AMERICAN THORACIC SOCIETY DOCUMENTS

Home Oxygen Therapy for Adults with Chronic Lung Disease

An Official American Thoracic Society Clinical Practice Guideline: Executive Summary

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This official clinical practice guideline of the American Thoracic Society was approved September 2020

Background: Evidence-based guidelines are needed for effective delivery of home oxygen therapy to appropriate patients with chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD).

Methods: The multidisciplinary panel created six research questions using a modified Delphi approach. A systematic review of the literature was completed, and the Grading of Recommendations Assessment, Development and Evaluation approach was used to formulate clinical recommendations.

Recommendations: The panel found varying quality and availability of evidence and made the following judgments: *1*) strong recommendations for long-term oxygen use in patients with COPD (moderate-quality evidence) or ILD (low-quality evidence) with severe chronic resting hypoxemia, *2*) a conditional recommendation against long-term oxygen use in patients with COPD with moderate chronic resting hypoxemia, *3*) conditional recommendations for ambulatory oxygen use in patients with COPD (low-quality evidence) or ILD (low-quality evidence) with severe exertional hypoxemia, *4*) a conditional recommendation for ambulatory liquid-oxygen use in patients who are mobile outside the home and require >3 L/min of continuous-flow oxygen during exertion (very-low-quality evidence), and *5*) a recommendation that patients and their caregivers receive education on oxygen equipment and safety (best-practice statement).

Conclusions: These guidelines provide the basis for evidence-based use of home oxygen therapy in adults with COPD or ILD but also highlight the need for additional research to guide clinical practice.

Keywords: mobility; hypoxemia; quality of life; chronic obstructive pulmonary disease; interstitial lung disease

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Am J Respir Crit Care Med Vol 202, Iss 10, pp 1345–1359, Nov 15, 2020

DOI: 10.1164/rccm.202009-3608ST
Internet address: www.atsjournals.org

Summary of Recommendations

Chronic Obstructive Pulmonary Disease

- **In adults with chronic obstructive pulmonary disease (COPD) who have severe chronic resting room air hypoxemia,* we recommend prescribing long-term oxygen therapy (LTOT) for at least 15 h/d** (*strong recommendation, moderate-quality evidence*).
  **Severe hypoxemia is defined as meeting either of the following criteria: 1) $Pa_{O_2} \leqslant 55$ mm Hg (7.3 kPa) or oxygen saturation as measured by pulse oximetry (Sp_{O_2}) $\leqslant 88\%$; 2) $Pa_{O_2} = 56$–59 mm Hg (7.5–7.9 kPa) or $Sp_{O_2} = 89\%$ plus one of the following: edema, hematocrit $\geqslant 55\%$, or P pulmonale on an ECG.*
- **In adults with COPD who have moderate chronic resting room air hypoxemia,* we suggest not prescribing LTOT** (*conditional recommendation, low-quality evidence*).
  **Moderate hypoxemia is defined as an Sp_{O_2} of 89–93%.*
- **In adults with COPD who have severe exertional room air hypoxemia, we suggest prescribing ambulatory oxygen** (*conditional recommendation, low-quality evidence*).

Interstitial Lung Disease

- **For adults with interstitial lung disease (ILD) who have severe chronic resting room air hypoxemia, we recommend prescribing LTOT for at least 15 h/d** (*strong recommendation, very-low-quality evidence*).
- **For adults with ILD who have severe exertional room air hypoxemia, we suggest prescribing ambulatory oxygen** (*conditional recommendation, low-quality evidence*).

Liquid Oxygen

- **In patients with chronic lung disease who are mobile outside of the home and require continuous oxygen flow rates of >3 L/min during exertion, we suggest prescribing portable liquid oxygen (LOX)** (*conditional recommendation, very-low-quality evidence*).

Education and Safety

- **For patients prescribed home oxygen therapy, we recommend that the patient and their caregivers receive instruction and training on the use and maintenance of all oxygen equipment and education on oxygen safety, including smoking cessation, fire prevention, and tripping hazards** (*best-practice statement*).

Introduction

Five million adults live with chronic lung disease in the United States, with more than one million prescribed LTOT (1, 2), defined as oxygen prescribed for at least 15 h/d. The rationale for the provision of LTOT in adults is based on the survival benefit reported by two randomized clinical trials (RCTs) published over three decades ago that examined the effect on mortality of home oxygen therapy in patients with severe COPD and hypoxemia (3, 4). Since then, an additional clinical trial has examined the role of home oxygen therapy in patients with COPD and moderate resting hypoxemia or exertion-only hypoxemia (LOTT [Long-Term Oxygen Therapy Trial]) (5).

Although several professional societies and groups have published clinical practice guidelines for home oxygen therapy (6–12), most have not incorporated the recent LOTT results. Recent data highlight differences in home oxygen needs and experiences across different lung diseases, lifestyles, and oxygen supply requirements (13–16). For example, the physiologic mechanisms of hypoxemia differ between obstructive and restrictive lung diseases. The rapid and steep rate of exertional desaturation for patients with ILD differs from that of those with COPD (17, 18). These considerations highlight the need for guidelines specific to individuals with COPD and ILD, the two major diagnoses for which oxygen therapy is prescribed (19).

The 2017 American Thoracic Society (ATS) workshop on optimizing home oxygen therapy identified the lack of evidence-based clinical practice guidelines for appropriate use of home oxygen as a critical gap (20). Workshop proceedings suggested a need for additional research on portable oxygen technology, advocacy for improved financing of oxygen therapy, and updated guidelines for policy, advocacy, and practice. The purpose of this guideline panel was to develop clinical guidelines targeting healthcare providers who care for adults living with chronic lung disease who need oxygen in the community, outside of inpatient and emergency settings.

Methods

This clinical guideline was developed in accordance with policies and procedures of the ATS. The guideline included 4 co-chairs and 18 voting members: 11 pulmonary/critical care physicians, 4 nurses, 1 registered respiratory therapist, 1 physiotherapist, and 1 patient representative (Box 1). We used the Grading of Recommendations Assessment, Development and Evaluation approach to appraise the quality of evidence and to formulate, write, and grade recommendations (Tables 1 and 2) (21). To facilitate interpretation of our recommendations, we adopted a published terminology for home oxygen therapy (Table 3) (22). For our systematic review, we defined severe hypoxemia as $Sp_{O_2} \leqslant 88\%$ or $Pa_{O_2} \leqslant 55$ mm Hg (7.3 kPa), moderate hypoxemia as having an Sp_{O_2} of 89–93% or a Pa_{O_2} 56–60 mm Hg (7.5–8.0 kPa), and we defined severe exertional hypoxemia as an $Sp_{O_2} \leqslant 88\%$. However, we found substantial variability in definitions for severe hypoxemia

This Executive Summary is part of the full official ATS clinical practice guideline, which readers may access online at http://www.atsjournals.org/doi/abs/10.1164/rccm.202009-3608ST. Only the Executive Summary is appearing in the print edition of the *Journal*. The article of record, and the one that should be cited, is: Home Oxygen Therapy for Adults with Chronic Lung Disease: An Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med* 2020;202:e121–e141.

