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Review

Home Oxygen Therapy (HOT) in Stable Chronic Obstructive Pulmonary Disease (COPD) and Interstitial Lung Disease (ILD): Similarities, Differences and Doubts

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Abstract: This narrative paper reviews the current knowledge of Home Oxygen Therapy (HOT) in stable Chronic Obstructive Pulmonary Disease (COPD) and Interstitial Lung Disease (ILD), two major causes of Long-Term Oxygen Therapy (LTOT) prescription. There is evidence that LTOT improves survival in COPD subjects with chronic severe respiratory failure. HOT is also used to contrast exercise and sleeping hypoxemia and to improve Quality of Life (QoL) and symptoms. Ambulatory Oxygen Therapy (AOT) did not assure generalized improvements in symptoms and Quality of Life (QoL) of COPD subjects. There is short-term evidence in a real-life study that AOT may improve QoL in ILD subjects with Exercise Oxygen Desaturation (EOD) and exertional dyspnea. There are some differences between guidelines and practices, which translate into variations in characteristics and rates of ILD and COPD subjects admitted to LTOT and AOT. Indications on titration of oxygen flow and the best oxygen delivery device for optimal management of AOT in COPD and ILD subjects are often vague or lacking. More work is needed for optimizing and customizing HOT in COPD and ILD subjects.

Keywords: Chronic Obstructive Pulmonary Disease (COPD); Interstitial Lung Disease; oxygen therapy; survival; dyspnea; devices; Quality of Life

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1. Introduction

Home Oxygen Therapy (HOT) is often used in subjects with chronic pulmonary diseases. HOT is realized by increasing the percentage of oxygen in the gas inspired by the patient. This is obtained either by enriching the air with Liquid Oxygen (LOX) and Gaseous Oxygen (GOX) or by extracting nitrogen from air with concentrators (OCs). We send the interested reader to a devoted review for extensive description of oxygen delivery devices [1]. Briefly, these three delivery systems offer similar clinical results, but have different characteristics, summarized in Table A1. Each of these systems includes portable delivery devices. Although there is no clear definition of weight and size, a portable device is generically defined as the oxygen delivery device suitable for Ambulatory Oxygen Therapy (AOT), usually prescribed to subjects who go outside the home regularly.

HOT has several causes of prescription and use, displayed in Table A2, with large overlaps [2]. The long-term prescription of HOT for at least 15 h a day to reverse chronic severe respiratory failure (defined as arterial oxygen tension, $PaO_2 \leq 55/7.3$ mmHg/kPa, or PaO_2 56–59/7.4–7.8 mmHg/kPa and hypoxemic organ damage) is the aforementioned Long-term Oxygen Therapy (LTOT). Severe hypoxemia is a marker of advanced disease and unfavorable prognosis. Chronic Obstructive Pulmonary Disease (COPD) and Interstitial Lung Disease (ILD) are the most common causes of LTOT prescription. According to the Swedish registry, in the period between 2016 and 2019, COPD and ILD accounted for about 67% and 18% of LTOT prescriptions, respectively [3].

COPD is a highly prevalent syndrome characterized by persistent airflow limitation, due to the chronic inhalation of harmful particles, mainly tobacco smoke [4]. The GBD study has estimated a prevalence of COPD worldwide at 3.9% [5].

ILD is a syndrome characterized by extensive lung fibrosis. Idiopathic Pulmonary Fibrosis (IPF) [6], the most common and severe variety of ILD, has an adjusted prevalence in the range of 0.33–4.51 per 10,000 persons [7]. A subset of subjects with other ILDs, approximately approaching 20–30% of cases, also shows an evolving course, similar to that of IPF, defined as Progressive Fibrosing ILD [8,9]. This narrative review will summarize the current knowledge on the use of HOT in subjects with COPD and ILD. We will only consider subjects in the stable state and exclude those with Obstructive Sleep Apnea syndrome (OSA), a common sleeping breathing disorder, that is primarily managed with treatments other than HOT.

