PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

FINAL RESEARCH REPORT

Comparing Two Methods to Improve CPAP Use among Patients with COPD and Obstructive Sleep Apnea — The O_2VERLAP Study

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TABLE OF CONTENTS

ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) are 2 major chronic conditions that affect millions of Americans. When OSA and COPD coexist, they are collectively referred to as "overlap syndrome." OSA is prevalent in 10% to 15% of the 15 million patients diagnosed with COPD. Patients with both conditions are commonly prescribed medical devices for management, continuous positive airway pressure (CPAP) for OSA, and oxygen therapy for COPD. Because our early work found that most patients with OS use CPAP but a relatively low percentage of them use oxygen therapy, this study focused on improving the use of CPAP. Although CPAP is the most efficacious treatment for OSA, its use by patients is low relative to the prescription to use CPAP whenever asleep. Suboptimally treated OSA impairs next-day functioning.

Objectives: The project comprised 3 separate but related phases: (1) patient and stakeholder engagement activities; (2) focus groups to learn more from our patient community about the proposed comparative effectiveness research (CER) study; and (3) finalizing and carrying out the O_2VERLAP study, which was a large-scale, CER study examining 2 interventional approaches to improve treatment device adherence and outcomes. The main aims of this randomized controlled trial were as follows:

- *Aim 1:* To compare the effectiveness of proactive care (PC; ie, a web-based peer-coaching education and support intervention based on scheduled interactions and outreach) vs reactive care (RC; ie, education and support based on limited scheduled interactions and patient-initiated contacts) on improving adherence to CPAP therapy in patients diagnosed with both COPD and OSA.
- *Aim 2:* To compare the effectiveness of the 2 intervention groups on patient-centered outcomes, including daytime functioning, sleep quality, and daytime symptoms.

Methods: Participants were primarily recruited from 3 communities (COPD, OSA, and PCORnet) through electronic methods. They were given access to the study website to learn more and, if interested, could choose to provide e-consent and complete a self-report eligibility questionnaire. Inclusion criteria included being aged ≥40 years, having diagnoses of both COPD and OSA, and having been prescribed CPAP therapy. Participants were then randomly assigned to 1 of the 2 groups, with outcomes assessed at baseline, after an intervention period of 6 weeks, and after a follow-up at 12 weeks. Baseline CPAP adherence data were also collected for the 30-day period before randomization. The study primary outcome was CPAP adherence, defined as the amount of time that CPAP was worn each day at the prescribed pressure; the secondary outcomes were sleep quality, daytime functioning, and daytime sleepiness.

Results: The study enrolled 332 participants and randomly assigned 294. The mean (SD) CPAP adherence levels for the PC and RC groups were 6.1 (3.1) and 7.3 (2.4) hours/night (baseline), 6.3 (2.7) and 7.4 (2.2) hours/night (6 weeks), and 5.9 (3.0) and 7.2 (2.5) hours/night (12 weeks), respectively. The groups significantly differed in CPAP adherence at baseline ($P < .001$). There was no significant difference in change in CPAP adherence between the 2 study groups at either

6 weeks (difference = 0.18; 95% CI, −0.16 to 0.52; *P* = .29) or 12 weeks (difference = −0.05; 95% CI, −0.39 to 0.29; *P* = .78). There were also no significant differences in the change in patient-reported outcomes (ie, daytime functioning, sleep quality, and daytime sleepiness) at 6 weeks or 12 weeks.

Conclusions: In a group of patients with both COPD and OSA who used CPAP therapy, no difference was found between the provision of PC and RC. We found an unexpectedly high baseline CPAP adherence level, which meant that any improvement due to the intervention would have been very small and difficult to detect. The study was potentially underpowered to find a very small effect size, given the sample size. The high baseline CPAP adherence level may have been related to selection bias, due to the reliance on electronic recruitment methods (ie, email, social media, newsletters). Participants in both study groups were very satisfied with the care provided.

Limitations: The study was designed as a large, national, electronic recruitment–only study of patients diagnosed with both COPD and OSA. Because it relied on electronic recruitment, the study was limited to patients who had access to those electronic methods of outreach. Future studies of this kind would benefit from more stringent inclusion and exclusion criteria to ensure the studies are limited to patients who are having some difficulty with CPAP use or to new users.

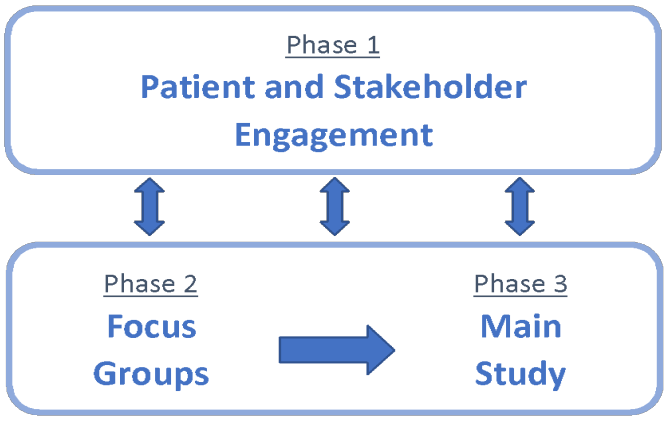
BACKGROUND

Patient-Powered Research Networks Research Demonstration Projects Within PCORnet

In the past, PCORI supported patient-powered research networks (PPRNs), which are communities of patients interested in participating in the clinical research process as part of PCORnet (National Patient-Centered Clinical Research Network: https://pcornet.org/). In 2015, PCORI launched the PPRN Research Demonstration Project initiative within PCORnet to support PPRNs in conducting comparative clinical effectiveness research on questions that are important to, and inclusive of, patients and other stakeholders. The initiative provides the foundation for the present project.

This research project comprised 3 separate but related phases: (1) patient and stakeholder engagement activities across the entirety of the project; (2) focus groups to learn more from our patient community about the proposed comparative effectiveness research (CER) study; and (3) finalizing and carrying out the O_2VERLAP study, which was an ambitious, large-scale CER study examining 2 interventional approaches to improve treatment device adherence and outcomes. Figure 1 illustrates how the phases were related to each other during the O_2VERLAP project period. Patient and stakeholder engagement (phase 1) was foundational for our project and took place from grant application through study dissemination. The focus groups (phase 2) were conducted before commencing the main study (phase 3).

Figure 1. Three Phases of the O_2VERLAP Project



Overlap Syndrome Overview

Chronic obstructive pulmonary disease (COPD) is a group of progressive and debilitating respiratory conditions that affect 15 million to 25 million Americans[1] and more than 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 department visits.[4] Obstructive sleep apnea (OSA) is a prevalent chronic medical condition characterized by repeated stops (apneas) and near stops (hypopneas) of breathing during sleep, due to collapse of the tissues in the upper airway.[5] These breathing disturbances last 10 seconds or longer and cause repeated sleep disruptions and oxygen desaturations that lead to important consequences, including daytime sleepiness and increased risk of cardiovascular problems. OSA affects 17% of adults and more than 25% of older adults,[6] with rates increasing in association with the obesity epidemic.[7] Sleep apnea aggregates in families,[8] affects all age groups, and disproportionately affects minority populations[9] and those from poor neighborhoods.[10] OSA requires immediate and ongoing therapy because it lowers blood oxygen levels, disrupts sleep, and is associated with hypertension (including pulmonary hypertension), myocardial infarction, stroke, atrial fibrillation, cor pulmonale, and early death. OSA also results in increased risk of depression, anxiety, cognitive issues, erectile dysfunction, irritability, daytime sleepiness, and motor vehicle crashes.[11-18]

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 overlap syndrome.[19] OSA is prevalent in at least 10% to 15% of patients diagnosed with COPD.[20] Although the prevalence of OSA is similar in patients with COPD as in those 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 of COPD, demonstrating the importance of OSA treatment.[21]

It is thought that overlap syndrome is clinically distinct from either condition alone and that patients with this syndrome have a worse prognosis compared with patients who have only COPD or only OSA, for several reasons that have important implications for diagnosis, treatment, and outcome.[22] Studies that have examined the efficacy of CPAP therapy for overlap syndrome have shown that CPAP use is associated with improved walking capacity[23] and longer survival in patients with COPD who are hypercapnic,[24] and that higher levels of CPAP adherence are associated with better outcomes.[21] However, of the approximately 80% of patients who initially accept CPAP therapy, most patients fall into a partial use pattern of 3 to 5 hours/night. Appendix 1 provides CPAP adherence data from studies that focused on improving adherence in new CPAP users. The overall mean adherence of the control groups of 4.0 hours/night supports the notion that CPAP is not used to the extent prescribed in the typical clinical population. The Appendix 1 table also shows that adherence levels in the United States tend to be lower than those outside the United States. 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%.[25] This evidence highlights the importance of providing the overlap syndrome patient population with the tools necessary to improve adherence to CPAP therapy.

Interventional Approaches

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.[26] In a review of web-based interventions for diabetes management, successful intervention components included goal setting, personalized coaching, interactive feedback, and online peer support.[27] A review of home telemonitoring interventions in patients with heart failure showed that the interventions helped reduce all-cause mortality and hospitalizations.[28] The literature is evolving relatively quickly. Within the field of sleep medicine, Carl Stepnowsky, PhD, has shown that both remote telemonitoring by providers[29] and an interactive web portal accessed and used by patients with OSA can improve CPAP adherence.[30] More recent evidence has shown that simply providing patients with access to their CPAP data improves adherence.[31] Patients who use CPAP have always been able to read limited summary data on their machines, but new

technologies now allow patients to view more of their CPAP adherence and efficacy data online, along with education about how to understand this information. The O_2VERLAP study's intervention was developed with this evidence in mind and therefore combined a proactive, patient-centered, peer-coaching system together with an online educational curriculum that enabled easy access to the CPAP adherence and efficacy data by both coaches and participants. The intervention was designed to address common adherence barriers using CPAP therapy, as well as adherence facilitators.

The 2 intervention groups were designed to help answer the question of whether an organization should "staff up" to provide a dedicated, multifaceted intervention and support for patients, or "staff down" and provide intervention and support only on an as-needed basis. Although the main medical decisions for CPAP therapy (eg, regarding change in pressure level or in CPAP mode) need to be made by a qualified, licensed medical professional, the interventional approach for this study was meant to be a supportive and informational adjunct to medical care provided by a licensed provider. Evidence suggests that the health care system as designed can only provide limited support for patients who are prescribed CPAP therapy, with evidence showing that CPAP adherence rates have been level for 2 decades.[32] Ideally, our intervention should be deployed within a health care system; however, an argument can be made that it could also be deployed by home medical equipment (HME) companies, patient advocacy organizations, or other similar kinds of organizations that play supportive roles for patients.

Summary

The goals of this project were to carry out a large, national CER project and to learn more about doing so within PCORnet via the PPRN Research Demonstration Project initiative. The main aims of the O_2VERLAP study were as follows:

- *Aim 1:* To compare the effectiveness of proactive care (PC; a web-based peer-coaching education and support intervention) vs reactive care (RC; ie, education and support based on limited scheduled interactions and patient-initiated contacts) on improving adherence to CPAP therapy in patients diagnosed with both COPD and OSA. The

hypothesis was that the participants in the PC group would have higher CPAP adherence levels than would those in the RC group.

- *Aim 2:* To compare the effectiveness of the 2 intervention groups on patient-centered outcomes, including daytime functioning, sleep quality, and daytime symptoms. The hypothesis was that participants in the PC group would have improved daytime functioning, improved sleep quality, and fewer daytime symptoms than those in the RC group.

As such, the study team was tasked not just with carrying out an ambitious CER project but doing so in the PCORI spirit of "doing research differently" through an extensive patient and stakeholder engagement plan (phase 1). The engagement plan started at funding application outset when the core study team went out to their communities to learn more about the interest level in this project, and the community communicated that they were very interested in this topic. From that point, a team with key patient, research, clinician, and advocacy stakeholders designed the funding application and then carried out the projects with a relatively large study team and stakeholder advisory board (SAB). In addition, we reached out to more than 40 different organizations for study promotion. This effort included significant interactions with a specific stakeholder group (HME organizations) that has traditionally not engaged with research in the past. The following section provides more information and details about project engagement activities.

PATIENT AND STAKEHOLDER ENGAGEMENT

Patient and stakeholder engagement (phase 1) was fundamental in this project and started by having a central role when the team came together to work on the original funding application. In the "Patient Engagement" section, we first describe the patient–community focus groups that were held as part of phase 2 and then provide descriptions of some specific patient engagement activities that were accomplished during the project period. The "Stakeholder Engagement" section focuses on important feedback provided by the SAB.

Patient Engagement

Patient–Community Focus Groups (Phase 2)

In phase 2, our team carried out a series of focus groups to learn more about the outcomes and interventions important to our patient community. The focus groups were designed to help inform the final plans for our main scientific study. A total of 17 participants (70% women, 30% men) were included; their mean age was 65.1 years (SD, 11.2; range, 47-84 years). Because the team was unsure which focus group method would be the most informative, we planned 3 types of groups: (1) teleconference (audio only; n = 6); (2) in-person (n = 4); and (3) web-based platform (n = 7). The 3 types of focus groups differed in delivery only: (1) teleconference was conducted via telephone; (2) in-person was conducted by a moderator in the same room with participants; and (3) the web-based platform was conducted using the COPD Foundation's COPD360Social platform both in real time and asynchronously.[33] There was a great deal of discussion and time spent deciding how to optimally run the web-based platform focus group. The team decided to first run a 2-hour synchronous group in which study team members engaged participants in real time, which was then immediately followed by 72 hours of asynchronous time. During this time period, users could return to the platform and answer questions and provide follow-up responses at their leisure. The same questions were asked of each group.

The study team found that the transcript from the telephone and web-based focus groups produced the most coded phrases (n = 40 and 32, respectively), whereas the in-person

transcript produced the fewest coded phrases (n = 16). The study team interpreted this difference as likely primarily due to the extra informal interactions that participants had in person that they were not expected to have by phone or online. In other words, participants connected more interpersonally when they were physically present with each other than when they were communicating by phone or online.

The focus groups had 2 sets of findings, 1 related to the intervention and 1 related to the planned outcome measures. In terms of the intervention, the participants were most concerned about mask fit and comfort, as a CPAP use barrier and facilitator, respectively. Other factors identified as affecting CPAP use included nasal dryness and issues concerning insurance coverage of the device. In terms of patient-centered outcomes, it was very clear that participants who experienced a disturbed night's sleep had an impaired ability to function during the following day. Some used the expression "not being able to get out of bed." Others used the phrases "not being able to do the kinds of activities that I want to do" and "not having the energy I need during the day." Many mentioned the need to take naps the following day to manage their fatigue, which cut into time available to do typical day-to-day activities. It was clear from the focus groups that the most important outcome for patients with overlap syndrome was their ability to function during the day. Because of this finding, our study team elevated the patient-reported outcome (PRO) of daytime functioning in the main scientific study. More details can be found in the focus group manuscript in Appendix 2.

Individual Patient Engagement Activities

The study included numerous opportunities for patient engagement activities given that it was funded as a PPRN Research Demonstration Project. During the process of pulling together the funding application, 2 patient advocacy organizations had patient members who were part of the team, so patients had the opportunity to provide input from as early as the project planning stages. Other key areas of patient engagement included (1) incorporating the patient perspective throughout the project and (2) paying special attention to recruitment efforts. The project's first activity was to assemble the aforementioned series of focus groups, which were designed to obtain the patient's perspective on several key study components.

Although not specifically covered in the previous section, it was in no small part patients finding patients via word of mouth that allowed the project team to successfully carry out those focus groups.

The patient stakeholders also provided support for the study's recruitment efforts. Not only did they assist with the preparation of all participant-facing materials (including emails and social media posts) to ensure they were readable and understandable, they also were instrumental in O_2VERLAP study promotion efforts:

- After completing study participation, 2 participants were asked to post on the COPD Foundation's Facebook page about their experience participating in the O_2VERLAP study and to encourage others to join. One of those participants decided to post regularly.

- Bill Clark, patient co-investigator, patient representative for the COPD Foundation, and O_2VERLAP SAB member, who moderates the COPD 360Social interactive platform, maintained close interactions with the COPD community by posting and responding to extra study promotion messages on COPD 360Social. Mr Clark also reached out to COPD Foundation state captains when needed.

- Theresa Shumard, patient advocate with the American Sleep Apnea Association (ASAA), was a member of the study team who reached out to >30 Facebook patient groups and organizations to post about the study and help spread the word about it. She then monitored each of those sites weekly to answer questions and respond to comments. Ms Shumard also reached out to online communities of patients with sleep apnea and attended several regional sleep meetings.

- Frank R. Salvatore, Jr, and Sarah Vaughn, with the American Association of Respiratory Care (AARC), and Keith Siegel, with Siegel Respiratory Consulting, Inc, are respiratory therapists (RTs) who provided the RT intervention component for the O_2VERLAP study. Mr Siegel and Mr Salvatore posted on their personal Facebook pages and directly reached out to friends and colleagues both individually and while attending professional conferences. Ms Vaughn also engaged in study outreach both directly and while attending professional conferences.

- The COPD Foundation maintains a network of patient state captains across the country. COPD Foundation study team members used this network on several occasions during this project. The state captains helped provide informal feedback on the main scientific

study, helped recruit for the focus groups and the main scientific study, and identified interested people to assist with our project webinars.

Stakeholder Engagement

SAB meetings were held every 2 to 3 months throughout the project. A total of 10 meetings were convened from October 2016 to November 2019. During each of the meetings, the study team would present SAB members with the study's progress and challenges and ask them to share ideas and additional efforts that could be implemented to overcome those challenges. At the last SAB meeting, held on November 19, 2019, the study team presented a study overview with results and preliminary data analysis, because study recruitment had recently ended. That final meeting was also used to thank all SAB members for their engagement with the project.

Stakeholder members maintained their involvement with the project over time. Our first meeting on October 31, 2016, started with 19 of our 20 members in attendance. The attendance at each meeting after that ranged from 14 to 16 members. The following sections describe several of the broader topics discussed with the SAB and how the study and its methods were improved as a result.

Study Inclusion and Exclusion Criteria

The group brainstormed ideas related to how the study team might plan for national electronic recruitment. Ideas ranged from message awareness to how to identify specific groups of patients. The group also discussed how the team might obtain a representative sample of patients with overlap syndrome. Importantly, early feedback from the SAB informed the eligibility criteria and planned focus of the study to include patients diagnosed with both medical conditions (ie, COPD and OSA) and who were prescribed and are currently using, to some extent, both oxygen therapy and CPAP therapy. Feedback, particularly from our clinician stakeholders, suggested that this would result in a limited sample of only the most ill. The recommendation was to loosen the criteria for oxygen therapy use. All stakeholders agreed this would be an important decision for the study. The study team adopted this recommendation.

Study Measures

The findings from our focus groups were presented in detail to the SAB regarding raising the importance of daytime functioning. After much discussion, the SAB members agreed to use the Patient-Reported Outcomes Measurement Information System (PROMIS) instrument, which measure health outcomes from the patient perspective and has the benefit of providing an additional non–sleep-specific measure of daytime functioning. In other words, the SAB and study team agreed that the Functional Outcomes of Sleep Questionnaire (FOSQ) was the predominant measure within the sleep field but that having an additional measure from PROMIS would benefit the study. The group decided to use the Sleep-Related Impairment scale from PROMIS. Because of the advantages that the PROMIS scales afforded, the group ultimately decided to use additional PROMIS measures for the study. More details can be found in the Methods section.

Participant Reimbursement

Participant reimbursement, from the patient perspective, was an ongoing topic of conversation in the SAB meetings before study start. In 1 of the webinars listed in Table 1, participant reimbursement was a significant component. The SAB discussed the potential levels of reimbursement for a patient's time as a study participant and compared with other similar studies. The study team and SAB members together decided on the participant reimbursement of $25 for this study, in the form of an online gift card, on completion of each of the 3 surveys, conducted at baseline, 6-week follow-up, and 12-week follow-up.

Table 1. Dates and Names of Completed O_2VERLAP Project Webinars

	Date	Webinar title	Team members involved
1	May 2, 2018	Why Should I Participate in Research?	Hugo Campos, Will Headapohl, Adam Amdur, Carl Stepnowsky, PhD
2	May 31, 2018	Including LGBTQ, Gender, Sex Minorities in Research	Mitchell Lunn, MD
3	July 29, 2018	Sharing Results of Research with Patients	John Linnell, Hugo Campos, Adam Amdur, Carl Stepnowsky, PhD
4	October 31, 2018	Peer-based Interventions in Chronic Illnesses	Carl Stepnowsky, PhD
5	November 21, 2019	O_2VERLAP study: Lessons Learned	Sergio Martinez, Elisha Malanga, Carl Stepnowsky, PhD

Abbreviation: LGBTQ, lesbian, gay, bisexual, transgender, queer or questioning.

Study Promotion Campaigns

The topic of study promotions was likely the most discussed topic across all SAB meetings. The reason for this was clear: study promotion was 1 of the study's most significant concerns. In addition, many SAB members also had access to patients who were diagnosed with 1 or both of the study's medical conditions (ie, COPD and/or OSA). So, as the study team developed the methods of study promotion, we would discuss the ideas and approaches with the SAB for feedback. Once a study promotion toolkit was finally developed for the study, SAB members were asked for assistance. Several of the most important topics the SAB provided feedback on included (1) type of messaging for study promotion and (2) recommendations concerning study promotion details, including how to work with external organizations and respect the existing communications schedules of the organizations with their communities.

