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Oxygen in Patients with Fibrotic Interstitial Lung Disease: An International Delphi Survey

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Take Home Message: Supplemental oxygen should be recommended for patients with fibrotic interstitial lung disease in cases of severe resting hypoxemia, or exertional hypoxemia particularly with attributable symptoms or exercise limitation.

Abstract

Rationale: Patients with fibrotic interstitial lung disease frequently develop resting or exertional hypoxemia. There is heterogeneity in clinical practice and a paucity of evidence guiding supplemental oxygen use in this patient population. The objectives of this study were to build international expert-based consensus on the indications and goals of supplemental oxygen from the perspective of health-care providers, and identify potential barriers to its access.

Methods: Semi-structured interviews and a comprehensive literature search informed items for the Delphi survey, with items not meeting consensus included in the second round. The third round contained survey questions regarding regional funding coverage for oxygen therapy. *A priori* definitions of consensus were median scores of 4 (agree) to 5 (strongly agree) for 'agreement', 1 (strongly disagree) to 2 (disagree) for 'disagreement', or 3 (unsure) with an interquartile range of 0 to 1.

Results: 42/45 (93%) experts completed all three survey rounds, representing 17 countries. 20/36 items met consensus for agreement or disagreement, ten items met consensus for unsure, and five items did not meet consensus. Experts agreed that oxygen should be recommended for patients with severe exertional hypoxemia, and in cases of exertional desaturation to <85-89%, particularly with attributable symptoms or exercise limitation. There are regional differences in funding coverage for oxygen, based on desaturation thresholds, clinical symptoms and testing requirements.

Conclusions: Experts achieved consensus on 20 items guiding supplemental oxygen use in fibrotic interstitial lung disease. These data may inform research, clinical recommendations, and funding policy.

Introduction

Interstitial lung disease (ILD) represents a large and heterogeneous group of disorders that can lead to progressive symptoms of dyspnea, cough, and exercise intolerance. Among those with advanced fibrotic ILD, hypoxemia is common. Impaired gas exchange develops due to ventilation-perfusion mismatching, diffusion limitation, and vascular abnormalities.(1-3) Exertional hypoxemia, in the absence of resting hypoxemia, is a common characteristic of fibrotic ILD that is often more severe than in other lung diseases such as chronic obstructive pulmonary disease (COPD).(4) In addition, both exertional and resting hypoxemia have been associated with increased mortality in this patient population.(5, 6)

Important patient-centered priorities for individuals with fibrotic ILD include improving dyspnea, exercise capacity, and health-related quality of life (HRQoL).(7) Supplemental oxygen is commonly prescribed in routine clinical practice with these goals in mind, however, robust evidence to support its long-term use is lacking. Several small studies of short-term oxygen use in patients with ILD have shown that it can improve dyspnea, endurance, and walking distance.(8-10) However, other studies have failed to identify symptomatic or physiologic benefits.(11, 12) Data in patients with isolated exertional hypoxemia are limited but a recent randomized crossover trial demonstrates that short-term oxygen use is associated with improved HRQoL in patients with fibrotic ILD.(13) No studies have adequately evaluated the role of long-term oxygen on outcomes such as disease progression or mortality in ILD, in either resting or ambulatory hypoxemia. Recommendations for long-term oxygen therapy for resting hypoxemia in ILD are largely extrapolated from trials conducted in COPD, where a survival benefit is well established.(14, 15) Clinical guidelines on the management of idiopathic pulmonary fibrosis (IPF) and other ILDs are also subject to limitations imposed by current gaps in knowledge. While most recommend oxygen therapy for patients with IPF and resting hypoxemia,(16-18) there are inconsistent recommendations for other common clinical scenarios such as isolated exertional hypoxemia.