This is a corrected version of the article; it was updated on April 15, 2021. See erratum: *Am J Respir Care Med* 2021;203:1045–1046; https://www.atsjournals.org/doi/full/10.1164/rccm.v203erratum7.

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This document has an online supplement, which is accessible from this issue's table of contents at www.atsjournals.org.

Box 1

"The ability to get out of the house and continue my activities is top of the chart in importance! There is no way I want to become a couch potato . . . All the oxygen equipment was 'dumped' on me. I knew nothing and was in a daze. I am sure that the delivery guy gave me some instructions when it was delivered but I retained nothing. . . . My first concern was to find a better solution than the shoulder carry bag that the oxygen company provided. I needed to be hands free to play tennis. . . . I spent a couple of years perfecting my system of how to carry enough tanks to a tennis match (requires 6–8 tanks). I did a lot of Internet research to find carts or carrying cases for tanks. I have settled on a rolling cart that was designed to carry wine bottles to tasting parties. Perfect size for 6 tanks . . . It is a pain to have to plan out a day of activities with oxygen. What is the elevation, how far will I have to walk, how many tanks do I need, where can I recharge my POC [portable oxygen concentrator]? There may come a day when you can't do these things so enjoy every minute you have. When I don't get enough tanks it makes me mad as hell . . . I still do not let down my guard down around the supplier. I never know when their business decisions will again affect my life."
—Supplemental home oxygen user

across studies. Thus, we also considered studies using different thresholds and reported the definitions used by study authors. We have provided suggested thresholds for hypoxemia in our conclusions. A detailed description of the methods is available in the online supplement.

Results

The final recommendations are summarized in Table 4, with the review of evidence and conclusions detailed below for each question.

Question 1: Should long-term oxygen be prescribed for adults with COPD who have severe chronic resting room air hypoxemia?

Evidence. The critical outcome for this question was mortality, and five studies were assessed (3, 4, 23–25) (*see* Table E2 in the online supplement), only two of which were RCTs (3, 4). There was moderate-quality evidence on the effects of LTOT on mortality because of imprecision in estimating the treatment effects. The two RCTs defined severe resting hypoxemia as either a $Pa_{O_2} \leq 55$ mm Hg (7.3 kPa) or a $Pa_{O_2} \leq 59$ mm Hg (7.9 kPa) plus one of the following: edema, hematocrit $\geq 55\%$, or P pulmonale on ECG (3); or as Pa_{O_2} 40–60 mm Hg (5.3 kPa) and at least one previous episode of ankle edema (4). The NOTT (Nocturnal Oxygen Therapy Trial) (3) indicated a 2-year mortality-risk reduction of 55% in those prescribed continuous LTOT (24 h/d) compared with only nocturnal oxygen (relative risk, 0.45; 95% confidence interval [CI], 0.25–0.81). The MRC (Medical Research Council) study (4) indicated a 5-year mortality-risk reduction of 59% in those with LTOT (15 h/d) compared with no oxygen (relative risk, 0.41; 95% CI, 0.17–0.98). Data from the NOTT and MRC studies were not pooled because of differences in definitions of severe hypoxemia, durations of home oxygen therapy, comparators, time points of measurement, and populations. In the NOTT study (3), LTOT improved survival compared with nocturnal oxygen in patients with a higher Pa_{CO_2}, lower arterial pH, lower FVC, more severe nocturnal hypoxemia, lower hematocrit, lower mean pulmonary arterial pressure (PAP), and lower pulmonary vascular resistance (PVR). The NOTT authors were surprised to find smaller, nonsignificant differences in mortality between treatment groups in participants with higher baseline hematocrit, pulmonary arterial pressure, or PVR (3). Of note, however, the direction in the trend toward improved mortality in these individuals was similar to the trend in those with less impaired hemodynamics, and the mean PAP threshold used to separate subgroups (overall group median) was higher than the one used in the currently accepted definition of pulmonary hypertension. The MRC study did not report mortality benefits according to baseline characteristics (4). There was very-low-quality evidence on the effects of LTOT on healthcare use (24, 25). No study that met our inclusion criteria directly reported on the other important outcomes of dyspnea, fatigue, health-related quality of life (HRQL), exercise capacity, or physical activity in patients who received LTOT versus no LTOT.

For the outcome of safety, the systematic review identified cases of fires, burns from smoking around oxygen equipment, nosebleeds, and tripping over the equipment (26). The LOTT trial, the largest study of LTOT to date, found that for every 100 person-years, the rate of fires was 0.08, the rate of burns from smoking around oxygen equipment was 0.12, the rate of burns from oxygen around an open flame was 0.04, the rate of burns from LOX frost was 0.16, the rate of nosebleeds was 0.35, and the rate of tripping/falling over oxygen equipment was 0.90 (5). For all COPD Medicare beneficiaries who used home oxygen, those who had an emergency room visit for a burn injury were twice as likely to be prescribed oxygen in the preceding 90 days compared with those without burn injury (27).

Table 1. Certainty of Evidence

Evidence Quality	Definition
High	High confidence that the estimated effect is close to the true effect.
Moderate	Moderate confidence that the estimated effect is close to the true effect, but with a chance that the true effect is considerably different.
Low	Low confidence in the estimated effect. Higher likelihood that the true effect is considerably different from the estimated effect.
Very low	Very low confidence in the estimated effect. High likelihood that the true effect is considerably different from the estimated effect.

Table 2. Implications of Clinical Guideline Recommendations by Stakeholder

Stakeholder	Strong Recommendation	Conditional Recommendation
Patient	The majority of patients would want the recommended course of action in this situation, and only a small number would not.	Many patients in this situation would prefer the recommendation, but a substantial number may not. This is an opportunity for shared decision-making between the clinician and patient.
Clinician	Most individuals should receive the course of action that is recommended. There is a low chance that additional formal decision aids are needed to help individuals make decisions consistent with their values and preferences, and adherence to this recommendation could be used as a performance indicator or quality criterion.	Different choices will be applicable to different patients, and additional factors will need to be considered in addition to the recommendation in order for a patient to make a decision according to their values and preferences. Decision aids may be needed to assist individuals in making their best choice. This is an opportunity for shared decision-making between the clinician and patient.
Policy-maker	The recommendation can be widely adapted as policy and can be used for performance indicators.	Policy-making will require substantial additional debate and involvement of many and/or additional stakeholders. The likelihood of regional variance is also higher, and performance indicators would need to take into consideration any additional deliberation that has occurred.

Conclusions. The panel concluded that the balance of desirable and undesirable effects supported the use of LTOT in patients with COPD with severe resting hypoxemia. The size of the desirable anticipated effects of LTOT on mortality is large, with decreased 2-year and 5-year mortality (critical outcome). The NOTT trial (3) reported that patients with severe hypoxemia associated with ventilatory compromise (on the basis of Pa_{CO_2}, arterial pH, and FVC) were more likely to benefit from LTOT and did not identify differences in mortality benefit according to pulmonary hemodynamics (on the basis of PVR and pulmonary arterial pressure), with a slightly larger benefit being shown in those with relatively milder hemodynamic disturbances. However, these were subgroup analyses, and similar analyses were not performed in the MRC study (4), so the panel concluded that there is insufficient evidence to recommend preferentially prescribing LTOT to specific subgroups of patients with COPD and severe hypoxemia.

