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Characteristics at the time of oxygen initiation associated with its adherence: Findings from the COPD Long-term Oxygen Treatment Trial☆

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ABSTRACT

Rationale: Characteristics associated with adherence to long-term oxygen therapy (LTOT) in COPD remain unclear.
Objectives: To identify patient characteristics at the time of oxygen initiation associated with its adherence.
Methods: We conducted a secondary analysis of data from 359 COPD participants assigned to oxygen in the Long-term Oxygen Treatment Trial. Participants were prescribed continuous (n = 214) or intermittent (n = 145) oxygen based on desaturation patterns at study entry. At the time of initial prescription, participants rated their perceived readiness, confidence, and importance to use oxygen on a 0–10 scale (0 = not at all, 10 = very much). During follow-up, they self-reported average hours per day of use (adherence). Adherence was averaged over short-term (0–30 days), medium-term (months 9–12), and long-term (month 13 to last follow-up) intervals. Multivariable logistic regression models explored characteristics associated with high adherence (≥16 h/day [continuous] or ≥8 h/day [intermittent]) during each time interval.
Results: Participant readiness, confidence, and importance at the time of oxygen initiation were associated with high short- and medium-term adherence. For each unit increase in baseline readiness, the odds of high short-term adherence increased by 21% (odds ratio [OR] 1.21, 95% confidence interval [CI] 1.05–1.40) and 94% (OR 1.94, 95% CI 1.45–2.59) in the continuous and intermittent groups, respectively. In both groups, high adherence in the medium-term was associated with high adherence in the long-term (continuous, OR 12.49, 95% CI 4.90–31.79; intermittent, OR 38.08, 95% CI 6.96–208.20).
Conclusions: Readiness, confidence, and importance to use LTOT at initiation, and early high adherence, are significantly associated with long-term oxygen adherence.

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Abbreviations list

BD	bronchodilator
CI	confidence interval
COPD	chronic obstructive pulmonary disease
FEV_1	forced expiratory volume in 1 s
FVC	forced vital capacity
LOTT	Long-term Oxygen Treatment Trial
LTOT	long-term oxygen therapy
MMRC	modified Medical Research Council
OR	odds ratio
SD	standard deviation
SGRQ	St. George's Respiratory Questionnaire

1. Introduction

Although long-term oxygen therapy (LTOT) prolongs life in patients with chronic obstructive pulmonary disease (COPD) who have severe resting hypoxemia [1,2], adherence to treatment has been reported to be as low as 45–70% [3,4]. Many factors—physiological, psychosocial, and oxygen treatment-related—determine adherence to LTOT. Reasons for low adherence, previously assessed in patients already using LTOT, include cumbersome and unreliable equipment, no perceived benefit, embarrassment and stigma, and lack of social support [3–14].

Bandura's Social Cognitive Theory states that understanding and addressing both efficacy and outcome expectations are required for behavior change [15]. Specifically, believing that one is capable of using the oxygen (efficacy expectation) and knowing the importance of wearing oxygen (outcome expectation) are needed to effect the behavior changes of using and adhering to LTOT [15]. In clinical practice at the time of LTOT initiation, provider counseling focuses on outcome expectations (importance), and little is known about patient efficacy expectations [4,16,17]. It is not uncommon that oxygen is prescribed and delivered to the home with no formal assessment of the patient's self-efficacy (readiness and confidence) to use oxygen. In a survey of oxygen users, approximately one-third of patients felt “very” or “somewhat” unprepared to operate oxygen equipment [18]. Furthermore, there is a paucity of information about differences in adherence to LTOT in patients recently prescribed continuous (24 h/day) or intermittent oxygen (e.g., with exertion and during sleep), and factors associated with adherence in these two groups at various points in time after initiating LTOT (e.g., first 30 days vs. after the first 12 months) [4,16,17].

In the Long-term Oxygen Treatment Trial (LOTT), participants with COPD and moderate resting hypoxemia or normal resting saturation and moderate hypoxemia during exercise were randomly assigned to no supplemental oxygen or to supplemental oxygen [19,20]. Participants assigned to supplemental oxygen received it either continuously or intermittently with exercise and sleep based on resting and exercise desaturation patterns at trial entry. They also received an adherence intervention to promote oxygen use, which included regular participant self-assessments of readiness, confidence, and importance to use oxygen. The LOTT did not find a benefit of supplemental oxygen for these specific participants with COPD [19]. Nevertheless, the participants started on oxygen as part of LOTT provide a unique opportunity to assess expectations and characteristics at the time of oxygen initiation that are associated with treatment adherence. These findings may inform strategies to promote adherence in other COPD populations prescribed LTOT.

