper training in the protection of PHI.

Access Control

DatStat maintains Standard Operating Procedures to ensure physical and network security. The DatStatoffice manager and IT specialist are tasked with provisioning and de-provisioning physical and network access as employees are on-boarded and separated from the organization. Standard Operating Procedures are also used to outline the processes in place to ensure data security and data integrity asrelated to federal compliance.

Privacy and Compliance

DatStat employees exhibit a core competence and sensitivity to the implementation of confidentiality andsecurity measures required to maintain the standards associated with patient and research participant data. Moreover, each full-time and part-time DatStat employee has completed the following training courses:

- *HIPAA awareness for Business Associates*, from HIPAATraning.comor *HIPAA awareness training*, from Resource Management Inc.
- *Protecting Human Research Participants*, from NIH Office of Extramural Research
- *21 CFR Part 11 training*, from Computer System Validation

Business Continuity & Incident Management

DatStat maintains Standard Operating Procedures for incident response and disaster recovery. Furthermore, all data is stored in a secure hosting facility with redundant power supplies, seismic protection, and nearly unlimited bandwidth capabilities over a cross-configured, multi-homed

network. The data center is audited annually for SSAE 16 Type II compliance, which has replaced the well-knownSAS 70 requirements.

Data Breach and Incident Response

DatStat employs hardware firewalls utilizing Watchguard Live Security to monitor for and stop intrusions,viruses, and other malicious activity, this coupled with server hardening and event logging are configured together to prevent any security incidents. In the event of an incident, DatStat IT personnel are immediately notified, an investigation begins, and customers are notified per their BAAs. Investigationsinclude a review of firewall traffic logs, server event logs, and other data points to determine the extentof the breach, if one occurred. If a breach or other incident is determined to have taken place, any affected customers are again notified per their BAA with regards to the date and time, potential data breached or lost, and other details related to the incident as well as a timeline and roadmap to restoration of service and recovery of the system.