2. Literature Search

We performed a literature search using the electronic platform Medline Pubmed, for articles published in English up to May 2022. The following keywords were used: "Chronic respiratory failure", "Chronic respiratory diseases", "Respiratory Failure", "Respiratory Insufficiency", "Oxygen Therapy", "Supplemental oxygen", and "Oxygen, inhalation therapy". Each of these terms was then combined with: "pulmonary disease, chronic obstructive", "COPD", "chronic bronchitis" or "Interstitial Lung Fibrosis", "Interstitial Lung disease", and "Idiopathic Pulmonary Fibrosis". The reference list of the retrieved articles was tracked down. Titles and abstracts were analyzed, selecting studies considered as pertinent for our search. Full selected studies were read, also looking for other relevant studies or reviews. No quality evaluation of papers was performed. This review was not registered.

3. Frequency, Significance and Varieties of Hypoxemia in Subjects with COPD and PF-ILD

3.1. COPD

Chronic severe respiratory insufficiency is a relatively uncommon complication of COPD, occurring in approximately 2% of cases [10].

Independently of resting daytime hypoxemia, many COPD subjects show Exertional Oxyhemoglobin Desaturation (EOD) and/or Sleeping Oxyhemoglobin Desaturation (SOD). Although there is a lack of full agreement on their definition, EOD is often defined as a decrease in oxyhemoglobin saturation (SpO_2) of at least 5% from resting baseline values and an exertional nadir of less than 90%; SOD is generally invoked when more than 30% of overnight sleep time is spent with SpO_2 of less than 90% in the absence of an intermittent hypoxemic pattern. Up to 40–50% of COPD subjects with daytime resting mild hypoxemia or normoxemia show EOD [11,12]. EOD has been associated with severe prognosis and an increased risk of exacerbation and deterioration of Quality of Life (QoL) in COPD subjects [12–16]. Isolated SOD has been observed in up to one-third of COPD populations [17,18]. SOD may worsen prognosis [16]. In a study involving 59 COPD subjects who did not qualify for LTOT, the group with SOD did not show impairment in QoL and sleep quality [19].

3.2. PF-ILD

Subjects with PF-ILD have fast progression: the median transplant-free survival time of PF-ILD subjects with chronic severe hypoxemia was 0.76 years vs. 1.77 years in COPD subjects with chronic respiratory failure [3,10]. Subjects with ILD have more frequent and profound EOD than those with COPD [20]. In a study including a large population of 400 subjects with ILD, 54% had EOD and up to 80% of those with FVC values less than 50% of the predicted theoretical value [21]. EOD is a predictor of exertional dyspnea, reduced exercise activity and mortality in ILD [22–26]. Some studies have found that SOD is common in subjects with ILD [27–29]. The prevalence of isolated OD in subjects with ILD is not well defined. Pitsiou et al., found SOD in 23 out of 33 IPF subjects with no OSA [30].

In a study involving 35 subjects with IPF, 26% had OSA and SOD, but only one patient had isolated SOD ($SpO_2 \leq 8\%$ for $\geq$5 min) [31]. Another study that evaluated 60 IPF subjects with overnight pulse oximetry found a sustained desaturation pattern suggestive of isolated SOD in 5% of cases [32]. Some studies have suggested that the coexistence of SOD may worsen outcomes in ILD cohorts [26–28,30], but the prognostic role of isolated SOD is unclear.

4. Effect of HOT on Prognosis in COPD and PF-ILD Subjects

4.1. COPD

The Medical Research Council (MRC) and Nocturnal Oxygen Therapy Trial (NOTT) randomized studies [33,34], conducted in the late 1970s (see main details of these seminal studies in Table A3), showed that LTOT for 15–24 h a day at oxygen flow able to reverse hypoxemia (PaO_2> 60 mmHg/8 kPa) improved the survival of COPD subjects with chronic severe respiratory failure.