In this secondary analysis of LOTT data, we explore characteristics associated with high oxygen adherence. We hypothesize that self-efficacy constructs, such as readiness and confidence, are strongly associated with high adherence. We also hypothesize that characteristics associated with high adherence differ over short-, medium-, and long-term intervals of follow-up and between those initiated on continuous versus intermittent oxygen.

2. METHODS (see the Appendix for additional details)

2.1. Study design

In brief, the LOTT was a multicenter randomized controlled trial of supplemental oxygen therapy versus no supplemental oxygen therapy (no placebo, unblinded) for patients with stable COPD and moderate resting hypoxemia or normal resting saturation and moderate hypoxemia during exercise [19,20]. Participants had post-randomization follow-up for at least one and up to six years [19,20]. LOTT was approved by the institutional review board at each participating center, and all participants provided written informed consent.

2.2. Study population

Our study population consisted of the participants randomized to supplemental oxygen therapy in the LOTT. Previous publications have described LOTT eligibility criteria and the characteristics of study participants at trial entry [19,20].

2.3. Supplemental oxygen prescription

Participants with moderate resting hypoxemia at trial entry received a prescription for continuous oxygen, while those with normal saturation at rest and desaturation during exercise at trial entry were prescribed intermittent oxygen [19,20]. Patients in the intermittent oxygen group were prescribed oxygen for exercise and during sleep. LOTT did not evaluate patients for hypoxemia during sleep. All patients randomized to supplemental oxygen received a stationary system and a portable oxygen delivery system.

2.4. Oxygen adherence intervention

LOTT participants randomized to receive supplemental oxygen therapy also received an adherence intervention that investigators designed to promote use of LTOT. The oxygen adherence intervention was comprised of regular telephone contacts by research staff. Study-trained and certified adherence educators delivered the oxygen adherence intervention. At each contact, staff used motivational interviewing techniques to explore the participant's perceptions of readiness, confidence and importance to use oxygen and to address ambivalence towards use by discussing their self-identified barriers and solutions to it [20]. Participants received the ongoing oxygen adherence intervention while follow-up outcomes were assessed. Participants self-reported their perceived readiness, confidence, and importance to use LTOT (each on a scale of 0–10, where 0 = not at all and 10 = very much) at the time of treatment initiation, when they knew whether they would receive continuous or intermittent oxygen. Contacts began at the visit when participants were assigned to oxygen, followed by telephone calls weekly during the first month, monthly for 6 months, and bi-monthly in months 6–10, and visits yearly through the end of follow-up [20].

2.5. Oxygen adherence assessments

At each follow-up adherence contact, participants estimated average hours (0–24) of oxygen use per day in the prior week. Every 4 months, at contacts comprising the LOTT's follow-up visit schedule for all randomized participants, participants randomized to oxygen also self-reported oxygen use separately for stationary and portable oxygen, by selecting the average daily hours of oxygen use in the prior week from categories of ≤4, 5–8, 9–16, or 17–24 h/day. The two streams of

self-reports were merged for analyses.

We defined short-, medium-, and long-term time intervals as specified in Table 1 and calculated each participant's average daily oxygen use in each of the three intervals. We defined high adherence to supplemental oxygen as average supplemental oxygen use ≥16 h/day (2/3 of the expected time) for those assigned to continuous supplemental oxygen therapy, and ≥8 h/day for those assigned to intermittent supplemental oxygen therapy [19]. It is reasonable to expect patients to be in bed for 7–8 h and to be active 3–4 h a day. We estimated that the majority would wear oxygen approximately 12 h a day. Thus, the definition of high adherence in the intermittent group (at least 8 h/day) is based on use during 2/3 of the expected time.

