Physical Activity After COPD Exacerbations

BY

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THESIS

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LIST OF ABBREVIATIONS

CMS	Centers for Medicare and Medicaid Services
COPD	Chronic obstructive pulmonary disease
IQR	Interquartile range
IRB	Institutional Review Board
ISWT	Incremental shuttle walk test
PROMIS	Patient-Reported Outcomes Measurement Information System
SD	Standard deviation
US	United States

SUMMARY

A 12-week prospective cohort study involving patients with chronic obstructive pulmonary disease (COPD) recently discharged from the hospital was conducted to evaluate the feasibility of implementation of a physical activity promotion program, identify barriers and facilitators to implementation, and estimate time-related changes in physical activity and patient-reported outcomes.

Several barriers to recruitment and retention were identified following initiation of the study. The goal of the implemented study modifications were to establish a more inclusive eligibility criteria and decrease in study burden, particularly reducing the number of outpatient visits, and adding flexibility to the timing and setting of the baseline study visit. Target recruitment was reached following these protocol modifications.

The Incremental Shuttle Walk Test was found not to be a feasible outcome in future clinical studies involving patients with COPD following hospital discharge. However, daily step counts were found to be a feasible and suitable surrogate for it. There was high correlation between daily step counts in any week with adjacent weeks, indicating limited within-person variability in daily physical activity over the course of the study. Patient reported outcomes with variability over time due to factors not accounted for in the study are unlikely to be suitable outcomes for future clinical studies in this population.

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I. INTRODUCTION

A. Background

Chronic Obstructive Pulmonary Disease (COPD) affects at least 15 million adults in the United States (US) and is responsible for 750,000 hospitalizations each year.¹ As approximately 20% of patients hospitalized for a COPD exacerbation are rehospitalized within 30 days of discharge, the Centers for Medicare and Medicaid Services (CMS) has implemented financial penalties for hospitals with higher than expected risk-standardized rehospitalizations.^{2,3} However, recent studies indicate that the high risk of poor outcomes in patients with COPD recently discharged extend well beyond the initial 30 days, with an estimated 12-month readmission rate of 64%.⁴ Although there is clear evidence that pulmonary rehabilitation after hospital discharge improves outcomes in patients with COPD, including rehospitalizations, its impact is limited due to poor reach and adoption.^{5,6} It is estimated that less than 10% of eligible patients start the program after hospital discharge and that a significant proportion of those do not complete it ^{6,7} There are multiple reasons for this poor attendance, but limited availability of programs, as well as transportation and financial difficulties have been identified as common barriers in multiple studies.^{8,9} In response to these barriers, in recent years there has been significant interest in home-based pulmonary rehabilitation. Physical activity promotion programs have been implemented in patients with stable COPD with benefits comparable to that of traditional outpatient pulmonary rehabilitation.¹⁰⁻¹² However, few programs to date have evaluated the efficacy such a program in patients recently discharged from the hospital belonging to an ethnically underrepresented backgrounds.¹³

B. Study objectives

In anticipation to implementing a program specific to the needs of patients recently discharged from the hospital at an urban minority-serving institution, we sought to understand the baseline levels of functional capacity and daily physical activity in this population. The study's objectives were to:

- a) Evaluate the feasibility and fidelity of implementation of the study procedures.
- b) Identify barriers and facilitators to the implementation of the study procedures to guide the development of the home-based physical activity promotion program.
- c) Estimate the time-related changes in functional capacity, objectively measured physical activity parameters, and patient-generated outcomes in a cohort of patients recovering from COPD exacerbations following hospital discharge.

II. METHODS

A. Study design

This 12-week prospective cohort study involved patients with COPD hospitalized or recently discharged from the hospital for respiratory symptoms (Table I). The initial study design required patients to attend 5 in-person outpatient study visits (eligibility/baseline visit, followed by visits on weeks 1, 2, 4 and 12; Figure 1, panel A). During each outpatient visit, participants answered questionnaires regarding their physical, mental and social health (Patient-Reported Outcomes Measurement Information System, PROMIS) and their healthcare utilization, and performed an Incremental Shuttle Walk Test (ISWT) to assess their functional capacity. The eligibility/baseline and follow-up visits, participants were asked to carry pedometers for daily physical activity monitoring. To reduce participant burden, outpatient visits were scheduled around the time of clinical appointments and participants received monetary compensation. The study was approved by the University of Illinois at Chicago Institutional Review Board (IRB# 2015-0989).

ST	UDY DESIGN
Design	Prospective cohort study
Planned number of sites and patients	Total enrollment of 50 participants at 1site
Planned recruitment period	1 year
Follow-up	3 months
Endpoints	Primary: ISWT
	Secondary: mean daily step counts, PROMIS
	depression, anxiety, fatigue, physical function,
	satisfaction with social roles and activities, ability
	to participate in social roles and activities

TABLE I



FIGURE 1. PACE study schema. A. Original study design, B. Study design following protocol modifications

B. Participant population

The inclusion and exclusion criteria were designed to recruit patients with a recent COPD hospitalization who received their outpatient are at the University of Illinois at Chicago and were unable to attend pulmonary rehabilitation (Table II). Additional eligibility criteria included airflow obstruction by spirometry, inability to attend pulmonary rehabilitation and no medical contraindications to participation, as determined by the patient's physician.

TABLE II ORIGINAL ELIGIBILITY CRITERIA AND PROTOCOL CHANGES INITIATED TO IMPROVE PATIENT RECRUITMENT.

Original criteria	Protocol amendments to improve patient recruitment		
Inclusion oritoria			
- Physician diagnosis of COPD	- Physician diagnosis of COPD		
- Hospitalized for COPD exacerbation	- Hospitalized for respiratory symptoms		
- ≤4 weeks since hospital discharge	- \leq 3 months since hospital discharge		
- Airflow obstruction by spirometry*	- Criterion deleted		

Exclusion criteria

- Medical contraindication as determined by	
the treating clinician	
- Resting SpO2 <90% refractory to	
supplementalO2 (or in a patient	
unable/unwilling to use supplemental O2)	
- Physical inability to participate in a walking	
program	
- Moderate or severe cognitive impairment	
- Resting electrocardiogram with new ST	
changes, tachyarrythmia, bradycardia or	- QTc prolongation criterion deleted
prolonged QTc interval	
- Enrollment in pulmonary rehabilitation	- Criterion deleted
- Enforment in pullionary reliabilitation	
- Unable to communicate in English	
- Declines to provide informed consent	

During the study we implemented protocol amendments to modify the eligibility criteria. The goal of these modifications was to increase the reach of the study and allow participation to additional patients who may eventually benefit from the intervention.