LTOT comes with a moderate level of undesirable anticipated effects, including the physical and mental burden of using oxygen equipment, reduced ability to travel outdoors, difficulty accessing oxygen equipment during travel, and sleep disturbance from equipment noise (10, 28). The costs of implementation vary across geographic areas (29–33). The panel concluded that cost-effectiveness considerations probably favor the use of LTOT, after placing high value on reducing mortality and lower value on cost and resource use. Severe hypoxemia was defined using different thresholds in the two RCTs ($Pa_{O_2} \leq 55$ mm Hg [7.3 kPa] or $Pa_{O_2} \leq 59$ mm Hg [7.9 kPa] plus one of the following: edema, hematocrit $\geq 55\%$, or P pulmonale on ECG [3]; vs. Pa_{O_2} of 40–60 mm Hg [5.3–8.0 kPa] [4]). Because a mortality benefit was demonstrated in both studies, the panel concluded that either definition of severe hypoxemia is clinically justified. Neither clinical trial reported Sp_{O_2}-based thresholds for severe hypoxemia. We recognize that the relationship between Sp_{O_2} and Pa_{O_2} can vary because of an individual's pH, 2,3-diphosphoglycerate levels, Pa_{CO_2}, and temperature. However, the guideline panel concluded that providing approximate thresholds for Sp_{O_2} that correspond to the Pa_{O_2} thresholds used in the NOTT and MRC studies would improve the usability of the guideline report in circumstances in which arterial blood-gas measurements were not available.

In addition, the two clinical trials used slightly different definitions of "chronic." In the NOTT study (3), chronic was defined as meeting the definition of severe hypoxemia on "at least two occasions >1 week apart over a 3-week observation period" while the patient was free of exacerbations. In the MRC study (4), chronic was defined as meeting the Pa_{O_2}-based criteria for hypoxemia on "two repeated measurements at least 3 weeks apart." For implementation purposes, we define chronic resting hypoxemia as resting hypoxemia in the absence of a reversible cause. Although the NOTT and MRC trials used definitions that required repeated measures 3 weeks apart, this may not be possible or necessary in clinical practice. Reassessment recommendations include retesting after exacerbation and also in the setting of chronic disease (Table 5).

The panel agreed that a target saturation of 90% was preferred, as opposed to 88% in some guidelines, to avoid prolonged episodes of desaturation with minimal activity.

ATS recommendation. In adults with COPD who have severe chronic resting room air hypoxemia, we recommend prescribing LTOT for at least 15 h/d (strong recommendation, moderate-quality evidence).

Question 2: Should long-term oxygen be prescribed for adults with COPD who have moderate chronic resting room air hypoxemia?

Evidence. For this question, mortality was the critical outcome. The panel concluded that the quality of evidence for mortality in patients with moderate chronic resting room air hypoxemia was low because of imprecision of estimated treatment effects. The LOTT study included participants who had moderate hypoxemia at rest (room

Table 3. Terminology for Home Oxygen Therapy

Term	Definition
Ambulatory oxygen	Oxygen delivered during exercise or activities of daily living.
Continuous-flow oxygen	Oxygen delivered at a constant flow rate, regardless of the respiratory rate, in contrast to pulse-dose oxygen (*see below*).
Continuous oxygen	Oxygen prescribed 24 h/d.
Home oxygen	Oxygen delivered in a home, also known as domiciliary oxygen. It includes not only long-term oxygen but also short-term, nocturnal, palliative, ambulatory, and short-burst oxygen. It excludes oxygen use in healthcare and emergency settings.
Long-term oxygen	Oxygen that is delivered to patients with chronic hypoxemia, in most cases for the remainder of the patient's life. Long-term oxygen therapy is prescribed for at least 15 h/d.
Nocturnal oxygen	Oxygen delivered during sleep time only.
Palliative oxygen	Oxygen to relieve dyspnea. Palliative oxygen may be provided continuously, nocturnally, or during ambulation. Short-burst oxygen therapy falls into this category.
Portable oxygen	Oxygen delivered through systems that are sufficiently lightweight so that they can be carried or pulled by patients and allow them to leave their home (e.g., oxygen cylinders or canisters carried or pulled in trolleys or portable oxygen concentrators).
Pulse-dose oxygen	Oxygen delivered during inspiration only in such a way that the quantity of oxygen administered is influenced by the respiratory rate. The delivery system is at rest while the patient is exhaling.
Short-burst oxygen	Brief and intermittent oxygen administration before and/or after exercise, generally used as needed, in the absence of known hypoxemia.
Short-term oxygen therapy	Oxygen provided temporarily, during a period of severe hypoxemia (e.g., during the course of and shortly after an exacerbation of COPD).

Definition of abbreviation: COPD = chronic obstructive pulmonary disease.
There are several types of home oxygen therapy. This table is provided to assist in standardizing the terminology and is adapted by permission from Reference 22.

air Sp_{O_2} of 89–93%, no Pa_{O_2} threshold specified) and, after a change in study design during the trial because of low recruitment, also included participants who desaturated only with exertion ($Sp_{O_2} \geq 80\%$ for $\geq$5 min and $<90\%$ for $\geq$10 s during a 6-min-walk test [6MWT]) (5). At the request of the guideline panel, the LOTT group conducted additional analyses, comparing the risk of death with and without LTOT in the 419 participants with moderate hypoxemia at rest (57% of LOTT participants; Table E3). There was no difference between groups in time to death (hazard ratio, 0.95; 95% CI, 0.59–1.50). There were similar findings in a previous RCT of 135 patients with COPD and a Pa_{O_2} of 56–65 mm Hg (7.5–8.7 kPa) (34); the relative hazard of survival for no oxygen versus LTOT was 0.92 (95% CI, 0.57–1.47).

The panel concluded that the quality of evidence for effects on HRQL with LTOT in patients with COPD and moderate hypoxemia was moderate. Improvements in St. George's Respiratory Questionnaire (SGRQ) favored the use of LTOT at 4-month follow-up in those with both moderate resting and exertional desaturation (mean difference [MD], −3.30; 95% CI, −6.50 to −0.10), but no significant differences were found at 12 months. There were no differences between groups in the Quality of Well-Being Scale (5). Safety data from the LOTT trial (5) were reported in question 1.

Conclusions. The panel concluded that the balance of desirable and undesirable effects did not support use of LTOT for patients with moderate resting room air hypoxemia, on the basis of the available data. On the basis of the LOTT study, we defined moderate resting hypoxemia as an Sp_{O_2} of 89–93%. The corresponding Pa_{O_2} was not reported (5). The panel made a conditional recommendation against LTOT, placing high value on the absence of a proven mortality reduction and low value on short-term improvement in HRQL (observed at 4 mo but not 12 mo). The costs and burden of the treatment appear to outweigh the minimal benefit of LTOT on critical or important outcomes in adults with COPD with moderate resting room air hypoxemia. Therefore, discussions regarding prescribing continuous oxygen in this population offer opportunities for shared decision-making between the clinician and patient.