2.6. Statistical analysis

We compared baseline characteristics between the oxygen prescription groups using Fisher's exact test, chi-squared test, or analysis of variance. Multivariate logistic regression was used to explore characteristics associated with high adherence (yes vs. no) in each of the 6 groups determined by oxygen prescription (continuous, intermittent) and time interval (short-, medium-, long-term) [21]. The candidate set of characteristics for high adherence in the short-term included baseline factors chosen *a priori* for their potential impact on adherence: 1) constructs from the Social Cognitive Theory: self-reported ratings of readiness, confidence, and importance and 2) general or COPD-related health experiences and symptoms. The candidate sets of characteristics for high adherence in the medium-term and long-term included the candidate characteristics for high adherence in the short-term plus post-randomization measures of COPD exacerbation and high adherence or not during the prior interval. All models adjusted for age, race, and sex. For each analysis, best subsets variable selection identified the model with the lowest Akaike information criterion out of all possible models for the candidate set of characteristics [21–23]. Model fit was assessed using the Hosmer-Lemeshow test [24]. Analyses were completed in SAS (Cary, NC) or STATA (College Station, TX).

3. RESULTS (see the Appendix for additional details)

3.1. Participant characteristics

Three hundred sixty-eight participants were randomized to supplemental oxygen in the LOTT; 359 (97.6%) completed at least one oxygen adherence contact and were included in this analysis. Two hundred and fourteen participants (59.6%) were prescribed continuous oxygen, 68 (31.8%) of whom had resting hypoxemia only. One hundred forty-five participants (40.4%) were prescribed intermittent oxygen during exercise and sleep.

Compared to those starting intermittent oxygen, participants who started continuous oxygen had significantly higher pack-years of cigarette smoking, body mass index, post-bronchodilator forced expiratory volume in 1 s (FEV_1), prevalence of coronary vascular disease and diabetes mellitus, and lower prevalence of prior participation in pulmonary rehabilitation (Table 2). At baseline, participants started on continuous oxygen had significantly lower readiness and confidence scores to use oxygen (7.6 ± 2.7 vs. 8.9 ± 1.9, P < 0.0001 and 8.4 ± 2.1 vs. 8.8 ± 1.6, P = 0.02, respectively), and a trend of lower perceived importance of oxygen use (7.8 ± 2.5 vs. 8.3 ± 2.3, P = 0.05), compared to those initiated on intermittent oxygen (Table 2).

3.2. Characteristics of self-efficacy are associated with high oxygen adherence

In multivariable analysis, higher ratings of readiness and confidence to use oxygen were strongly associated with high adherence in the first 30 days of oxygen use (Table 3). For each unit increase in readiness, there was a 21% (odds ratio (OR) 1.21, 95% confidence interval [CI] 1.04–1.40, P = 0.008) increase in the odds of high adherence in the continuous group and a 94% (OR 1.94, 95% CI 1.45–2.59, P < 0.001) increase in the odds of high adherence in the intermittent group (Table 3).

3.3. Characteristics associated with high oxygen adherence differ over time

Female sex, higher self-reported importance to use oxygen at oxygen initiation, and high adherence in the first 30 days were significantly associated with high adherence in the medium term of 9–12 months in multivariable analysis in both the continuous and intermittent use groups. For each unit increase in baseline rating of importance, there was a 23% (OR 1.23; 95% CI 1.04–1.44, P = 0.01) increase in the odds of high adherence in months 9–12 in the continuous group and a 38% (OR 1.38, 95% CI 1.10–1.73; P = 0.005) increase in the intermittent group (Table 3). For the continuous group, the odds of high adherence in months 9–12 was 15.85 (P < 0.001; 95% CI 7.24–34.73) times greater for those with high adherence compared to low adherence in the first 30 days. For the intermittent group, the odds ratio was 5.11 (P = 0.005; 95% CI 1.63–15.97).

High long-term adherence in months 13 to the end of follow-up was associated with high oxygen adherence in the medium-term of months 9–12. Compared to those with low adherence in the medium-term, those with high adherence in the medium-term had greater odds of high adherence in the long-term: OR 12.49 (P < 0.001; 95% CI 4.90–31.79) and OR 38.08 (P < 0.001; 95% CI 6.96–208.20) in the continuous and intermittent groups, respectively (Table 3).

3.4. Characteristics associated with high oxygen adherence differ by prescription group

In the continuous group, a history of participation in pulmonary rehabilitation was significantly associated with high adherence in the short-term, while current smokers were less likely to have high

Table 1
Definitions for duration of follow-up and level of oxygen adherence.

	Definition
Duration of Follow-up	
Over all follow-up	Oxygen equipment delivery day through end of follow-up
Short-term	Oxygen equipment delivery day through day 30
Medium-term	Days 270 through day 365 (months 9 through 12)
Long-term	Days 366 through end of follow-up (months 13 to end)
Oxygen Adherence	
Participants prescribed continuous oxygen (24-h)	
Low	< 16 h/day on average
High	≥16 h/day on average
Participants prescribed intermittent oxygen (during exercise and sleep)	
Low	< 8 h/day on average
High	≥8 h/day on average

Table 2
Baseline participant characteristics by oxygen prescription group.