C. <u>Recruitment and retention process measures</u>

Electronic medical records were screened to identify patients with COPD admitted to University of Illinois Hospital, a 465-bed academic medical center and minority-serving institution located in Chicago, Illinois, and patients attending the outpatient clinics who had been recently hospitalized. Following assent from the treating clinicians, patients who met the eligibility criteria (Table II) were approached in their hospital or clinic rooms for enrollment. If participants were approached in the outpatient setting, the baseline visit was completed immediately following the clinical visit. If participants were initially approached and provided informed consent while hospitalized, demographic information and clinical history was collected, but other study activities were deferred until the patient was discharged from the hospital.

During the recruitment period, barriers to recruitment and retention were investigated by means of quantitative and qualitative data collection. We calculated rates of recruitment (percent of screened participants who consented to participate in the study), retention (percent of consented participants who completed the study), study visit completion (percent of consented participants who completed each study visit), outcome data collection (percent of participants with available data for each outcome) to inform decisions regarding protocol modifications. Qualitative data included the reasons for ineligibility and for declining to participate as they were documented in the study forms.

D. Analysis

We employed descriptive statistics and calculated the pre-specified process measures before and after implementing each protocol modification. Daily physical activity was analyzed as the mean daily step count over 7 days. The list of reasons why participants declined to participate was coded thematically by an investigator who reviewed the compiled raw data and coded the responded using an adaptation of grounded theory analysis. Pearson's correlations were used to calculate associations within each outcome measure over time. Wilcoxon rank sum tests were used to compare differences in mean daily physical activity according to participant healthcare utilization and baseline functional capacity. Wilcoxon signed rank tests were used to compared time-related changes in patient-reported outcomes.

III. RESULTS

A. Participant recruitment and retention

The recruitment period was planned for 1 year. Over the first 6 months of recruitment, 81 hospitalized and 13 recently discharged patients were screened; 54 (57% of 94) were approached for enrollment, 44 (87% of 54) were considered eligible for informed consent, and 29 (66% of 44) provided informed consent. However, only 8 (28% of 29) remained in the study after completing the baseline visit (Figure 2). The reasons for exclusion after obtaining clinician assent to approach participants were varied and included no diagnosis of COPD or a COPD exacerbation on subsequent evaluation by their provider, medical contraindications to participation (e.g., electrocardiogram abnormalities), care discontinuity e.g., patients not attending follow-up outpatient appointments) and new enrollment in pulmonary rehabilitation following hospital discharge. At this point, declining to participate remained a relatively minor reasons for non-participation (26% of approached patients).

B. Measures to improve recruitment and retention

A variety of modifications were implemented over the course of the study to enhance patient recruitment and to make recruitment more inclusive. As detailed in Table II, several inclusion and exclusion criteria were revised by protocol amendment to make them more reflective of the hospitalized patients with COPD and extended the eligibility window after hospital discharge to three months. Participants planning to attend or continue pulmonary rehabilitation after their hospitalization were also permitted to participate as previous studies have found that



a- 1 participant who completed the baseline visit at a time not included in this graph

b- 1 participant who was active after the baseline visit not included in this graph as the participant completed the baseline visit at a time not included in this graph

FIGURE 2. PACE study recruitment vs. time

a significant proportion of patients who start pulmonary rehabilitation do not complete the program.⁶ To decrease participant burden, the number of study visits was decreased from 5 to 3 (Figure 1, panel B) and transportation to and from study visits was arranged on request using a ride-sharing service. Last, we allowed participants to complete the baseline study visit independently from their post-discharge clinical visit. As a safety precaution, participants who completed the baseline visit as a dedicated study visit (i.e., not immediately after a clinical encounter) met and were examined by a member of the research staff with a clinical background (Medical Doctor or Advance Practice Nurse) to ensure that no changes in clinical condition had occurred since hospital discharge. QTc interval prolongation on electrocardiogram was removed as an exclusion criterion as it is not an exclusion criterion for pulmonary rehabilitation and albuterol, first-line therapy for COPD, can prolong the QTc interval.^{14,15} Participants who would have been eligible after the protocol modifications were invited to re-consent and attend a new baseline visit if they were still within the eligibility window.

C. Study performance after protocol modifications

Recruitment continued for an additional 4 months following implementation of the modifications described above. Although an improvement in consent rates were seen after implementation of the modifications, given the time lag between informed consent (performed while hospitalized) and the baseline visit after hospital discharge, the increase in number of participants completing the baseline visit was not observed for several weeks (Figure 2). Given the decreased participant burden, the rate of consented patients attended baseline visits also improved (45% to 67%) and due to the inclusive inclusion criteria only one participant who attended the baseline visit was

found to be ineligible to continue participation in the study during this period. Overall, a total of 22 participants continued in the study after the baseline study visit.

D. Barriers to participation

Over the course of the study, 26 participants declined to participate, 14 and 12 before and after implementing the study modifications, respectively. Patients approached for enrollment in the study identified reasons for declining to participate included competing priorities, such as the clinical appointments for treatment of comorbidities for them or for family members (n=7), competing priorities (n=7) and limited transportation (n=5) (Table III). Lack of interest and limited personal benefits were relatively less common reasons for declining to participate. Two participants withdrew from the study after informed consent, but prior to their baseline visit due to the need to focus on other priorities, such as care of other chronic conditions.