The large open, randomized, parallel Long-term Oxygen Treatment Trial (LOTT) has been promoted to clarify the role of LTOT in survival of 738 stable COPD subjects with moderate (SpO_2 89–93%) resting daytime hypoxemia and/or EOD, defined as SpO_2 < 90% for >10 s during the 6-Minute Walking Test (6MWT). At a median follow-up of 18.4 months, the active group did show no advantage in the primary outcomes, survival and time to the first hospitalization, over the placebo arm [35].

The randomized, double-blind, placebo-controlled International Nocturnal Oxygen (INOX) study (that excluded subjects with OSA: i.e., Apnea–Hypopnea Index >14/h) investigated the role of nocturnal HOT in 243 stable COPD patients with isolated SOD (who did not qualify for LTOT). The primary outcome, a composite score including death or the occurrence of criteria for switching to LTOT, did not differ between groups at follow-up of 4 years [36].

4.2. PF-ILD

An Italian parallel study (not published in extenso, 22) including 62 participants (49 of whom had IPF) with PF-ILD and chronic severe respiratory failure treated half of the subjects with placebo and half with LTOT using LOX. There was no difference in mortality between groups at one (OR, 0.50; IC 95%, 0.15–1.61), two (OR, 1.76; 95% CI, 0.64–4.86), and three years of treatment (OR, 0.99; 95% CI, 0.16–6.26) [37].

The role of HOT in ILD subjects with isolated EOD and/or SOD for improving prognosis is not defined.

5. Effect of HOT on Quality of Life, Exercise Capacity and Exertional Dyspnea in COPD and ILD Subjects

5.1. COPD

Beneficial effects of supplemental oxygen on dyspnea and exercise capacity have been observed during exercise laboratory tests in COPD, but not convincingly replicated in daily life [38]. The largest controlled study [39] that involved 143 COPD subjects with exertional dyspnea but no severe resting hypoxemia evaluated the significance of AOT at a flow of 6 lpm prescribed during physical activity (through a cylinder of weight 4.2 kg when full) for 12 weeks. There was a trend towards improvement in both treatment arms. The group receiving HOT showed a statistically significant difference of 11 m in the distance walked at 6MWT, but no difference in QoL using the Chronic Respiratory Questionnaire (CRQ). The average daily oxygen usage was 40 min. Of note, EOD was shown in 35% of participants and its presence was not predictive of the outcome. No significant advantage of LTOT was also observed in secondary outcomes, including QoL and distance travelled in the 6MWT, of the LOTT study; however, a bias of this study was reluctance to participate for subjects complaining of severe exertional dyspnea [35]. The SUPPlemental Oxygen in pulmonary Rehabilitation Trial (SUPPORT) [40] evaluated the significance of oxygen supplements during rehabilitation activities in 111 stable moderate-to-severe COPD subjects with EOD.

The active group did not significantly improve QoL and exercise capacity compared to the placebo group. In the INOX study, sleeping HOT did not assure any advantage in exacerbation rates and QoL by changes in the St. George Respiratory Questionnaire (SGRQ) and the generic Short Form Heath Survey 36 (SF-36) scores over time at 3- and 4-year follow-up [36].