	Continuous (24-h; N = 214)	Intermittent (during exercise and sleep; N = 145)	P[a]
Demographics			
Age (years; mean ± SD)	68.0 ± 6.9	68.5 ± 8.3	0.58
White race	86.4%	82.1%	0.30
Hispanic ethnicity	3.3%	2.1%	0.75
Female gender	25.7%	29.7%	0.47
Exposures, symptoms, and physiologic measures			
Lives with a smoker	13.6%	17.2%	0.37
Current smoker	33.2%	24.8%	0.10
Pack-years tobacco cigarette smoking (mean ± SD)	65.7 ± 39.2	57.7 ± 26.7	0.03
Wheeze or whistling in chest	55.1%	51.7%	0.52
Nasal dryness or bloody nose or discharge ≥ 1x/mo	40.7%	43.5%	0.66
MMRC dyspnea score			
1	28.0%	22.8%	0.37
2	30.4%	32.4%	
3	34.6%	40.7%	
4	7.0%	4.1%	
Body mass index (kg/m^2; mean ± SD)	29.9 ± 6.8	27.2 ± 5.7	< 0.0001
Hemoglobin (g/dL; mean ± SD)	14.6 ± 1.5	14.4 ± 1.4	0.12
6-min walk distance (ft; mean ± SD)	1035 ± 319	1100 ± 307	0.06
Post BD FEV_1 (L; mean ± SD)	1.38 ± 0.47	1.22 ± 0.51	0.002
Post BD FEV_1 percent predicted (%; mean ± SD)	48 ± 15	45 ± 18	0.08
Post BD FEV_1/FVC (mean ± SD)	0.48 ± 0.13	0.44 ± 0.13	0.003
Healthcare utilization and comorbidities			
Pulmonary rehabilitation ever	21.5%	36.6%	0.003
Ever used home oxygen prior to entry	29.4%	30.3%	> 0.99
COPD exacerbation in 3 months prior to entry	17.3%	17.2%	0.99
Hospitalization in year prior to entry[b]	23.2%	20.8%	0.69
Coronary vascular disease	38.3%	24.8%	0.009
Diabetes	23.8%	13.8%	0.02
Osteoarthritis, sciatica, chronic back problem	47.2%	53.1%	0.28
Psychosocial measures			
Ratings of Social Cognitive Theory constructs (scored 0–10)			
Readiness to use oxygen (mean ± SD)	7.6 ± 2.7	8.9 ± 1.9	< 0.0001
Confidence in using oxygen (mean ± SD)	8.4 ± 2.1	8.8 ± 1.6	0.02
Importance of using oxygen (mean ± SD)	7.8 ± 2.5	8.3 ± 2.3	0.05
SGRQ total score (mean ± SD)	49.7 ± 19.3	50.7 ± 16.9	0.60
Epworth sleepiness score (mean ± SD)	7.3 ± 4.0	6.3 ± 3.8	0.03

SD = standard deviation; MMRC = modified Medical Research Council; FEV_1 = forced expiratory volume in 1 s; FVC = forced vital capacity; COPD = chronic obstructive pulmonary disease; SGRQ = St. George's Respiratory Questionnaire.

[a] Fisher's exact test, chi-square test, or *t*-test for difference between groups.

[b] Status re: hospitalization in year prior to entry was missing for 24 continuous patients and 1 intermittent patient; collection of this data item began after protocol revisions instituted in September 2009.

adherence in the short-term in multivariable analysis (Table 3). In the intermittent group, those with a higher 6-min walk distance were less likely to have high adherence in the medium term. Participants in the intermittent group with comorbidities of cardiovascular disease, osteoarthritis, or back problems had a lower odds of high oxygen adherence in the medium- and long-term.

4. Discussion

This secondary study of LOTT participants randomly assigned to receive supplemental oxygen coupled with an oxygen adherence intervention demonstrates that high self-reported ratings of readiness and confidence to use oxygen at the time of treatment initiation are associated with high adherence in COPD participants with moderate hypoxemia at rest or with exertion prescribed LTOT. This is a novel and clinically meaningful finding as it highlights efficacy expectations that can be enhanced through counseling prior to oxygen initiation to improve treatment adherence. In addition, early oxygen adherence predicts later adherence. We also show that characteristics associated with high adherence differ initally and over time, and between those prescribed continuous versus intermittent oxygen. Importance was significantly associated with medium-term adherence, suggesting that efficacy expectations are important in the short-term while outcome expectations are important in the medium-term.