Because of this critical feedback, we structured our external calls and presentations around these ideas. For example, we would first find out from an external organization how often they communicated with their community and by what methods. By finding common ground, we could then best collaboratively explore and negotiate what that organization might be able to do for study promotion. Some partners were able to go above and beyond initial expectations of what they could do, whereas other partners were unable to engage in study

promotion. We generally found that if an organization or group had experience communicating with their communities about research opportunities, they were able to help with study promotion; those external groups who had little or no experience generally found it difficult to take this next step. is HMEs were an example of this latter group. In the end, HMEs had limited communications with their communities (ie, consumers), and very few had communicated research opportunities. That said, the HMEs were all very cordial and wanted to help; in the end, however, promoting research studies did not align with their business priorities.

One additional point to make on study promotion is that 1 SAB member emphasized the potential yield the study could get by promoting it to the Veterans Health Administration (VHA), which is the largest integrated health care system in the United States, with more than 9 million patients. In addition, OSA incidence is known to be high in patients receiving care from the VHA. At the time, the study had already enrolled approximately 5 veterans. The SAB and study teams discussed this possibility at length, but the key issue was that most VHA medical centers do not allow non-VHA studies to be advertised. Dr Stepnowsky had checked with his local VHA medical center to confirm this was the case.

CPAP Data Sharing

The topic of CPAP data sharing was the second most challenging aspect of the study. The original funding application had planned to use a simple proxy measure of CPAP use, but the planned device had limitations. Once the decision was made by the study team, with SAB input, to focus on CPAP therapy, it was also decided that the study should obtain the CPAP adherence and efficacy data from the manufacturer's servers. This resulted in a significant challenge to the study. Although the machines and data may be owned by the patients, the HME companies are, in fact, the data stewards. What this meant was that our study team needed to help our participants facilitate the HME company's data sharing with the study. The SAB was critical in listening to the study team's plans and providing feedback on what might and might not work. In the end, we made several key changes to our methods to maximize our opportunity to have patient data shared with the study. This feedback and change in our methods resulted in an improvement in data sharing from 25% at the beginning of recruitment

to 93% by study end. Feedback from the SAB suggested this could be an important patient-centered topic for a “lessons learned” or “road map” (ie, instructional) type of manuscript focused on this issue. It could also be related to how to perform real-world data research, given the increase in the use of wearable devices as an example of this data-access need for research.

Webinars

The SAB provided important feedback and discussion of both the potential webinar topics and their content. The list of our 5 webinars can be found in Table 1. The webinar topics determined the primary audience of interest and all were inclusive of the patient perspective. In addition, there was much discussion about whether the webinars should be specific to the O_2VERLAP study or be made more general. Because the project was funded as a PCORI PPRN Research Demonstration Project, the study team and SAB all thought that for the webinars to have the most value on PCORnet Commons, they should be kept general. The webinars were provided to PCORI for upload to PCORnet Commons.

Summary

The inclusion of the variety and number of stakeholders was important to the success of this project. Patient stakeholders from both patient communities (ie, those with COPD and those with OSA) were included from project outset and helped establish the patient focus and orientation of the team. We took advantage of opportunities for patient involvement and feedback throughout the project, with an emphasis on patient-facing materials, recruitment efforts, and webinars. The SAB provided feedback in several important study areas, including measure selection, inclusion and exclusion criteria, and CPAP data sharing. The core study team greatly benefited from the stakeholder engagement.

METHODS

Study Overview

The O_2VERLAP study was a PPRN Research Demonstration Project within PCORnet to support the PPRNs in conducting comparative clinical effectiveness research on questions that are important to patients and other stakeholders. As such, the main scientific study of the project was informed by what we learned from the focus groups, as discussed in the Patient and Stakeholder Engagement section.

The main aims of the O_2VERLAP study were as follows:

- *Aim 1:* To compare the effectiveness of PC (web-based peer-coaching education and support intervention) vs RC (ie, education and support based on limited scheduled interactions and patient-initiated contacts) on improving adherence to CPAP therapy in patients diagnosed with both COPD and OSA.
- *Aim 2:* To compare the effectiveness of the 2 intervention groups on patient-centered outcomes, including daytime functioning, sleep quality, and daytime symptoms.

Study Setting

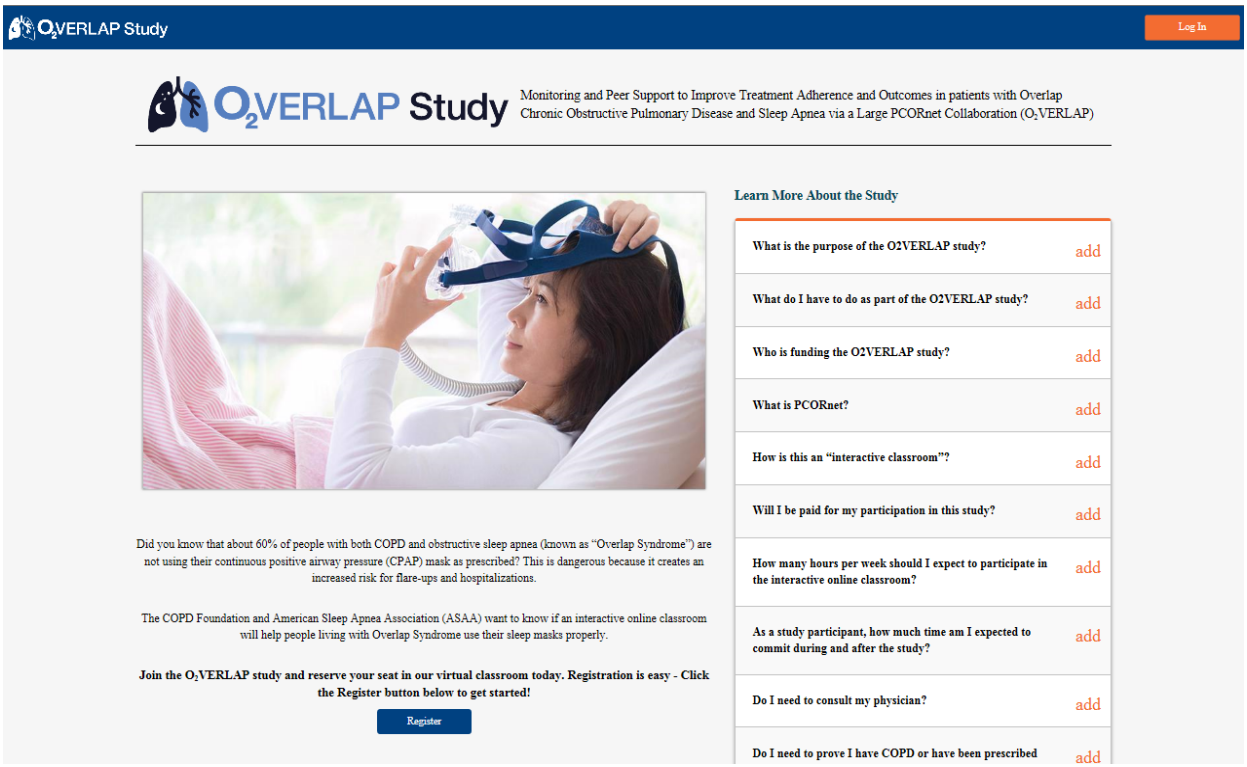
The O_2VERLAP study was designed to be national in scope and did not take place within any defined health care system. Primary study offices were located within the COPD Foundation and the University of California, San Diego (UCSD). The study was carried out via a web portal, which was hosted by DatStat, Inc (Seattle, WA). As a PPRN Research Demonstration Project initiative, an overarching goal of the project was to determine how a research study might be best carried out within PCORnet in collaboration with PCORnet partners and collaborators.

At the start of this project, the PCORI-funded PPRNs and Clinical Data Research Networks (CDRNs) were all fully operational. The PPRNs that agreed to join the COPD PPRN and be a part of this project included PRIDEnet (San Francisco, CA); PI Connect (Towson, MD); Health eHeart Alliance (San Francisco, CA); and the ABOUT Network (Tampa, FL). This project was unique in that it was 1 of the few PPRN Research Demonstration Projects that included a

CDRN (pSCANNER; principal investigator [PI]: Lucila Ohno-Machado; UCSD, La Jolla, CA), which comprised 9 large health care systems, including the 5 University of California (UC) medical centers (UCSD; UC Los Angeles [UCLA]; UC San Francisco [UCSF]; UC Irvine; and UC Davis). The PPRNs and CDRN assisted with study outreach and recruitment.

Figure 2 shows the study home page. The study's online portal was used to educate potential participants about the study design, obligations, and study inclusion criteria. Home-page content and FAQs were carefully thought out by the study team for interested potential participants to use. The study portal also housed digital e-consent and HIPAA forms, as well as the PI's and project coordinator's contact information, so participants could reach out if they had any questions or concerns.

Figure 2. Screenshot of O_2VERLAP Study Home Page



Recruitment

Overview

The O_2VERLAP study relied almost entirely on electronic recruitment methods, including emails, social media posts, electronic newsletters, website home-page banners, and interactive platforms or forums; some supplemental nonelectronic methods (ie, in-person study promotional activities) also were used, including presenting at conferences, exhibiting at health fairs, and via word of mouth. The study promotion methods used the following definitions:

- *Community*: a group of people with some defining or common characteristic
- *Audience*: a defined subgroup of community
- *Method*: a specific type of communication (eg, email, social media post)

Based on these definitions, a campaign consisted of sending a message via a defined method to a defined audience. A short way to express our approach is "campaign = audience + method." Appendix 3 provides an extensive list of the study promotional efforts and describes the community, audience, method, number of contacts, and total reach over the duration of the project, which took place from February 2018 to July 2019. Eighteen of the 46 campaigns were deployed multiple times over the 18-month recruitment period. Appendix 3 also provides more details on the recruitment campaigns, including (1) description of the 3 different message types that were used; (2) description of how a reminder email sent 3 to 5 days after the initial email was considered standard practice; and (3) additional information about Facebook and Twitter posts.

Recruitment Metrics

Each campaign comprised an audience and a method for reaching that audience. One primary recruitment metric was the size of the audience. For most campaigns, audience size was either known or could be estimated. For example, if we had a list of email addresses, then the number of individuals we emailed was a known quantity. On the other hand, newsletters or newspapers might report an estimated circulation number. Other metrics included the number

and percentage of enrolled participants. The number of enrolled participants is simply a count of the number of enrolled participants for that specific campaign. The percentage of enrolled participants refers to the number of enrolled participants divided by the audience size of that campaign.

URL Analytics

The study web vendor (DatStat, Inc, Seattle, WA) provided 2 ways for tracking participant interaction data. The first was through their URL key pairing functionality, commonly described as "referral URLs." With this tool, we generated URLs for participant recruitment that contain a specific piece of information, such as a recruiting site or campaign. When participants clicked the URL in an invitation email or manually entered the URL from a mailer or site recruitment poster, they were taken to the DatStat portal and the referring ID was stamped into their session. Participants who registered had their participant record updated automatically using the data stamped in the session, which effectively linked that participant to the recruitment campaign used.

DatStat Connect platform was also tied to Google Analytics and user flow was tracked with a Google Analytics Tracking ID. This gave more generic information on the types of sites (eg, social media, Google, direct URL) from which patients were being referred. Google Analytics is a product feature; thus, it is tied to all major site functions, such as registration, log-in events, and pagination, but it is not customizable to specific implementations. For specific recruitment details based on an individual study, the referral URL functionality was recommended by DatStat.

Participants

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: being aged ≥40 years; being able to speak and read English; having diagnoses of both COPD and OSA; having a prescription of CPAP therapy; and having access to the internet and a personal computer, tablet, or smartphone (to complete the online study activities). In addition, the CPAP device needed to have wireless connectivity

(via an internal or external modem). Exclusion criteria for the O_2VERLAP study were being a non-English speaker and having a life expectancy of ≤6 months.

Onboarding

Signing up for the O_2VERLAP study was a 2-step process: (1) registration and (2) consent. Because the consenting process was done via the study platform, hereafter it is referred to as an e-consent. The e-consent encouraged potential participants to discuss participation with their family and friends, should they want additional support. The last page of the e-consent form included a checklist for the participant to review and interactively check off. The list included confirmation that the participant understood the study design, described the low risk for participating, and confirmed that the participant comprehended and met the eligibility criteria. Those who did not sign consent were contacted by study staff via phone and email to confirm they did in fact intend to stop and not continue with consenting into the study. Recontacting this group was considered another lesson learned for the project, because during this process, we found a group of people who did want to continue to step 2 but did not because they either had technical issues moving on to the next step or were unsure of how to continue to the consent portion.

After an individual digitally signed the e-consent form, they were then prompted to take a first survey which relied on self-reported confirmation that they met the study's eligibility criteria. If an individual responded to a question in a way that indicated they did not meet the eligibility criteria, the study team was notified by email to schedule a call and confirm that the individual was truly ineligible to participate.

When an e-consent was signed, it also triggered an email to the study team to notify them and to prompt the team to reach out to the newly enrolled individual for their first study phone call with the study coordinator. The purpose of the Confirmation of Eligibility (CoE) phone call was to verbally confirm that the individual met the study's eligibility criteria. If the study coordinator confirmed that the consented individual was, in fact, eligible, the outcome was documented in the study portal through the corresponding CoE survey; the study

coordinator then proceeded to complete additional forms that provided evidence of the participant's eligibility (ie, CPAP device information, medical history survey, and demographics survey). In addition to the portal tracking all participants as they signed up, the study team also kept a study screening log (ie, a password-protected Excel spreadsheet) that captured all individuals who registered and e-consented and also documented the following scenarios: those who subsequently failed to meet inclusion criteria on the initial self-reported CoE survey, those who subsequently failed to meet inclusion criteria on the CoE phone call with the study coordinator, and all who were eligible for the study and would continue on to the next tasks.

After confirming someone's eligibility, study staff had to contact the participant's HME company to request access to the participant's CPAP data. This data sharing process involved the HME company adding the O_2VERLAP study's sleep lab to their participant's integrator and physicians list on the EncoreAnywhere (Philips Respironics data platform; Koninklijke Philips N.V.) for Philips devices or AirView (ResMed data platform; ResMed, Inc) for ResMed devices. This technique would allow a wireless flow of their CPAP data from the data platform to the O_2VERLAP study portal, which would display the participants' nightly CPAP data metrics (ie, hours used, Apnea-Hypopnea Index [AHI], and mask leak) displayed in user-friendly graphs on the portals for the coordinator and participant to view.

Potential participants who either had an older CPAP model, did not have a device from 1 of the major CPAP manufacturers, or no longer had their device were given an opportunity to obtain a machine with a newer model either on their own or through the ASAA CPAP Assistance Program. Approximately 35 individuals received a CPAP device or accessory replacements so they could participate in the study.

Interventions and Comparators or Controls

The study design was a comparison of 2 intervention groups: PC and RC. Once participants met all eligibility criteria and completed the RT introductory call, they would be assigned the next available participant identification number (PIN) from a preset randomization scheme spreadsheet that was tied to a specific randomized group assignment. This process was carefully handled only by the study coordinator and allocation was tracked in the password-

protected Excel randomization scheme spreadsheet. Simple randomization to the 2 groups was based on the use of a random number generator (https://www.rand.org/).

In both groups, participants first received their introductory phone call from their assigned research study RT (ie, not their personal RT). On this introductory call, RTs would follow a scripted questionnaire to review the participant's baseline CPAP adherence data and work with the participant to set 3 SMART (Specific, Measurable, Attainable, Relevant, and Timely) goals for improvement. The set goals were reviewed with the PC group at the end of the intervention. Once the RT introductory call was completed, the PIN was assigned from the preset randomization scheme spreadsheet, and the baseline survey would become available to the participant via the online portal. For PC group participants, the online curriculum opened next.

PC Group

PC is considered the study intervention. If an individual was randomly assigned to the PC group, their involvement included the following:

- Week 1:
  - An introductory call from an RT and a COPD Information Line coach who acted as peer coaches in health topics covered in the curriculum
  - Access to module 1 of the online curriculum
- Weeks 2 to 4:
  - Weekly dyadic peer coaching calls by COPD Information- Line coaches
  - Access to modules 2 through 6 of the online educational curriculum, covering topics on COPD, OSA, and overlap syndrome
- Week 5:
  - Access to module 7, the final module in the curriculum
  - COPD Information Line coach call and RT follow-up call on completion of module 7

Participants in the PC group also had online access to their CPAP adherence monitoring data to track their progress as they advanced through the study program, as well as access to a chat function in the portal to ask questions or contact the study team throughout the intervention period.

RC Group

The RC group of the study was given access to an RT who would make an introductory call during week 1. Participants in the RC group were given the phone number of the COPD Information Line that they could contact to seek advice about any aspect of CPAP therapy or information about general health topics related to overlap syndrome. The RC group participants also had online access to their CPAP adherence monitoring data. They had access to general informational COPD and OSA materials via the website. The primary characteristic of the RC group was that they had access to the same educational materials as the PC group but were not required to go through them; they were also provided with the contact information for support. When the team was pulling the grant proposal together, the perspective was that of a patient advocacy nonprofit organization providing this education and support outside of the care system in an adjunctive way. From that perspective, the patient advocacy team was proactive in providing education and support, and any study participants would be reactive if they took the initiative to seek this information and support.

Online Curriculum

A previous online COPD educational curriculum was used as the model for the O_2VERLAP educational curriculum. The study team met to develop the specific outline. Two sleep education specialists were identified by the ASAA to write the content under the supervision of Dr Stepnowsky, who has developed several OSA- and CPAP-specific curricula for previous CPAP adherence studies. Table 2 provides the module titles and the lessons, divided by chapters, that make up each module. There was a total of 22 chapters, 1 of which was an introduction. Of the 21 topical chapters, 11 were focused on OSA/CPAP, 7 on COPD/oxygen, and 3 on both content areas.

Table 2. Content of the Online Educational Curriculum

Module	Title	Chapter	Topic
1	Introductions	1	Meet the Team
2	Fundamentals of COPD	1 2 3	Some Basic Health Care Info After Your Diagnosis Lung Pathology Exercise Limitations
3	A Review of Sleep Apnea and CPAP	1 2 3	Understanding Sleep Apnea Consequences of Sleep Apnea What Is Positive Airway Pressure?
4	Review of Your CPAP Equipment	1 2 3	Concerns About Wearing CPAP Solutions to Problems When Using CPAP Concerns About Wearing CPAP
5	Supply Chain Logistics	1 2 3 4 5	Supply Chain Logistics Cleaning Equipment Maintenance of Equipment Traveling with CPAP Feelings About CPAP
6	Oxygen Therapy	1 2 3 4	Why You Need Oxygen Testing for Low Oxygen Levels Types of Oxygen Systems Oxygen Delivery Devices
7	Using Oxygen with CPAP	1 2 3	Supplemental Oxygen Used with CPAP Aspects of Overlapping CPAP and Oxygen Therapies Practical Applications: Combines CPAP and Oxygen Therapies

Abbreviations: COPD, chronic obstructive pulmonary disease; CPAP, continuous positive airway pressure.

Modules Completed

Of the 153 participants randomly assigned to the PC group, 120 (78%) completed all 7 modules in the online curriculum. Participants needed to complete all of the pages and activities in a chapter before advancing to the next chapter. Similarly, participants needed to complete all of the chapters within a module before advancing to the next module. There were 33 (22%) participants who did not complete all 7 modules. The following number of participants completed each number of modules: 6 modules (n = 3); 5 modules (n = 2); 4 modules (n = 2); 3 modules (n = 11); 2 modules (n = 8); 1 module (n = 2); and 0 modules (n = 4). One participant who withdrew after randomization never started the curriculum.

Coach Contact

RT contact. Both PC and RC group participants received the same scripted RT introductory coach call before randomization. Of the 153 participants, 151 (99%) who were randomly assigned to the PC group and 134 of the 141 (95%) who were randomly assigned to the RC group received the RT introductory coach call. Some participants did not receive the RT introductory call because, in the first few weeks of the study, our process was to randomly assign participants first and then complete the RT introductory coach call; as a result, 9 participants (n = 2 in the PC group; n = 7 in the RC group) advanced too far along into the intervention before training of the RT coaches was completed. The study team decided to change the workflow to complete the RT introductory coach call before randomization to prevent this from occurring again. A second scheduled RT call was made only to PC group participants on completion of the online curriculum.

COPD Information Line coach contact. Only participants who were randomly assigned to the PC group of the intervention and completed the baseline assessment received their first COPD Information Line coach phone call. Four other consecutive weekly calls were scheduled with the participant and the COPD Information Line coach, totaling 5 calls. There were no scheduled calls for the RC group, but the participants were given the contact details to reach out to the Information Line coaches for support, which represented the “reactive” component of the RC intervention. Table 3 provides descriptive data on the number of calls made by the RTs and COPD Information Line coaches by group.

Table 3. Number of Information Line Coach and RT Coach Calls by Group

Coach calls	PC	RC	Total
Total	830	138	938
No. per participant, mean (SD; range)	5.5 (2.1; 1-11)	1.0 (0.2; 1-2)	3.4 (2.7; 1-11)

Abbreviations: PC, proactive care; RC, reactive care; RT, respiratory therapist.