Given the paucity of data, it is unknown which fibrotic ILD patients are most likely to derive benefit from supplemental oxygen, and in which clinical scenarios. This contributes to important variability in prescribing practices and funding coverage, including pre-testing algorithms that differ geographically due to regional infrastructure.(19) We conducted an international Delphi survey in an effort to develop a consistent best practice approach to supplemental oxygen use in patients with fibrotic ILD. The objectives of this Delphi study were to build expert-based consensus on the indications and goals of supplemental oxygen therapy and to identify potential barriers to its prescription and funding coverage. This study specifically focused on these goals from a health care provider's perspective and was not designed to address the perspectives and experiences of patients living with fibrotic ILD. Some of these results have been previously presented in abstract form [at the upcoming 2019 American Thoracic Society International Conference, reference when available].

Methods

This study was approved by the Conjoint Health Research Ethics Board, University of Calgary (REB17-1669_REN1) and all participants provided informed consent.

Identification of Delphi Survey Items

One investigator (KJ) conducted individual, semistructured telephone interviews with recognized ILD experts, selected based on research experience in ILD and supplemental oxygen, and representing diverse practice regions. Open-ended questions regarding the indications, goals, and practical challenges of oxygen use in ILD patients were posed to all participants (see interveiw guide in the supplementary material). Interviews were transcribed and analysed by two investigators (RL and CH) using a content analysis approach.(20, 21) Results of the qualitative interviews and a comprehensive literature review informed survey items for the first Delphi round.

Participant Panel Selection

Panelists were identified through contacts from the professional networks of KJ, AH, and JM, or through publication and citation records. We aimed for an international group of ILD experts with a range of clinical and research experience, representing a diversity of geographical practice locations. An initial list of potential participants with their region and country of practice was created. Aiming to achieve representation in age, gender, health care provider profession, and career stage, the initial list was culled. The final list had proportionally greater representation from larger geographical regions (e.g United States) or smaller regions with an established track record of publications on the specific study content (e.g Australia, United Kingdom). The identified experts, including those who participated in the qualitative interviews, were invited to participate in the first round of the Delphi survey.

Delphi Survey Execution

The Delphi study was conducted in accordance with the reporting standards developed in CREDES (Conducting and REporting of DElphi Studies).(22) Surveys were disseminated and completed online using Qualtrics® software. Surveys were administered approximately three weeks apart and participants were given two weeks to complete their responses. Email reminders were sent to maximize participation rates, and participants not completing a round of the survey were not invited to subsequent rounds. Items in the first two rounds were rated using a five-point Likert scale, where items were rated as '1 -strongly disagree', ' 2 - disagree', '3 - unsure', '4 - agree', and '5 - strongly agree'. The *a priori* definitions of consensus were median scores of 4-5 for 'agreement', and 1-2 for 'disagreement', with an interquartile range (IQR) of 0 to 1. A median score of 3 with IQR of 0 to 1 was considered consensus for 'unsure'. These definitions were chosen to represent the spread of responses for each item.(23) Items not meeting consensus in round one were repeated in round two, while items meeting consensus were removed from subsequent surveys.

In the first round, participants could provide feedback and suggest additional survey items for round two, with responses reviewed to identify original items within the scope of the study for subsequent inclusion. If deemed appropriate, first-round survey items were revised for clarity prior to dissemination in the second round. During round two, participants were given the distribution of group answers for survey items repeated from round one and provided new survey items. They also answered one multiple choice question about the peripheral oxygen saturation (SpO_2) threshold below which they recommend exertional supplemental oxygen, a suggestion from the first round. In round three, participants were asked about regional funding policies for patients meeting the indications for supplemental oxygen use, as defined by consensus from prior rounds. Additional questions focused on the availability of clinical investigations agreed upon by earlier consensus. Answers were 'yes or no', but participants could provide optional text.

Statistical Analysis

Descriptive statistics were used to characterize the study participants. Quantitative group results for each item (median) and the level of dispersion (IQR) were calculated to identify items meeting the *a priori* definitions of consensus for agreement, disagreement, or unsure after rounds one and two. A sensitivity analysis was conducted using an alternative method of determining consensus, defined as ≥70% agreement for either 1 or 2, 4 or 5, or 3. Results from round 3 were summarized descriptively. Statistical analyses were performed using STATA (version 15.1, StatCorp, College Station, Texas).