Reasons	# of patients ^a
Co-morbidity (personal or family)	7
Competing priorities	7
Limited transportation	5
No reason/uninterested	4
Physical limitations	4
Burden of study procedures	3
No direct benefit	1

 TABLE III

 REASONS FOR DECLINING TO PARTICIPATE IN THE PACE STUDY

a- participants may have declined for more than one reasons

E. Participant characteristics

Limited demographic and clinical information was obtained from participants who provided informed consented while hospitalized but did not attend the baseline visit. Overall, the 22 participants who remained in the study after the baseline visit were predominantly African American (90%), women (68%) and had high school education or les (72%), as shown in Table IV. Participants had a mean of 1.8 (standard deviation, SD 1.1) hospitalizations in the year prior to enrollment. Participants often reported comorbidities, including those associated with chronic pain (connective tissue disease, osteoarthritis, chronic back pain) or limited mobility (stroke). Additionally, some of the comorbidities reported by participants have symptoms that can either overlap (e.g., dyspnea in patients with heart failure) or exacerbate (e.g., perception of dyspnea in patients with comorbid depression) those of COPD.

Participants had a mean ISWT distance lower than the age-adjusted normal values (788 for 60-69-year-old individuals). Additionally, participants reported more anxiety, less physical function, less satisfaction with participation in social roles and activities, and less ability to participate in social roles and activities compared to the general US population (at least 0.5 SD difference from T-score 50).

F. Feasibility of outcome collection

Although the ISWT distance was collected in the majority of participants (18/22, 86%) at the baseline, ISWT collection rates was lower at subsequent study visits, with only 18% (4/22) of participants performing the test on all three study visits. With exception of two study visits where clinical study staff was not available to supervise the test and one where the patient did not have

Characteristic	Baseline measure,
A_{de} (vears) mean (SD)	11=22 63.8 (7.07)
Famela conder = r(0/2)	15(690/)
remain gender, in (%)	13 (08%)
African American race, n(%)	20 (90%)
High school education or less	16 (72%)
Current smoker, n(%)	5 (23%)
Body mass index (kilograms/square meter), median (interquartile range), missing=2	32.5 (27.1, 41.0)
Hospitalizations in previous year, mean (SD)	1.8 (1.1)
Comorbidities, n(%)	
Connective tissue disease	5 (23%)
Depression	4 (18%)
Heart failure	7 (32%)
Osteoarthritis	3 (13%)
Chronic back pain	6 (27%)
Stroke	5 (23%)
ISWT distance (meters), median (interquartile range), missing=3	110 (30, 210)
PROMIS measures, mean (SD)	
Anxiety, missing=1	55.4 (8.2)
Depression	53.0 (8.5)
Fatigue, missing=1	50.9 (9.1)
Physical function	37.3 (8.5)
Ability to participate in social roles & activities	41.4 (8.0)
Satisfaction with participation in social roles & activities, missing=1	42.3 (9.7)

 TABLE IV

 PARTICIPANT DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

time to perform the test, the reason for failure to perform the ISWT was uncontrolled COPD or comorbidities, including uncontrolled chronic pain.

Outcome collection rates for daily physical activity and patient-reported outcomes was higher. Daily physical activity data was available for 80% of weeks participants were enrolled in the study. Patient reported outcome data (PROMIS measures were available for >90% of participants at each of the study visits completed.

G. Daily physical activity and patient-reported outcomes

Daily physical activity data was collected starting at the baseline visit, which occurred a mean (SD) of 21 (19.5) days after hospital discharge. The median (interquartile range, IQR) daily step count was 3,101 (1,144 to 5,330) in week 1 of the study. On study completion (week 12), the media (IQR) daily step count was 3,142 (1,511 to8,125) with a median (IQR) within-person change of 203 (-160 to 1,633) steps. The correlation coefficient between daily step counts at week 1 and 12 was 0.70. There was high correlation between daily step counts at any week with adjacent weeks (R>0.82; Figure 3), indicating limited within-person variability in daily physical activity over the course of the study. Interestingly, the week-to-week correlation coefficient is higher is the later weeks of the study. It is possible that the increased correlation is due to participants with a higher (above the median) ISWT distance at the baseline visit had higher mean daily step counts compared to participants with ISWT distances below the median value (3,727 vs. 1,144 steps, respectively, p=0.03). This difference in daily step counts according to baseline ISWT was not significant at week 12 (3,799 vs. 1,033 steps, respectively, p=0.07).

Week 1	r=0.82	2									
1 A ¹	Week 2	r=0.83	ĺ.								
ني را مغرب		Week 3	r=0.92	!							
et	زير		Week 4	r=0.8	5						
i v ·			13 11 22	Week 5	r=0.92	2					
			de la	11.12	Week 6	r=0.88	3				
		3			· · · · · · · · · · · · · · · · · · ·	Week 7	r=0.96	3			
1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.		· · · · ·		۰ ۲۰۰۰ ۲۰۰۰ ۲۰۰۰ ۲۰۰۰		a star	Week 8	r=0.98			
		· · · ·						Week 9	r=0.93	3	
		· · · · ·	· · · ·	1	1				Week 10	r=0.96	
			·				1.11		1	Week 11	r=0.98
		1	e					. 7			Week 12

FIGURE 3. Within-person variation in mean daily steps counts, by study week

Participants who were hospitalized or died while enrolled in the study had lower daily step counts than participants who were not hospitalized, however this difference was not statistically significant (1,836 vs. 4,296 steps, respectively, p=0.13).

Compared to the baseline visit, there was no significant change in any of the PROMIS T-score domains at week 12 (Wilcoxon signed rank test p>0.05 for all measures; Table V). There was high correlation between Physical function, anxiety and satisfaction with social roles T-scores at baseline and week 12, indicating minimal within-person variation. Within-person variation was higher for the remaining PROMIS measures.