These findings suggest that the initiation of LTOT and the immediate 30 days thereafter are critical times to focus educational and motivational efforts that may have long-lasting effects on adherence. Sources of patient instruction and support are currently limited, which mostly include the delivery person (64%) and less commonly the clinician (8%) [18]. Our study provides guidance for the content of provider communications, namely to assess and optimize patients' self-efficacy, perceived readiness and confidence, to use oxygen when it is initially prescribed. Our findings can potentially guide the development of future interventions to enhance long-term adherence [25].

Oxygen use prior to trial entry did not predict high adherence during the trial. Providers should not take previous oxygen use as reassurance that the patient will use and adhere to a new prescription. Participation in pulmonary rehabilitation predicted short-term high oxygen adherence. We speculate that this setting allowed opportunities for providers to educate patients about the use of LTOT, which facilitated adherence. One-third of the participants assigned to continuous oxygen were active cigarette smokers, which was significantly associated with lower odds of high adherence at 30 days. Individuals who are active smokers prescribed continuous oxygen require ongoing education to maintain high oxygen adherence, compared to those starting intermittent oxygen.

The strengths of this analysis include the large, well characterized study population, assessments at the initiation of LTOT, a theoretical framework for behavior change, and longitudinal follow-up over a long duration. We acknowledge that the group of COPD participants who

Table 3
Characteristics associated with high adherence to LTOT in the short-, medium-, and long-term by oxygen prescription group.