Results

Expert Survey Participants

Ten out of ten (100%) invited experts participated in the semi-structured individual interviews (Table 1). A total of 45 ILD experts were invited by email to participate in

the Delphi survey, including those completing the interviews, with 42/45 (93%) completing all three rounds. The survey participants had a mean age of 51 years (SD=8.5), 19 (45%) were female, 39 (93%) were physicians, 3 (7%) were nurses, with a mean of 19.1 years (SD=9.3) in independent clinical practice, and an average 77% (SD=22) of clinical time dedicated to patients with ILD. Experts represented 17 countries and five continents.

Survey Items

Based on the semi-structured expert interviews and literature review, 32 items were included in the first round of the survey (Figure 1). Twenty-three items met consensus and were excluded from the second round. Nine items were repeated in the second round, with four new items. After the second round, eight items met consensus and four did not. The third survey round contained 16 questions regarding regional funding criteria and access to supplemental oxygen and physiological testing for patients with fibrotic ILD.

Delphi Survey Results

A total of 18 items met consensus for agreement, and two met consensus for disagreement (Table 2). All experts strongly agreed that oxygen should be recommended in cases of severe resting hypoxemia (ie. PaO_2 <55 mmHg/SpO_2 < 89%, or PaO_2 <60 mmHg and cor pulmonale and/or polycythemia). There was consensus that oxygen be recommended with the goals of addressing a broad range of symptoms, functional impairments, and/or physiological derangements. There was consensus that resting hypoxemia leads to pulmonary hypertension in patients with fibrotic ILD, and that the development or worsening of exertional hypoxemia provides evidence of clinical deterioration. There was consensus that patients with exertional hypoxemia should not be advised to use oxygen during sleep without objective testing documenting nocturnal desaturation, and that all patients should undergo such screening tests. All experts strongly agreed that newer portable oxygen delivery systems should be developed in order to reduce the burden of use in patients with fibrotic ILD.

Ten questions met consensus for unsure, and four did not meet consensus (see Table S1 in the supplementary material). Experts were unsure if pulmonary hypertension develops as a consequence of isolated exertional or nocturnal desaturation, or if oxygen therapy can slow the development of existing pulmonary hypertension. Experts were unsure if supplemental oxygen prevents adverse clinical outcomes such as hospitalization or acute exacerbation, or if oxygen therapy impacts survival in patients with fibrotic ILD. No consensus was reached on whether oxygen should be titrated according to symptom alleviation, and whether it should be continued for physiological benefit in cases with no symptomatic improvement. In the sensitivity analysis, 15/20 (75%) items would still have met consensus for agreement or disagreement using a definition of ≥70% agreement. Five items would not have met consensus including whether patients should undergo a screening test for nocturnal hypoxemia, if oxygen should be titrated to achieve SpO_2 >89%, and regarding potential concerns about oxygen toxicity (Table 2).

Exertional desaturation threshold

19/42 (45%) experts recommended oxygen below an SpO_2 threshold of <89%, 9/42 (21%) recommend it at a threshold <90%, and 9/42 (21%) at a threshold <85%. A minority (4/42) do not recommend oxygen or do not use an SpO_2 threshold, and 1 recommended it below an SpO_2 threshold <80% (Figure 2). Throughout the survey, experts indicated that their recommended desaturation threshold would be considered in the context of symptoms, exercise tolerance, and patient preference.

Regional funding policies

In the third round survey, nearly all experts (41/42; 98%) reported that supplemental oxygen would be funded in their region for fibrotic ILD patients with severe resting hypoxemia (defined as PaO_2<55 mmHg/SpO_2<89%, or PaO_2<60 mmHg and cor pulmonale and/or polycythemia). For isolated exertional desaturation, access to oxygen funding varied depending on the SpO_2 threshold, and the presence or absence of symptoms attributable to the hypoxemia (Figure 3). The