5.2. PF-ILD

Supplemental oxygen can improve endurance time, dyspnea and exercise capacity of ILD subjects during exercise laboratory tests [41–43]. These benefits have been replicated in real-life conditions. The 2-week open randomized crossover Ambulatory Oxygen (AmbOx) study [44] evaluated the role of AOT with GOX cylinders of about 2 kg (titrated during the 6MWT to either maintain SpO_2 values >90% for more than half of the test or to a maximum continuous flow rate of 6 lpm) prescribed during daily activities in 76 not hypoxemic (baseline resting SpO_2 values >94% whilst breathing air) subjects with PF-ILD and isolated EOD (defined as $SpO_2 \leq 88\%$ at 6MWT; mean values of about 85%). The group on AOT showed a significant improvement both in total score of the King's Brief ILD questionnaire, a validated tool for assessing QoL in ILD subjects, with a Mean Difference (MD) of 3.7 points, just below the estimated Minimal Clinically Important Difference (MCID) of 3.9 and in the domains of dyspnea and activity and thoracic symptoms. There was also a significant improvement in the SGRQ (MD, −3.6; MCID equal to −4). Significant (and beyond MCID) improvement in dyspnea was also detected using the University of California, San Diego Shortness of Breathing Questionnaire (UCSD-SOBQ). The results of the AMBOX study are important, but other data are needed for evaluating the long-term impact of AOT on QOL and exercise capacity of PF-ILD subjects. To our knowledge, the role of nocturnal HOT in isolated SOD of ILD subjects has not been investigated.

6. The Issue of Adherence to HOT and the Role of the Delivery Device

Adherence to HOT does not seem to differ between COPD and ILD subjects [45], but, overall, it is a challenge. Non-adherence, defined as a lower number of performed daily hours of HOT than prescribed, was already observed in the NOTT study [33], where the average number of hours in which LTOT was practiced was 17.7 h per day against a prescription of 24 h per day.

It is believed that the availability of a portable device in subjects on LTOT assured higher daily outdoor activities [46] and adherence [47]. A survey of 417 US subjects on LTOT evaluating the impact of different portable oxygen delivery devices found the highest satisfaction and better QoL using LOX, that also assured a higher perceived mobility score than in that with GOX [48]. However, in the real-life Multicenter Italian Study on Oxygen Therapy Adherence (MISOTA) study, where 84% of 1504 subjects on LTOT had LOX with a portable device, only 40% declared they used it daily [49]. These findings show that the provision of the most appreciated oxygen delivery devices does not automatically translate into optimal adherence for subjects on HOT.

Another variety of non-adherence to HOT occurs when the proper oxygen flow is not respected, being supplied higher or lower than prescribed. This result may be due to the fear that the prescribed flow of HOT is dangerous or the supply runs out before being replaced, or simply to the lack of clear indications. Comparing the hours of oxygen prescribed and performed in a large cohort of subjects on LTOT, a significant difference was observed at rest, but was much more evident at night and during exercise [49]. The prescribed delivery device may not meet the subject's needs in terms of required flow or supply. In an online survey of 836 oxygen users, nearly half (47%) of participants used a portable OC despite knowing that the device did not produce adequate oxygen flow to meet their prescribed needs [50]. Domiciliary High Flow Nasal Cannula oxygen therapy (HFNC) is an emerging add-on device that might reduce dyspnea and improve exercise capacity, not only by improvements in pulmonary gases, but even by changes in the mechanics of the respiratory systems. At present, there is limited access of the HFNC devices at home, as

they are not currently supplied with an internal battery and are relatively large to transport considering the need for a distilled-water chamber. However, some studies have shown that HFNC is capable of reducing dyspnea, exacerbation rates and hospitalization in COPD subjects with chronic respiratory failure and with mild hypoxemia [51–53]. In ILD subjects with EOD, the use of HFNC can also improve exertional capacity more than the standard oxygen therapy [54,55].

7. Discussion

There is evidence that LTOT improves survival in subjects with COPD and severe chronic respiratory failure, but not in subjects with PF-ILD, where unfavorable progression is faster and, possibly, the benefits of LTOT cannot fully unfold to achieve significance. However, it is considered unethical to exclude subjects with PF-ILD and severe chronic respiratory failure from LTOT prescription. As recent treatments could possibly improve survival in PF-ILD subjects, the benefits of LTOT could become more evident.

Some large studies have shown that LTOT does not offer generalized advantages to COPD subjects with moderate chronic hypoxemia, EOD and/or SOD. In addition, AOT is not always associated with increased physical activity, but often with increased levels of sedentary live. It is known that higher daily physical activity improves survival and QoL. Apart from subjects who quality for LTOT, this seems to support the view that AOT should only be prescribed to selected COPD subjects.