Study Outcomes

The primary study outcome was CPAP adherence, which was objectively measured by the CPAP device, with data sent wirelessly to the study team. All participants were assigned a baseline survey package. Together the surveys measure several important patient-centered outcomes, including daytime sleepiness, daytime functioning, and COPD functioning. Based on our focus group findings, consultation with the SAB, and discussions with the study team, the patient-reported study outcomes included (1) daytime functioning (as measured by the FOSQ and the PROMIS Sleep-Related Impairment scale); (2) sleep quality (as measured by the Pittsburgh Sleep Quality Inventory [PSQI] and the PROMIS Sleep Disturbance tool); and (3) symptoms (as measured by the COPD Assessment Test [CAT], Epworth Sleepiness Scale [ESS], and PSQI Daytime Dysfunction subscale).

CPAP Adherence

CPAP adherence was operationally defined as the number of hours that CPAP was used at the prescribed pressure per day (ie, over a defined 24-hour period). The sources of CPAP data were the CPAP manufacturer websites (AirView and EncoreAnywhere). Because these 2 manufacturers represent approximately 85% of the CPAP marketplace in the United States, only participants with 1 of these CPAP devices were included in the study. In addition, the study included 2 measures of CPAP efficacy: mask leak, which was defined as the amount of air that escaped (liters per minute) and the AHI, which is a measure of the number of apneas and hypopneas per hour of CPAP use. These metrics were available to the participants via the portal, and the coaches used these metrics to provide feedback on how well CPAP was working to control OSA. Suggestions to improve CPAP use were based on these metrics. For example, if mask leak was moderate to high, suggestions to improve the mask fit were discussed. These 2

metrics were intended for interventional purposes, but there were no plans to analyze them, given that CPAP adherence was the study's primary outcome.

Measures of Daytime Functioning

Functional Outcomes of Sleep Questionnaire. In our qualitative work with the community of patients with overlap syndrome, we discovered that the most important outcome to patients is daytime functioning. The FOSQ measures impact of sleepiness on activities of daily living (ADLs).[34,35] The FOSQ-10 consists of 10 questions on a scale of 1 to 4 (1 = extreme difficulty, 4 = no difficulty). A lower score indicates more difficulty with ADLs due to lack of sleep. The FOSQ total score is the mean of subscale scores (ie, vigilance, productivity, social outcome, intimacy, activity) multiplied by 5. The scores range from 5 (maximum difficulty) to 20 (no difficulty). Change in FOSQ total score is calculated from baseline to end point, with higher (positive) values representing improvement. The worst possible change value would be −15 and the best would be +15.

PROMIS survey. Clinical measures are important but may not reflect the day-to-day functioning and well-being of patients with chronic diseases. The PROMIS initiative of the National Institutes of Health was developed to advance the methodology and application of PROs among patients with chronic diseases for use in research and clinical practice.[36,37] The study used 2 related PROMIS 8-item sleep scales (sleep-related impairment and sleep disturbance), as well as the following additional PROMIS measures: global health (2-item measure); physical functioning (4-item measure); ability to participate in social roles and activities (4-item measure); anxiety (4-item measure); depression (4-item measure); pain interference and intensity (4-item measure); and cognitive functioning (4-item measure). All PROMIS measures are scored in the following way: (1) sum the total (follow instructions for a prorated score if any items are missing for a measure) and (2) translate the total score (or prorated score) to a T-score per PROMIS instructions. A T-score is a standardized score with a mean of 50 and SD of 10. PROMIS scores are interpreted with higher scores representing more of the concept being measured.

Pittsburgh Sleep Quality Index. The PSQI is a self-rated, 19-item questionnaire used to assess sleep quality and disturbances over the previous 1 month.[38] The PSQI measures 7 areas of sleep: (1) subjective sleep quality, (2) sleep latency, (3) sleep duration, (4) habitual sleep efficiency, (5) sleep disturbances, (6) use of sleep medication, and (7) daytime dysfunction. Items are scored on a Likert scale, with 0 being indicative of better sleep and the maximum value of 3 being indicative of poor sleep. PSQI scores can range from 0 to 21, with higher scores indicating worse sleep quality. The PSQI total score was used in our study unless otherwise specified.

COPD Assessment Test. The CAT is a simple, 8-item health status instrument for patients with COPD, which is highly practical,[39] has good psychometric properties, and has been shown to be responsive to pulmonary rehabilitation and recovery from exacerbation.[40-43] CAT scores range from 0 to 40, with higher scores representing a more severe impact of COPD on a patient's life. The minimally important clinical difference score has been shown to be 2 points.[44,45] The CAT includes a sleep item and an energy item, which is relevant to those patients with overlap syndrome.

Epworth Sleepiness Scale. The ESS is an 8-item validated measure of daytime sleepiness and is the most widely used subjective measure of excessive daytime sleepiness in research and clinical settings.[46,47] The questions on the ESS ask respondents to estimate how likely they are to doze in a variety of different situations, with 0 meaning they would never doze and 3 meaning they would have a high chance of dozing. The range of ESS scores is 0 to 24, with higher scores indicating a higher level of sleepiness. The ESS can be used to discriminate the sleepiness level of patients with OSA from that of healthy controls.[48]

Functional Comorbidity Index. The Functional Comorbidity Index (FCI) is a validated measure of comorbidity with functional level as the outcome of interest.[49] The FCI is composed of a list of 18 comorbid medical conditions that the study respondents self-reported having or not having. The conditions are simply summed, such that a higher number represents higher comorbidity.

Other Measures

Demographics

The sociodemographic information we collected included age, sex, race, ethnicity, sexual orientation, and income. Additional participant characteristics included smoking status, geographic location, years since diagnosis, and comorbidities.

Oxygen Therapy Adherence

Oxygen therapy adherence was assessed by self-report. Several items asked about whether oxygen therapy was administered, as well as type and timing of oxygen therapy.

Satisfaction

Participant satisfaction was assessed by self-report for each communication with the study staff (coach, RT, other), by method (phone or online). Participants were asked to provide a rating based on a scale of 1 (dissatisfied) to 10 (satisfied).

Sample Size Calculations and Power

The power analysis was based on the primary hypothesis that CPAP adherence (ie, the number of hours that CPAP was used in a 24-hour period) would be improved in the PC group in the first 6 weeks compared with the RC group. A sensitivity analysis was conducted by considering a range of sample sizes from 100 to 180 participants per group. Assuming a 2-sided type I error of α =.05, we could detect a standardized effect size (for the difference in CPAP adherence between the PC and RC groups) ranging from 0.296 to 0.398 with 80% power. These calculations indicate we would have sufficient power to detect a small to medium standardized effect size (0.325) in adherence between the PC and RC groups if enrolling 150 participants per group. By definition, standardized effect sizes are unitless and their advantage is that the size of the effect can be compared across studies.

Time Frame of Study

Study recruitment started in January 2018 and ended in July 2019. Data collection occurred at baseline, 6 weeks, and 12 weeks.

Data Collection and Sources

Questionnaires/Surveys

The study team collected all questionnaire/survey data electronically or by phone, using the study's Coordinator and Participant portals. Both portals contained questionnaires for all users to complete that would become available according to a previously established time-sensitive workflow that started with a Self-Report Eligibility questionnaire, completed by the participant in the Participant portal after signing consent. Completion of the Self-Report Eligibility questionnaire would then trigger a consequent form for the coordinator to complete in the Coordinator portal (eg, the CoE questionnaire, Demographics, Medical History).

The randomly assigned participants then completed 3 main questionnaires that were available to them via the Participant portal. Those time-sensitive questionnaires were the baseline, 6-week follow-up, and 12-week follow-up surveys. Each time point had a 2-week window during which the questionnaire was available online to the participant. Participants were offered an incentive of a $25 online gift card that was emailed to them on completion of each survey. Reminder phone calls were made and email reminders sent to those participants who had a survey due, to inform them of the approaching follow-up window due date. Any surveys that were not completed by their due date were considered missing.

CPAP Data

CPAP data were included in the study in 2 ways. First, a data workflow integration was established such that data calls were made 2 times each week (on Monday and Wednesday) to populate the O_2VERLAP study portal. These data were used by both participants and interventionists to monitor progress and intervene as necessary. An intermediary, Corepoint Health (Frisco, TX), was contracted to provide data integration services and provide middleware

between the CPAP manufacturer servers and the O_2VERLAP study portal. More than 90% of the data were transmitted successfully. Second, to use a comprehensive and accurate CPAP adherence and efficacy data set, our research team engaged in a double check of every CPAP data point in our data set to be sure it was consistent with the data at the source, namely, the manufacturer's servers. Given the unexpected and novel findings of the very high CPAP use levels found in this study, we are confident in our conclusions because of our extensive CPAP data quality-assurance efforts. See Appendix 4 for more details.

Analytical and Statistical Approaches

Overarching Approach to Analyses

Preliminary analyses began by examining the distribution of study variables and providing descriptive statistics (ie, mean, median, SD, quartiles for continuous variable, frequency, and percentage for categorical variables) about the study population. Patient characteristics were compared between study groups by Wilcoxon rank-sum tests (or Fisher exact tests, as appropriate). Variables on which the groups differ initially were explored as covariates in subsequent analyses. The primary analyses were intent to treat (including all enrolled participants), and all analyses were performed using 2-sided tests with $\alpha = .05$. Mean differences and 95% CIs were reported with the *P* values. Summary metrics were reported by mean (SD), unless otherwise specified. Analyses were conducted using R statistical software.[50] Analysis plans that addressed each hypothesis are described in the following sections.

Analyses for Study Primary Aim

We hypothesized that CPAP adherence at the 6-week time point would be improved in the PC group compared with the RC group. A random-effects model was used to compare the mean CPAP adherence over 6 weeks between the PC and RC groups. Daily CPAP adherence data were used for analysis. A random intercept was included in the model to account for the correlation between repeated measures of CPAP adherence over each assessment period as well as the correlation among 3 assessment periods (baseline, week 6 during the intervention, and 6 weeks after the intervention [week 12]) within each patient. A multivariable random-

effects model was used to assess the difference in CPAP adherence between the PC and RC groups, with adjustment for potential covariates. Adjustments were made to correct for baseline imbalances across study groups and to adjust for variables known to influence the outcome. Baseline demographics and other clinically important characteristics were assessed for imbalance among the study groups, using Wilcoxon rank-sum test, chi-square, or Fisher exact test, and their association with the outcome was assessed using a simple random-effects model. These variables were included as covariates in the multivariable model if found to be moderately associated with the outcome or unbalanced ($P < .15$) across groups. All covariates significant at $P < .10$ were kept in the final model.

Analyses for Study Secondary Aims

We hypothesized that improvement in patient-centered outcomes at 6 weeks and 12 weeks would be larger in the PC group than in the RC group. The change in patient-centered outcomes from baseline to week 6 and week 12 was compared between the PC and RC groups. The difference in change of each outcome was assessed using analysis of covariance (ANCOVA), with intervention group as a main effect and baseline score as a covariate. A linear random-effects model was fit to assess the change from baseline to week 6 and the change from baseline to week 12 by considering the correlation of measurements (at baseline, week 6, and week 12) within each participant. A multivariable linear random-effects model was used to assess the difference in change scores between groups, with adjustment for baseline characteristics using approaches similar to those described for the primary aim.

The PRO measurements are divided into 3 categories: daytime functioning, sleep quality, and daytime symptoms. Daytime functioning was deemed the most important PRO per our focus groups. Daytime functioning was measured by the FOSQ. Sleep quality was measured by the PSQI. Daytime symptoms were measured by the ESS.

Exploratory Analyses

We conducted additional exploratory analyses that were unanticipated at study outset: examination of CPAP data use levels. CPAP adherence data, measured in duration of use per

night, is most meaningful when compared relative to total sleep time (TST) and/or total sleep period (TSP). Because we did not have an objective measure of TST in this study, we opted to use TSP from the PSQI. Descriptive statistics and Pearson correlation coefficient were used.

Addressing Heterogeneity of Treatment Effects

To evaluate the heterogeneity of treatment effects, we assessed the interaction between treatment group and several baseline patient characteristics including age, sex, education, and socioeconomic status. If an interaction was significant, the treatment effect was estimated separately for each study subgroup.

Handling of Missing Data

We included all available data for the analyses using a random-effects model. The mixed-effects method allows the inclusion of participants with missing data or those who were terminated early in the study, without relying on data imputation procedures. We also performed ANCOVA, which only included participants with complete data to compare the change score with adjustment for baseline score. Because the results from the random-effects model and ANCOVA were consistent, we only provide results of the former.

Changes to the Original Study Protocol

There were 4 key changes to the original study protocol: (1) medical device adherence (ie, oxygen therapy), (2) focus on CPAP adherence, (3) measure selection, and (4) study time frame.

Adherence to 2 Medical Devices (Original Plan)

In the original study protocol, we planned to study adherence to the 2 medical interventions that are prescribed for patients with both COPD and OSA: oxygen therapy and CPAP, respectively. It became clear during our qualitative focus-group work that less than half of patients with overlap syndrome used oxygen therapy at night, whereas all of them reported using CPAP therapy. Because of this observation, we changed the study protocol to primarily

focus on the use of CPAP therapy, with a limited focus on oxygen therapy, given the relatively low base rates of its use found in this specific patient group.

Adherence to CPAP Device (Revised Plan)

The original study protocol acknowledged the potential difficulty of enrolling patients with OSA using CPAP therapy and being able to obtain their CPAP data. When a study takes place within a single health care system, typically the patients with OSA in that health care system only use a few HME provider companies. Even though most CPAP devices are owned by the patient, the HME companies are considered the CPAP data stewards, those who play an oversight or data governance role. Practically, this means that for us to obtain access to the CPAP data for our study, we needed the permission of both the patient and the HME company. Because the study was designed as a national study that was enrolling existing CPAP users, we could not limit the potential number of HME companies with whom we would have to work to obtain the CPAP data.

For this reason, the original study protocol was designed to use an innovative device (Evermind, Nashville, TN) designed to obtain a proxy measure of CPAP use. This small device plugs into the wall, and the power cord of the CPAP device plugs into it. The measurement concept was simple: whenever the CPAP blower drew electrical power, the device would measure the power surge. When power was being used, so was the CPAP. In this way, we could easily obtain a proxy measure of CPAP use for any CPAP make or model, regardless of age or interconnectivity of device.

However, once the study became solely focused on CPAP adherence, the study team decided, based on feedback from our patient community, that the project should use the most rigorous CPAP data (ie, the data obtained by the CPAP device itself), which were sent to the manufacturers' servers and made available to the research team. The study team decided to use the most commonly used CPAP devices (ResMed and Philips Respironics). More details on CPAP data sharing methods are provided in the Discussion section.

Measure Selection

The qualitative focus groups were instrumental in helping the study team finalize its measure selection. The focus groups determined that by far the most important outcome to patients was daytime functioning. Originally, daytime functioning was considered a tertiary outcome, but its importance was elevated to the most important secondary measure (CPAP adherence remained the primary outcome) because of this important work in listening to the patient community.

Study Time Frame

The only change that was made to the original milestones was a 2-month, no-cost extension request in May 2019 to give us more time to recruit and reach our 100% recruitment milestone. For the project to meet our original date of May 31, 2019, for the 100% recruitment milestone, the study needed to have each of our planned campaigns perform well. Although we were close to meeting our milestone, in the end several campaigns either did not do as well as they had in the past (eg, social media posts on Facebook); were unable to be implemented (namely, PRIDEnet; Health eHeart Alliance; and 2 UC pSCANNER sites: UCLA and UCSF); or resulted in fewer-than-expected patients with COPD and OSA (UC Irvine). The no-cost extension allowed the main research period to be changed from May 31 to July 31, 2019, and consequently pushed back each subsequent milestone by 2 months.

RESULTS

Recruitment Campaign Results

An O_2VERLAP study campaign was defined as sending a message via a defined method to a defined audience. Table 4 shows the 4 primary communities used in this study; the recruitment method type for each; the actual or estimated size of each audience; and the total number and percentage of participants who were enrolled in the study from each community and audience.

Table 4. O_2VERLAP Study Campaigns: Number and Percentage of Participants Enrolled by Campaign

Community (No. [%])	Campaign		Audience size[a]	No. enrolled	Enrolled, %
	Audience	Method			
COPD (162 [49])	COPD PPRN emails	Emails	858	60	6.99
	COPD Foundation Facebook	Social media	199 519	28	0.01
	Alpha-1 Registry	Emails and letters	5161	27	0.52
	COPD *PPRN Newsletter*	e-Newsletter	6700	20	0.30
	PELICAN Study	Email and phone call	158	8	5.06
	Faces of COPD Newsletter	e-Newsletter	40 000	9	0.02
	O_2VERLAP survey	Phone call	47	7	14.89
	COPD Foundation homepage banner	Website landing page	147 000	2	0.00
	State captains	Word of mouth	120	1	0.83
OSA (66 [20])	ASAA emails	Emails and e-newsletter	21 169	32	0.15
	ASAA newsletter				
	ASAA Facebook	Social media	93 070	25	0.03
	ASAA website homepage	Website landing page	118 838	5	0.00
	SleepHealth Mobile emails	Emails	9409	4	0.04
PCORnet (58 [17])	pSCANNER (UCSD Health)	Emails and letters	24 008	54	0.22
	pSCANNER (UCI Health)	Emails	284	1	0.35
	PRIDEnet	Emails	506	3	0.59
	Health eHeart	Social media	5349	0	0.00
	PI Connect	Emails and social media	180	0	0.00
Miscellaneous (46 [14])	Web browsing and word of mouth	Web browsing and word of mouth	—	25	—
	ResearchMatch	Emails	1062	11	1.04
	The Pulmonary Paper	Hardcopy newspaper	35 000	3	0.01
	Friends 4 friends	Social media	886	2	0.23
	11 private Facebook groups	Social media	30 441	3	0.01
	AARC	Social media and flyers	61 248	2	0.00

Abbreviations: —, missing data due to difficulty of measuring accurately; AARC, American Association of Respiratory Care; ASAA, American Sleep Apnea Association; COPD, chronic obstructive pulmonary disease; PELICAN, Peer-Led O_2 InfoLine for Patients and Caregivers; PPRN, patient-powered research network; pSCANNER, Patient-Centered Scalable National Network for Effectiveness Research; UCI, University of California, Irvine; UCSD, University of California, San Diego.

[a]Audience size may be a count or an estimate.

The only audience for which we could not determine a total size was the "Web browsing and word of mouth" audience, because it was difficult to measure accurately. At study outset, we knew that we needed to carefully track the yield of our campaigns because our project was staffed to accommodate approximately 20 to 30 new participants per month in combination with the current participants who needed to be followed each month as well. This meant that our campaigns needed to meet a range of new participants each month, without going too far above or below the required number. The more we understood the projected yield of a campaign, the better we could plan for which type of campaign and when it should begin. So, for each campaign that allowed it, we counted the number of individuals for each campaign method. For the word-of-mouth and web-browsing audiences, we could not accurately keep track of how many people engaged in each. For this reason, audience size is missing for these 2 campaign types.

Table 5 provides a summary of the study home-page web analytics results that were a function of the study campaigns. Table 5 is a summary of the full table in Appendix 5. It also provides a summary of the analytics by community. The term "sessions" here is defined as a period during which a user is actively engaged or viewing the website or post. Note the highest number of sessions for the COPD and OSA communities occurred with 2 campaigns that were based on "boosted" posts (ie, paying for additional posts). The 2035 sessions resulting from the highest-yielding COPD campaign were more than double that of the next highest-yielding COPD campaign. Likewise, the 13 193 sessions resulting from the highest-yielding OSA campaign were >13 times more than the next highest-yielding OSA campaign. Appendix 5 lists the number of trackable URLs that were assigned to each campaign. This number is nearly equivalent to the number of times that a campaign was promoted. We point this out because the number of sessions appears to be primarily a function of the size of the community and the number of times a campaign was promoted. We believe an additional factor may have come into play, namely, that the campaign text and images (eg, see Figure 2) primarily emphasized sleep apnea and CPAP, which would have appealed to the OSA community more than to the other communities.

Table 5. O_2VERLAP Study Home-Page Web Analytics[a]

Community	No. of sessions[b]	Pages/session[c]	Average session duration, s[d]
COPD	148.9 (405.1; 2-2035)	3.3 (2.0; 1.0-8.8)	353.73 (254.5; 0-868.8)
OSA	812.2 (3007.4; 1-13 193)	1.4 (0.4; 1-2.3)	88.46 (82.9; 0-245)
PCORnet	95.8 (182; 1-669)	1.8 (0.6; 1-2.9)	173 (184.8; 0-613.5)
Miscellaneous	17.2 (22.4; 1-56)	1.7 (0.8; 1-3.5)	227.7 (495.1; 8.5-1627)
Total	270.8 (1499.2; 1-13 193)	2.3 (1.5; 1-8.8)	237.2 (285.3; 0-1627)

Abbreviations: COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnea; PCORnet, National Patient-Centered Clinical Research Network.

[a]Data are reported as mean (SD; range).

[b]Total number of sessions within the date range. A session is the time a user is actively engaged with a website, app, etc. All usage data (eg, screen views, events, e-commerce) are associated with a session.