Continuous Group				*Intermittent Group*			
	Odds ratio	95% CI	P		Odds ratio	95% CI	P
Short term (1st 30 days; N = 212)				**Short term (1st 30 days; N = 145)**			
Age at trial entry (per year)	1.00	(0.96, 1.05)	0.99	Age at trial entry (per year)	1.06	(0.99, 1.12)	0.09
White race (vs. other)	0.57	(0.22, 1.45)	0.24	White race (vs. other)	0.73	(0.23, 2.36)	0.60
Female (vs. male)	0.85	(0.42, 1.72)	0.66	Female (vs. male)	2.08	(0.72, 5.99)	0.18
Self-reported rating of readiness to use oxygen at randomization (per unit)	1.21	(1.05, 1.40)	0.008	Self-reported rating of readiness to use oxygen at randomization (per unit)	1.94	(1.45, 2.59)	< 0.001
Exacerbation in 3 mos prior to trial entry (yes vs. no)	2.37	(0.97, 5.78)	0.06	Exacerbation in 3 mos prior to trial entry (yes vs. no)	0.37	(0.12, 1.11)	0.08
Ever participated in pulmonary rehabilitation as of trial entry (yes vs. no)	3.02	(1.29, 7.05)	0.01	Ever diagnosed with cardiovascular disease as of trial entry (yes vs. no)	0.22	(0.08, 0.60)	0.003
Self-reported rating of confidence in using oxygen at randomization (per unit)	1.24	(1.03, 1.50)	0.03	MMRC dyspnea score at trial entry (per unit)	0.58	(0.32, 1.04)	0.07
Current tobacco smoker at trial entry (yes vs. no)	0.49	(0.25, 0.96)	0.04	SGRQ total score at trial entry (per unit)	1.02	(0.99, 1.05)	0.16
Model goodness of fit: Hosmer-Lemeshow $\chi 2$ (df = 3) = 4.30 with P = 0.23, indicating good fit.				Model goodness of fit: Hosmer-Lemeshow $\chi 2$ (df = 3) = 3.84, P = 0.28, indicating good fit.			
Medium term (months 9–12; N = 208)				**Medium term (months 9–12; N = 139)**			
Age at trial entry (per year)	0.96	(0.91, 1.01)	0.10	Age at trial entry (per year)	1.11	(1.03, 1.20)	0.007
White race (yes vs. no)	0.94	(0.33, 2.70)	0.90	White race (vs. other)	0.68	(0.15, 2.97)	0.60
Female (vs. male)	0.35	(0.15, 0.86)	0.02	Female (vs. male)	0.24	(0.07, 0.79)	0.02
High adherence in the 1st 30 days since starting oxygen (yes vs. no)	15.85	(7.24, 34.73)	< 0.001	High adherence in the 1st 30 days since starting oxygen (yes vs. no)	5.11	(1.63, 15.97)	0.005
Self-reported rating of importance of using oxygen at randomization (per unit)	1.23	(1.05, 1.44)	0.01	Self-reported rating of importance of using oxygen at randomization (per unit)	1.38	(1.10, 1.73)	0.005
Exacerbation in 1st 8 months since starting oxygen (yes vs. no)	2.32	(0.99, 5.43)	0.05	Wheeze or whistling in chest at trial entry (yes vs. no)	6.15	(2.03, 18.68)	0.001
Post BD FEV_1 at trial entry (per L)	0.45	(0.18, 1.10)	0.08	6-min walk distance at trial entry (per 10 ft)	0.97	(0.95, 0.99)	0.002
Ever used home oxygen before trial entry (yes vs. no)	1.97	(0.89, 4.37)	0.10	Hemoglobin level at trial entry (per g/dL)	0.53	(0.33, 0.87)	0.01
				Living with a smoker at trial entry (yes vs. no)	6.25	(1.41, 27.80)	0.02
Model goodness of fit: Hosmer-Lemeshow $\chi 2$ (df = 3) = 3.33, P = 0.53, indicating good fit.				Ever diasagnosed with cardiovascular disease as of trial entry (yes vs. no)	0.26	(0.07, 0.94)	0.04
				Current tobacco smoker as of trial entry (yes vs. no)	0.36	(0.11, 1.15)	0.08
				Ever diagnosed with osteoarthritis, sciatica, chronic back problems as of trial entry (yes vs. no)	0.41	(0.15, 1.14)	0.09
				Exacerbation in 3 mos prior to trial entry (yes vs. no)	3.61	(0.82, 15.76)	0.09
				Model goodness of fit: Hosmer-Lemeshow $\chi 2$ (df = 3) = 1.24, P = 0.74, indicating good fit.			
Long term (month 13 to end of follow-up; N = 187)				**Long term (month 13 to end of follow-up; N = 133)**			
Age at trial entry (per year)	1.08	(1.01, 1.16)	0.02	Age at trial entry (per year)	0.96	(0.89, 1.04)	0.34
White race (yes vs. no)	1.46	(0.46, 4.58)	0.52	White race (vs. other)	5.35	(0.95, 30.06)	0.06
Female (vs. male)	2.04	(0.71, 5.84)	0.19	Female (vs. male)	2.11	(0.44, 10.23)	0.35
High adherence in months 9–12 (yes vs. no)	12.49	(4.90, 31.79)	< 0.001	High adherence in months 9–12 (yes vs. no)	38.08	(6.96, 208.20)	< 0.001
High adherence in the first 30 days (yes vs. no)	2.95	(1.17, 7.43)	0.02	High adherence in the 1st 30 days (yes vs. no)	3.33	(0.91, 12.22)	0.07
6-min walk distance at trial entry (per 10 feet)	0.99	(0.98, 1.01)	0.20	6-min walk distance at trial entry (per 10 feet)	0.98	(0.96, 1.00)	0.05
SGRQ total score at trial entry (per unit)	1.03	(1.01, 1.06)	0.01	Hospitalized in year prior to trial entry (yes vs. no)	20.22	(1.54, 266.25)	0.02
Hemoglobin level at trial entry (per g/dL)	1.37	(1.00, 1.88)	0.05	Ever diagnosed with osteoarthritis, sciatica, chronic back problems as of trial entry (yes vs. no)	0.23	(0.06, 0.89)	0.03

(*continued on next page*)

Table 3 (*continued*)

Continuous Group				*Intermittent Group*				
	Odds ratio	95% CI	P		Odds ratio	95% CI	P
Self-reported rating of readiness to use oxygen at randomization (per unit)	1.18	(0.98, 1.41)	0.08	Epworth Sleepiness Scale score at trial entry (per unit)	1.18	(0.98, 1.42)	0.08
Post BD FEV_1 at trial entry (per L)	2.32	(0.87, 6.20)	0.09				
Model goodness of fit: Hosmer-Lemeshow $\chi 2$ (df = 3) = 5.25, P = 0.15, indicating good fit.				Model goodness of fit: Hosmer-Lemeshow $\chi 2$ (df = 3) = 3.40, P = 0.33, indicating good fit.			