By contrast, the AMBOX study has shown short-term symptomatic advantages of AOT in PF-ILD subjects with EOD. As displayed in Table A4, the results of some recent studies on the topic are not yet incorporated into some guidelines on HOT with differences in indications, characteristics and rates of subjects admitted to LTOT and AOT in different countries [2,56–59]. Indications on the titration of oxygen flow and the best oxygen delivery device, mainly during exercise and sleep, are also vague or lacking [2,56–59]. The American Thoracic Society (ATS) [2] has recently updated the indications to LTOT, supporting the use of LOX with a portable device for those subjects who leave the house and require AOT at a continuous flow during exercise >3 lpm [2]. The same ATS guideline has emitted a conditional recommendation against the use of LTOT in subjects with COPD and resting moderate hypoxemia and for AOT prescription in COPD and ILD subjects with EOD [2]. There is no indication in subjects with PF-ILD and moderate resting chronic hypoxemia [2]. Many authors think [60] that the pathophysiology of ILD is different from COPD and that persistent hypoxemia, linked to increased oxidative stress and chronic inflammation, might predispose to the development of lung fibrosis. There is good agreement among researchers in the practice of AOT prescription for subjects with ILD, EOD and related symptoms [61]. In a study of 200 subjects with PF-ILD with EOD who do not qualify for LTOT, 58 (29%) were prescribed AOT [21]. Less agreement on AOT prescription was found in the presence of EOD but no related symptoms as well as in the presence of dyspnea but no EOD [61]. There was also no agreement whether oxygen should be titrated according to symptom relief or to reverse EOD [61]. Some studies are ongoing to evaluate the role of different oxygen delivery devices that could be prescribed individually in subjects with EOD [62,63]. Technology advancements might possibly help the clinician to manage the issue of proper oxygen titration for HOT. Some devices are being developed that continuously measure oxyhemoglobin saturation and automatically adjust the oxygen flow to the level useful for keeping the saturation value at the desired value even during exercise and sleep [64–66]. However, this requires clear indications on the oxygen titration in the different situations of everyday life. Regarding the issue of SOD, there is no evidence on the usefulness of nocturnal HOT in the absence of chronic severe hypoxemia. However, due to high prevalence of OSA, all COPD and ILD subjects should possibly undergo at least a screening overnight cardiorespiratory test. Other studies should clarify the diffusion and the role of isolated SOD in ILD subjects.

8. Conclusions

Studies of HOT in COPD and ILD subjects have obtained some different results. There are also some differences in HOT prescription and use among COPD and ILD subjects. The issue of oxygen titration and the best oxygen delivery device are also unclear, mainly in subjects with high oxygen requirements, such as many patients with PF-ILD and EODThere is an urgent need for new effective portable devices for AOT and recommendation for their titration.

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Appendix A

Table A1. Main characteristics of the oxygen sources for HOT in the stable state.