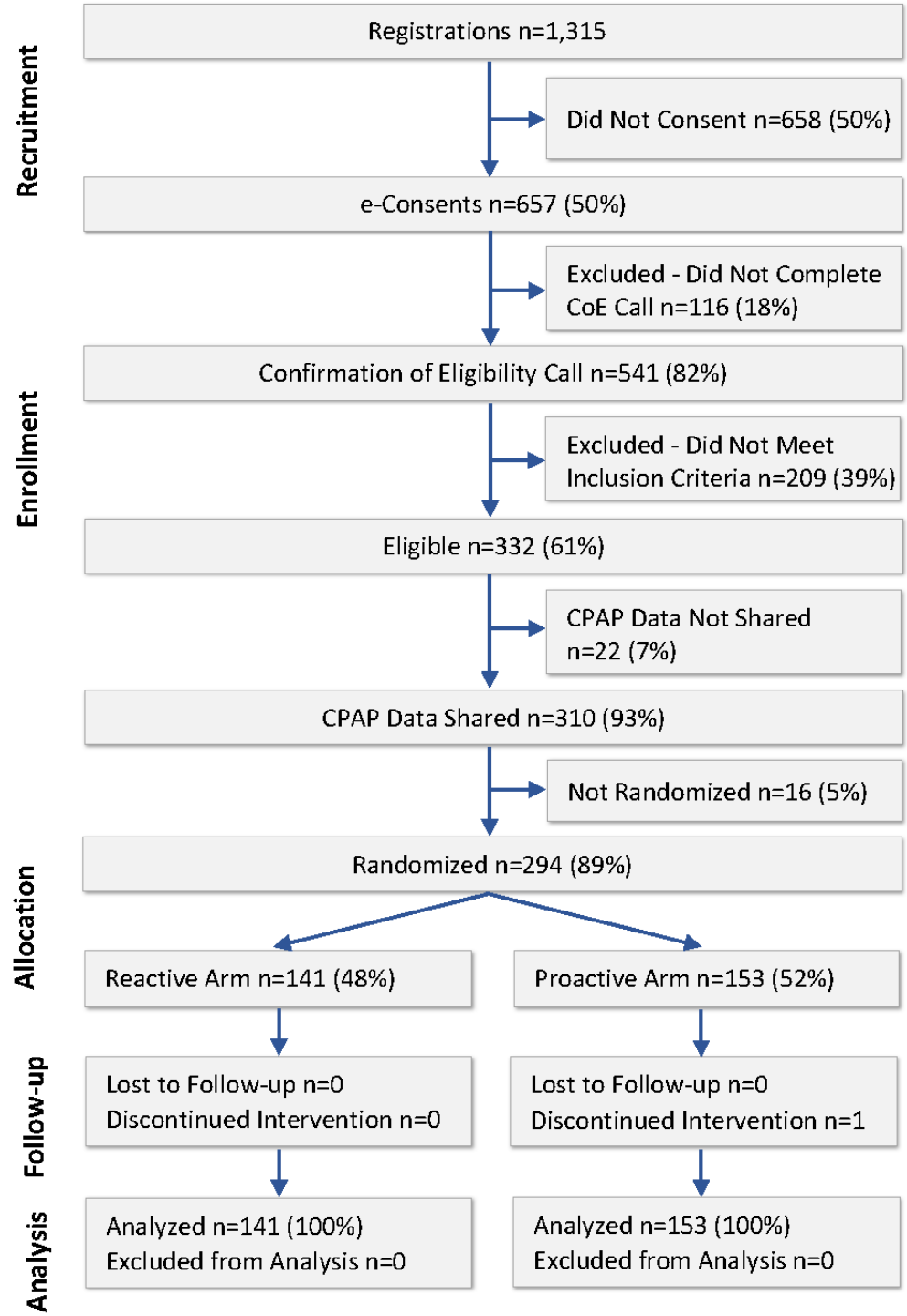
[c]The average number of pages viewed during a session (average page depth). Repeated views of a single page are counted.

[d]The average length of a session in seconds.

Participant Flow

Figure 3 shows the study CONSORT diagram. All study recruitment efforts in aggregate resulted in 1315 individuals registering for the O_2VERLAP study on the study home page. Of those who registered, 657 individuals (50%) proceeded to sign consent, whereas 658 did not. Of the 657 who consented, a total of 541 participants (82%) completed the CoE phone call, and 116 (18%) were either not reached or were reached but decided they did not want to proceed with the study.

Figure 3. O_2VERLAP Study CONSORT Diagram



Abbreviations: CoE, Confirmation of Eligibility; CPAP, continuous positive airway pressure.

Study Ineligibility

The O_2VERLAP study goal was to enroll 330 participants and randomly assign 300 of them, which factored in a 10% prerandomization attrition rate. On July 31, 2019, the study reached its enrollment goal with 2 additional participants when 332 (61%) of the 541 who completed the CoE phone call were found to be eligible to participate. The remaining 209 (39%) were deemed ineligible for the study. Table 6 provides a breakdown of the reasons for ineligibility and then categorizes them by diagnosis, device, and miscellaneous reasons. The diagnosis category had the highest number (n = 134), followed by device (n = 69) and miscellaneous (6).

Table 6. Number of Persons Ineligible to Participate and Reason for Study Ineligibility (n = 209)

No.	Reason	Category
107	Did not have a COPD diagnosis	Diagnosis
49	Did not have a wireless modem in their CPAP device	Device
24	Did not have an OSA diagnosis	Diagnosis
16	Did not have a prescription for CPAP	Device
4	Not 40 y of age	Miscellaneous
4	Using a Trilogy device[a]	Device
3	Did not have either OSA or COPD diagnosis	Diagnosis
2	Were receiving hospice care and considered too ill	Miscellaneous

Abbreviations: COPD, chronic obstructive pulmonary disease; CPAP, continuous positive airway pressure; OSA, obstructive sleep apnea.
[a]Trilogy devices are not dedicated CPAP devices.

"Did not have a COPD diagnosis" was the most common reason for ineligibility because of 2 related factors: (1) the high volume of the ASAA campaign's study promotional efforts to their OSA community, and (2) OSA is more common in people diagnosed with COPD than the reverse.

Study Eligibility: Cumulative and Monthly Enrollment

Figure 4 and Figure 5 show study enrollment over the 18-month recruitment period. Figure 4 shows the cumulative enrollment, which appears to be relatively smooth, with participant enrollment ahead of goal for the first half of the study and then slightly behind the goal. Figure 5 shows the monthly enrollment figures and demonstrates the monthly variability of enrollment that the project experienced due to the relatively unknown campaign yields. The study team needed to estimate campaign yields to attempt to enroll the goal of 20 to 30 new participants per month. In other words, the team tried to avoid over- or under-enrolling in any 1 month, given considerations about coach staffing and time effort.

Figure 4. Cumulative Enrollment Over 18-Month Recruitment Period (February 2018-July 2019)

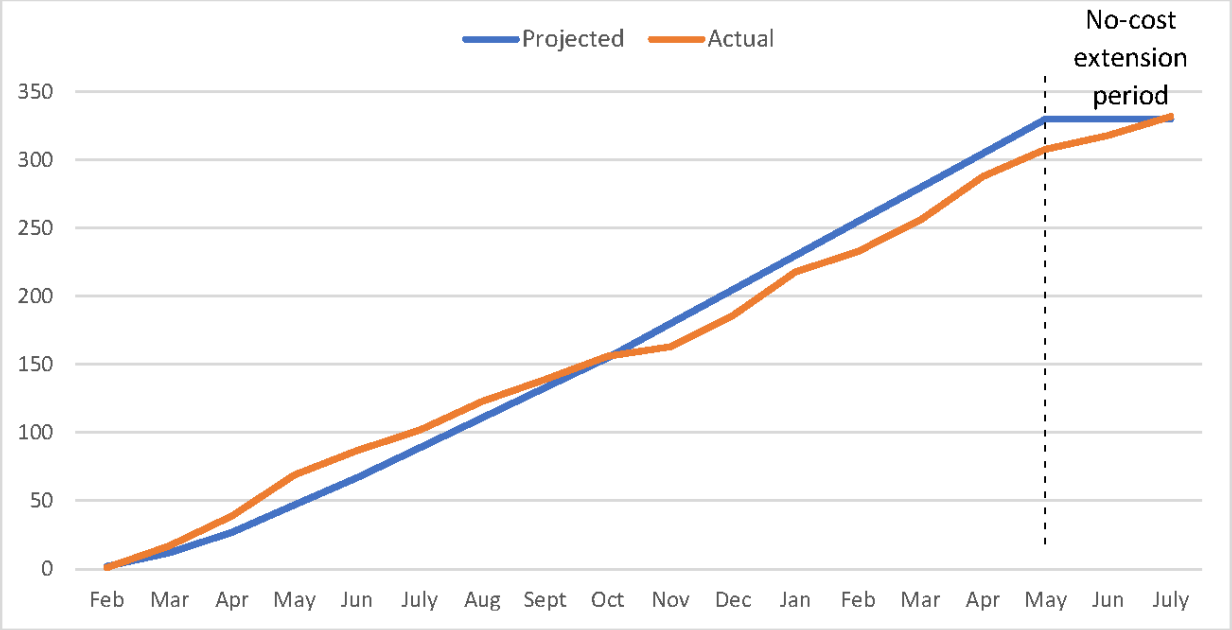
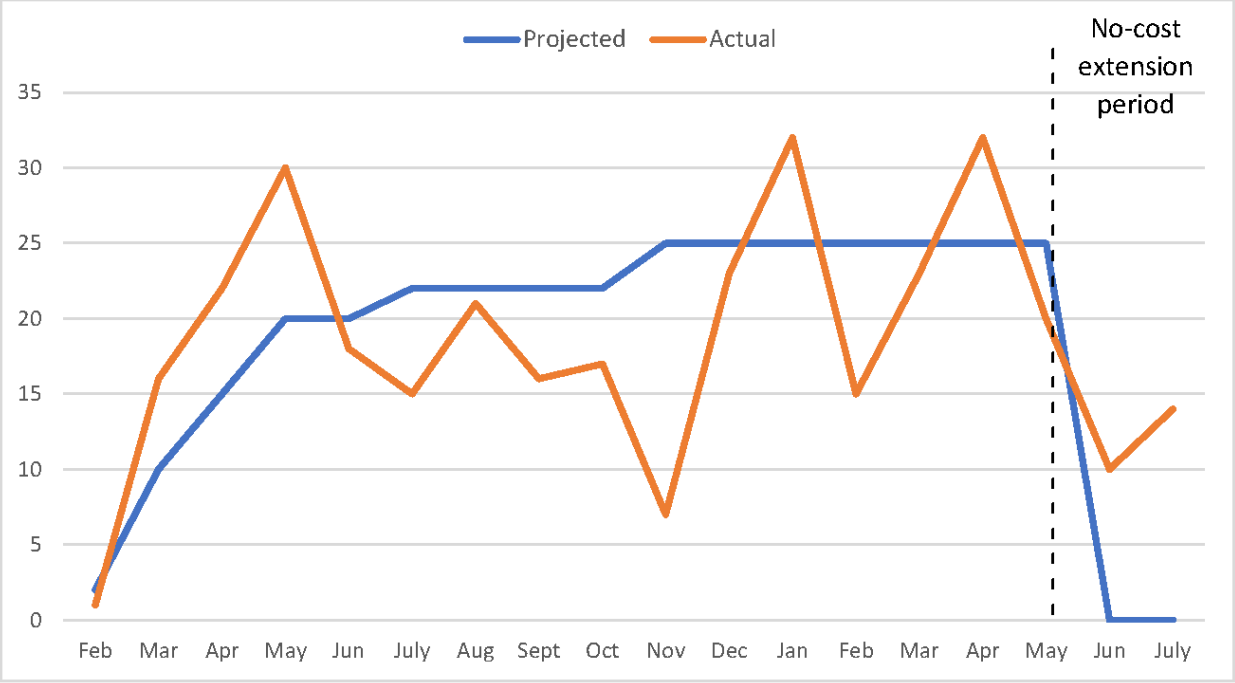


Figure 5. Monthly Enrollment Over 18-Month Recruitment Period (February 2018-July 2019)



CPAP Data Sharing

Once participants were considered eligible and enrolled in the study, we required 1 additional step before they could be randomly assigned: getting permission for CPAP data sharing. We successfully obtained permission to share the CPAP data of 310 (93%) of 332 enrolled participants. We were concerned that data sharing would be 1 of the most significant challenges to the study. In the end, only 22 participants (7%) withheld permission for CPAP data sharing. Of the 22 who did not share CPAP data, 7 were on hold or never provided their device serial number or HME name and contact information; 6 withdrew during this time; 6 had data transmission issues; 2 were nonresponsive; and 1 died during this time. Two reasons we think participants withdrew or declined at this point were that (1) for some of these individuals, it was likely the result of the data sharing process taking a long time, and the initial interest in participating in the study naturally waning over time; and (2) they changed their mind about participating and wanted to leave the study before being randomly assigned.

To successfully obtain CPAP data sharing permissions from CPAP providers, the study team had to work with each participant's HME provider. At study outset, 1 concern with using

this methodology was that potentially we would have to work with 330 different HME companies. However, in the end, we found that we "only" had to work with 132 different HMEs. We found that our study had multiple participants in some of the large national HMEs. Ultimately, the study had >10 participants in 5 HMEs, 3 to 10 participants in 9 HMEs, 2 participants in 11 HMEs, and 1 participant in 94 different HME companies. Importantly, those 5 HMEs with which >10 of the study participants were associated accounted in total for 151 participants, or 49% of the total. Those 5 HMEs were as follows: O_2VERLAP HME account (n = 69), which included the participants who were not associated with an HME at the time of enrollment; Lincare (Clearwater, FL; n = 37); Apria Healthcare (Lake Forest, CA; n = 28); VHA (Washington, DC; n = 14); and Sleep Data, Inc (San Diego, CA; n = 11). The study team was able to establish efficient working relationships with these large national HME organizations, without which the study may not have been able to achieve its recruitment goals. One of those HME accounts was not associated with an existing HME company, which we discuss next.

The CPAP data sharing process would have caused this study to fail had it not been for the study team's creation of its own HME account for participants who were no longer being followed by an HME company or who had opted out of being followed by an HME. This O_2VERLAP study HME account included 69 participants. In addition, the support of the ASAA CPAP Assistance Program was instrumental in helping some participants receive updated CPAP devices with wireless capabilities. The 69 participants represented 22% of the 310 from whom we successfully obtained CPAP data. Given the study's ambitious timeline in needing the full 18 months for study recruitment, it was clear that without doing this, the study would have been unable to meet its objectives. The Discussion section provides more coverage of this issue, with an emphasis on the challenges that patients face in obtaining their own medical data.

Eligible and Enrolled Participants Who Did Not Move Forward With the Study

Of the 310 participants who reached the CPAP data sharing point of the study workflow, there were an additional 16 participants who did not move forward to the randomization phase for 2 reasons: they either "declined" to move forward with the study (n = 9) or the study team

was unable to contact them despite multiple attempts by phone and email to reach them for randomization (n = 7). We put the word “decline” in quotation marks because some told us they no longer wished to participate in the study. Others simply said they were no longer interested in the study and did not elaborate.

Randomization

A total of 294 (89%) of the 332 enrolled participants were randomly assigned to 1 of the 2 intervention groups: 153 were randomly assigned to the PC group and 141 to the RC group. In comparing the 38 participants (who signed informed consent but were not randomly assigned) with the 294 participants (who met all study criteria and were randomly assigned), there were no significant differences in any demographic characteristic.

Main Study Findings

The main study was conducted on a sample size of 294 participants. This section summarizes the findings by category: sample characteristics, primary and secondary aims, and exploratory analyses.

Sample characteristics

Women and men comprised 47.3% and 52.7% of the sample, respectively. The mean age of the sample was 64.0 (SD, 9.6) years and ranged from 41 to 89 years. Table 7 shows the sample characteristics.

Table 7. Sample Characteristics

Characteristic	Response	PC		RC	
		No.	%	No.	%
Current marital status	Married	90	58.8	76	53.9
	Divorced	33	21.6	30	21.3
	Single	14	9.2	17	12.1
	Widowed	12	7.8	9	6.4
	Domestic partner	2	1.3	4	2.8
	Separated	1	0.7	4	2.8
	I do not want to answer	1	0.7	1	0.7
Highest level of education	Some high school (10th or 11th grade)	5	3.3	2	1.4
	Completed high school (or GED)	10	6.5	22	15.6
	Some college or vocational training	63	41.2	57	40.4
	Completed bachelor's degree	35	22.9	28	19.9
	Some graduate training	3	2.0	1	0.7
	Completed graduate degree	37	24.2	30	21.3
	I do not want to answer this question	0	0	1	0.7
Hispanic	No	144	94.1	138	97.9
	Yes	9	5.9	3	2.1
Race	White	132	86.3	128	90.8
	Black or African American	10	6.5	6	4.3
	Multiple races	7	4.6	6	4.3
	Asian	0	0	1	0.7
	Other	4	2.6	0	0.0

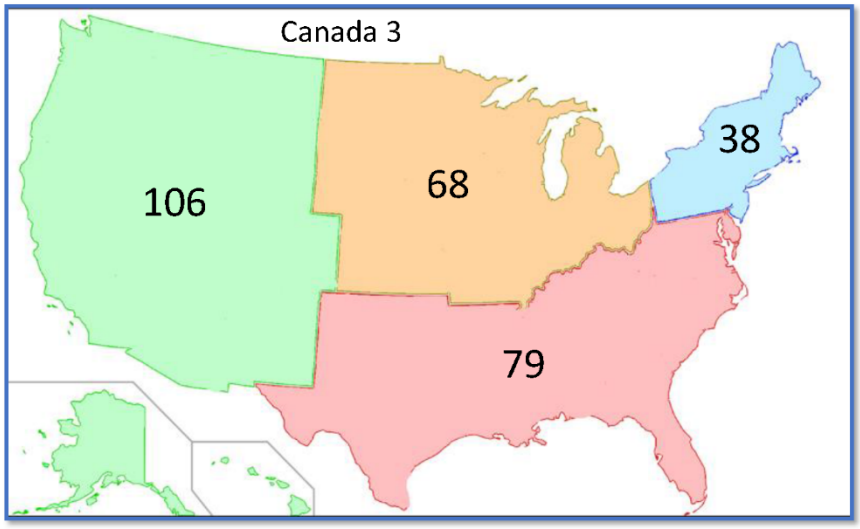
Characteristic	Response	PC		RC	
		No.	%	No.	%
Total annual household income, $	<15,000	14	9.2	11	7.8
	15 000-25 000	18	11.8	15	10.6
	25 001-35 000	15	9.8	13	9.2
	35 001-50 000	20	13.1	13	9.2
	50 001-65 000	8	5.2	10	7.1
	65 001-80 000	10	6.5	10	7.1
	80 001-100 000	11	7.2	11	7.8
	100 001-135 000	11	7.2	14	9.9
	>135 000	14	9.2	5	3.5
	I do not want to answer this question	29	19.0	37	26.2
	I am not sure	3	2.0	2	1.4
How do you manage on the income you have available?	It is impossible	4	2.6	3	2.1
	It is difficult most of the time	21	13.7	16	11.3
	It is difficult some of the time	45	29.4	41	29.1
	It is never difficult	58	37.9	47	33.3
	I am not sure/I do not want to answer	25	16.3	34	24.1
Sexual orientation	Straight	141	92.2	132	93.6
	Gay	7	4.6	5	3.5
	Lesbian	2	1.3	3	2.1
	Bisexual	2	1.3	1	0.7
	Decline to answer	1	0.7	0	0.0

Abbreviations: PC, proactive care; RC, reactive care.

Geographic distribution. Figure 6 provides a map of the United States color-coded by region (West, Midwest, South, Northeast). The map is based on US Census regions and divisions.[51] The map shows the geographic distribution of the O_2VERLAP study sample size of 294 participants. The study included 3 participants from Canada with dual citizenship who had residences in both the United States and Canada but who were living in Canada during the time of the study. The study IRB advised that this was allowed per its policies. The study team attempted to ensure geographic diversity during the study.

Appendix 6 provides 2 supplemental data tables that show the decision-making by the team at the 11-month time point and then the final geographic distribution. The final rates for each of the 4 regions, from highest to lowest, were as follows (in number of participants per 10 million): West, 12.6; Midwest, 9.9; Northeast, 6.7; and South, 6.3. Rates were calculated by dividing the number of participants enrolled in a region by the population of that region.

Figure 6. Geographic Distribution of O_2VERLAP Study Participants by US Region and Canada



Years since COPD and OSA diagnoses. Table 8 provides the number (percentage) of participants with the lengths of time since diagnosis for both COPD and OSA. Note that 54% and 58% of the sample was diagnosed with OSA and COPD ≥6 years ago, respectively. Relatively few participants were diagnosed <2 years ago (19% OSA and 10% COPD).

Table 8. Years Since COPD and OSA Diagnoses (N = 293)

Years since diagnosis	OSA, No. (%)			COPD, No. (%)		
	PC	RC	Total OSA	PC	RC	Total COPD
0	4 (1)	8 (3)	12 (4)	4 (1)	6 (2)	10 (3)
1	25 (9)	18 (6)	43 (15)	13 (4)	7 (3)	20 (7)
2-5	44 (15)	36 (12)	80 (27)	46 (16)	47 (16)	93 (32)
6-10	36 (12)	28 (10)	64 (22)	34 (12)	33 (11)	67 (23)
>10	44 (15)	50 (17)	94 (32)	56 (19)	47 (16)	103 (35)

Abbreviations: COPD, chronic obstructive pulmonary disease; CPAP, continuous positive airway pressure; OSA, obstructive sleep apnea; PC, proactive care; RC, reactive care.