ATS recommendation. In adults with COPD who have moderate chronic resting room air hypoxemia, we suggest not prescribing LTOT (conditional recommendation, low-quality evidence).

Question 3: Should ambulatory oxygen be prescribed for adults with COPD who have severe exertional room air hypoxemia?

Evidence. For our critical outcome of HRQL, we examined studies that included patients with COPD who had severe isolated exertional desaturation (35–41) as well as those who had exertional desaturation but were eligible for LTOT (42–46) (Table E4). Overall, the quality of the evidence was low and included only two parallel-group RCTs of ambulatory oxygen (39, 46), of which only one included blinding to the intervention (39).

Isolated exertional desaturation. Meta-analysis of three studies (36, 39, 40) found a small but significant improvement in the dyspnea-related quality-of-life domain of the Chronic Respiratory Disease Questionnaire (standardized mean difference, 0.42; 95% CI, 0.04–0.79;

Table 4. Summary of ATS Recommendations

Question	ATS Recommendation	Strength of Recommendation and Level of Evidence
COPD		
Question 1: Should long-term oxygen be prescribed for adults with COPD who have severe* chronic resting room air hypoxemia?	In adults with COPD who have severe chronic resting room air hypoxemia, we recommend prescribing LTOT for at least 15 h/d.	Strong recommendation, moderate-quality evidence
Question 2: Should long-term oxygen be prescribed for adults with COPD who have moderate† chronic resting room air hypoxemia?	In adults with COPD who have moderate chronic resting room air hypoxemia, we suggest not prescribing LTOT.	Conditional recommendation, low-quality evidence
Question 3: Should ambulatory oxygen be prescribed for adults with COPD who have severe exertional room air hypoxemia?	In adults with COPD who have severe exertional room air hypoxemia, we suggest prescribing ambulatory oxygen.	Conditional recommendation, low-quality evidence
ILD		
Question 4: Should long-term oxygen be prescribed for adults with ILD who have severe chronic resting room air hypoxemia?	For adults with ILD who have severe chronic resting room air hypoxemia, we recommend prescribing LTOT for at least 15 h/d.	Strong recommendation, very-low-quality evidence
Question 5: Should ambulatory oxygen be prescribed for adults with ILD who have severe exertional room air hypoxemia?	For adults with ILD who have severe exertional room air hypoxemia, we suggest prescribing ambulatory oxygen.	Conditional recommendation, low-quality evidence
Liquid oxygen		
Question 6: Should portable liquid oxygen be provided for adults with chronic lung disease who are prescribed continuous oxygen flow rates of >3 L/min during exertion?	In patients with chronic lung disease who are mobile outside of the home and require continuous oxygen flow rates of >3 L/min during exertion, we suggest prescribing portable liquid oxygen.	Conditional recommendation, very-low-quality evidence
Education		
Education and safety for patients and caregivers	For all patients prescribed home oxygen therapy, we recommend that the patient and their caregivers receive instruction and training on the use and maintenance of all oxygen equipment and education on oxygen safety, including smoking cessation, fire prevention, and tripping hazards.	Best-practice statement

Definition of abbreviations: ATS = American Thoracic Society; COPD = chronic obstructive pulmonary disease; ILD = interstitial lung disease; LTOT = long-term oxygen therapy.
*On the basis of two clinical trials, severe hypoxemia is defined as meeting either of the following criteria: *1*) $Pa_{O_2} \leq 55$ mm Hg (7.3 kPa) or oxygen saturation as measured by pulse oximetry (Sp_{O_2}) ≤ 88% or *2*) Pa_{O_2} = 56–59 mm Hg (7.5–7.9 kPa) or Sp_{O_2} = 89% plus one of the following: edema, hematocrit ≥ 55%, or P pulmonale on an ECG.
†On the basis of a single clinical trial, moderate hypoxemia is defined as an Sp_{O_2} of 89–93%. The corresponding Pa_{O_2} was not reported in that study.

$I^2 = 12\%$) in favor of ambulatory oxygen, but mean changes were generally less than the minimal clinically important difference (MCID) in all three studies (47). Improvements with oxygen in individual participants could not be predicted by sex, exercise response to hyperoxia, or severity of desaturation, airflow obstruction, or dyspnea (39). One study using the SGRQ found no difference between supplemental oxygen and compressed room air (40), whereas another using the 36-Item Short-Form Health Survey (36) observed a significant difference in favor of ambulatory oxygen in multiple survey domains (48). The acute effects of oxygen on functional exercise capacity were assessed using multiple tests. Oxygen improved the 6-minute-walk distance by 28.9 m (95% CI, 16.1–41.9 m; $I^2 = 0\%$) (36, 37), increased exercise endurance on a cycle ergometer by 5.8 minutes (95% CI, 2.23–9.37 min) (41), increased exercise capacity by 17.9 W (95% CI, 8.10–27.70 W) (38), and increased steps walked on a 5-minute-walk test (14.9; 95% CI, 0.85–28.94) (40). We meta-analyzed the results of three studies reporting on the Borg dyspnea score at the end of exercise (36, 37, 41) and found a reduction of 1.11 U (95% CI, 0.53–1.69 U; $I^2 = 39\%$) in favor of ambulatory oxygen (Borg MCID = 1.0 U) (49). No studies reported the long-term effects of ambulatory oxygen on exercise capacity beyond acute laboratory or field tests, and no studies reported effects on physical activity in daily life.

Table 5. ATS Recommendation: Education and Safety Considerations

For patients prescribed home oxygen therapy, we recommend that the patient and their caregivers receive instruction and training on the use and maintenance of all oxygen equipment and education on oxygen safety, including smoking cessation, fire prevention, and tripping hazards (*best-practice statement*).

Safety	• Provide safety education to patients and caregivers regarding tripping and falls, decreasing fire risk by not smoking or allowing smoking inside the home, the use of inline devices, avoidance of activities around an open flame or spark, and the use of nonpetroleum nasal products.*†
	• Instruct liquid-oxygen users on avoidance of skin burns from contact with frosted parts on liquid-oxygen-device connectors.‡
	• Provide guidance on transporting and traveling safely with oxygen.
	• Confirm the presence of back-up devices for emergencies or power loss.
Smoking	• Instruct current smokers or caregiver smokers on treatment of tobacco dependence and refer to appropriate resources.
	• In some regions, smoking is an absolute contraindication to home oxygen therapy§. One guideline suggests advising the patient that oxygen provides limited clinical benefit for those who continue to smoke.‖
	• Alert patients and caregivers that use of e-cigarettes, or vaping, is associated with burn accidents in e-cigarette smokers receiving home oxygen therapy.¶
Education	• Tailor patients' education to their health literacy and cultural contexts.
	• Incorporate effective evaluation and return demonstration of their ability to use their prescribed devices both in the home and in ambulatory settings.
	• Instruct patients and caregivers on troubleshooting equipment problems.
	• Consider access to appropriate equipment on the basis of patients' physical, physiologic, and lifestyle/mobility needs.
Monitoring	• Reassess patients' oxygen needs, acknowledging that the frequency would vary by disease characteristics, such as rate of progression. Clinical support for monitoring at home by nurses and respiratory therapists is rare in the United States but common in other regions.**
	• Reassess oxygen needs for patients who are newly prescribed oxygen after hospital discharge to confirm ongoing oxygen requirements.††
	• Advise patients to bring their portable device to healthcare visits to assess its effectiveness and to reinforce self-management.