For each outcome, the model shown is that with the lowest Akaike information criterion (16, 17). Odds ratios, 95% confidence intervals, and P values (Wald chi-squared tests) were determined from multiple logistic regression of high adherence in the indicated time frame (yes vs. no) on the candidate set of characteristics. For each model, inclusion of age, race and sex was forced; the other characteristics were identified by best variable subsets selection (15) using the Akaike information criterion and were selected from the candidate set of characteristics for the outcome (20 for short-term adherence; 22 for medium-term adherence; and 23 for long-term adherence). See Appendix for additional details.

LTOT = long-term oxygen treatment; MMRC = modified Medical Research Council; BD = bronchodilator; FEV_1 = forced expiratory volume in 1 s; SGRQ = St. George's Respiratory Questionnaire.

volunteered for LOTT may not represent the general population of patients who meet current guidelines to initiate LTOT. These results must also be interpreted in the context of participants receiving an embedded intervention to promote oxygen adherence during the trial. Despite this best case scenario of an adherence intervention, 42.5% of the continuous group and 25.5% of the intermittent group had low adherence during the first 30 days. It is unlikely that the adherence intervention confounded the results, as we focus on baseline measurements of self-efficacy constructs, and ratings of readiness and confidence tended to be unchanged over time (see Appendix). In fact, high oxygen adherence decreased over time in the continuous group (see Appendix).

The LOTT showed no significant benefit with oxygen in the population studied. Our findings might not apply to patients with COPD and severe hypoxemia who may have greater motivation to adhere with oxygen treatment believing that it is necessary for their health. Nevertheless, our participants may have enrolled in the LOTT with the belief that supplemental oxygen would improve their health, and participants like the ones we studied may progress to meet the current guidelines, so understanding their barriers to adherence is relevant. Our findings may also be relevant to understanding adherence to other behavior changes often promoted in persons with COPD such as engagement in physical activity, bronchodilator medication use, and use of action plans for acute exacerbations.

Oxygen use was assessed by self-report which generally over-reports use compared to objective measures [26–29]. Thus, there may be a response bias overclassifying high adherence in LOTT. However, we previously found good agreement between self-reports of oxygen use with objective measurement of serial concentrator meter readings in 100 LOTT participants for whom meter readings were available [19]. Our definitions of oxygen adherence have precedence as cut-offs of $>$ 15 h per day or $>$ 17–18 h per day have been previously used to define adherence and oxygen use that is efficacious [1,3,27,30,31]. We do not know the level of physical activity or the sleep patterns of the participants in the intermittent group to determine how many hours of daily oxygen they should have used. Nevertheless, our definition of high oxygen adherence, $\geq$8 h/day, appears to be a reasonable estimate in this population.

We acknowledge that our assessment of readiness, confidence, and importance is not based on a validated questionnaire with known psychometric properties and minimum clinically important differences. Nevertheless, the wording of the questions used to assess readiness, confidence, and importance are based on face validity and the responses are modeled on the commonly used visual analog scale.

5. Conclusions

Efficacy and outcome expectations assessed by self-reported readiness, confidence, and importance to use oxygen are associated with high adherence among LOTT participants assigned to supplemental oxygen. While characteristics that are associated with high adherence depend on the time from the initiation of treatment and type of oxygen prescription, it appears that once high adherence is established it is likely to continue. This finding highlights the importance of early intervention to promote adherence to supplemental oxygen use.

Author contributions and guarantor statement

Conception and design: Marilyn L. Moy, Kathleen F. Harrington, Anne L. Fuhlbrigge.

Analysis and interpretation: Alice L. Sternberg, Marilyn L. Moy, Kathleen F. Harrington, Anne L Fuhlbrigge, Jerry Krishnan, James Tonascia, Richard Casaburi, Roger Yusen, Ai-Yui Tan.

Drafting the manuscript for important intellectual content: all authors.

All authors read and approved the final manuscript. Alice L.

Sternberg and James Tonascia had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Summary conflict of interest statement

Drs Moy, Albert, Diaz, Kanner, Krishnan, Panos, Stibolt, and Yusen have nothing to disclose.

Dr. Stoller has no conflicts relevant to this work.

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Dr. Au reports grants from NIH/NHLBI during the conduct of the study and personal fees from Gilead Sciences and Novartis Inc, both outside the submitted work.

Dr. Casaburi reports stock ownership in Inogen, Inc., outside the submitted work.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2019.02.004.

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