Comorbidities. The FCI was used; the mean number of medical conditions was 6.4 (SD, 2.7; range, 2-17). When the optional write-in medical conditions were included, the mean was 8.4 (SD, 2.9; range, 2-17). The top 5 endorsed medical comorbidities in this sample were visual impairment (ie, cataracts, glaucoma): 182 (54.8%); obesity (body mass index [BMI] ≥ 30): 180 (54.2%); arthritis: 177 (53.3%); peripheral vascular disease: 168 (50.6%); and upper gastrointestinal disease: 148 (44.6%).

Supplemental oxygen therapy use. The study design resulted in 100% of study participants having and using CPAP therapy. We also found that 44% (n = 144) of all participants were using oxygen therapy to some degree, meaning that 56% (n = 184) were not using oxygen therapy.

Smoking. In terms of smoking status, 233 participants (70.2%) reported being past smokers, 27 (8.1%) current smokers, 71 (21.4%) never having smoked, and 1 (0.3%) refused to answer. The past smokers reported smoking for 31.4 years (SD, 12.3; range, 1-60) and 9.7 packs/week (SD, 5.4; range, 1-30). The current smokers reported smoking for 35.1 years (SD, 12.3; range, 15-59) and 5.6 packs/week (SD, 4.5; range, 1-24).

Satisfaction. Participants in both groups were presented with an automated online satisfaction survey within the Participant portal after a communication task with an RT and/or

Information Line coach was completed. The questions on the satisfaction survey were as follows: (1) Who did you have a study communication with? Response options: Information Line coach, RT, or other. (2) Was your communication by phone or portal messaging? Response options: video, phone, or online (chat). (3) Communication Satisfaction score (1-10 scale). The purpose of the last question was to rate the participant's satisfaction regarding their perceptions of the quality of communications with either an RT or a COPD Information line coach. For the PC group, the satisfaction survey also appeared after communication via a chat function in the study portal. Table 9 provides a summary of the satisfaction surveys completed and scores based on a range from 1 to 10, with higher scores indicating greater satisfaction.

Table 9. Satisfaction Survey Scores for Coach's Communications[a]

RT coaches		Information Line coaches		Total
Chat (n = 4)	**Phone (n = 341)**	**Chat (n = 6)**	**Phone (n = 448)**	**N = 799**
9.7 (0.5; 8.9-10)	9.5 (0.9; 4-10)	8.6 (1.5; 6.9-10)	9.5 (0.8; 5-10)	9.5 (0.9; 4-10)

Abbreviation: RT, respiratory therapist.
[a]Data reported as mean (SD; range).

Primary Aim: CPAP Adherence

The primary aim of the study was to examine the effect of the intervention (ie, PC or RC) on CPAP adherence. Table 10 provides the adherence values by group and time point. Time point refers to the 3 assessment time points (baseline, 6 weeks, and 12 weeks). The groups differed at baseline, with the RC group (7.3 hours/night) using CPAP slightly more than the PC group (6.1 hours/night; $P < .001$) during the 30 days before study start.

Table 10. CPAP Adherence by Group and Study Time Point[a]

Group	Baseline	Wk 6	Wk 12
Total (N = 294)	6.7 (2.8; 0-17.8)	6.8 (2.5; 0-17.4)	6.5 (2.8; 0-18.3)[b]
RC (n = 141)	7.3 (2.4; 0-14.1)[c]	7.4 (2.2; 0-12.8)[d]	7.2 (2.5; 0-12.8) [d]
PC (n = 153)	6.1 (3.1; 0-17.8)[c]	6.3 (2.7; 0-17.4) [d]	5.9 (3.0; 0-18.3) [d]

Abbreviations: CPAP, continuous positive airway pressure; PC, proactive care; RC, reactive care.
[a]Data reported as mean (SD; range) hours/night of CPAP use.
[b]The total group week-12 adherence level was lower than total group baseline adherence ($P = .047$).
[c]The PC and RC groups differed at baseline ($P < .0001$).
[d]No difference in change of adherence between PC and RC groups at 6 weeks ($P = .78$) or 12 weeks ($P = .29$).

In an unadjusted linear random-effects model, the interaction between time point and intervention group was not significant, which indicated no significant difference in change of CPAP adherence between the 2 study groups in either week 6 (difference = 0.18; 95% CI, −0.16 to 0.52; $P = .29$) or week 12 (difference = −0.05; 95% CI, −0.39 to 0.29; $P = 0.78$). Removing the interaction term from the model, we found that overall, the week-12 CPAP adherence level was significantly lower than at baseline (difference = −0.17; 95% CI, −0.34 to −0.002; $P = .047$) while controlling for the group, and the PC group had lower CPAP adherence compared with the RC group while controlling for the time point (difference = −1.16; 95% CI, −1.75 to −0.58; $P < .001$).

CPAP adherence was significantly related ($P < .15$) to race, ethnicity, income, education, and smoking status, but not related to age, sex, or marital status. Adding the identified covariates to a multivariable model resulted in similar findings as found in the analysis that was not adjusted for these additional baseline characteristics.

Secondary Aim

The secondary aim of the study was to examine the relationships between group assignment and the following PROs: daytime functioning, sleep quality, and daytime symptoms. Table 11 provides a summary of these measures by group and time point.

Table 11. PROs by Group and Study Time Point[a]

Measure (score range)	Group[b]	Baseline	Wk 6	Wk 12
FOSQ[c] (5-20)	Total group	14.5 (3.7; 3.5-20)	14.9 (3.4; 3.5-20)	14.9 (3.4; 3.5-20)
	RC	14.8 (3.5; 5.8-20)	15.2 (3.0; 8.8-20)	15.1 (3.2; 7.0-20)
	PC	14.1 (3.8; 3.5-20)	14.6 (3.7; 5.0-20)	14.6 (3.6; 4.3-20)
PSQI[d] (0-21)	Total group	8.8 (4.2; 0-20)	8.4 (4.1; 1-20)	8.0 (4; 0-19)
	RC	8.1 (4.1; 1-20)	7.9 (4.1; 1-20)	7.6 (4.0; 1-19)
	PC	9.4 (4.2; 0-20)	8.8 (4.1; 1-19)	8.4 (4.1; 0-19)
ESS[e] (0-24)	Total group	9.0 (5.1; 0-23)	8.8 (4.7; 0-23)	8.2 (4.7; 0-24)
	RC	8.5 (4.8; 0-21)	8.4 (4.3; 0-20)	7.8 (4.0; 0-17)
	PC	9.5 (5.4; 0-23)	9.2 (5.0; 0-23)	8.5 (5.2; 0-24)

Abbreviations: ESS, Epworth Sleep Scale; FOSQ, Functional Outcomes of Sleep; PC, proactive care; PROs, patient-reported outcomes; PSQI, Pittsburgh Sleep Quality Index; RC, reactive care.
[a]Data reported as mean (SD; range) hours/night.
[b]The sample size for each group was as follows: total (N = 294), RC (n = 141), and PC (n = 153).
[c]Higher scores indicate better daytime functioning.
[d]Higher scores indicate worse sleep quality.
[e]Higher scores indicate more daytime sleepiness.

FOSQ 10-item tool. Baseline scores on the FOSQ 10-item tool (FOSQ-10) did not differ between the 2 groups ($P = 0.16$), with a mean score of 14.8 for the RC group and 14.1 for the PC group. In an unadjusted linear random-effects model, the interaction between time point and intervention group was not significant, which indicated no significant difference in change in FOSQ-10 score between the 2 study groups in either week 6 (difference = 0.12; 95% CI, −0.53 to 0.77; $P = .72$) or week 12 (difference = 0.16; 95% CI, −0.51 to 0.83; $P = .64$). Removing interaction from the model, we found that the week-6 FOSQ-10 score was marginally significantly higher than at baseline (difference = 0.32; 95% CI, −0.01 to 0.64; $P = .06$) while controlling for the group, and the PC group had a marginally significantly lower FOSQ-10 score compared with the RC group while controlling for the time point (difference = −0.64; 95% CI, −1.39 to 0.12; $P < .10$). The results from a multivariable random-effects model with adjustment for baseline covariates were similar to those of the unadjusted analysis.

PSQI. Baseline scores on the PSQI were significantly different between the 2 groups (*P* = .01), with a mean score of 8.1 for the RC group and 9.4 for the PC group. In an unadjusted linear random-effects model, the interaction between time point and intervention group was not significant, which indicated no significant difference in change in PSQI score between the 2 study groups in either week 6 (difference = −0.26; 95% CI, −0.93 to 0.42; *P* = .46) or week 12 (difference = −0.07; 95% CI, −0.77 to 0.63; *P* =.85). Removing interaction from the model, we found that the week-12 PSQI score was significantly lower than at baseline (difference = −0.59; 95% CI, −0.94 to −0.24; *P* =.001) while controlling for the group, and the PC group had a significantly higher PSQI score compared with the RC group while controlling for the time point (difference = 1.19; 95% CI, 0.29-2.09; *P* < .01). The results from a multivariable random-effects model with adjustment for baseline covariates were similar to those of the unadjusted analysis.

ESS. Baseline scores on the ESS were not significantly different between the 2 groups (*P* = .16), with a mean score of 8.5 for the RC group and 9.5 for the PC group. In an unadjusted linear random-effects model, the interaction between time point and intervention group was not significant, which indicated no significant difference in change in ESS score between the 2 study groups in either week 6 (difference = −0.06; 95% CI, −0.84 to 0.73; *P* = .89) or week 12 (difference = −0.15; 95% CI, −0.96 to 0.66; *P* = .72). Removing interaction from the model, we found that the week-12 ESS score was significantly lower than at baseline (difference = −0.66; 95% CI, −1.06 to −0.25; *P* = .002) while controlling for the group, and the PC group had a marginally significantly higher ESS score than that of the RC group while controlling for the time point (difference = 0.92; 95% CI, −0.14 to 1.98; *P* = .09). The results from a multivariable random-effects model with adjustment for baseline covariates were similar to those of the unadjusted analysis.

Exploratory Analyses

CPAP use relative to TSP. CPAP is prescribed for use during sleep, and nearly all patients use it for some portion of their TSP. Patients seldom use CPAP for longer than their

TSP. However, per anecdotal reports, some patients may use CPAP during nonsleep periods because they like how it helps with their breathing.

TSP was calculated as uptime minus bedtime, and its units are in hours. The source of uptime and bedtime data was the PSQI. Table 12 provides the TSP by group and time point. Note that the average TSP for the entire group at each time point was quite high, at 8.1 hours/night, and that it ranged quite substantially from 2 hours on the low side to 14 hours on the high side.

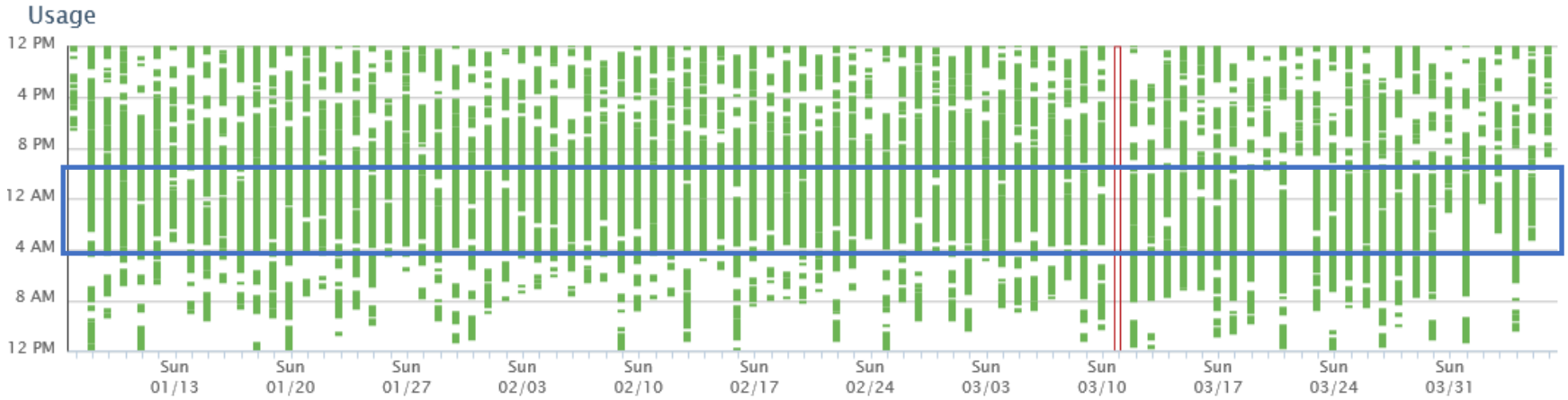
Table 12. TSP by Group and Study Time Point[a]

Group	Baseline	Wk 6	Wk 12
Total group	8.1 (1.7; 2-14)	8.1 (1.6; 3-13)	8.1 (1.7; 3-14)
RC	8.2 (1.7; 5-13)	7.9 (1.5; 4-12)	8.0 (1.8; 4-13)
PC	8.2 (1.7; 2-14)	8.3 (1.7; 3-13)	8.2 (1.7; 3-14)

Abbreviations: PC, proactive care; RC, reactive care; TSP, total sleep period.
[a]Data reported as mean (SD; range) hours/night.

Figure 7 shows a time graph of CPAP use over the course of an approximately 90-day period for 1 nonidentified participant. The green bars indicate the times when CPAP was used during each 24-hour period. Breaks in the green bar indicate when the CPAP mask was removed. The single red bar on March 11 indicates a day when CPAP was not used. The blue box indicates when a normal, approximately 8-hour TSP typically occurs (ie, 10 PM to 6 AM). The green bars outside of the blue box show those times when CPAP was used outside of the normal sleep period.

Figure 7. Time Graph of CPAP Use by Day[a]



Abbreviation: CPAP, continuous positive airway pressure.

[a]These data are from 1 O_2VERLAP participant to graphically demonstrate when CPAP is likely used during sleep (ie, inside the blue box) and likely used outside the main sleep period (ie, outside the blue box). The green bars indicate the times when CPAP was used during each 24-hour period. The y-axis represents a 24-hour period (12 PM to 12 PM), and the x-axis shows the number of days (in this case, approximately 90 days).

The percentage of CPAP use during TST was calculated using the following ratio: CPAP use (hours) divided by TSP (hours), which we here refer to as the *CPAP to TSP ratio*. A CPAP to TSP ratio of 1.0 means that a CPAP user who slept 6 hours used CPAP for the full 6 hours. A ratio of 2.0 means that a CPAP user who slept 6 hours used CPAP for 12 hours. The mean CPAP to TSP ratio at baseline was 83% (SD, 33%; range, 0%-223%) and at 12 weeks was 87% (SD, 32%; range, 0%-297%). Table 13 provides the CPAP to TSP ratio by group and time point.

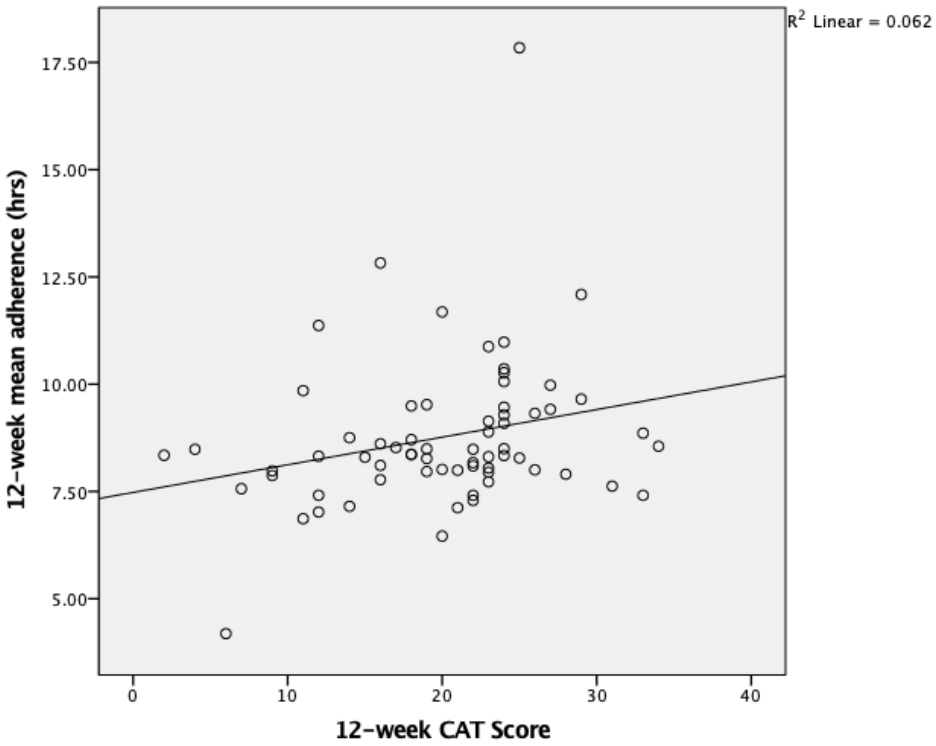
Table 13. CPAP to TSP Ratio[a] by Group and Time Point[b]

Group	Baseline	Wk 6	Wk 12
Total group	82.9 (33.4; 0-223)	87.9 (30.3; 0-219)	87.1 (32.2; 0-297)
RC	84.4 (35.5; 0-223)	91.4 (34.1; 0-223)	88.8 (37.7; 0-297)
PC	81.5 (31.5; 0-164)	84.6 (26.1; 2-159)	85.6 (26.1; 4-158)

Abbreviations: CPAP, continuous positive airway pressure; PC, proactive care; RC, reactive care; TSP, total sleep period.
[a]The ratio is a percentage calculated by CPAP adherence (hours) divided by TSP (hours).
[b]Data reported as mean % (SD; range).

Our SAB suggested there might be a relationship between severity of COPD and CPAP use. The team examined the relationship between COPD severity as measured by the CAT score and CPAP adherence. For the entire group, there was a nonsignificant relationship between the CAT score and CPAP adherence at the 12-week time point. However, when the subgroup of high CPAP users (defined as CPAP to TSP ratio >1.0) was analyzed separately, the correlation coefficient was 0.250 (P = .04). Figure 8 shows the scatterplot for this subgroup.

Figure 8. Scatterplot of CAT Score by CPAP Adherence[a]



Abbreviations: CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; CPAP, continuous positive airway pressure.

[a]This figure shows the relationship between COPD severity (as reflected in an increased CAT score on the x-axis) and CPAP adherence at the 12-week time point for participants with a CPAP to TSP ratio >1.0.

DISCUSSION

Main Study Findings

In the O_2VERLAP study, we did not find a difference between the 2 intervention groups (PC and RC) in CPAP adherence or PROs. The baseline CPAP adherence level for the entire sample was 6.7 hours/night (SD, 2.8; range, 0-17.3 hours/night), and the mean CPAP to TSP ratio at baseline was 83% (SD, 33%; range, 0%-223%). This very high CPAP level at baseline (ie, before the start of the intervention) represents the goal of interventional studies (see Appendix 1) and is therefore considered an unexpected and novel finding of this study. Possible reasons for the high baseline CPAP use level may be due, in part, to the shortened study time frame and use of electronic recruitment methods that resulted in a sample of very consistent CPAP users at baseline. High adherence rate at baseline appears to have resulted in a ceiling effect, meaning that there was little room for improvement for both groups.

In addition, the baseline difference between the 2 groups (RC: 7.3 hours/night; PC: 6.1 hours/night) was also a surprising finding. Most interventional studies show an effect of increasing CPAP use levels by 1.0 to 1.5 hours/night, but those studies are of new CPAP users, not existing users, as in our study.[32] The baseline use level represented a ceiling above which improvement can be difficult. To our knowledge, this high level of CPAP use in patients diagnosed with COPD and OSA is a finding that has not been previously reported in the medical literature.

Several reasons may account for the uniquely high CPAP use level found in this study relative to past studies reported in the literature. Appendix 1 provides the weighted mean adherence level for the overall group (3.48 hours/night across 18 studies and 4000 participants) and for US-based studies (3.11 hours/night) as reference values to put into context the adherence levels found in the present study. The mean age group in this study was of retirement age, so the participants likely were free in the daytime hours to use CPAP. It appeared that more use, especially for daytime CPAP users, was associated with worse COPD severity. It may be that other published studies did not have samples with the degree of COPD severity that our sample had. Finally, the present study was unique in its national, electronic

recruitment method conducted via the COPD and OSA communities. It may be that patients who are actively involved in monitoring social media channels and who are willing to respond to research opportunities are in some ways different than those who are not.

The study as designed can help answer the question, Should a clinic or patient advocacy organization be more proactive in setting up online and personnel support for their communities? In the end, because we found patients who were already using CPAP at a high level, the findings of the present study cannot help answer this contextual question. In fact, because there was a downward trend in the PC group at 12 weeks (after an initial slight increase), it may be that providing structured support to active, consistent users has a slightly negative effect. The recommendation from the study team to a clinic or organization that is considering staffing up or providing minimal resources would be to do the latter and build up only if the demand can be quantified. This is not to say that support should not be provided. Support should continue to be provided, just on an as-needed basis based on documentation of poor adherence. Good care for chronic illness is providing the right support at the right time to the right person.[52]

In addition to carrying out this large, national CER study, the study team learned a great deal about (1) the pros and cons of using electronic methods (primarily direct emails and social media posts) to carry out study promotional efforts; and (2) the complex issue of the health care system providing the sharing of medical device data to patients, specifically with CPAP devices. We discuss these 2 areas next.

Study Recruitment: Key Lessons Learned

We learned several important lessons concerning conducting primarily electronic recruitment in a large-scale, national study. We organize our findings by lessons learned about social media expertise, messaging, working with PCORnet partners, and using social media platforms.