Definition of abbreviation: e-cigarette = electronic cigarette.
*Reported in safety findings of LOTT (Long-Term Oxygen Treatment Trial) (5, 26).
†Risk of burn injury reported in 17-year national study in Sweden (5, 26).
‡Apria Patient/Caregiver Instructions–Liquid Oxygen (86).
§Thoracic Society of Australia and New Zealand Clinical Practice Guidelines on Adult Domiciliary Oxygen (9).
‖British Thoracic Society guidelines for home oxygen use in adults (93).
¶Described in a study on home oxygen programs and funding in Canada (10, 94).
**Home support noted in 29-year prospective long-term oxygen therapy data (19).
††Data on patient recovery from hypoxemia in patients with chronic obstructive pulmonary disease after hospital discharge (95) and importance of retesting (96).

Resting and exertional hypoxemia. Six RCTs (42–46, 50) met our inclusion criteria; however, none included results for our critical outcome of HRQL. In one randomized crossover study of LTOT users, ambulatory oxygen had no effect on dyspnea (51). Ambulatory oxygen acutely increased the distance patients walked in 12 minutes if not carrying walkers or shopping trolleys (42), acutely improved the distance walked on the incremental shuttle walk test (MD, 27.3 m; 95% CI, 14.7–39.8 m) (50), and acutely improved endurance time by 4.70 minutes compared with room air (95% CI, 3.76–5.64 min) (45). We meta-analyzed the results from three studies reporting on the Borg dyspnea score (44, 45, 50) and found a reduction of 0.59 U (95% CI, 0.18–0.99 U; $I^2 = 25\%$) in favor of ambulatory oxygen.

There is also a substantial body of evidence regarding the patient and caregiver burden associated with the use of ambulatory oxygen, including managing the equipment, being embarrassed using it outside the home, fear of cylinders running out, reduced ability to travel, equipment noise that may affect social activities, difficulty obtaining portable oxygen concentrators, and poor access to information about effective use of oxygen equipment (14, 52, 53).

Conclusions. For people with COPD and severe exertional hypoxemia, we did not find consistent evidence that ambulatory oxygen delivered clinically significant improvements in the critical outcome of HRQL, whereas effects generally favored ambulatory oxygen (low Grading of Recommendations Assessment, Development and Evaluation evidence). In studies examining the acute effects of oxygen during exercise testing, there were clinically significant improvements in endurance time and walk distance. Improvements in exercise capacity were seen both in those with isolated exertional hypoxemia and in those eligible for LTOT. The effects of ambulatory oxygen on dyspnea during exercise testing were inconsistent. Effects on mortality, fatigue, and physical activity in daily life were not reported. We defined exertional hypoxemia as an $Sp_{O_2} \leq 88\%$. In patients who are eligible for LTOT, prescription of ambulatory oxygen may be important to increase the daily hours of oxygen usage (54). Standardization of the level of exertion is critical when assessing the effects of oxygen on dyspnea (55, 56). This recommendation places a high value on increasing HRQL and the potential for facilitating physical activity outside the home and places a lower value on cost, inconvenience, and resource use.

ATS recommendation. In adults with COPD who have severe exertional room air hypoxemia, we suggest prescribing ambulatory oxygen (conditional recommendation, low-quality evidence).

Question 4: Should long-term oxygen be prescribed for adults with ILD who have severe chronic resting room air hypoxemia?

Evidence. For the critical outcome of mortality, no studies were found that met all of our inclusion criteria. A 2001 Cochrane systematic review (57) reported the results from one unpublished RCT in which severe resting hypoxemia was defined as a Pa_{O_2} of

45–60 mm Hg (6.0–8.0 kPa), slightly above our prespecified cutoff of a $Pa_{O_2} \leq 55$ mm Hg (73 kPa) (Table E5). There was no significant difference in mortality between the LTOT and room air groups after 1 year (odds ratio [OR], 0.50; 95% CI, 0.15–1.61), 2 years (OR, 1.76; 95% CI, 0.64–4.86), or 3 years (OR, 0.99; 95% CI, 0.16–6.26). As conclusions about mortality are based on one unpublished RCT, the quality of evidence was very low (Table E5). Because of the paucity of any direct evidence on patients with ILD, we chose to consider indirect evidence from our first population, intervention, comparison, and outcome question, which considered patients with COPD and severe resting hypoxemia (6, 58–60).

Safety data in ILD were scarce but included a qualitative study in patients with idiopathic pulmonary fibrosis, noting tripping as a hardship after being on oxygen for 9–12 months (61). The panel agreed that the safety data for patients with COPD on LTOT would be similar for patients with ILD on LTOT.

Conclusions. The panel judged the perceived benefits of LTOT to treat severe chronic resting hypoxemia to be substantial for most adults living with ILD, on the basis of indirect evidence from trials in COPD. LTOT for severe resting hypoxemia may confer a survival benefit and prevent organ dysfunction due to severe sustained hypoxemia, including the prevention of pulmonary hypertension. Other benefits may include relief of breathlessness as well as improvements in disability and HRQL. The primary undesirable consequences are listed in question 1. Overall, the panel deemed the substantial desirable consequences of LTOT to outweigh the undesirable consequences of untreated severe resting hypoxemia. Despite the very-low-quality evidence available to the panel, ethical concerns about withholding LTOT were strong factors in our decision-making. Other guidelines similarly base recommendations on COPD evidence (7, 62). For patients with ILD, we have applied the same definition of severe resting hypoxemia as was applied for those with COPD (question 1). The assessment of pulmonary hypertension should be considered, as it is a predictor of increased mortality in patients with idiopathic pulmonary fibrosis and is also a predictor of worsening lung function, worsening functional status, increased oxygen needs, and increased risk of acute exacerbation (6, 58–60).

ATS recommendation. For adults with ILD who have severe chronic resting room air hypoxemia, we recommend prescribing LTOT for at least 15 h/d (strong recommendation, very-low-quality evidence).

Question 5: Should ambulatory oxygen be prescribed to adults with ILD who have severe exertional room air hypoxemia?

Evidence. The quality of evidence was low, with no parallel-group RCTs and only one study, the AmbOx (Ambulatory Oxygen in Fibrotic Lung Disease) trial (63), reporting the effects of ambulatory oxygen used during daily activities. In this randomized, 2-week, unblinded, crossover trial in patients with fibrotic ILD with isolated exertional hypoxemia ($Sp_{O_2} \leq 88\%$), a significant improvement in the King's Brief ILD questionnaire was found in favor of ambulatory oxygen for the total score (MD, 3.7; 95% CI, 1.8 to 5.6), breathlessness/activities score (MD, 8.6; 95% CI, 4.7 to 12.5), and chest symptoms score (MD, 7.6; 95% CI, 1.9 to 13.2). The MCID for the total score is 3.9 points (64, 65). There was also a significant improvement in the SGRQ total score (MD, −3.6; 95% CI, −6.7 to −0.6) and activity score (MD, −7.5; 95% CI, −12.4 to −2.5), with the MCID for the SGRQ being 4 U (66). Dyspnea with activities of daily living was assessed using The University of California, San Diego, Shortness of Breath Questionnaire, showing a decrease by 8 U (95% CI, 3.6 to 12.4 U). The MCID is 5 U (63, 67). Despite the clear challenges posed by ambulatory oxygen, also highlighted in the qualitative component of the trial, two-thirds of patients decided to continue with ambulatory oxygen at the end of the study.