majority of experts reported that oxygen would be funded based on a desaturation threshold set at <89%, with broader access to funding based on lower desaturation thresholds and the presence of hypoxia-attributable symptoms. In contrast, most experts (30/42; 71%) report no access to oxygen funding at an exertional desaturation threshold set at <90%, regardless of symptoms. Though not included in our clinical scenarios of exertional desaturation, some respondents noted that improved exercise tolerance must also be demonstrated prior to funding approval in their practice location. Notably, 4/42 (9·5%) and 10/42 (24%) experts reported that no funding coverage would be available for an exertional SpO_2 <80% with or without hypoxemia-attributable symptoms, respectively. All experts reported routine access to physiological testing for exertional desaturation such as 6-minute walk test or shuttle walk, at their ILD referral centre. The majority (81%) report routine access to overnight oximetry testing or sleep testing for assessment of nocturnal desaturation. Where 12% of experts practice, obese patients with fibrotic ILD are required to undergo a polysomnogram prior to being eligible for oxygen funding. As part of their regional oxygen funding algorithm, an arterial blood gas was reported as required by 19/42 (45%) in cases of resting desaturation, and 11/42 (26%) in cases of isolated exertional desaturation. 40/42 (95%) experts reported that funding policies are consistent across different etiologies of fibrotic ILD, and only 8/42 (19%) reported specific oxygen funding policies for fibrotic ILD patients with an anticipated survival of less than six months.

Discussion

In this study, our expert panel achieved consensus on 20 items that can be used to guide supplemental oxygen use in patients with fibrotic ILD. We further identified several areas where respondents were unsure or where consensus could not be met, suggesting future areas where research efforts should be focused. Finally, we identified discrepancies between scenarios where clinicians would recommend oxygen and poor patient access, based on regional funding criteria or testing requirements. These findings may be used to develop clinical practice

recommendations and funding policies for supplemental oxygen for this patient population, pending more robust evidence. A proposed approach to the assessment and prescription of supplemental oxygen for patients with fibrotic ILD is presented in Figure 4.

Overall, experts agreed that supplemental oxygen is a safe therapeutic intervention that should be considered in conjunction with patient wishes and goals, and that newer portable systems should be developed to facilitate its use. There was consensus to recommend oxygen in cases of severe resting or exertional hypoxemia, and that nocturnal desaturation is an important clinical parameter. Experts agreed that the goals of oxygen use are multi-faceted, primarily aiming to improve the patient experience, targeting symptoms and/or exercise tolerance. Experts recommend oxygen use in cases of symptomatic exertional desaturation, highlighting the different approach to oxygen prescription for patients with fibrotic ILD compared to patients with COPD. A large randomized trial found that supplemental oxygen did not improve survival, functional status, or quality of life in stable COPD patients with moderate resting hypoxemia or isolated exertional desaturation.(24) However, these findings should be extrapolated with caution to patients with fibrotic ILD, given the differing physiology and severity of exertional desaturation between these groups.(4, 25)

The only clinical scenario for which there was 100% strong agreement to recommend oxygen was in cases of severe resting hypoxemia, consistent with published guidelines for ILD management.(16, 17, 26) Some country-specific recommendations suggest ambulatory oxygen for patients with ILD or IPF if breathlessness or exercise limitations exist in the context of exertional desaturation (17, 26). In our study, most experts recommended oxygen below an exertional desaturation threshold between 85-89%, and particularly when patients have symptoms or exercise intolerance that improved with oxygen therapy. Given the dynamic and effort-dependent nature of exertional desaturation, expert commentary suggested that a single measured SpO_2 in isolation provides

inadequate data to guide oxygen prescription. Desaturation level should likely be considered in conjunction with symptoms, exercise tolerance and possibly with evidence of improvement in these parameters with oxygen therapy.

All clinical decisions, including the use of supplemental oxygen, should be made in partnership with patients and where appropriate, caregivers. Prior qualitative and mixed-methods studies have addressed the goals of oxygen use from both health care provider and patient perspectives.(27-29) The summarized goals appear consistent, primarily focused on improving symptoms and exercise tolerance. The current study focused uniquely on health care providers' opinions regarding the indications and goals of oxygen for patients with fibrotic ILD. We wanted to understand the recommendations being made by clinicians, as this is inexorably related to how information is presented to patients. The discussion of anticipated benefits and potential risks or complications of therapy can influence a patient's decision to accept or decline treatment in shared decision-making models.(30) In the absence of definitive evidence, we hope that our findings can provide a framework for such discussions. Further studies addressing internationally diverse patient and caregiver perspectives would add important data guiding the role of oxygen. Despite differences in clinical practice patterns among our experts, there was a consensus that clinicians should consider the balance of benefits versus burdens of supplemental oxygen for individual patients with fibrotic ILD, an essential point underlying all work on this topic.