Type of Oxygen	Gaseous Oxygen (GOX)	Liquid Oxygen (LOX)	Oxygen Concentrator (OC)
Variety of models and oxygen Supply	Many types of cylinders with different weight and size. The smallest cylinders are portable devices with a capacity of 150–170 L and weight of 2.5 kg when full. The largest cylinders have an oxygen capacity of about 7000 L with weight di 70–80 kg	Many types of tanks containing up to 30–40 L of LOX. The smallest tanks are portable devices, said strollers, with weight of 2–3 kg when full	Some varieties of concentrators. The greatest models have weight of 10–25 kg, permitting greateer oxygen supply. The smallest devices, said portable concentrators, have smaller size and weight (even 2–3 kg) and rechargable batteries
Disadvantages	Need of regular replacing the empty with full cylinders	Loss of oxygen are expected up to 0.5–1 kg of lox per day even if not used. Need of a distributional network	Noise and vibrations from the device Elettrically powered The smallest devices can only assure either intermittent oxygen flow or relatively low flows
Advantages	Available worldwide. Noise free Oxygen may be stored for long-term periods without any loss of content if not used	Storing of large content of oxygen in limited volumes:1 L of LOX produces up to 860 L of GOX. Tanks of 30–40 L can last for 10–14 days for continuous HOT at flow of 2–3 lpm. Ease transfill of oxygen from the mother unit into the stroller Noise-free The strollers can assure good mobility outside the home and acceptable autonomy of delivery	Uninterrupted supply of oxygen Do not require regular replacement of oxygen, but only periodical (and emergency) maintenance/assistance The smallest devices can assure good mobility and autonomy outside the home.
\Strong issues	Good mobility No need for distribution network Low mobility Acceptable autonomy. Refillable from methor unit	Deliver oxygen for long-term consuption	
Assistance Disadvantage		with periodic visits to replace the empty with full tanks	

Table A2. Main motivations of Home Oxygen Therapy prescription.

Cause	
Long-term continuous Oxygen Therapy	Oxygen delivered to subjects with stable severe resting hypoxemia
Ambulatory Oxygen Therapy	Oxygen delivered during physical activities of everyday life
Nocturnal Oxygen Therapy	Oxygen only delivered during sleep time. This treatment is usually administered in the presence of Sleeping Oxygen Desaturation (SOD)
Symptomatic Oxygen Therapy	Oxygen delivered to contrast symptoms and mainly to relieve dyspnea and to improve exercise tolerance. This treatment may be administered in the presence or in the absence of Exertional Oxygen Desaturation (EOD). It also includes brief and intermittent oxygen release before and/or after exercise, generally used as needed for symptomatic reasons and defined as short-burst oxygen

Table A3. Some characteristics of main studies evaluating the significance of LTOT in COPD subjects with chronic severe respiratory hypoxemia.

Study/No Reference	No (% Males)	Mean Age, Years	Mean $PaCO_2$ Values *, mmHg	Mean PaO_2 Values *, mmHg	FEV1% pred	Inclusion Criteria	Prescribed O_2, Hours a Day	Survival Rate, Primary Outcome	Other Outcomes
MRC/34°	87 (74)	58	50	54	NA	$PaO_2 \leq 60$ §	15 vs. no O_2	† *45%* vs. *67%* [1]	≈ hosp
NOTT/35	203 (79)	65	44	51	30	$PaO_2 \leq 55/PaO_2 \leq 59$ ^	24 vs. 12	† *22%* vs. *41%* [2]	≈ hosp, SIP; MMPI, POMS; Ht

* = baseline results at arterial blood gas analysis evaluated in the stable state at rest; °No AOT source; titration: minimal oxygen flow able to achieve resting PaO_2 values greater than 60 mmHg at arterial blood gas analysis. § = at least an episode of right heart failure and FEV1 pred < 1,2 l; ^ coexistence of oedema, hematocrit $\geq$ 55 or pulmonary p at EKG (3 mm in II, III, aVF); [1] at 5 year follow-up; [2] at 2 year follow-up; † = ; ≈: no significant differences; hosp = hospitalization rate; POMS= Profile of Mood States, SIP = SIckness of Impact Profile, MMPI, Minnesota Multiphasic Personality Inventory; Hy = hematocrit.

Table A4. Recommendations of guidelines on HOT.