A 2016 Cochrane systematic review (68) found no benefits of ambulatory oxygen over room air in patients with ILD for change in 6-minute-walk distance, the endurance shuttle walk test, or the Borg dyspnea score. One study reported an acute improvement in endurance time by 118.7 seconds (95% CI, 23.9 to 213.5 s) (69) with ambulatory oxygen. Meta-analysis of three newer studies showed that ambulatory oxygen acutely improved 6-minute-walk distance by 18.57 m (95% CI, 11.14 to 25.99 m; $I^2 = 0\%$) compared with room or cylinder air (Table E6) and reduced the Borg perceived-exertion score (0.37 U; 95% CI, 0.19 to 0.54 U; $I^2 = 0\%$), but no significant difference was found regarding the Borg dyspnea score (MD, −0.72; 95% CI, −1.70 to 0.27; $I^2 = 73.28\%$) (63, 70, 71). Oxygen increased exercise duration by 57.67 seconds (95% CI, 0.22 to 115.12 s; $I^2 = 0\%$) without significant improvement in the maximal work rate (MD, 10.34 W; 95% CI, −3.59 to 24.26 W; $I^2 = 0\%$) in participants undergoing cardiopulmonary exercise testing (72, 73).

The Cochrane review did not report any serious adverse events or side effects (68). However, the panel agreed that risks of transporting cylinders, burns, fires, and tripping would be potential safety concerns for patients with ILD using oxygen during exertion within and outside the home.

Conclusions. Weak evidence supports the use of ambulatory oxygen in people with ILD because of the benefit to HRQL, but certainty is low, as the medium- to long-term effects are unknown. In laboratory studies, the improvements in exercise capacity tended to favor ambulatory oxygen but were generally small, and effects on physical activity in daily life were not examined. Qualitative studies undertaken in patients with ILD report negative physical and psychosocial impacts of ambulatory oxygen therapy that persist despite acceptance that ambulatory oxygen may be inevitable as disease progresses (74). Patients and caregivers report that there may be unmet expectations for symptom relief (particularly with regard to dyspnea), challenges related to the use of cumbersome or complicated equipment, embarrassment when using ambulatory oxygen in public, reduced independence for patients, and increased caregiver burden, marking an important trade-off between benefits and inconvenience (61, 74, 75). Therefore, it is likely that some patients will choose not to use ambulatory oxygen. We defined exertional hypoxemia as an $Sp_{O_2} \leq 88\%$.

ATS recommendation. For adults with ILD who have severe exertional room air hypoxemia, we suggest prescribing ambulatory oxygen (conditional recommendation, low-quality evidence).

Question 6: Should portable LOX be provided for adults with chronic lung disease who are prescribed continuous oxygen flow rates of >3 L/min during exertion?

Evidence. Three modes of portable oxygen delivery are available for patients' use

Table 6. Characteristics of Portable Oxygen Devices

	Metal Oxygen Cylinders	POCs	LOX
Size and weight	Available in multiple sizes from 2.5 to 9 kg (E cylinder in United States, which requires a trolley)*	Vary in weight (1.5–10 kg), noise, battery life, oxygen purity (87–95%), maximum breath rates, and settings (pulse flow, continuous flow, or both)†‡	Medium to large canister ranges between 2.5 and 4 kg
Filling	Some stationary concentrators allow patients to fill smaller oxygen cylinders in their home, (home-fill units), but these last <1 h on continuous-flow rates >3 L/min and therefore are inadequate for high-flow patients	No filling; POCs "concentrate" oxygen by extracting nitrogen from ambient air. They run off of a battery and can be recharged	Patients refill portable canisters from a larger home reservoir of LOX One liter of LOX expands to 860 L of gaseous oxygen
Pulse setting or continuous-flow capacity§	Oxygen-conserving devices using pulse-flow technology can be attached to metal cylinders to prolong the duration of supply by releasing oxygen only during inspiration Because of differences in an individual patient's ability to trigger a pulse dose of oxygen, and the volume delivered with each pulse at different respiratory rates, they may be insufficient for patients who require continuous oxygen with exertion at >3 L/min, such as those with interstitial lung disease, lung transplantation candidates, and others with severe hypoxemia	At a given pulse-flow setting, POCs differ as to the volume of oxygen (ml) per pulse, inspiratory time, and triggering sensitivity and may not consistently sense patients' inspiratory efforts to trigger the device* Pulse settings are based on an oxygen volume unique to each device, not a standardized L/min methodology	Portable LOX technology allows delivery of continuous-flow oxygen up to 15 L/min via a lighter and longer-duration device
Duration of supply	A single E tank with a stroller will last approximately 1.9 h on 6 L/min. Multiple cylinders are needed for high-flow (>3 L/min) patients to be out of the home >2–4 h‖	All POCs depend on a battery supply that depletes more rapidly with higher settings, higher respiratory rates, and the use of continuous-flow settings	A medium LOX canister will last 3 h at 6 L/min of continuous flow
Cost	Metal oxygen cylinders range from US$50 to US$100; additional costs for a regulator or oxygen-conserving device. Commonly supplied by U.S. DME companies	In the United States, many DME companies offer POCs as a portable option together with a stationary concentrator; individuals can also purchase them for US$2,000–4,000	Cost estimates are approximately four times higher per patient compared with POCs or metal-cylinder options because of the requirements for DME companies to access and store LOX, use specially outfitted delivery trucks, and provide weekly refill servicing¶
Travel	Metal cylinders not allowed for air travel	POCs are the only carry-on portable oxygen device allowed by the Federal Aviation Administration for air travel; some airlines may provide oxygen cylinders for emergency in-flight use only**	Liquid oxygen not allowed for air travel

Definition of abbreviations: DME = durable medical equipment; LOX = liquid oxygen; POCs = portable oxygen concentrators.
*The availability of different oxygen devices varies by geographic region, and some jurisdictions do not have smaller metal oxygen cylinders.
†POCs vary in pulse technology, oxygen purity, and triggering sensitivity (78, 87–91).
‡The few POCs that currently provide a maximum of 3 L/min on a continuous-flow setting weigh over 9 kg and require a trolley.
§For all devices, if an oxygen-conserving device is used, the patient should be tested using that device during exertion, similar to what they would do in daily life, to ensure adequate oxygenation. A continuous-flow setting of 5 L/min and a pulse-flow setting of "5" may not deliver equivalent volumes of oxygen, despite direct marketing claims.
‖Patients depend on their DME company to deliver an adequate number of cylinders per week or month.
¶LOX costs are higher than costs for POCs or metal cylinders (81).
**The Federal Aviation Administration stipulates which POCs are allowed for use during air travel (92).