Instrument, mean T-score (SD)	Baseline	Week 12	Mean change ^a	r ^b	
Anxiety	55.45 (8.21)	54.05 (8.27)	-0.42 (5.15)	0.82	
Depression	53.05 (8.46)	53.04 (8.08)	-0.15 (6.84)	0.66	
Fatigue	50.93 (9.12)	49.03 (7.59)	-1.44 (7.16)	0.70	
Physical function	37.28 (8.48)	36.24 (9.35)	0.23 (4.26)	0.89	
Satisfaction w/ participation in social roles	42.33 (9.73)	43.91 (10.62)	1.15 (7.63)	0.75	
Ability to participate in social roles	41.57 (7.97)	42.53 (9.10)	1.88 (7.68)	0.61	

TABLE VWITHIN-PERSON VARIATION IN PATIENT-REPORTED
OUTCOMES (PROMIS MEASURES)

a- Mean within-person change, Wilcoxon signed rank test p>0.05 for all measures

b- Pearson correlation coefficient

IV. DISCUSSION

This study involving patients with COPD hospitalized or recently discharged from the hospital was designed to evaluate the feasibility of recruiting participants into a pragmatic mobile-health supported physical activity promotion program, to assess the barriers and facilitators to participation and to determine baseline levels of functional capacity, daily physical activity and patient reported outcomes. The study was designed to minimize participant burden to promote participation, particularly among those unable to attend a traditional outpatient pulmonary rehabilitation program. Although this study was observational, and it did not involve delivery of an intervention, study participants were asked to attend multiple outpatient study visits following enrollment and to carry a pedometer.

Unfortunately, participant completion rates of the baseline visit were initially much lower than the projected target for the study. During the initial recruitment efforts, multiple barriers to recruitment and retention were identified, including those relating to limited socioeconomic resources, such as limited transportation, and competing priorities, such as, such as the treatment for comorbidities (e.g., hemodialysis for end-stage renal disease) or being the caregiver for other family members with chronic illnesses. Following implementation of the protocol modifications, including the decrease of study visits to five to three, study accrual improved allowing us to reach our target recruitment. Although participants were compensated for their time and transportation costs, and complimentary transportation upon request was being added to the study visits, given the baseline illness (COPD with a recent hospitalization) and comorbidity burden, it was thought that further decreasing the burden of participation was a necessary modification to increase recruitment and retention. Our approach to participant recruitment, approaching patients while hospitalized or during follow-up clinic appointments, was successful in enrolling patients into the study. Over the course of the study, we discovered that outpatient clinic visits are busy (e.g., patients meet with multiple providers, such as physicians and pharmacists), participants can be stressed about seeing their provider after a hospitalization or about delays in seeing the provider, or have limited time for the visit, such as patients with pre-arranged transportation. Coordinating study visits with outpatient clinic appointments, a study feature designed to minimize participant burden, resulted in limitations to participation due to the participant's competing priorities.

As part of the protocol modifications, study eligibility criteria were modified to be more inclusive. The goal of these modifications was to enroll a patient population that would be more representative of the general population of patients with COPD hospitalized at our institution. Given the diagnostic uncertainty that can occur when a patient with multiple comorbidities present to the hospital with acute dyspnea, they can be treated for more than one condition (e.g., diuretics for decompensated heart failure and systemic steroids for a COPD exacerbation), the protocol was modified to allow participation of patients with a history of COPD who were hospitalized for respiratory symptoms. Additionally, airflow obstruction by spirometry was removed as an eligibility criterion. A significant number of patients diagnosed with COPD do not undergo spirometry in routine clinical practice.¹⁶ When hospitalized for dyspnea, these patients are typically treated for a COPD exacerbation, leading to financial penalties to health systems if they are rehospitalized, regardless of the spirometry results.³ These observations, particularly in the setting that recent studies have shown that patients with a history of smoking

and lack of airflow obstruction by spirometry can have respiratory exacerbations, highlighted the need to further understand patterns of functional capacity and daily physical activity while recovering from a hospitalization in these patients.¹⁷

In recent years, increases attention has been given to clinical trial recruitment and retention. A recent study showed that of more than 2,500 clinical trials, almost 20% of them were terminated early for insufficient accrual or were completed with less than 85% of the target enrollment.¹⁸ A recent multi-center randomized comparing the efficacy of tiotropium to placebo to improve pulmonary function and clinical outcomes in 1,208 patients with COPD recently discharged from the hospital across. The study was terminated after randomizing 158 participants over 18 months.¹⁹ Several modifications were implemented in this trial to improve recruitment, including expanding the eligibility criteria, extending the recruitment period from 12 to 18 months, increasing the number of study sites and expanding the times of the day study visits could take place at. Additionally, the investigators provided participant compensation for transportation and provided participants with educational materials and gifts. Despite these changes, recruitment no significant change in the rates of enrollment was observed. With these modifications, the investigators reduced barriers to entry and provided incentives to participate in the study. However, no significant changes were made to the burden of participation, such as the number or duration of the study visits. Additionally, although participants were compensated for transportation following the modifications, it is likely they still had the logistical burden of arranging it, particularly shortly after hospital discharge, a time when other priorities can be overwhelming. Given these considerations, our findings that decreasing the number of study visits and arranging transportation for study participants, among other modifications,

significantly improved recruitment and retention indicate future studies should be designed to have the minimal possible footprint to enroll and retain participants.

Several findings of this cohort study have informed the development of the future physical activity promotion pilot clinical trial. First, as only 18% of participants completed the ISWT on all three study visits, this test is not a feasible outcome to be included in future studies involving patients with COPD recently discharged from the hospital. However, as participants with above median ISWT had significantly higher mean daily step counts it is possible that daily step counts can be used as a surrogate measure for ISWT. Second, the high within-person variation over time of some outcome measures, such as PROMIS Ability to participate in social roles and activities, indicate that it is possible that factors not accounted for in the study influence within-person variation. This variability decreases the measure's utility as an outcome as the effect of the intervention may be dampened by factors not captured in the study. Last, although measures, such as PROMIS Anxiety have low within-person variation over time, mechanistically it is only indirectly linked to the intervention (physical activity promotion), limiting its utility as the pilot clinical trial's primary outcome. However, this will be an important measure to collect as secondary outcomes as it will likely inform the development of future studies.