Social Media Expert

First and foremost, the earlier a project can bring a social media expert on board, the better. Our team developed the experience and skill in social media campaigns, but it would have been far more effective from study outset had we brought this person onboard at the start. They could have helped write the initial email/social media post text and headers and engaged in A/B (or similar) testing to determine which text and headers performed the best. A/B testing refers to creating 2 separate versions of a social media post ("A" vs "B") to evaluate which post is more effective. A social media expert could have helped identify and design graphics that were catchy and met the specific requirements for research on Facebook and other social media outlets. They also could have helped us understand the fine details of social media posts and their measurement. For a defined research network such as PCORnet, it is highly recommended that the central coordinating personnel search for and identify a highly qualified individual who is available on a recharge basis for individual projects. Alternatively, identifying a group of qualified individuals to hire as part-time staff or consultants is another possibility.

Message Content, Timing, and Frequency

Many lessons were learned regarding message content and timing. As described, our team primarily used 3 different types of messaging: (1) initial general content; (2) text geared toward the individual recipient, but with an additional request for that individual to promote the study to their family and friends; and (3) "last chance," which communicated an end-of-project urgency. In addition to the content of the messaging, the timing is important as well. We found that mid-week campaigns (eg, Tuesday-Thursday) tended to work better than weekend campaigns (eg, Friday-Monday) because of the potential for getting overlooked in weekend activities. Finally, 18 (51%) of 35 campaigns were only implemented once. Given that we found objective evidence for the continued very good yield of implementing ≥2 campaigns to a single audience, this in hindsight appears to be a lost opportunity. The lesson learned here is, if possible, to screen potential study-promotion partners for their willingness to engage in >1

outreach to their community. The benefit to the study is the possibility of needing to work with fewer partners to achieve study goals.

Working With Partners

We first discuss this topic generally and then divide it into PCORnet partners and non-PCORnet partners. Generally, the key point we found was to be respectful of the existing communication methods and practices of a partner organization. We ended up creating an internal framework for our calls, such that each call (1) first discussed the current community communication methods of the organization (eg, timing, methods, size, inclusion of research); (2) assessed interest in research in general and O_2VERLAP specifically; and (3) then discussed the possibility of the partner engaging in O_2VERLAP communications and how that might look. We would then provide an email summary of the call and schedule a follow-up call to finalize details.

Our study team found that the willingness of PCORnet partners to help with study recruitment was in no small part related to the PCORI funding cycle. All the PCORnet CDRNs and PPRNs were nearing the end of the funding cycle when the O_2VERLAP project had <6 months to go. In addition, future funding from PCORI to remain a PCORnet member was in doubt because the People-Centered Research Foundation was established, particularly for the PPRNs. We strategically decided to recruit from the COPD and OSA communities first, given the higher likelihood of having both medical conditions, which was a prerequisite for study participation. Despite initial enthusiasm and verbal agreement from many PCORnet partners, when it came time to engage in study recruitment messaging, many either opted not to participate or to send a single communication. In no small part because of this issue, our study team had to request a no-cost extension to the project to send additional emails to UCSD and UC Irvine, to achieve our recruitment milestone.

The study team found a variety of issues with non-PCORnet partners. These types of partners were quite diverse. We attempted to go beyond the medical nonprofit organizations and health care systems that were part of the broad network by going to the medical device

suppliers themselves. This included a wide of range durable medical equipment or HME providers, from umbrella or membership organizations, to large national companies, to smaller regional companies, and to online-only companies. We asked them if they would consider communicating with their customers to promote a research study. Although we received a fair amount of interest in communicating with patients who used their services, in the end we found that very few had formal, planned communications with their customers, and that for those that did, the HME providers were either unwilling or reluctant to help with the study. In the end, we do not believe that O_2VERLAP was promoted by an HME company via a single campaign. However, we did find 2 HME companies that were willing to post about O_2VERLAP. We also found an online CPAP HME company that was willing to post about the study in their online community. Finally, we identified 1 online forum geared toward medical conditions that asked for $25,000 for a single post, despite language in their Terms of Conditions that promised their community that 1 of their stated goals was to inform them about research opportunities (ie, they would inform their community about research opportunities but at a very high cost, one that is prohibitive for all but industry research).

Facebook

For this study, we used Facebook a great deal, with ultimately very poor returns. The primary issue with Facebook is that the fate of a post directed to a defined community cannot be tracked. For example, if an HME organization has a Facebook community with 20 000 individuals, Facebook was unwilling to tell us whether that post would reach all 20 000 individuals or a subset. Based on our analytics, it appeared that it reached a subset of that defined group. We therefore engaged in "paid boosts" to increase coverage. After using a couple of metrics to define the demographic we were interested in (but not having the ability to target people with known or suspected COPD or OSA), we found that paid boosts were a very poor use of limited study resources. Only if a study is recruiting a sample that is consistent with the metrics that Facebook allows for boosting would we recommend consideration of a paid boost. Finally, Facebook defines an *impression* as "the number of times an instance of an ad [or post] is on screen."[53] For our study, the activity was a study-related Facebook post.

Importantly regarding the Facebook definition, there is no guarantee that an impression was actually read or not. That said, we did include a trackable URL in the Facebook post, so if an individual clicked on the link to the O_2VERLAP study home page, we kept track of those clicks objectively. What we could not measure was the number of times the post was read (whether in full or in part) but not clicked.

Twitter

Twitter, on the other hand, collects a fee only when a Tweet is clicked. From this perspective, paying for clicks on Twitter makes far more sense than paying for a boost that may or may not be seen on Facebook. That said, we found the Twitter audience to be significantly smaller, and it did not appear to include the demographic the study required. In further comparing Facebook and Twitter, individuals on Facebook appear to be socialized to read a wider variety of content than those who use Twitter, where most users appear to be interested in very specific kinds of content. Participation in research appears to be very rare on Twitter.

CPAP Data Sharing: Lessons Learned and Patient Access to Their Own Data

Lessons Learned

In the previous sections of this report, we provided a relatively basic background on CPAP data sharing methods and results. In this section, we provide more details on the specific strategies developed and deployed based on collaboration between the study team and the SAB that allowed the study team to move from a data sharing rate of 25% to our final sharing rate of 93%. Five specific strategies were used:

1. Improvements to the documents that were faxed to HME companies. These included a more detailed cover letter on COPD Foundation letterhead to increase study credibility, a copy of the signed and dated participant consent form, and clear instructions on the specific steps required to data share.

2. The consent form language was modified to more directly state that the participant agreed for their CPAP medical data to be shared between their provider or HME and the study team.

3. The study team created a template based on key HIPAA elements and then refined the form with the HME and others to create a final acceptable form for release of records.

4. We worked with a national HME umbrella organization to try to facilitate discussions with key contacts at the largest HME companies, and then we tried to work with key contacts within each organization to facilitate data sharing.

5. We involved many stakeholders in this process: the study team, SAB, our IRB, health care attorneys, individual HME organizations, national HME umbrella organizations, national patient advocacy associations (eg, AARC), and HIPAA specialists.

Given that the use of these strategies took several months to develop and deploy, we recommend that researchers who are trying to engage in participant medical-device data sharing take a multipronged approach to foster the sharing of such data for research:

- Early planning is essential; we should have met directly with HME companies during the study planning phase to address how best to approach this issue, especially because HMEs are relatively unaccustomed to being part of research.

- Understand the barriers and issues facing clinical service providers and discuss ways to overcome them.

- Identify the most likely solutions and their implementation.

- Reach out to experts and specialists who have the knowledge required to help accomplish the study's goals.

Patient Access to CPAP Data

CPAP data sharing was covered in the Methods and Results sections from the perspective of the study and in the Engagement section from the perspective of the SAB. In terms of CPAP data sharing from the perspective of a patient, patients have the right to access their medical information and data. The VHA has determined that patients own their CPAP devices and that they have a right to access their data.[54] In the private sector, HME companies act as data stewards; that is, patients do not have direct and easy access to the data on their

own medical devices. Instead, they must formally request permission to access their data. The study team found that this access via a third party ranges from being easy to very difficult.

Limitations and Subpopulation Considerations

The present study had limitations. The study had an ambitious time frame and depended on electronic recruitment methods that were conducted primarily through the COPD and OSA communities and PCORnet partners. The recruitment findings showed that the most success was with participants who had already been research participants and who were known to have both COPD and OSA. It may be that, in the end, these participants were more active in taking care of themselves, as demonstrated by their willingness to be part of existing patient communities and by the high CPAP adherence levels they demonstrated. Perhaps the most important finding of this study is also its most significant shortcoming. In terms of subpopulations, it appeared that in the subgroup of the most active CPAP users, greater COPD severity was associated with more use. It seems that there is a previously unidentified subgroup of patients with a high rate of CPAP use who are using CPAP during the daytime to help with their breathing. It should also be mentioned that the sample was predominately White, non-Hispanic, and well educated; therefore, research in other populations is warranted to determine generalizability of study findings or whether findings would be different in other populations.

Future Research

There are several important recommendations for research based on the findings of the O_2VERLAP study. From a clinical perspective, future researchers should better understand the factors associated with daytime use of CPAP in patients with overlap syndrome and whether there is a physiological benefit that supports the perceived benefit. The present study was unique in that it is 1 of the few that examined current CPAP users. Most CPAP adherence studies examine new users (ie, naive to CPAP). The interventional approaches used in this study should be performed with new users. Providers and clinics are often unsure how much support to provide to new users and such a study could help provide that information.

We have several recommendations with regard to methodological findings from this study for future research. The first concerns PCORI's contracting and negotiation process, which allows a wonderful opportunity to make significant improvements to a study. With respect to O_2VERLAP, in hindsight, significantly more attention should have been paid to the changes to the study that increased the scientific rigor but also the time and effort to support that additional rigor. Closely related to this issue is the use of social media for study recruitment. Methodological studies are needed to learn how best to use social media platforms cost-effectively for research study recruitment.

Patient Perspectives on the Study

The following quotes from O_2VERLAP study participants were just 2 of many that showed appreciation for having a resource available to supplement the care they were receiving from the professional medical team.

> *I had a good chat with the overlap people today. The young lady I spoke with was very polite to me and helped me set some goals as well as some good information.* (PIN 20024)

> *Thank you for the kindness, but it was truly my pleasure. And I learned much from the course to my benefit. . . . These studies and trials are the way to beat this and it would be my honor to contribute.* (PIN 20152)

CONCLUSIONS

The O_2VERLAP study did not find a difference between the intervention groups (PC and RC) in CPAP adherence or outcomes, which appears to be due in part to the shortened study time frame and use of electronic recruitment methods that resulted in very high baseline CPAP use levels in this sample of patients diagnosed with both COPD and OSA. This remarkably high level of CPAP use is a finding that has not been previously reported in the medical literature. In addition to carrying out a large, national CER study, the study team learned a great deal about (1) the advantages and disadvantages of carrying out research within PCORnet; (2) the value that an SAB brings to a large trial; (3) the pros and cons of using electronic methods (primarily direct emails and social media posts) to carry out study promotional efforts; and (4) the complex issue of the health care system providing the sharing of medical-device data with patients, specifically those who use CPAP devices.

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Stepnowsky CJ, Amdur A, Clark W, et al. Monitoring and peer support to improve treatment adherence and outcomes in patients with overlap chronic obstructive pulmonary disease and sleep apnea via a large PCORnet collaboration (O_2VERLAP). October 31-November 2, 2017; Washington, DC.

Martinez S, Sullivan J, Pasquale C, et al. The O_2VERLAP study: a PCORnet research demonstration project. September 18-20, 2019; Washington, DC.

Associated Professional Sleep Societies Meeting Presentation Abstracts

Martinez S, Deering S, Sullivan J, et al. The O_2VERLAP Study: high CPAP use in overlap syndrome patients. *Sleep.* 2020;43:A265.

Deering S, Shumard T, Zamora T, et al. CPAP adherence relative to sleep duration and sleep period in different study populations. *Sleep.* 2020;43:A260.

ACKNOWLEDGMENTS

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APPENDICES

Appendix A. CPAP Adherence Interventional Studies Summary Table

CPAP Adherence Interventional Studies. This table provides a summary of the CPAP adherence levels in the control and interventional groups of studies focused on improving CPAP adherence in new CPAP users (mean±SD).

Study	Year	N	Control Group	Intervention Group	Follow -up	Country
Lugo	2019	186	5.63 ± 1.64	5.68 ± 1.38	3 mos	Spain
Dickerson	2018	14	5.14 ± 2.0	6.07 ± 1.7	1 mo	USA
Hwang	2018	167	3.8 ± 2.5	4.8 ± 2.3	3 mos	USA
Turino	2017	100	4.9 ± 2.2	5.1 ± 2.1	3 mos	Spain
Munafo	2016	122	4.7 ± 2.1	5.1 ± 1.9	1 mo	USA
Frasnelli	2016	113	4.6	5.3	1 mo	Switzerland
Bakker	2016	83	3.3 ± 2.7	4.4 ± 2.9	6 mos	USA
Dawson	2015	75	3.6 ± 29.0	4.31 ± 32.3	10 wks	USA
Dantas	2015	41	5.7 ± 1.3	5.7 ± 1.4	1 mo	Portugal
Chen	2015	80	4.35 ± 1.71	6.32 ± 1.25	12 mos	China
Parathasarathy	2013	39	4.0 ± 2.0	5.2 ± 2.0	1 wk	USA
Lettieri	2013	2116	3.1 ± 2.6	3.5 ± 1.9	1 mo	USA
Deng	2013	110	5.28 ± 0.67	5.59 ± 0.56	1 mo	China
Bartlett	2013	206	4.1	3.5	6 mos	Australia
Olsen	2012	106	3.25 ± 2.83	4.85 ± 2.55	1 mo	Australia
Fox	2012	75	1.7 ± 2.0	3.2 ± 2.45	3 mos	Canada
Sparrow	2010	250	1.48	2.4	6 mos	USA
Richards	2007	100	2.51 ± 2.70	5.38 ± 2.55	1 mo	Australia

Notes: Study = First author last name; N = sample size; Control and Interventional Group: CPAP adherence reported as mean±SD; Country = country in which the study was performed.

The overall unweighted mean of the control groups was 3.98 hours per night. A weighted mean based on the study sample size and was 3.48 hours per night for the control groups. A subgroup analysis was also performed on those studies done in the USA vs outside of the USA, finding weighted mean adherences rate of 3.11 and 3.26 hours per night, respectively.

Appendix B. Focus Group Manuscript

Appendix 2: Focus Group Manuscript

Outcomes Important to Patients Diagnosed with Both COPD and Sleep Apnea: Findings from the O_2VERLAP Study

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This article has an online data supplement.

Abbreviations: chronic obstructive pulmonary disease, **COPD**; continuous positive airway pressure, **CPAP**; overlap syndrome, **OS**; obstructive sleep apnea, **OSA**. =

Keywords: chronic obstructive pulmonary disease; focus groups; obstructive sleep apnea; qualitative analysis; patient reported outcomes.

Funding: The study was funded by the Patient-Centered Outcomes Research Institute (PCORI) contract PPRND-1507-3166.

Abstract

Introduction: Few studies have asked overlap syndrome (OS) patients what continuous positive airway pressure (CPAP) therapy use outcomes are particularly important to them, while also considering their self-reported CPAP adherence barriers and facilitators. This study conducted a series of focus groups to learn about the abovementioned issues with the goal of applying these findings to the design of a larger PCORI-funded scientific study, the O_2VERLAP Study.

Methods: People previously diagnosed with both chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA), who were current or recent past users of the standard therapy for each condition (*i.e.*, supplemental oxygen and continuous positive airway pressure therapy, respectively) were included. Three qualitative focus groups were run using different communication modalities: (1) teleconference (audio only); (2) in-person; and (3) web-based.

Results: The focus groups included a total of 17 participants. The telephone and online focus groups resulted in more relevant transcripts, while the in-person focus groups had far fewer excerpts able to be coded. The participants were most concerned about mask fit and comfort. Other key factors affecting CPAP use included nasal dryness and issues concerning insurance. The most important outcome to patients was daytime functioning.

Discussion: This work found that telephone and web-based qualitative focus groups resulted in greater topical discussions than an in-person focus group, likely due to the customary socializing that occurs in-person. The study identified (1) CPAP use barriers and facilitators that helped guide intervention development for the larger study and (2) daytime functioning as the most important outcome for patients.

Introduction

The goals and activities of disease management can be different for patients and providers. Oftentimes, providers tend to be more focused on objective clinical parameters (*e.g.*, test results) while patients are more focused on subjective factors (*e.g.*, how they feel and function during the day). This is perhaps even more true when patients are dually diagnosed. Patients who are diagnosed with both chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) are often referred to as having Overlap Syndrome (OS).[1] OSA is prevalent in at least 10-15% of patients diagnosed with COPD.[2] The prevalence rate of OSA is similar in patients with COPD as in the general population; individuals with both of these conditions that do not use OSA therapy at night during sleep have an increased risk of death and more hospitalizations from acute exacerbations, demonstrating the importance of OSA treatment.[3]

The first-line therapy for OSA patients is continuous positive airway pressure (CPAP). CPAP provides pressure to the airway to act as a pneumatic “splint” to keep the airway open during sleep.[4]

Overlap Syndrome (OS) may be clinically distinct from either COPD or OSA alone. Patients with OS have a worse prognosis compared with patients with only COPD or OSA for several reasons that have important implications for treatment and outcome.[5] Studies that have examined the efficacy of CPAP therapy for OS have shown that CPAP use is associated with improved walking capacity[6] and longer survival in COPD patients who are hypercapnic,[7] and that higher levels of CPAP adherence are associated with better outcomes.[3] However, of the ~80% of patients who initially accept CPAP therapy, most patients fall into a partial use pattern of 3-5 hours per night.[8,9] 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%.[10] This evidence highlights the importance of providing this patient population the tools necessary to improve use of their prescribed medical device therapies.

There are several outcomes related to both COPD and OSA that are routinely measured by researchers and clinicians, but few studies to date have asked which of these outcomes are important to OS patients. Additionally, few studies to date have focused on better understanding OS patient CPAP therapy barriers and facilitators. One qualitative study focused on the role of partners, finding that to the extent that partners were involved and supportive of therapy, use of CPAP therapy tended to be better.[11] Another focused on the communication patterns between healthcare personnel and patients during the initial CPAP visits, finding that there were certain aspects of communication that better facilitated patient-centered communications.[12] And another qualitative study focused on studying CPAP use trajectories, finding that there seemed to be two unique pathways: a route of devotion, which was described as the pathway whereby patients tended to experience immediate benefits and became devoted, regular users of CPAP; and a route of negotiation, which was described as the pathway characterized by lower perceived benefits and therefore more irregular use patterns.[13] While these studies all provided various insights in CPAP use factors, none directly investigated defined barriers and facilitators of CPAP use.

The study team had an opportunity to investigate both CPAP use facilitators and barriers and outcomes important to patients using qualitative methods as part of the O_2VERLAP Study, which was funded by the Patient-Centered Outcomes Research Institute (PCORI) under the Partnerships to Conduct Research (PaCR) mechanism. The goal of PaCR projects was to support the PCORI Patient-Powered Research Networks (PPRNs) in conducting comparative clinical effectiveness research on questions that are important to, and inclusive of, patients and other stakeholders.

The study team's first task was to conduct a series of focus groups with Overlap Syndrome patients about their experiences with CPAP therapy. More specifically, the goal was to better understand important patient-centered outcomes, treatment barriers, and treatment facilitators and so that the study team could develop and refine a peer-led web-based coaching intervention, which was the focus on the main scientific study of the O_2VERLAP project. The goal of the intervention of the larger scientific study was to improve therapeutic adherence and patient-centered outcomes in individuals with COPD and OSA.

Methods

The protocol was limited in scope to the conduct of three focus groups with the express purpose of identifying outcomes important to patients with both COPD and OSA, as well as identifying treatment barriers and facilitators. Details about the participants, recruitment methods, focus groups methods, and qualitative analysis are provided next. The study and methods were approved by Western IRB (Puyallup, WA).

Description of participants

Patients who had been diagnosed with both chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) were included. Participants were either current or recent past users of the primary therapeutic medical device for each condition, namely: supplemental oxygen and continuous positive airway pressure therapy (CPAP), respectively. Participants who reported using only one device were considered for inclusion in the focus groups on an individual basis.

Recruitment

Several types of recruitment were employed. The study team included representatives from both the COPD Foundation (Miami, FL and Washington, DC) and the American Sleep Apnea Association (Washington, DC). Both groups reached out to their members to inform them about these focus groups. They were notified of the study either verbally or electronically through posts to community on-line forums or through email. Online websites and forums included COPD360SOCIAL, the COPDF Facebook page, COPDF-related patient advocacy groups on Facebook, and the American Sleep Apnea Association Facebook page. Any interested individuals were invited to participate in the focus groups by calling a toll-free phone number for more information. The electronic nature of the recruitment strategy allowed other study partners to easily share the approved recruitment messages with their own constituents. In all cases, potential focus group participants were directed to contact the COPD Foundation's study coordinator for more information. Only IRB-approved messaging and scripts were used. For direct email, only one contact attempt was made. All recruitment materials were in English only.