Figure 1. Examples of stationary and portable oxygen devices in the United States. Illustration by Patricia Ferrer Beals.

outside of the home: metal cylinders of compressed gaseous oxygen, portable oxygen concentrators, and LOX canisters (Figure 1 and Tables 6 and E11). LOX has previously been used for those with higher flow requirements of up to 15 L/min via a relatively lightweight device with a longer duration of oxygen supply to facilitate mobility and time spent outside of the home, but efficacy is unclear. Since the implementation of the Medicare National Competitive Bidding Program by the Centers for Medicare and Medicaid Services (CMS) in the United States in 2011, Medicare beneficiary claims for portable LOX declined from 966,846 in 2004 to 97,690 in 2016 (76), reflecting lower CMS reimbursement to durable medical equipment (DME) companies with subsequent elimination of LOX and transition to "nondelivery" home-fill gaseous oxygen systems (77–79) and heavier E cylinders. The impact of this decline in the availability and adequacy of portable oxygen devices in the United States has been profound, with the overarching theme being restricted mobility and isolation due to inadequate portable options (13, 14, 16, 20, 80). The panel agreed that portable LOX for individuals requiring >3 L/min of continuous-flow oxygen was an important problem to address, both because limited mobility affects our critical outcome of HRQL and because the symptoms associated with exertional hypoxemia in patients with high-flow oxygen needs may be substantial.

The literature search did not yield any studies that met our inclusion criteria, which specified that patients be prescribed continuous oxygen flow rates of >3 L/min during exertion, so we synthesized the literature for six studies on patients with COPD (44, 46, 81–84) who had lower or unreported flow rates (Table E7). A multicenter RCT (81) compared the use of stationary oxygen concentrators (alone or in combination with small oxygen cylinders) with LOX (stationary and portable) and found significant differences in the Sickness Impact Profile score favoring LOX for the domains of mobility (MD, −4.57; $P = 0.043$), body care (MD, −5.83; $P = 0.011$), ambulation (MD, −8.46; $P = 0.017$), social interaction (MD, −5.27; $P = 0.023$), and total score (MD, −3.38; $P = 0.018$) (81) (MCID is a change of 5 U) (85). No difference in oxygen saturation was observed on the 6MWT (44, 84) or 2-minute-walk test (83) between LOX and concentrators. The Borg dyspnea score did not differ significantly after the 6MWT (MD, −0.10; 95% CI, −1.23 to 1.03) (44) or 2-minute-walk test (MD, −0.40; 95% CI, −1.36 to 0.56) (83). In adherence assessments, LOX groups used oxygen for 3 hours (95% CI, 1.97 to 4.03 h) (46) to 6.50 hours (95% CI, 4.43 to 8.57 h) (83) longer each day compared with those solely using stationary devices. LOX users spent more time outside the home than metal-cylinder users (MD, 4.0 h; 95% CI, 0.9 to 7.1 h) (82, 83) and were more likely to leave the home (83).

Conclusions. Despite the absence of studies examining the use of continuous-flow LOX at >3 L/min, the panel judged that the desirable consequences and benefits outweighed the undesirable consequences and harms of portable LOX therapy. This recommendation places a high value on HRQL and mobility outside of the home and places a lower value on costs and resource use. Indirect evidence demonstrated improvements in some domains of HRQL, improved adherence, and increased time spent outside the home. LOX provides opportunity for increased community mobility and participation for patients with severe hypoxemia who would otherwise be unable to leave the home. Patients who are caregivers for others, have paid employment or classroom education needs outside the home, or are attending pulmonary rehabilitation sessions to prepare for lung transplantation will have greater ability to effectively engage in such activities by having a longer duration of oxygen supply. Undesirable consequences unique to LOX included the need for the manual ability to fill portable canisters from a large reservoir and risk of skin burns from frost leaks when filling portable canisters (86).

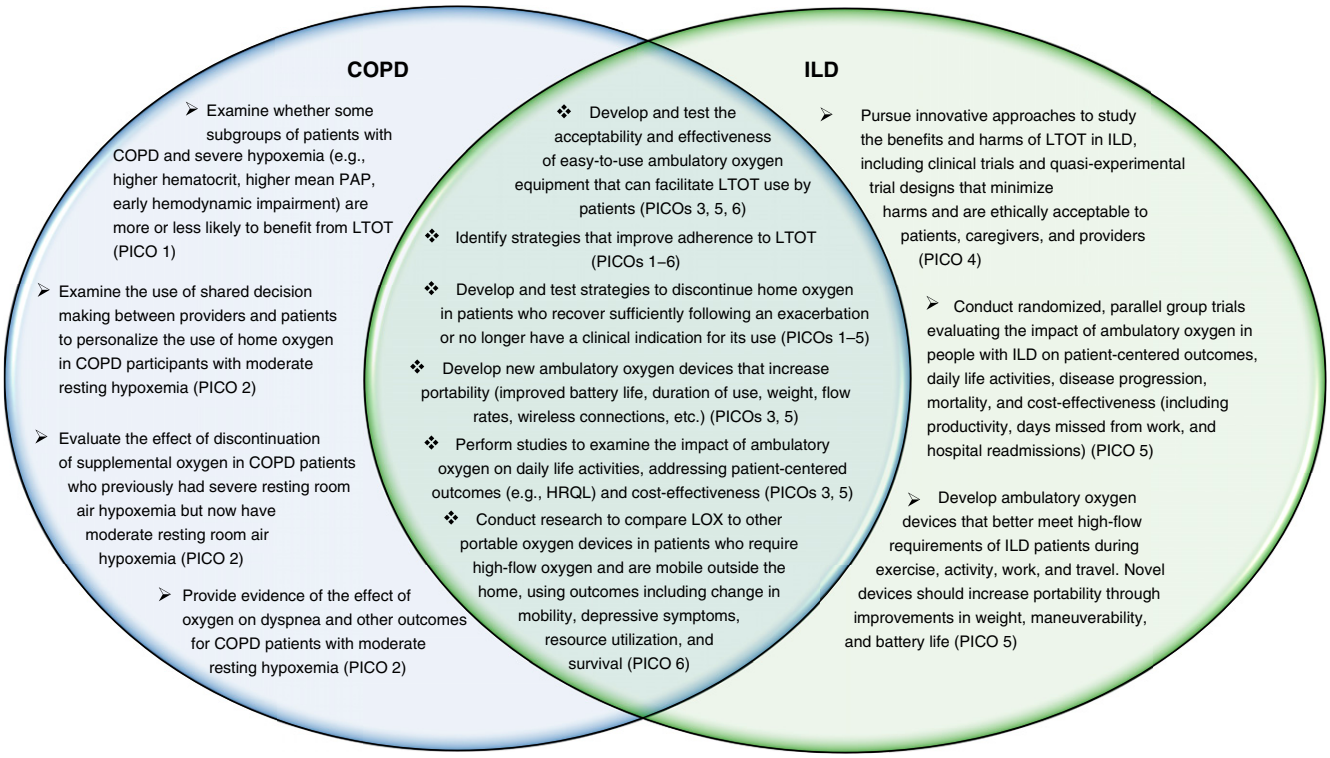

Figure 2. Research needs. COPD = chronic obstructive pulmonary disease; HRQL = health-related quality of life; ILD = interstitial lung disease; LOX = liquid oxygen; LTOT = long-term oxygen therapy; PAP = pulmonary arterial pressure; PICO = population, intervention, comparison, and outcome.