The Delphi technique is a validated methodology used in healthcare research to develop consensus-based recommendations when robust evidence is lacking. Through iterative questionnaires, a group of experts provides their opinion after considering the collective responses of prior rounds, while maintaining anonymity.(22, 23) We believe that the Delphi technique was a justified research tool to identify current best practices in supplemental oxygen use among patients with fibrotic ILD. Based on expert input representing 17 countries, access to oxygen funding appears heterogeneous by practice location. In some regions, there are few

barriers to oxygen funding, while in others oxygen is only accessible if patients pay for the equipment themselves, or if they qualify via pre-defined testing algorithms. One quarter of experts reported that no oxygen funding is available for patients with exertional desaturation <80% in the absence of attributable symptoms, highlighting the heterogeneity of access to this therapy in different practice areas. Standardizing the clinical indications for oxygen may make access more equitable across regions, but this is a complex goal given the variability in health care systems, and oxygen reimbursement policies worldwide. Furthermore, technological advances should be prioritized to reduce the burden of portable oxygen devices for advanced lung disease patients.(31, 32)

This study has limitations. First, our participant selection strategy was not based on pre-defined or publication-based criteria. Rather, we sought to achieve representative diversity of experience and opinion from a large pool of potential international ILD experts. We believe this is particularly important with our study question, given the lack of high-quality evidence. In support of our expert selection approach are the very high participation and survey completion rates. Participants from the Asian and African continents are under-represented in this survey and future work should aim to better understand clinical practice patterns in these regions. Based on the survey design of this study, we were unable to further qualify the expert responses to define specific clinical scenarios in which supplemental oxygen would be used. Given the unique circumstances of each patient encounter, this was not feasible. Finally, the consensus among experts does not necessarily equate to scientific truth or clinical validity, and lack of consensus highlights differences in perspectives regarding complex issues. A Delphi survey is not a substitute for rigorous prospective studies, and many of the questions posed herein, including those meeting consensus, should be further addressed in randomized trials of oxygen therapy, where possible.

Conclusions

An international group of ILD experts achieved consensus on 20 items to guide supplemental oxygen use in patients with fibrotic ILD. Desaturation severity, hypoxemia-attributable symptoms, exercise tolerance, and patient preference should be considered when recommending oxygen. While there is a lack of evidence to guide clinical recommendations, oxygen is an important component of patient management and well-designed prospective studies are urgently needed to answer outstanding questions. The current data may provide a framework to guide clinical decision-making and funding policy for oxygen therapy in this patient population, pending the availability of high-quality evidence.

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Contributorship statement: RKL and KAJ conceived of the study, all authors made substantial contributions to the study design, data analysis, and data interpretation, RKL and KAJ drafted the manuscript, all authors critically appraised and approved the final version of the submitted manuscript.

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Tables

Table 1: Expert Characteristics

Characteristic	Expert Interview (n=10)	Modified Delphi (n=42)
Response rate, n/total (%)	10/10 (100)	42/45 (93)
Age (years), mean (SD)	50.1 (8.2)	50.5 (8.5)
Female gender, n (%)	6 (60)	19 (45)
Country, n (%)		
Argentina	--	1 (2.4)
Australia	1 (10)	5 (11.9)
Belgium	--	1 (2.4)
Brazil	--	1 (2.4)
Canada	--	4 (9.5)
Denmark	--	1 (2.4)
France	--	2 (4.8)
Germany	1 (10)	2 (4.8)
Greece	--	1 (2.4)
Iceland	--	1 (2.4)
Italy	--	3 (7.1)
Japan	--	1 (2.4)
Mexico	--	1 (2.4)
The Netherlands	1 (10)	2 (4.8)
Spain	1 (10)	2 (4.8)
United Kingdom	3 (30)	3 (7.1)
United States	3 (30)	11 (26.2)
Occupation, n (%)		
Physician	8 (80)	39 (93)
Nurse	2 (20)	3 (7)
Years in clinical practice, mean (SD)	19.9 (10)	19·1 (9.3)
% of time dedicated to interstitial lung disease, mean (SD)	92 (14)	77·3 (22.3)