Types of Focus Groups

The study team conducted three unique focus groups using the following modalities: (1) teleconference (audio only); (2) in-person; and (3) web-based platform. The rationale for using these three kinds of focus groups was to avoid limiting the amount of data collected; as it related to the study teams short time frame, as it related to the limited mobility of participants and as an opportunity to compare the usefulness of modes which, in comparison to in-person focus groups, are preferable for many reasons, including increased accessibility, timeliness and improved resource allocation. Further, because the main study was national in scope, we realized an opportunity to begin practicing digital recruitment methods that would be used in the larger study, which was applicable to: (1) teleconference and (2) web-based platform focus groups.

The focus groups differed only in communication modality: (1) the teleconference focus group was conducted via telephone; (2) the in-person focus group was conducted by a moderator physically located in the same room with the participants; and (3) the web-based platform focus group was conducted using the COPD Foundation's COPD360Social platform, both in real-time and asynchronously, using a moderator led private 'chat room'.

There was a fair amount of discussion and time spent deciding how to optimally run the web-based platform focus group. The team decided to run an initial two-hour synchronous (*i.e.*, real-time) group where study team members engaged with participants in real-time. The initial two-hour period was immediately followed by a 72-hour period of possible asynchronous communication; during the initial two-hours participants were made aware of the opportunity to provide more information over the following three days. We encouraged participants to return and answer questions or provide follow-up responses at their convenience.

The study team planned to have between five and eight participants in all the "live" focus groups to allow for substantive participation. The basis for this decision was focus group best practices, which recommends that fewer than five participants may limit the conversation and yield poor data while more than ten can be unwieldy. The in-person focus group had four participants, the phone focus group had five participants and the web-based focus group had eight participants.

Number of Focus Groups

It is well known that it takes more than one focus group on any one topic to produce valid results.[14] The commonly accepted number of groups is usually three or four. This is the rationale that was used to decide to run three focus groups.

Focus Groups Methods

In-person and telephone. All focus groups participants were consented verbally over the phone and sent copies of the studies IRB-approved consent information sheet. Focus group participants were introduced by first name and ground rules were established by the moderator and participants. Focus groups lasted approximately 90 minutes and were audio-recorded. Audio recordings were then transcribed for analysis. A brief questionnaire was given prior to the start of the in-person focus groups to assess participant demographics and to capture current therapeutic medical device characteristics. The telephone participants filled the same survey out online via SurveyMonkey prior to participation.

Web-based platform. The participation instructions used for the in-person and telephone-based focus groups was also deployed for the web-based focus group. This focus group took place over 3 consecutive days after being live (*i.e.*, interactions occurring in real-time) for a period of approximately ninety minutes. The text of the conversations was captured online via a private discussion forum and then converted into transcript format, similar to the in-person and phone focus groups.

Data Handling

The phone and in-person focus groups were audio recorded. The conversations were moderated in such a way as to keep participants anonymous. First names only were used to converse and moderate the discussion. Recordings were submitted to a contract vendor for transcription (www.rev.com) and all personal health information (PHI), though it may have been discussed anonymously, was redacted from the records. The conversations from the online focus group were transcribed into a document and securely sent to Dr. Stepnowsky for analysis.

Qualitative Analysis

Qualitative analysis was a two-stage process using thematic analysis. The first stage involved the coding and classification of the data by reviewing the transcripts for potential conceptual categories, using the focus group and interview questions as initial categories. Two types of codes were employed: 1) deductive codes that represented expected themes, as identified by our stakeholders and from the medical literature, were applied to the data; 2) inductive codes that emerged organically were applied to the data. Emergent themes were identified based on recurrence and similarities and differences noted across the transcripts.

A codebook was developed from the themes and includes a detailed description of each code, inclusion and exclusion criteria, and examples of the code in use. The basis for the codebook was based on a recently published article.[11] Coding was undertaken with reference to the codebook. Coded data was analyzed to describe the different dimensions and commonalities of each theme, their distribution across categories of patient selection and the patterns and linkages between themes. This allowed the team to build concepts grounded in the data to explain the observed phenomena and to have a shared understanding of the meaning and context of each theme and code. The transcripts were coded independently by two coders. The median intercoder reliability was 0.95 (95% CI, 0.92 to 0.98) as measured by Cohen's kappa. Differences in coding were discussed and resolved by consensus. After identifying all themes, final codes were applied to the transcripts to summarize the final themes and relevant quotes using Dedoose qualitative analysis software.[15] A commonly used outcome metric is a count of the frequency of each code. Dedoose provides functionality to create a word cloud, which is a data visualization method to graphically show the most frequently used coded words and/or phrases.

Focus Group Questions

Online data supplement 1 provides the script used to begin each focus group and the list of questions used to engage participants in discussion. The questions were designed to generate the kinds of discussions that can yield the kind of information that will be important for the goals of the subsequent larger scientific study, including both a focus on outcomes important to patients and to discussion of barriers and facilitators of device use. The questions started more generally and then became more specific.

Results

Focus Group Date and Duration

All synchronous discussions lasted about 90 minutes and were scheduled for midday eastern standard time (EST) to accommodate different time zones. This time of the day was selected because alertness level tends to be best for this patient group during this time period. The online focus group remained open for comments after the synchronous portion for 72 hours and was considered the asynchronous portion of the online focus group.

Recruitment Methods

All recruitment was accomplished through established COPD and OSA patient communities. Interested individuals were directed to call or email the COPD Foundation study research coordinator. Recruitment messaging and graphics were all submitted to WIRB for approval prior to engagement. The COPD Foundation (COPDF) and American Sleep Apnea Association (ASAA) both used various online communities to promote the focus groups after receiving WIRB approval, including: COPD360Social, COPDF Facebook page, COPDF twitter account, ASAA Facebook page, and ASAA twitter account. Facebook was the primary and most successful source of social media recruitment. The focus groups were promoted organically for about seven days and then utilized Facebook's option for boosting posts and placing an advertisement.

Participant Demographics

The recruitment period was approximately twenty-five days (including weekends), during which time approximately 50 inquiries were received. Of the fifty inquiries received, 17 individuals were able to participate in the focus groups. Sixteen of those individuals had both COPD and OSA while one individual had only a diagnosis of OSA.

The average age of participants was 65 years old, 70% were female and 30% male, and most of the participants ethnic background was white or Caucasian. The average household income of participants was $35,000-$50,000 annually. These demographics are consistent with those who are known to have the Overlap Syndrome. Most individuals reported that it was difficult to manage their financial needs on an annual basis with their reported household income. The participants average level of education was a completed high school diploma or G.E.D. with some college or vocational training. 100% of participants used positive airway pressure devices at night and 47% used both supplemental oxygen and positive airway pressure devices at night. Only 52% of participants reported using their CPAP device as prescribed and only 75% of supplemental oxygen users reported using their oxygen therapy as prescribed.

Qualitative Data Analysis

Facilitators and Barriers. Table 1 provides a summary of the code counts while the full coding table is provided in online data supplement 2. The codes are summarized across the three focus groups. Interestingly, the most codes were from the telephone (40) and on-line (32) focus groups, while the in-person (16) focus group had far fewer (~50%) excerpts coded. Table 1 shows the codes which have a count of 3 or more. The following facilitators had a count of 2: addition of humidifier; decreased energy; napping; and feeling refreshed in the morning. The following barriers had a count of 2: dryness; inconvenience when traveling; and don't want to put CPAP back on after getting up during the night.

Table 1. Coding Summary. This table provide a count of the codes for both CPAP use facilitators and barriers. Each code was organized by category and sub-category.

Code	Count	Sub-Category	Category
FACILITATORS			
Comfortable mask	5	Motivators	Barriers and motivators of CPAP use
Improved energy	4	Beneficial Effects	Use of Both CPAP and Oxygen
Spouse support	4	Motivators	Barriers and motivators of CPAP use
Improved sleep	3	Beneficial Effects	Use of Both CPAP and Oxygen
Tracking CPAP	3	Motivators	Barriers and motivators of CPAP use
BARRIERS			
Uncomfortable mask	8	Barriers	Barriers and motivators of CPAP use
Insurance/cost	4	Barriers	Barriers and motivators of CPAP use

Interestingly, the role of the mask had a large impact for the participants as both a CPAP use barrier and facilitator. When participants described barriers or problems with therapy, they focused primarily on the mask, its poor fit and how uncomfortably it felt to wear. On the other hand, a comfortable mask was identified by other participants as the most important facilitator of CPAP therapy. Perceived benefit in the form of improved energy and improved sleep were other key facilitators. Having a supportive spouse or partner was another identified important facilitator. Several participants also found the tracking of their CPAP data via phone applications (*i.e.*, apps) to be an important facilitator as well. Other key barriers, beyond an uncomfortable mask, included: nasal dryness resulting from CPAP use and the cost of care maintaining a functioning CPAP device and related insurance issues. It is important to note regarding the most important issue of mask fit being comfortable or uncomfortable that this issue including some related aspects as well, including ability to breath with the mask on.

Another aspect coded, which might indicate poor mask fit and is also a cause of discomfort, is the perceived ability to breath with mask on. It is important to note that there is often an adjustment period using a CPAP mask that, regardless of mask fit, requires users to overcome an initial sensation of asphyxiation or perceived breathing cessation when using the mask. This may be true when a person is first diagnosed with OSA and becoming acquainted with CPAP therapy or may be true when an experienced user is transitioning to use a new or different style CPAP mask. All of our focus group participants were seasoned CPAP therapy users

Figure 1 shows the word cloud for the codes across the three focus groups. This word cloud included all coded items, including those from the discussion on the intervention format options.

Figure 1. Word cloud for the codes across the three focus groups.

Intervention Format. In terms of intervention format options, participants were overall enthusiastic about obtaining peer support, which in various ways they communicated as being perceived as a method that is more tailored and customizable to their individual circumstances as compared to members of their clinical care teams. They expressed the difficulty in obtaining the feedback that they needed within the clinical care system. The kind of feedback that they sought was related to general support and understanding for living day in and day out with the OSA and COPD and needing to use a treatment device on a nightly basis. While the clinical care team excelled in their technical expertise, peers were described as being more helpful with psychosocial support and empathy. The reader is referred to the bottom of online data supplement 2 for a full list of the codes related to the intervention. Of note, peer intervention (count = 7); social media channels (count = 6); and patient advocacy organizations (count = 5) were all listed as important sources of information about CPAP therapy.

Patient-Centered Outcomes. It was very clear from the transcripts that a disturbed night's sleep results in a less than optimal ability to function the following day, and for several folks, a very difficult time functioning the next day. Some used the expression of "*not being able to get out of bed*." Others used the phrase of "*not being to do the kinds of activities that I want to do*" and "*not having the energy I need during the day*." Many participants mentioned the need to take naps the following day to manage their fatigue, which cut into time available to do typical day-to-day activities. In total, 15 out of 17 expressed the importance of daytime functioning as the most important outcome of managing their OSA.

Patient perspectives. A qualitative analysis would not be complete without a summary of some of the patient's thoughts and comments pulled out in their entirety. Online data supplement 3 contains a list of quotes and comments from individual participants of the focus groups on a variety of issues.

Discussion

The three focus groups were designed to gain a better understanding of the use of medical devices (CPAP and supplemental oxygen therapy) in the treatment of COPD and OSA. Participants were clearly affected by both COPD and OSA and all were using the medical devices to some degree. However, the focus group discussions of these two main devices clearly indicate participants felt they had a very good handle on their use of oxygen therapy but were relatively unsatisfied by their experiences with CPAP therapy. And it is important to point out that the group of patients in our focus groups reported using CPAP regularly and having very good daytime functioning. The study team was surprised by the predominant focus of the discussions on CPAP therapy relative to oxygen therapy. This observation was also reflected in the participants' self-reported adherence for each therapy type, with 52% of the 17 participants using their CPAP device as prescribed and 75% of the eight oxygen users using their oxygen therapy as prescribed. However, this group of patients proved to be quite resilient

and adaptable as quite a few reported being able to adapt to CPAP therapy and derive a benefit after some personal trial and error. Even the most successful participants had stories to tell about their experiences, whether it be their perseverance in mask selection and comfort or negotiating with their insurance companies and/or durable medical equipment (DME) providers. While all new CPAP users have an adjustment period when starting to use therapy, what clearly distinguished this group of focus group participants was that none stopped using therapy, despite difficult times.

Feedback from the O_2VERLAP study's Stakeholder Advisory Board indicated that OS patients who are prescribed and use both medical device therapies (*i.e.*, supplemental oxygen therapy and CPAP therapy) may represent an overall less well group (*i.e.*, higher rates of comorbidities) and therefore comprise a relatively small percentage of potential participants in our larger study. We found, based on the three focus groups that were conducted, that not only do quite a few folks use both therapies, but that they are able to manage their COPD and OSA quite well. Several participants expressed their belief that they felt the best during the day if they used oxygen therapy at night in conjunction with CPAP therapy. Several participants who are not currently prescribed or using supplemental oxygen therapy mentioned that they feel they would benefit from a prescription and were motivated by our discussions to pursue this with their health care provider.

Resolve. The best word the study team could find to describe the spirit of what our focus group participants were communicating in the focus groups in balancing the CPAP facilitators and barriers was "*resolve*." Listening to the stories of patients who have managed their OSA and COPD for many years, what was heard was that the ones who managed their medical conditions most successfully had the resolve to: (1) use their medical device therapies regularly and (2) to troubleshoot problems and find solutions. One definition of resolve is a "*firm determination to do something*" and in this case, it is to manage sleep apnea on a regular basis and work through CPAP problems and issues so that daytime functioning is maximized. The level of resolve and determination exhibited by the participants in our focus group was remarkable.

Format of intervention. One of the themes that came through was that the participants felt that clinical staff are often limited in terms of the amount time that could be spent with patients, and that the use of other resources helped to fill this gap. Other resources included friends, family, community support, and social media support. To a person, folks were open to the type of intervention we were planning for the main study. Only two participants said that they would prefer to get all of their medical information from a physician or provider in the clinical care context. 16 out of 18 participants indicated that they would trust and rely on the type of intervention that we were planning. Importantly, several folks made the distinction of obtaining information from the "internet" vs. "patient advocacy non-profits" (they used phrases like, "from COPD Foundation" "or when I visit 360 [*short for COPD360SOCIAL*]." Of note, participants were not asked specifically to compare information sources they sought out, nor were they asked specifically about "non-profits," which we believe helps to provide more credence to this kind of finding from the focus groups.

Patient-centered outcomes. It was very clear that a disturbed night's sleep resulted in a less-than-optimal ability to function the following day in Overlap Syndrome patients, and for several folks, a very difficult time functioning the next day. Many participants mentioned the need to take naps the following day to manage their fatigue, which cut into time available to do typical day-to-day activities. The predominant theme expressed by the participants was a focus on next-day functioning. This finding helped inform the primary aims of the main O_2VERLAP study by increasing the importance of the measurement of daytime functioning.

Limitations. The focus group was reliant on identifying patients from each of the medical condition's patient advocacy organizations. It could be that individuals identified through these channels are somehow more motivated and able to take on challenges, given that they already were in some way associated with the organizations. Note, this statement is not meant to imply that the participants were active with the organizations; they were not. The study is also potentially limited by the sample size associated with each focus group type. It may be that had we run more focus groups with greater numbers that the findings would have been slightly different. That said, from quantitative studies of factors associated with CPAP use, mask fit and comfort tend to be one of the top factors found. This means that the findings of this study are consistent with the findings of patients with sleep apnea only.

Summary. The study has found that the most important outcome to Overlap Syndrome patients is daytime functioning. It has also identified both important CPAP facilitators and barriers as well as intervention formats important to, and preferred by, patients. In addition, what was clear from the groups were that effective use of CPAP was a key factor in next day functioning and was described by most as being more important than the use of oxygen therapy. All of these findings were incorporated into the main O_2VERLAP study. Importantly, the study team decided to primarily focus on CPAP therapy and changed the methods of the study to obtain and utilize CPAP adherence and efficacy data. The project was funded as part of the PCORI-funded PPRN Demonstration Project mechanism, and the study team is finding that the inclusion of patients and other relevant stakeholders at study outset can improve research process and quality.

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Appendix C. O_2VERLAP Study Promotion Efforts

Appendix 3: O_2VERLAP Study Promotion Efforts

As described in the Methods section, the O_2VERLAP Study relied almost entirely on electronic recruitment methods including emails, social media posts, electronic newsletters, web home page banners, and interactive platforms or forums, but also included some supplemental non-electronic methods (*i.e.*, in-person study promotional activities) including presenting at conferences, exhibiting at health fairs, and via word-of-mouth. The study promotion methods used the following definitions: *Community*: a group of people with some defining or common characteristic. *Audience*: a defined subgroup of community. *Method*: a specific type of communication (*i.e.*, email, social media post, etc.). Based on these definitions, a campaign was therefore comprised of sending a message via a defined method to a defined audience ("campaign = audience + method"). The table below provides an extensive list of the study promotional efforts and provides the community, audience name, method, number of contacts, and audience size over the duration of the project, which was from February 2018 to July 2019. Eighteen of the 46 campaigns were deployed multiple times over the 18-month recruitment period.

Table 1: Summary of O_2VERLAP Study Promotion

Community	Campaign		# Contacts*	Audience Size**
	Audience	Method		
COPD	COPD-PPRN emails	Emails	1	858
	COPDF Facebook	Social media	N/A	199,519
	Alpha-1 Registry	Emails & Letters	2	5,161
	COPD-PPRN Newsletter	e-Newsletter	3	6,700
	PELICAN Study	Email & Phone call	1	158
	Faces of COPD Newsletter	e-Newsletter	3	40,000
	OVERLAP survey	Phone call	1	47
	COPDF Homepage Banner	Landing page	N/A	147,000
	State Captains	Word of mouth	6	120
	COPD Twitter	Social media	1	17,000
	COPD 360Social	Social media	3	43,407

	COPD Praxis Buzz Newsletter	e-Newsletter	4	14,000
OSA	ASAA Emails	Emails	4	21,169
	ASAA Newsletter	e-Newsletter	2	---
	ASAA Facebook	Social media	N/A	93,070
	ASAA Homepage	Landing page	N/A	118,838
	SleepHealth Mobile emails	Emails	3	9,409
	SleepHealth Mobile Blog post	Social media	1	9,409
	ASAA Forum	Social media	4	1,400
	ASAA Twitter	Social media	2	5.524
	ASAA YouTube	Social media	1	12,000
	CAP Program	Bookmarks	1	2,237
PCORnet	pSCANNER (UCSD Health)	Emails & Letters	2	24,008
	pSCANNER (UCI Health)	Emails	1	284
	PRIDEnet	Emails	1	506
	PRIDEnet Facebook	Social media	1	8,376
	PRIDEnet Twitter	Social media	1	1,862
	Health e Heart Facebook	Social media	1	5,349
	Health e Heart Twitter	Social media	1	2,319
	PI Connect emails	Emails	1	180
	PI Connect Facebook	Social media	1	17,618
	PI Connect Twitter	Social media	1	3,097
Miscellaneous	Web browsing	Web browsing	N/A	---
	Word of mouth	Word of mouth	N/A	---
	ResearchMatch	Emails	2	1,062
	The Pulmonary Paper	Hardcopy paper	3	35,000
	Friends 4 friends	Social media	2	886
	11 private Facebook Groups	Social media	1	30,441

	AARC	Social media & Flyers	4	61,248
	AWAKE Coordinators	Emails	1	437
	SecondWind	Forum	1	20,000
	RTSleepWorld	Social media	1	2,953
	SleepyHead	Social media	1	21,106
	CPAPTalk	Forum	3	345
	Conferences	Poster & Flyers	2	---
	Other Facebook Groups	Social media	1	---

Note: See the Acronym List for explanation of acronyms used in this table.
*# contacts refer to the number of times that the audience was reached via the defined method.
**Audience size may be a count or an estimate.

Recruitment Campaign Details

For both email text and social media posts, all variations of our study promotion text messages were IRB-approved. Our study team realized during the project that the type of messaging was important, and that with more effective messaging, the yield of the campaigns could be improved. Our first messages were quite general and directed to patients with COPD and/or OSA. In one of our discussions, Madelaine Faulkner of Health eHeart Alliance suggested that we revise the message to broaden its scope. She called it the "Friends and Family" message. This message was also directed to patients with COPD and/or OSA, but this time extra wording was provided asking them to forward the message to anyone else that they may know who would be eligible or interested in learning more about the study. Our third message type was used in the last month of the recruitment period to inform potential participants that the end of the study will be July 31^{st,} 2019 in case anyone was "on the fence" regarding the study and that perhaps knowing the deadline would motivate them to sign up.

The # Contacts column in Table 1 represents the number of times that an audience was messaged. Email campaigns like PPRN, UCSD, ASAA sent an additional condensed message we called "Reminder email" 3 to 5 days after the initial email to remind potential participants of the original study announcement. The reminder email was not counted as a contact attempt. Email campaigns like UCSD and ASAA sent 2 to 4 email communications at various times in our 18-month recruitment period using the three different mentioned message variations. Reminder emails were sent 2 to 3 days after the primary email.

Social media campaigns, like COPD Foundation Facebook and ASAA Facebook campaigns, posted new or boosted existing posts on their Facebook pages many times during the 18-month recruitment period. The COPD Foundation posted study promotion announcements a total of seven times and the ASAA posted eleven times on their community's Facebook page. Using Facebook analytics, we were able to find that the seven COPD Foundation posts, in total had 24,000 unique views and the eleven ASAA Facebook posts had a total of 93,070 unique views. A similar abbreviated text of the different message variations where also IRB approved and used in all our social media posts.