Despite the modifications to the study design, the reach to the study was limited by factors relating to the study design, the health system and participants. First, more intensive engagement of the clinical providers is needed to inform them of the study design and goals, so they can best support their patients if they choose to participate. Second, despite the complimentary transportation, many patients were unable to attend the baseline outpatient study visit. Therefore, in the design of the pilot clinical trial we will propose eliminating outpatient study visits and perform study procedures exclusively through home visits and telephone calls. Last, despite the decreased burden of participation in the final cohort study design, patients declined to enroll due to competing priorities and perceived physical limitations (i.e., being too ill). In response to this barrier, we plan to include a component of self-management education, which includes education on the benefits of physical activity, and patient navigation to connect participants with publiclyavailable community resources that may decrease the burden of their competing priorities.

There are some limitations to this study. The main limitation to this study is the small sample size due to limited retention into the study (44%). Nevertheless, the lessons learned regarding recruitment and retention, particularly, the response to changes in eligibility criteria and study burden, could provide insight to future investigators planning clinical trials in this population. However, it is possible that these findings will not be applicable to other populations, such as those with different baseline levels of social support or economic resources. Additionally, some of the measures to facilitate participation, such as providing complimentary transportation may not be feasible if travel distances are extensive, such as in rural areas.

In conclusion, there are multiple challenges to enrolling participants in practice-based research following a hospitalization for COPD. In our original study design, the vast majority of patients hospitalized with COPD in this clinical setting were unable or ineligible to be enrolled as study participants. Modifications introduced to reduce the barriers of entry into the study and decrease the participant burden resulted in significant improvements in participant recruitment and retention. Although, the ISWT is not a feasible outcome for future studies in this population, daily physical activity, a robust, objective measure, may serve as a surrogate outcome. Investigators designing future real-world studies of interventions for COPD patients will need to consider a tailored recruitment strategy, and minimization of study burden on participants.

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13. Benzo R, Vickers K, Novotny PJ, Tucker S, Hoult J, Neuenfeldt P, Connett J, Lorig K, McEvoy C. Health Coaching and Chronic Obstructive Pulmonary Disease Rehospitalization. A Randomized Study. Am J Respir Crit Care Med 2016;194:672-80.

14. Spruit MA, Singh SJ, Garvey C, Zuwallack R, Nici L, Rochester C, Hill K, Holland AE, Lareau SC, Man WD, Pitta F, Sewell L, Raskin J, Bourbeau J, Crouch R, Franssen FM, Casaburi R, Vercoulen JH, Vogiatzis I, Gosselink R, Clini EM, Effing TW, Maltais F, van der Palen J, Troosters T, Janssen DJ, Collins E, Garcia-Aymerich J, Brooks D, Fahy BF, Puhan MA, Hoogendoorn M, Garrod R, Schols AM, Carlin B, Benzo R, Meek P, Morgan M, Rutten-van Molken MP, Ries AL, Make B, Goldstein RS, Dowson CA, Brozek JL, Donner CF, Wouters EF. An official american thoracic society/european respiratory society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med 2013;188:e13-64.

15. Proventil(R) HFA [package insert]. Northridge, CA: Merck & Co., Inc; 2012.

16. Joo MJ, Sharp LK, Au DH, Lee TA, Fitzgibbon ML. Use of spirometry in the diagnosis of COPD: a qualitative study in primary care. COPD 2013;10:444-9.

17. Woodruff PG, Couper D, Han MK. Symptoms in Smokers with Preserved Pulmonary Function. N Engl J Med 2016;375:896-7.

18. Carlisle B, Kimmelman J, Ramsay T, MacKinnon N. Unsuccessful trial accrual and human subjects protections: an empirical analysis of recently closed trials. Clin Trials 2015;12:77-83.

19. Ferguson GT, Beck B, Clerisme-Beaty E, Liu D, Thomashow BM, Wise RA, ZuWallack R, Make BJ. Recruiting Patients After Hospital Discharge for Acute Exacerbation of COPD: Challenges and Lessons Learned. Chronic Obstr Pulm Dis 2017;4:265-78.

VITA

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Valentin Prieto-Centurion, MD

FACULTY POSITIONS

October 2017-present	Assistant Professor of Medicine Section of Pulmonary, Critical Care, Sleep and Allergy Medicine University Of Illinois At Chicago, Chicago, Illinois	
July 2016-present	<i>Staff Physician</i> Jesse Brown VA Medical Center, Chicago, IL	
July 2016-September 2017	<i>Instructor of Medicine</i> Section of Pulmonary, Critical Care, Sleep and Allergy Medicine University Of Illinois At Chicago, Chicago, Illinois	
EDUCATION		
August 2016-present	<i>Master in Clinical and Translational Sciences</i> University of Illinois at Chicago, School of Public Health. Chicago, IL	
August 2005-May 2009	<i>Medical Doctor</i> Case Western Reserve University School of Medicine. Cleveland, OH	
August 2001-May 2005	Bachelor of Science in Chemical Engineering Rice University. Houston, TX	
POST-DOCTORAL TRAINING	G	
July 2012-June 2016	<i>Fellow</i> Section of Pulmonary, Critical Care, Sleep and Allergy Medicine University of Illinois at Chicago, Chicago, IL	
July 2009-June 2012	<i>Intern and Resident</i> Department of Medicine University of Chicago, Chicago, IL	
BOARD CERTIFICATIONS		
2012-2022 2015-2025 2016-2026	Critical Care Medicine, American Board of Internal Medicine Pulmonary Medicine, American Board of Internal Medicine Internal Medicine, American Board of Internal Medicine	
MEDICAL LICENSURE		
2012-2020 2012-2020 2012-2021	Licensed Physician and Surgeon, State of Illinois 036129688 Controlled Substance Licensure, State of Illinois, Available upon request DEA Licensure, Available upon request	
PROFESSIONAL SOCIETIES AFFILIATIONS		
2012-Present	American Thoracic Society	