ATS recommendation. In patients with chronic lung disease who are mobile outside of the home and require continuous flow rates of >3 L/min during exertion, we suggest prescribing portable LOX (conditional recommendation, very-low-quality evidence).

Panel Discussion

The panel agreed that for all patients receiving home oxygen therapy, including LTOT and ambulatory-only use, there was no acceptable alternative to providing patients and their caregivers with appropriate education related to home oxygen equipment use, oxygen safety, and self-management. These were recurring topics of discussion for all questions. A best-practice statement was included to address these recommendations (Table 5).

ATS Recommendation

For patients prescribed home oxygen therapy, we recommend that the patient and their caregivers receive instruction and training on the use and maintenance of all oxygen equipment and education on oxygen safety, including smoking cessation, fire prevention, and tripping hazards (best-practice statement).

Conclusions

Our systematic review revealed gaps in available data on the efficacy of supplemental oxygen. The need for guidance is high, given that the prescription of supplemental oxygen is common. Recommendations in this document reflect an integration of current evidence and clinical experience by a multidisciplinary expert panel. Figure 2 summarizes research needs identified by the panel.

For patients with severe resting hypoxemia, the prescription of LTOT to improve survival is supported by historical trials in patients with COPD. The panel also strongly recommends prescribing oxygen for patients with ILD with severe resting hypoxemia. Existing evidence and panel consensus suggest not prescribing LTOT for patients with COPD with moderate resting hypoxemia. The practice of initiating short-term oxygen therapy on hospital discharge in patients with severe hypoxemia is based on indirect evidence from the NOTT and MRC clinical trial populations with chronic hypoxemia. The harms and benefits of prescribing short-term oxygen therapy on hospital discharge deserves further study. Further research is also needed on the appropriate use of shared decision-making between patients and their clinicians for decisions regarding home oxygen therapy and on approaches to discontinue home oxygen in patients who no longer have severe resting hypoxemia.

This review confirmed scarce and inconclusive data to support the prescription of oxygen in patients who desaturate (sometimes markedly) with exertion, particularly during daily life activities outside of a laboratory setting. Emerging evidence suggests that ambulatory oxygen may improve HRQL in patients with ILD in the short term, but longer-term data are needed to evaluate patient-centered outcomes. This was identified as a critical research need to create evidence-guided practice for patients with ILD, who often experience severe

exertional hypoxemia. The urgency is underscored by the treatment's cumbersome nature, associated risks, and complex effects on patients, families, and caregivers.

No studies met the panel's criteria for the investigation of the benefits of LOX for patients who use >3 L/min of continuous-flow oxygen and spend regular time outside the home. The panel concluded that although an E tank or other large metal cylinder can adequately provide oxygen at up to 5 or 6 L/min, the patient would be restricted by the need to carry multiple E tanks to leave home for anything beyond a very short time period. The panel unanimously agreed that LOX should be offered to active patients on high-flow oxygen and that policies to accommodate this subgroup should be moved forward.

The minimal standard of care for all patients receiving home oxygen therapy must include education and training related to their oxygen equipment, oxygen safety, and self-management. Moreover, reassessment of patients' oxygen needs is critical when prescribed for severe chronic resting room air hypoxemia (after 60–90 d) and after hospital discharge after a COPD exacerbation (1–4 wk and again at 12–16 wk after hospital discharge) (12). Reassessing oxygen requirements would help to match a patient's evolving oxygen requirements with oxygen prescriptions (e.g., increase or decrease in oxygen flow rates, discontinuation), promote patient education (e.g., how to use new equipment, how to titrate oxygen flow to changes in levels of hypoxemia), and enhance communication with other providers (e.g., primary care and home health agencies).

We urge the research community and funding agencies to work together to develop a stronger evidence base that will guide clinical practice for oxygen prescription. Of critical importance is the involvement of engineers and those in related fields who can combine creativity with applied science to develop methods of raising arterial blood oxygen content to normal levels, even during intense exercise, without the burdens associated with current oxygen delivery systems. ■

This official clinical practice guideline was prepared by an *ad hoc* subcommittee of the ATS Assembly on Nursing.

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Author Disclosures: S.S.J. served on an advisory committee for the Pulmonary Fibrosis Foundation. A.E.H. served as a speaker for AstraZeneca and received research support from Air Liquide and Linde Healthcare. J.A.K. served on a data safety and monitoring board for Sanofi and received research support from Inogen, Patient-Centered Outcomes Research Institute, and ResMed. D.J.L. served on an advisory committee for Boehringer Ingelheim, Fibrogen, Galapagos, Genentech/Roche, and Veracyte; served as a consultant for Fibrogen, Galapagos, Galecto, Genentech/Roche, Patara, the Pulmonary Fibrosis Foundation, Sanofi, and Veracyte; received research support from Boehringer Ingelheim, Fibrogen, and Global Blood Therapeutics; and is an employee of and owns stock and stock options with Regeneron. B.C. served on an advisory committee for AstraZeneca, GlaxoSmithKline, Monaghan, and Sunovion; served as a consultant for GlaxoSmithKline and Monaghan; and served as a speaker for GlaxoSmithKline, Monaghan, and Sunovion. M.B.D. served on an advisory committee for AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, and Mylan; served as a consultant for AstraZeneca, Enterprise Therapeutics, GlaxoSmithKline, NovaVax, Parion, Philips Respironics, and Theravance; received research support from Boehringer Ingelheim; and received author royalties from Karger Publishing. C.G. served on an advisory committee, as a consultant, and as a speaker for Boehringer Ingelheim. V.P.-C. received research support from ResMed and is an employee of Vertex. E.A.R. served on an advisory committee for Roche; served as a speaker for Boehringer Ingelheim, Mundipharma, and Roche; and received travel support from Boehringer Ingelheim. C.J.R. served on an advisory committee for Boehringer Ingelheim and received research support from and served as a speaker for Boehringer Ingelheim and Roche. J.S. served as a consultant for Boehringer Ingelheim; served on an advisory committee, served as a speaker for, and received research support from Boehringer Ingelheim and Genentech; and served on the board of directors and has an intellectual property/patent unsold for Live Fully, Inc. M.E., M.G., B.A.G., T.H., B.J., T.K., S.L.K., K.L., A.S., A.-Y.M.T., and D.U. reported no relationships with relevant commercial interests.

Acknowledgment: The guideline panel thanks the ATS staff for their organization and support, which was critical to this project's completion and success. The authors also thank panel member Ms. Beverly Jackson for her insightful contributions as an oxygen user and as an advocate for those using home oxygen. The panel thanks the LOTT authors' sharing of their important data on patients with exertion-only hypoxemia and thanks the authors of the Moore and colleagues 2011 study (39) for providing additional study information.

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