We also wanted to note that we asked a past O_2VERLAP Study participant to write a comment about her participation in the study on COPD Foundation's Facebook. She posted, "*I did the study and learned so much about how to deal with the CPAP. The modules were easy, and the people were friendly, and I didn't even have to leave the house. Everything was by phone and online in my own time. It was great and I helped the cause*." It was good to see a past participant who had a good experience add a positive post about our study for others to read. In the future, this might be a method that other study teams consider asking of their past participants – the personal sharing of experiences could be a good way to help generate interest in research.

In addition, Newsletters and articles were circulated from organizations like COPD Foundation, ASAA, and the Pulmonary Paper with an O_2VERLAP study recruitment announcement. The study deadline date was also added to the O_2VERLAP study landing page so that other interested people could see that time to enroll was running out.

Appendix D. Remote CPAP Adherence Monitoring Setup Process and Data Integrity Check

Appendix 4: Remote CPAP Adherence Monitoring Setup Process and Data Integrity Check

Continuous positive airway pressure (CPAP) therapy data was an important component of the O2VERLAP study. It was used both for interventional and data analytic purposes. The data was provided via the study platform to both study participants and intervention coaches to help carry out the study intervention. CPAP adherence was considered the primary study outcome, and therefore was also used for data analytic purposes. This appendix provides details about how this data was obtained and used.

Participants were asked to provide the study team with the following CPAP information: serial number, brand, model, and HME provider. This information was necessary to coordinate access to the participant's remote adherence monitoring data collected wirelessly via their CPAP device modem. All study participants were required to have a ResMed or Philips Respironics brand CPAP device, with wireless modem, for this reason. Both ResMed and Philips Respironics have online systems for their CPAP device users (AirView and EncoreAnywhere, respectively). Home medical equipment (HME) companies and healthcare providers use these systems to log into as necessary for remote data collection, analysis and review. These two companies offer separate patient-specific apps, but they differ in a number of important ways so were not used for the current study. Instead, the study team created a patient-facing website specific for our participants.

The study team then coordinated with the participant's HME company to ensure that their online data profile was appropriately shared. This process included submitting a fax packet comprised of: (a) cover letter; (b) participant's study consent and HIPAA forms; and (c) detailed instructions on sharing either on AirView (ResMed) or EncoreAnywhere (Philips Respironics) data platform. The instructions document included a step-by-step guide to the HME for correctly adding the O_2VERLAP Study as an integration partner and the study's physician in the Physicians tab on 'Patient Details' of the participants profile. As such, both ResMed and Philips Respironics agreed to participate in the development of this study process and provided the following data variables via an 'Application Programming Interface' (API) workflow.

Data flowed from the ResMed AirView or Philips Respironics Encore Anywhere online systems to the necessary API's, and were managed by Corepoint Health Inc (Frisco, TX). Corepoint is an intermediary software company contracted to provide data integration services and provide middleware between the CPAP manufacturer servers and the O_2VERLAP Study portal. Corepoint Health then sent a password-protected excel spreadsheet with a download of the CPAP data linked to each participant's serial

number for importing in the O_2VERLAP Study portal (DatStat, Inc. Seattle, WA). The specified variables were represented graphically, on a bi-weekly basis, in the study portal charts for each participant in their record. Figure 1 shows a diagram of the data flow.

Figure 1: Diagram of CPAP data flow in the O_2VERLAP Study.

Data workflow integration was established such that data calls were made two times each week (Monday and Wednesday) to populate the O_2VERLAP Study portal. The CPAP data was included in the study to be used by both participants and interventionists to monitor progress and intervene as necessary.

Bi-weekly Updates on Critical Adherence Monitoring Data Variables:

1) Total Time Connected (*i.e.*, total time in minutes CPAP was used each 24-hour day)
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 and hypopneas that occur while wearing CPAP).

These three variables are critical, quantitative indications of the use and efficacy of CPAP therapy. Monitoring these CPAP therapy variables helped both the research participants and authorized research staff to tailor a participant's goal setting on a weekly basis, acknowledge progress, and troubleshoot any problems or difficulties. The participants randomized to the proactive care arm reviewed and discuss their data on a weekly basis with a peer coach to address these topics. Proactive care participants were also encouraged to call their peer coaches during regular business hours via the C.O.P.D. Information Line and were also encouraged to chat synchronously or asynchronously with peer coaches using the study portal.

CPAP Data Integrity Check. In order to ensure an accurate CPAP adherence dataset, our research team engaged in a doublecheck of each CPAP data value. Data at the source (the manufacturer online platforms) was compared to the data on our study platform. Early on we found that some data on our study platform was set to missing when in fact it should have been CPAP adherence = 0 hours per night. This is what originally prompted the data check. Over time, we ensured that our final data set reflected

true 0 adherence values and true missing values. In addition, because the implementation of middleware, we found that some nights had valid non-0 data but because of timing issues was not being obtained. Some duplicate nights were also found. Neither the duplicate nights nor the number of nights that were not coming through were enough to impact the intervention (*i.e.*, only affected 1-2 nights per week for some participants; trend data was still relatively easy to see). To summarize, all valid data (missing, 0, and non-0) from the source that was not consistent with the data on our study platform corrected. We had three staff members working on this data integrity check, including a check of each other. In doing this, we ensured that we ended up with a complete and accurate final dataset. Given the novel findings of the very high CPAP use levels found in this study, we are confident in our conclusions because of these extensive CPAP data quality assurance efforts.

Appendix E. Google Analytics for Trackable URLs for Each Study Promotion Campaign

Appendix 5: Google Analytics for Trackable URLs for Each Study Promotion Campaign

Community	**Audience**	**Unique Referral Link** (Short name)	**Sessions** [a]	**Pages / Session**[b]	**Average Session Duration** (sec)[c]
COPD	COPD PPRN	COPDPPRNEmail1	12	5.17	562.75
		COPDPPRNEmail2	24	6.92	670.21
		COPDPPRNEmail3	15	5.27	572.47
		COPDPPRNA	13	8.77	797.15
		COPDPPRNB	13	5.62	416.69
		COPDPPRNC	14	3.50	362.14
		COPDPPRND	7	4.57	268.00
		COPDPPRNE	6	2.83	113.00
		COPDPPRNF	14	3.86	445.00
		COPDPPRNH	72	4.00	370.56
		COPDPPRNI	9	2.56	429.00
		COPDPPRNJ	13	5.23	719.38
		COPDPPRNK	52	2.5	319.00
		COPDPPRNM	8	5	239.00
	COPD Facebook	COPDFFacebook1	2035*	1.18	48.11
		COPDFFacebook2	--	--	--
		COPDFFacebook4	173	1.36	75.92
		COPDFFacebook5	937	1.13	40.56
		COPDFFacebook6	354	1.38	68.00
	Alpha-1 Registry	Misc13	34	3.18	242.50
		Misc19	42	2.76	510.21
	COPD PPRN Newsletter	COPDPPRNG	166	3.53	365.23
		COPDPPRNL	65	2.08	220.00

	PELICAN Study	InfoLineEmail3	12	4.58	701.92
	Faces of COPD	Misc29	115	1.74	149.37
	State Captains	O2VERLAPMisc10	63	1.41	74.06
		Misc26	2	1.00	0.00
	COPD 360Social	COPD360Social1	12	1.58	868.83
	COPD Praxis Buzz	O2VERLAPMisc8	29	1.48	580.00
		Misc40	--	--	--
	COPD Twitter	COPDFTwitter1	--	--	--
		COPDFTwitter2	7	1.14	29.00
OSA	ASAA Emails	ASAAFacebook11	1	2.00	8.00
		O2VERLAPMisc4	--	--	--
		Misc22	261	2.03	239.23
		Misc35	274	2.2	245.00
	ASAA Newsletter	Misc23	--	--	--
	ASAA Facebook	ASAAFacebook1	1032	1.32	52.37
		ASAAFacebook2	13193*	1.12	31.90
		ASAAFacebook3	1	1.00	0.00
		ASAAFacebook4	141	1.3	81.00
		ASAAFacebook5	35	1.46	69.00
	ASAA Homepage banner	Misc42	90	1.21	92.00
	SleepHealth Mobile Emails	O2VERLAPMisc5	112	2.33	115.77
		Misc21	114	1.76	101.17
		Misc36	14	1.5	64.00
	ASAA Forum	Misc20	72	1.08	127.18
	ASAA Twitter	ASAATwitter1	12	1.00	5.67
		ASAATwitter2	2	1.00	0.00
		ASAATwitter3	62	1.15	237.19

		ASAATwitter4	8	1.38	172.13
	ASAA Webinar	Misc11	6	1.50	39.17
	ASAA YouTube	Misc18	1	1.00	0.00
PCORnet	pSCANNER (UCSD Health)	Misc12	137	2.68	344.59
		Misc28	57	2.91	613.46
		Misc34	200	2.11	408.00
		Misc38	669	2.19	221.00
	pSCANNER (UCI Health)	Misc41	46	2.02	196.00
	PRIDEnet Emails	PRIDEnet1	55	1.80	149.98
	PRIDEnet Facebook	PRIDEnet2	4	1.75	105.00
	PRIDEnet Twitter	PRIDEnet3	2	2	20.00
	Health e Heart Facebook	HeH1	24	1.13	19.88
		HeH2	1	1	0.00
		HeH4	5	1.00	0.00
	Health e Heart Twitter	HeH5	1	1	107.00
	PI Connect	Misc27	44	1.52	64.07
Misc.	ResearchMatch	Misc14	27	3.52	290.63
		Misc33	28	2.82	483.00
	Friends 4 friends	COPDFFacebook3	72	1.43	102.81
	AARC	O2VERLAPMisc3	35	1.11	93.23
		O2VERLAPMisc7	62	1.35	131.03
		AARC	2	4.50	1092.50
	SecondWind	O2VERLAPMisc9	--	--	--
		Misc30	--	--	--
		Misc31	1	1.00	78.00
	RTsleepworld	Misc24	--	--	--
		Misc25	--	--	--
		O2VERLAPMisc2	2	1.00	0.00

	NYU Pride Diversity Prog.	Misc32	1	2	54.00
	SleepyHead	Misc39	11	1	13.00
	Heart Community	Misc45	1	2	18.00
	PeP & Pulmonary Rehab	Misc17	56	1.16	94.23
	Villages	O2VERLAPMisc1	--	--	--
	Governing Board	O2VERLAPMisc6	48	1.38	71.25
	CPAPTalk	CPAPTalk1	43	1.33	77.00
	Conferences	Conference1	6	3.50	205.67
		Conference10	1	2.00	1627.00
	University of Arizona	Misc15	2	1.50	8.50
	Theresa Shumard Contacts	Misc44	3	1	108.00

Note: See the Acronym List for explanation of acronyms used in this table.

[a]*Sessions* = Total number of Sessions within the date range. A session is the period time a user is actively engaged with your website, app, etc. All usage data (Screen Views, Events, Ecommerce, etc.) is associated with a session.

[b]*Pages/Session* = Pages/Session (Average Page Depth) is the average number of pages viewed during a session. Repeated views of a single page are counted

[c]*Average Session Duration (sec)* = The average length of a Session in seconds.

*Boosted (i.e., study team paid for additional posts).

Appendix 6: Geographic Distribution

The first table shows the study enrollment status in January 2019 when the Midwest and West were enrolling at approximately the same rate (0.000073% and 0.000072%, respectively; % calculated as number enrolled/population per U.S. Census data), while the South and Northeast were slightly lower (0.000047% and 0.000046%, respectively). At this point in time the study had enrolled nearly 200 of the 332 total enrolled participants and needed to find new audiences. The decision was made to move forward in earnest with our CDRN partner (pSCANNER) who had a large presence in the West. Because of time (*i.e.*, for IRB approval) and practical consideration (willingness of each of the sites that comprised pSCANNER), the decision was made to approach the 5 University of California healthcare systems: UCLA, UCSD, UCSF, UC Irvine, and UC Davis. UC Davis had a policy of not allowing direct email of its patients. UCSF did not have the personnel bandwidth to assist on the project. UCLA only allowed patient messaging via the EMR, and discouraged their participation given their difficulties in recruitment for the PCORI-funded ADAPTABLE study. This left UCSD and UC Irvine who both allowed direct email communications with their patients.

Table 1: Geographic Distribution on 11th Month of Enrollment (January 2019)

Region	Division		Enrolled	Population	%
Northeast	1	New England (CT, ME, MA, NH, RI, VT)	10	14,862,429	0.000067 %
	2	Mid-Atlantic (NJ, NY, PA)	16	41,719,313	0.000038 %
		Subtotal:	**26**	**56,581,802**	**0.000046 %**
Midwest	3	East North Central (IL, IN, MI, OH, WI)	33	46,971,839	0.000070 %
	4	West North Central (IA, KS, MN, MO, NE, ND, SD)	17	21,408,695	0.000079 %
		Subtotal:	**50**	**68,380,534**	**0.000073 %**
South	5	South Atlantic (DE, FL, GA, MD, NC, SC, VA, DC, WV)	33	65,419,541	0.000050 %
	6	East South Central (AL, KY, MS, TN)	11	19,126,563	0.000058 %
	7	West South Central (AR, LA, OK, TX)	15	40,347,687	0.000037 %
		Subtotal	**59**	**124,893,791**	**0.000047 %**
West	8	Mountain (AZ, CO, ID, MT, NV, NM, UT, WY)	19	24,504,888	0.000078 %
	9	Pacific (AK, CA, HI, OR, WA)	37	53,671,406	0.000069 %
		Subtotal:	**56**	**78,176,294**	**0.000072 %**
		Total:	**191**	**328,032,421**	**0.000058 %**

Note: Each abbreviation refers to a State.

Table 2: Geographic Distribution on 18th Month, End of Enrollment (July 2019)

Region	Division		Enrolled	Population	%
Northeast	1	New England	15	14,862,429	0.000101%
	2	Mid-Atlantic	28	41,719,313	0.000067%
		Subtotal:	**43**	**56,581,802**	**0.000076%**
Midwest	3	East North Central	47	46,971,839	0.000100%
	4	West North Central	26	21,408,695	0.000121%
		Subtotal:	**73**	**68,380,534**	**0.000107%**
South	5	South Atlantic	51	65,419,541	0.000078%
	6	East South Central	15	19,126,563	0.000078%
	7	West South Central	26	40,347,687	0.000064%
		Subtotal	**92**	**124,893,791**	**0.000074%**
West	8	Mountain	29	24,504,888	0.000118%
	9	Pacific	92	53,671,406	0.000171%
		Subtotal:	**121**	**78,176,294**	**0.000155%**
		U.S. Total:	**329***	**328,032,421**	**0.000101%**

*Notes: Study Total = 332 based on U.S. (n=329) +Canada (n=3). Each abbreviation refers to a State.

Table 3: O_2VERLAP Study Enrollment by State

State	Count	State	Count	State	Count	State	Count	State	Count
AL	2	HI	2	ME	0	NJ	5	SD	1
AK	1	ID	4	MI	19	NM	3	TN	7
AZ	6	IL	9	MN	8	NV	3	TX	14
AR	3	IN	6	MO	10	NY	12	UT	4
CA	76	IA	5	MS	2	OH	8	VA	6
CO	4	KS	0	MT	2	OK	4	VT	0
CT	2	KY	4	NC	4	OR	7	WA	6
DE	0	LA	5	ND	0	PA	11	WI	5
FL	23	MA	12	NE	2	RI	0	WV	1
GA	5	MD	9	NH	1	SC	3	WY	3

Note: Study Total = 332 based on U.S. (n=329) + Canada (n=3). Each abbreviation refers to a State.

Appendix F. Geographic Distribution

The first table shows the study enrollment status in January 2019 when the Midwest and West were enrolling at approximately the same rate (0.000073% and 0.000072%, respectively; % calculated as number enrolled/population per U.S. Census data), while the South and Northeast were slightly lower (0.000047% and 0.000046%, respectively). At this point in time the study had enrolled nearly 200 of the 332 total enrolled participants and needed to find new audiences. The decision was made to move forward in earnest with our CDRN partner (pSCANNER) who had a large presence in the West. Because of time (*i.e.*, for IRB approval) and practical consideration (willingness of each of the sites that comprised pSCANNER), the decision was made to approach the 5 University of California healthcare systems: UCLA, UCSD, UCSF, UC Irvine, and UC Davis. UC Davis had a policy of not allowing direct email of its patients. UCSF did not have the personnel bandwidth to assist on the project. UCLA only allowed patient messaging via the EMR, and discouraged their participation given their difficulties in recruitment for the PCORI-funded ADAPTABLE study. This left UCSD and UC Irvine who both allowed direct email communications with their patients.

Table 1: Geographic Distribution on 11th Month of Enrollment (January 2019)

Region	Division		Enrolled	Population	%
Northeast	1	New England (CT, ME, MA, NH, RI, VT)	10	14,862,429	0.000067 %
	2	Mid-Atlantic (NJ, NY, PA)	16	41,719,313	0.000038 %
		Subtotal:	**26**	**56,581,802**	**0.000046 %**
Midwest	3	East North Central (IL, IN, MI, OH, WI)	33	46,971,839	0.000070 %
	4	West North Central (IA, KS, MN, MO, NE, ND, SD)	17	21,408,695	0.000079 %
		Subtotal:	**50**	**68,380,534**	**0.000073 %**
South	5	South Atlantic (DE, FL, GA, MD, NC, SC, VA, DC, WV)	33	65,419,541	0.000050 %
	6	East South Central (AL, KY, MS, TN)	11	19,126,563	0.000058 %
	7	West South Central (AR, LA, OK, TX)	15	40,347,687	0.000037 %
		Subtotal	**59**	**124,893,791**	**0.000047 %**
West	8	Mountain (AZ, CO, ID, MT, NV, NM, UT, WY)	19	24,504,888	0.000078 %
	9	Pacific (AK, CA, HI, OR, WA)	37	53,671,406	0.000069 %
		Subtotal:	**56**	**78,176,294**	**0.000072 %**
		Total:	**191**	**328,032,421**	**0.000058 %**

Note: Each abbreviation refers to a State.

Table 2: Geographic Distribution on 18th Month, End of Enrollment (July 2019)

Region	Division		Enrolled	Population	%
Northeast	1	New England	15	14,862,429	0.000101%
	2	Mid-Atlantic	28	41,719,313	0.000067%
		Subtotal:	**43**	**56,581,802**	**0.000076%**
Midwest	3	East North Central	47	46,971,839	0.000100%
	4	West North Central	26	21,408,695	0.000121%
		Subtotal:	**73**	**68,380,534**	**0.000107%**
South	5	South Atlantic	51	65,419,541	0.000078%
	6	East South Central	15	19,126,563	0.000078%
	7	West South Central	26	40,347,687	0.000064%
		Subtotal	**92**	**124,893,791**	**0.000074%**
West	8	Mountain	29	24,504,888	0.000118%
	9	Pacific	92	53,671,406	0.000171%
		Subtotal:	**121**	**78,176,294**	**0.000155%**
		U.S. Total:	**329***	**328,032,421**	**0.000101%**

*Notes: Study Total = 332 based on U.S. (n=329) +Canada (n=3). Each abbreviation refers to a State.

Table 3: O_2VERLAP Study Enrollment by State

State	Count	State	Count	State	Count	State	Count	State	Count
AL	2	HI	2	ME	0	NJ	5	SD	1
AK	1	ID	4	MI	19	NM	3	TN	7
AZ	6	IL	9	MN	8	NV	3	TX	14
AR	3	IN	6	MO	10	NY	12	UT	4
CA	76	IA	5	MS	2	OH	8	VA	6
CO	4	KS	0	MT	2	OK	4	VT	0
CT	2	KY	4	NC	4	OR	7	WA	6
DE	0	LA	5	ND	0	PA	11	WI	5
FL	23	MA	12	NE	2	RI	0	WV	1
GA	5	MD	9	NH	1	SC	3	WY	3

Note: Study Total = 332 based on U.S. (n=329) + Canada (n=3). Each abbreviation refers to a State.

Appendix G. Abbreviations/Acronyms

ASAA	American Sleep Apnea Association
CAT	COPD Assessment Test
CDRN	Clinical data research network
CoE	Confirmation of Eligibility
COPD	Chronic obstructive pulmonary disease
COPDF	Chronic Obstructive Pulmonary Disease Foundation
CPAP	Continuous positive airway pressure therapy
DFRR	Draft Final Research Report
ESS	Epworth Sleepiness Scale
FB	Facebook
FOSQ	Functional Outcomes of Sleep Questionnaire
FCI	Functional Comorbidity Index
OSA	Obstructive sleep apnea
OS	Overlap syndrome
PELICAN	PEer-Led o2 Info-line for patients and CAregivers (COPDF research study)
PCORI	Patient-Centered Outcomes Research Institute
PCORnet	National Patient-Centered Outcomes Network
PPRN	Patient-powered research network
PROMIS	Patient-Reported Outcomes Measurement Information System
PC	Proactive Care Group
pSCANNER	Patient-Centered Scalable National Network for Effectiveness Research
PSQI	Pittsburgh Sleep Quality Index
RC	Reactive Care Group
SAB	Stakeholder Advisory Board
TSP	total sleep period
Tw	Twitter
UC	University of California
UCI	University of California, Irvine
UCLA	University of California, Los Angeles
UCSD	University of California, San Diego
UCSF	University of California, San Francisco
VHA	Veterans Health Administration

Disclaimer:

The [views, statements, opinions] presented in this report are solely the responsibility of the author(s) and do not necessarily represent the views of the Patient-Centered Outcomes Research Institute® (PCORI®), its Board of Governors or Methodology Committee.

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