Guideline/No Ref.	LTOT	AOT	SOT	OT-ILD
TSANZ/55 ^	(a) $Pa(dr)O_2 \leq$ 55/7.3 mmHg/kPa (b) PaO_2 (dr) 56/7.4 to 59/7.8 mmHg/kPa plus hypoxic organ damage *****	(a) Subjects on LTOT mobile outdoors with desire to maximize their duration of HOT and exercise capacy *** (b) Occasionally not on LTOT but with exertional dyspnea and EOD; blinded confirmation of oxygen benefits is required **	Occasionally if SpO_2 < 88% for > 1/3 of sleep, mainly with pulmonary hypertension and polycythemia ****	$FiO_2 \rightarrow Pa(rd)O_2$ 60/8 mmHg/kPa or SpO_2 > 90%
ATS/2	(a) $Pa(dr)O_2 \leq 55/7.3$ mmHg/kPa or $SpO_2 \leq 88\%$ (b) PaO_2 (dr) 56/7.4 to 59/7.9 mmHg/kPa or SpO_2 89% plus oedema, hematocrit $\geq$ 55% or p pulmonale on ECG ***^^	(a) Subjects with EOD ^^^	No recommendation	No recommendation

Table A4. *Cont.*

Guideline/No Ref.	LTOT	AOT	SOT	OT-ILD
BTS/56	(a) $Pa(dr)O_2 \leq$ 55/7.3 mmHg/kPa (b) PaO_2 (dr) $\leq$60/8 mmHg/kPa plus oedema, hematocrit $\geq$ 55% or pulmonary hypertension"	(a) Subjects on LTOT imobile outdoors "" (b) Occasionally not on LTOT during exercise in a pulmonary rehabilitation programme and following after formal demonstration of improvement in exercise endurance """	not recommended in subjects with COPD with SOD but who fail to meet the criteria for LTOT $	Start on an oxygen flow rate of 1 L/min and titrated up in 1 L/min increments until SpO_2 > 90%. An ABG should confirm a PaO_2 value $\geq$ 60/8 mmHg/kPa"" Non-hypercapnic subjects on LTOT should increase their resting daytime flow rate by 1 L/min during sleep "" Oximetry may be performed to allow more accurate titration until a target PaO_2 value is achieved.
German/57–58	(a) $Pa(dr)O_2 \leq$ 55/7.3 mmHg/kPa (b) PaO_2 (dr) 55/7.3 to 60/8 mmHg/kPa plus polycythaemia and/or cor pulmonale"	(a) Subjects on LTOT who are mobile outdoors (b) Subjects not on LTOT, but with drops >5/0.7 mmHg/kPa and PaO_2 nadir < 55/7.3 mmHg/kPa during ergometric assessment (c) subjects not on LTOT with confirmation that AOT substantially improves exercise capacity	No recommandation	(a) $FiO_2 \rightarrow Pa(rd)O_2$ 60/8 mmHg/kPa (b) Exercise test to evaluate the necessary oxygen flow rate of AOT during exercise

Legend: TSANZ = Thoracic Society of Australia and New Zealand; ATS = American thoraacic Society; LTOT =Long-term Oxygen Therapy; AOT = Ambulatory Oxygen therapy; SOT= Sleeping Oxygen therapy OT = Oxygen Titration; EOD: Exercise Oxygen desaturation $Pa(dr)\ O_2$ = Arterial daytime resting Oxygen tension; SpO_2 oxyhemoglobin saturation level measured by pulse oximetry; $FiO_2 \rightarrow$ Flow rate of oxygen therapy set to maintain a predefined level of oxyten tension or oxyhemoglobin saturation.***** grade recommendation: A. Evidence:high; **** grade recommendation: A. Evidence:low; *** GRADE recommendation: A; evidence: very low; ** grade recommendation: C. Evidence: very low; * grade recommendation: A. Evidence: very low; "Evidence strong for COPD and very low for ILD subjects. "" Evidence strong; """ Evidence moderate; $ = "Evidence strong for COPD and moderate for ILD subjects. ^ no distintion between COPD and ILD; ^^ no distinction between COPD and ILD with recommandation A, but with moderate quality evidence in COPD and very low quality evidence in ILD; ^^^ no distinction between COPD and ILD with sconditional recommandation, but with moderate quality evidence in COPD and low quality evidence in ILD.

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