AWARDS AND HONORS

2018 2016-2017	Annals of the American Thoracic Society Reviewer Award National Institute of Health Program to Increase Diversity among Individuals
	Engaged in Health-Related Research
2016	American Thoracic Society Building Education to Advance Research (BEAR) Cage Finalist
2015	American Thoracic Society Fellows Track Symposium
2013, 2014	American Thoracic Society Abstract Scholarship Award
2010	American Institute of Chemical Engineering Best Applied Paper Award
2009	Case Western Reserve University, School of Medicine, Graduation Award for
	Outstanding Thesis,
2004, 2005	Rice University, Thomas W. Moore Award in Chemical Engineering
2002, 2005	Rice University President's Honor Roll
2003	Rice University, L J Walsh Award in Chemical Engineering
2001-2005	Rice University Edgar Odell Lovett International Scholarship

COMMITTEES AND OTHER SERVICE ACTIVITIES

2018-present	American Thoracic Society Supplemental Oxygen Therapy for Adults with Chronic
	Lung Disease Guideline Committee
2017-present	PCORnet Pulmonary Clinical Research Group
2016-present	American Thoracic Society Behavioral and Health Services Research Assembly
-	Program Committee
2017	American Thoracic Society Optimizing Home Oxygen Therapy Workshop
2017	World Health Organization mBreatheFreely program informal expert group member
2017	World Health Organization mBreatheFreely global workshop on mHealth for COPD and Asthma

SYMPOSIA / CONFERENCES

- 1. Co-chair, Poster discussion, American Thoracic Society International Conference, "Determinants of Outcomes and High-Value Care in COPD"; 2018
- 2. Faculty, Sunrise Seminar, American Thoracic Society International Conference, "Designing Behavior Change Interventions One Barrier at a Time", 2018
- 3. Co-chair, Poster discussion, American Thoracic Society International Conference, "Epidemiology and Outcomes of COPD and Asthma/COPD Overlap"; 2017
- 4. Faculty, Clinical Research Coordinator Forum, American Thoracic Society International Conference, "Spirometry"; 2016

INVITED LECTURES

- 1. *Physical Activity after COPD Exacerbations*. Presented at the Rosalind Franklin University of Medicine and Science Department of Medicine Grand Rounds. North Chicago, IL, December 2017
- 2. *Physical Activity after COPD Exacerbations*. Presented at the University of Illinois Department of Medicine Grand Rounds. Chicago, IL, February 2017
- 3. Obstructive Sleep Apnea-Chronic Obstructive Pulmonary Disease Overlap Syndrome. Presented at the University of Illinois Sleep Medicine Grand Rounds. Chicago, IL, November 2016

SELECTED PRESENTATIONS

- 1. Identifying patients for a supplemental oxygen registry. PCORnet Pulmonary Clinical Research Group, San Diego, CA, May 2018
- 2. Diagnosis and management of COPD. Pulmonary pathophysiology. University of Illinois College of Medicine, Chicago, IL, March 2018
- 3. Interstitial lung diseases. Pulmonary pathophysiology. University of Illinois College of Medicine, Chicago, IL, March 2018

- 4. Diagnosis and management of asthma. Pulmonary pathophysiology. University of Illinois College of Medicine, Chicago, IL, March 2018
- 5. Oxygen delivery. PCCSM Disease Oriented Clinical Conference, University of Illinois, Chicago IL, February 2018
- 6. Pulmonary rehabilitation. PCCSM Disease Oriented Clinical Conference, University of Illinois, Chicago IL, July 2017
- 7. Promoting Activity after COPD Exacerbations (PACE). Building Education to Advance Research (BEAR) Cage, American Thoracic Society, San Francisco, May 2016
- 8. Cardiac tamponade. Pulmonary Case Conference, University of Illinois, Chicago IL, May 2016
- 9. Emphysema. PCCSM Disease Oriented Clinical Conference, University of Illinois, Chicago IL, April 2016
- 10. A comparison of three methods to identify patients with COPD. Pulmonary Research Conference, University of Illinois, Chicago IL, September 2015
- 11. Severe asthma. PCCSM Disease Oriented Clinical Conference, University of Illinois, Chicago IL, August 2015
- 12. Non-24 hour sleep-wake disorder. Pulmonary Case Conference, University of Illinois, Chicago IL, August 2015
- 13. Pulmonary rehabilitation. PCCSM Disease Oriented Clinical Conference, University of Illinois, Chicago IL, April 2015

PEER-REVIEWED ABSTRACTS

- 1. Prieto-Centurion V, Coultas DB, Luo JJ, Ma J, Rand CS, Tan AM, Krishnan JA. Feasibility of Converting Patients to Participants in a Practice-Based Study to Promote Home-Based Physical Activity After a Hospitalization for COPD. American Thoracic Society, San Diego, CA, May 2018
- Prieto-Centurion V, Basu S, Bracken NE, Casaburi R, Gallardo III R, Gonzalez V, Grabarek M, Illendula SD, Proszasz J, Sandhaus RA, Sullivan J, Walsh LJ, Krishnan JA. Comparative Effectiveness of a PEer-Led Supplemental Oxygen InfoLine for Patients and CAregivers (PELICAN). American Thoracic Society (podium presentation), San Diego, CA, May 2018
- 3. Brillante C, Binder A, Luo J, Prieto-Centurion V. Can Smartphone-Based Pulse Oximeters Be Used for Monitoring Patients with Chronic Obstructive Pulmonary Disease. American Thoracic Society, San Diego, CA, May 2018
- 4. Rinne S, Resnick K, Elwy R, Melzer AC, Prieto-Centurion V, Jones BE, Slatore CG, Wiener RS. Importance of Multidisciplinary Collaboration to Reduce COPD Readmissions in VA. American Thoracic Society, San Diego, CA, May 2018
- 5. Tan AM, Mutso A, Pittendrigh B, Edwards D, McGowan D, Calhoun E, Villareal E, Zaidi F, Ursan I, Sullivan J, Walsh L, Williams M, Joo MJ, Gutierrez-Kapheim M, Bracken NE, DiDomenico R, Pickard S, Kazmi U, Prieto-Centurion V, Visvabharathy V, Krishnan JA. How Often Are Patients Admitted to the Hospital for Chronic Obstructive Pulmonary Disease Also Treated for Heart Failure and Vice Versa? American Thoracic Society, Washington, DC, May 2017
- 6. Krishnan JA, Bracken NE, Cerretta S, Gonzalez V, Grabarek M, Holm K, Porszasz J, Prieto-Centurion V, Sandhaus RA, Sullivan J, Walsh L, Casaburi R. What Oxygen Equipment Do Patients with COPD Have at Home? Ancillary Results of the PELICAN Study. American Thoracic Society, Washington, DC, May 2017
- 7. Tan AM, Vines DL, Prieto-Centurion V, Gutierrez-Kapheim M, Krishnan JA, Kallstrom TJ. Respiratory Therapist Home Oxygen for Chronic Obstructive Pulmonary Disease (RIsOTTO) Study: A National Survey. American Thoracic Society, Washington, DC, May 2017
- 8. Zaidi F, Buchcic BA, Prieto-Centurion V, Ramey NI, Bracken NE, Krishnan JA. Evaluation and Documentation of Oxygen Requirements in Patients Hospitalized with COPD: Time for Oxygen Reconciliation? American Thoracic Society, San Francisco, CA, May 2016

- 9. Choi N, Lederer P, Prieto-Centurion V, Onal E. Diffuse Alveolar Hemorrhage and Acute Respiratory Distress Syndrome Secondary to Mycoplasma Pneumoniae Infection in a Young Immunocompetent Patient. American Thoracic Society, San Francisco, CA, May 2016
- 10. Prieto-Centurion V, Zaidi F, Coultas DB, Casaburi R, Rand CS, Krishnan JA. *Comparison of Commercially-Available Pedometers for Potential Use for Promotion of Lifestyle Physical Activity*. American Thoracic Society, Denver, CO, May 2015
- 11. Prieto-Centurion V, Zaidi F, Bracken NE, Norwick L, Coultas DB, Casaburi R, Rand CS, Jaffe HA, Krishnan JA. *Patient Perspectives and Barriers to Pulmonary Rehabilitation Following Hospitalizations for Chronic Obstructive Pulmonary Disease Exacerbations*. American Thoracic Society, Denver, CO, May 2015
- 12. Zaidi F, Prieto-Centurion V, Bracken NE, Jaffe HA, Hauser J, Norwick L, Krishnan JA. *Reducing* avoidable readmissions following COPD exacerbations among US Veterans: The importance of teaching appropriate use of respiratory inhalers. American Thoracic Society, Denver, CO, May 2015
- 13. Prieto-Centurion V, Cheng Q, Juen J, Rolle AJ, Coultas DB, Schatz B, Krishnan JA. *GaitTrack: An Objective Measurement Of Gait Speed And Walk Distance Using Smartphone-Based Accelerometers In Patients With Asthma And Chronic Obstructive Pulmonary Disease*. American Thoracic Society (podium presentation), San Diego, CA, May 2014
- 14. Prieto-Centurion V, DiDomenico R, Godwin P, Grude-Bracken N, Gussin H, Jaffe HA, Joo MJ, Markos MA, Nyenhuis SM, Pickard AS, Pittendrigh B, Ramey NI, Schatz B, Sullivan J, Thomashow B, Williams MV, Krishnan JA. *A systematic review to reduce readmissions following COPD exacerbations*. American Thoracic Society (podium presentation), Philadelphia, PA, May 2013
- 15. Prieto-Centurion V, Rolle AJ, Au DH, Carson SS, Henderson A, Lee TA, Lindenauer PK, McBurnie M, Mularski RA, Naureckas ET, Vollmer W, Krishnan JA. *A comparison of three methods to identify patients with COPD*. American Thoracic Society, Philadelphia, PA, May 2013
- 16. Morales-Perez M, Lewis S, Seufferheld FJ, Bello-Bravo J, Koninckx-Horta J, Grude-Bracken N, DeLisa JA, Gonzalez V, Norwick L, Cannon C, Rolle AJ, Prieto-Centurion V, Gussin HA, Joo MJ, Nyenhuis SM, Jaffe HA, Pittendrigh BR, Krishnan JA. Use of an educational animated video as an inhaler technique teaching tool. American Thoracic Society, Philadelphia, PA, May 2013
- 17. Prieto-Centurion V, Huang F, Press VG, Naureckas E, Krishnan JA. *Assessment of spirometry of patients with obstructive lung disease in the hospital setting*. American Thoracic Society, Philadelphia, PA, May 2013

PEER-REVIEWED PUBLICATIONS

- 1. Prieto-Centurion V, Krishnan JA. Access to supplemental oxygen therapy a crisis (Letter to the editor). *Ann Am Thorac Soc.* 2018. (In Press).
- 2. Ferrer Marrero TM, Prieto-Centurion V, Jaffe HA, Thoracic splenosis: History is the key. *Respir Med Case Rep.* 2017;22:251-253
- 3. Zaidi F, Lee RS, Buchcic BA, Bracken NE, Jaffe HA, Joo M, Prieto-Centurion V, Tan AY, Krishnan JA. Evaluation and Documentation of Supplemental Oxygen Requirements is Rarely Performed in Patients Hospitalized With COPD. *Chronic Obstr Pulm Dis.* 2017;4(4):287-296
- 4. Prieto-Centurion V, Bracken N, Norwick L, Zaidi F, Mutso AA, Morken V, Coultas DB, Rand CS,

Marquez DX, Krishnan JA. Can commercially available pedometers be used for physical activity monitoring in patients with COPD following exacerbations? *Chronic Obstr Pulm Dis.* 2016; 3(3):636-642

- 5. Ursan ID, Krishnan JA, Pickard AS, Calhoun E, DiDomenico R, Prieto-Centurion V, Sullivan JB, Valentino L, Williams MV, Joo MJ, on behalf of the PArTNER investigators. Engaging Patients and Caregivers to Design Transitional Care Management Services at a Minority Serving Institution. *J. Health Care Poor Underserved*. (2016); 27:352–365
- Holm KE, Casaburi R, Cerreta S, Gussin HA, Husbands J, Porszasz J, Prieto-Centurion V, Sandhaus RA, Sullivan JL, Walsh LJ, Krishnan JA. Patient involvement in the design of a patient-centered clinical trial to promote adherence to supplemental oxygen therapy in COPD. *Patient*. 2016; 9(3):271-9
- 7. Zaidi F, Prieto-Centurion V, Krishnan JA. COPD Bundle to Prevent Hospital Readmissions and ED Visits (Letter to the editor). *Chest.* 2015; 148(3):e91
- 8. Krishnan JA, Gussin HA, Prieto-Centurion V, Sullivan JL, Zaidi F, Thomashow BM. National COPD Readmissions Summit: Integrating COPD into Patient-Centered Hospital Readmissions Reduction Programs. *Chronic Obstr Pulm Dis.* 2015; 2(1):70-80
- Prieto-Centurion V, Rolle AJ, Au DH, Carson SS, Henderson AG, Lee TA, Lindenauer PK, McBurnie MA, Mularski RA, Naureckas ET, Vollmer WM, Joese BJ, Krishnan JA. Multicenter study comparing case definitions used to identify patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2014; 190(9):989-995
- 10. Krishnan JA, Prieto-Centurion V. Reducing the risk of rehospitalization in patients with COPD exacerbations: Fewer known unknowns. *Ann Am Thorac Soc.* 2014; 11(5):797-798
- 11. Juen J, Cheng Q, Prieto-Centurion V, Krishnan JA, Schatz, B. Health Monitors for Chronic Disease by Gait Analysis with Mobile Phones. *Telemed J E Health*. 2014;20(11):1035-41
- 12. Prieto-Centurion V, Markos MA, Ramey NI, Gussin HA, Nyenhuis S, Joo MJ, Prasad B, Bracken N, DiDomenico R, Godwin P, Jaffe HA, Kalhan R, Pickard AS, Pittendrigh B, Schatz B, Sullivan JL, Thomashow BM, Williams MV, Krishnan JA. A systematic review of interventions to reduce readmissions following COPD exacerbations. *Annals Am Thorac Soc.* 2014; 11(3):417-424
- 13. Prieto-Centurion V, Gussin HA, Rolle AJ, Krishnan JA. Chronic obstructive pulmonary disease readmission at minority-serving institutions. *Annals Am Thorac Soc.* 2013; 10(6):680-684
- 14. Cheng Q, Juen J, Li Y, Prieto-Centurion V, Krishnan JA, Schatz BR. Gaittrack: Health monitoring of body motion from spatio-temporal parameters of simple smart phones. *Proceedings of the International Conference on Bioinformatics, Computational Biology and Biomedical Informatics.* Washington DC, USA: ACM. 2013. p. 897-906.
- Prieto-Centurion V, Huang F, Naureckas ET, Camargo CA, Charbeneau J, Joo MJ, Press VG, Krishnan JA. Assessment of Spirometry in Hospitalized Patients. *BMC Pulmonary Medicine*. 2012; 12:73
- 16. Davis VA, Parra-Vasquez ANG, Green MJ, Rai PK, Behabtu N, Prieto V, Booker RD, Schmidt J,

Kesselman E, Zhou W, Fan H, Adams W, Hauge RH, Fischer JE, Cohen Y, Talmon Y, Smalley RE, Pasquali M. True solutions of single-walled carbon nanotubes for assembly into macroscopic materials. *Nature Nanotechnology*. 2009; 4(12): 830-834.

17. Davis VA, Ericson LM, Parra-Vasquez ANG, Fan H, Wang Y, Prieto V, Longoria JA, Ramesh S, Saini RK, Kittrell C, Billups WE, Adams W, Hauge RH, Smalley RE, Pasquali M. Phase Behavior and Rheology of SWNTs in Superacids. *Macromolecules*. 2004; 37(1): 154-160.

RESEARCH SUPPORT

Active PCORI PCS-1504-30430 (PI: Jerry Krishnan, MD, PhD) 11/01/2017-12/15/2018 RofLumilast or Azithromycin to preveNt COPD Exacerbations (RELIANCE) Pragmatic clinical trial that will investigate whether daily azithromycin is non-inferior to daily roflumilast in patients at high risk of COPD exacerbations. Role: Site Principal Investigator

COPD Foundation (PI: Valentin Prieto-Centurion, MD) 05/15/2018-05/14/2019 Identifying patients for a supplemental oxygen registry – a pilot study Develop methods to identify patients prescribed supplemental oxygen in a PCORnet PPRN and CDRN. Establish guidelines to develop a registry of patients prescribed supplemental oxygen. Role: Principal Investigator

NIH K23 HL130524 (PI: Valentin Prieto-Centurion, MD)

07/01/2016-06/30/2021 Promoting Activity after COPD Exacerbations (PACE) The PACE study will develop and evaluate the feasibility of a home-based objectively-monitored behavioral intervention to increase physical activity in patients recovering from COPD exacerbations following hospital discharge. Role: Principal investigator

Completed PCORI CE-1304-6490 (PI: Jerry Krishnan, MD, PhD) 10/01/2013-09/30/2014 PEer-Led O2 Infoline for patients and CAregivers (PELICAN) The PELICAN study aims to develop and test a peer-led telephone line intervention to improve adherence to oxygen therapy in patients with COPD recently discharged from the hospital. Role: Co-investigator

NIH T32 HL082547 (PI: Patricia Finn, MD) 07/01/2012-06/30/2014 Respiratory Research Training Grant Institutional training grant to support research training. This grant supported the acquisition of basic skills required for patient-oriented clinical research. Role: Trainee (Fellow)

EDITORIAL ACTIVITIES

- Ad hoc reviewer, Annals of the American Thoracic Society
- Ad hoc reviewer, American Journal of Respiratory and Critical Care Medicine
- Ad hoc reviewer, BMC Pulmonary Medicine
- Ad hoc reviewer, Journal of the COPD Foundation
- Ad hoc reviewer, Thorax
- Ad hoc reviewer, BMJ Open
- Ad hoc reviewer, Pharmacy
- Ad hoc reviewer, Journal of Evaluation in Clinical Practice
- Ad hoc reviewer, Drugs Real World Outcomes