Abbreviations: SD=standard deviation

Table 2: Items meeting consensus for agreement or disagreement

Survey Item	Median score from 1-5 (IQR)	Sensitivity analysis, % agreement
Indications for supplemental oxygen		
Supplemental oxygen should be recommended for fibrotic ILD patients with severe resting hypoxemia (PaO_2 <55 mmHg/SpO_2 < 89%, or PaO_2 <60 mmHg and cor pulmonale and/or polycythemia).	5 (0)	100%
Supplemental oxygen should be recommended for fibrotic ILD patients with isolated exertional desaturation to <80%, regardless of symptoms.	5 (1)	74%
Recommendations for supplemental oxygen use should be consistent across different etiologies of fibrotic ILD.	4 (0)	92%
Supplemental oxygen should be recommended for fibrotic ILD patients with nocturnal hypoxemia in the absence of other causes such as sleep disordered breathing.	4 (1)	70%
Fibrotic ILD patients with isolated exertional hypoxemia should be advised to use supplemental oxygen during sleep, without the need for nocturnal oximetry testing.*	2 (1)	83%
Goals of supplemental oxygen		
Supplemental oxygen should be titrated to achieve an oxygen saturation above 89% at all times.	4 (1)	67%
I recommend supplemental oxygen to improve physical symptoms (e.g. fatigue, decreased energy) in patients with fibrotic ILD and evidence of resting or exertional desaturation.	4 (1)	83%

I recommend supplemental oxygen to improve psychological symptoms (e.g. cognition, mood) in patients with fibrotic ILD and evidence of resting or exertional desaturation.	4 (1)	60%
I recommend supplemental oxygen to improve dyspnea in patients with fibrotic ILD and evidence of resting or exertional desaturation.	4 (1)	84%
I recommend supplemental oxygen to improve functional capacity in patients with fibrotic ILD and evidence of resting or exertional desaturation.	4 (1)	86%
I recommend supplemental oxygen to prevent deconditioning in patients with fibrotic ILD and evidence of resting or exertional desaturation.	4 (1)	74%
I recommend supplemental oxygen to improve physiologic parameters such as oxygen delivery, cardiac output, and arterial oxygen content in patients with fibrotic ILD and evidence of resting or exertional desaturation.	4 (1)	71%
Other Considerations for Supplemental Oxygen Use		
Exertional hypoxemia should be periodically evaluated by objective standardized testing including but not limited to 6MWT, CPET, or Shuttle Walk in patients with fibrotic ILD.	5 (1)	88%
Prior to initiating and continuing supplemental oxygen prescription, the clinician should consider the balance of benefits versus burdens for individual patients with fibrotic ILD.	5 (1)	93%
Newer portable oxygen delivery systems should be developed in order to reduce the burden of use in patients with fibrotic ILD.	5 (1)	100%

Fibrotic ILD patients with isolated exertional hypoxemia should undergo a screening test for nocturnal hypoxemia.	4 (1)	67%
Oxygen toxicity is not a concern in most clinical scenarios where supplemental oxygen is prescribed for patients with fibrotic ILD.	4 (1)	65%
The development or worsening of exertional desaturation provides evidence of clinical deterioration in patients with fibrotic ILD.	4 (1)	86%
Resting hypoxemia leads to the development of pulmonary hypertension in patients with fibrotic ILD.	4 (1)	74%
In patients prescribed supplemental oxygen for isolated exertional hypoxemia, oxygen should be discontinued in those who do not report any improvement in symptoms or exercise capacity.*	2 (1)	57%

Abbreviations: ILD=interstitial lung disease, 6MWT=six minute walk test, CPET=cardiopulmonary exercise test, PaO_2=partial pressure of oxygen, SpO_2=peripheral oxygen saturation. *=consensus for disagreement

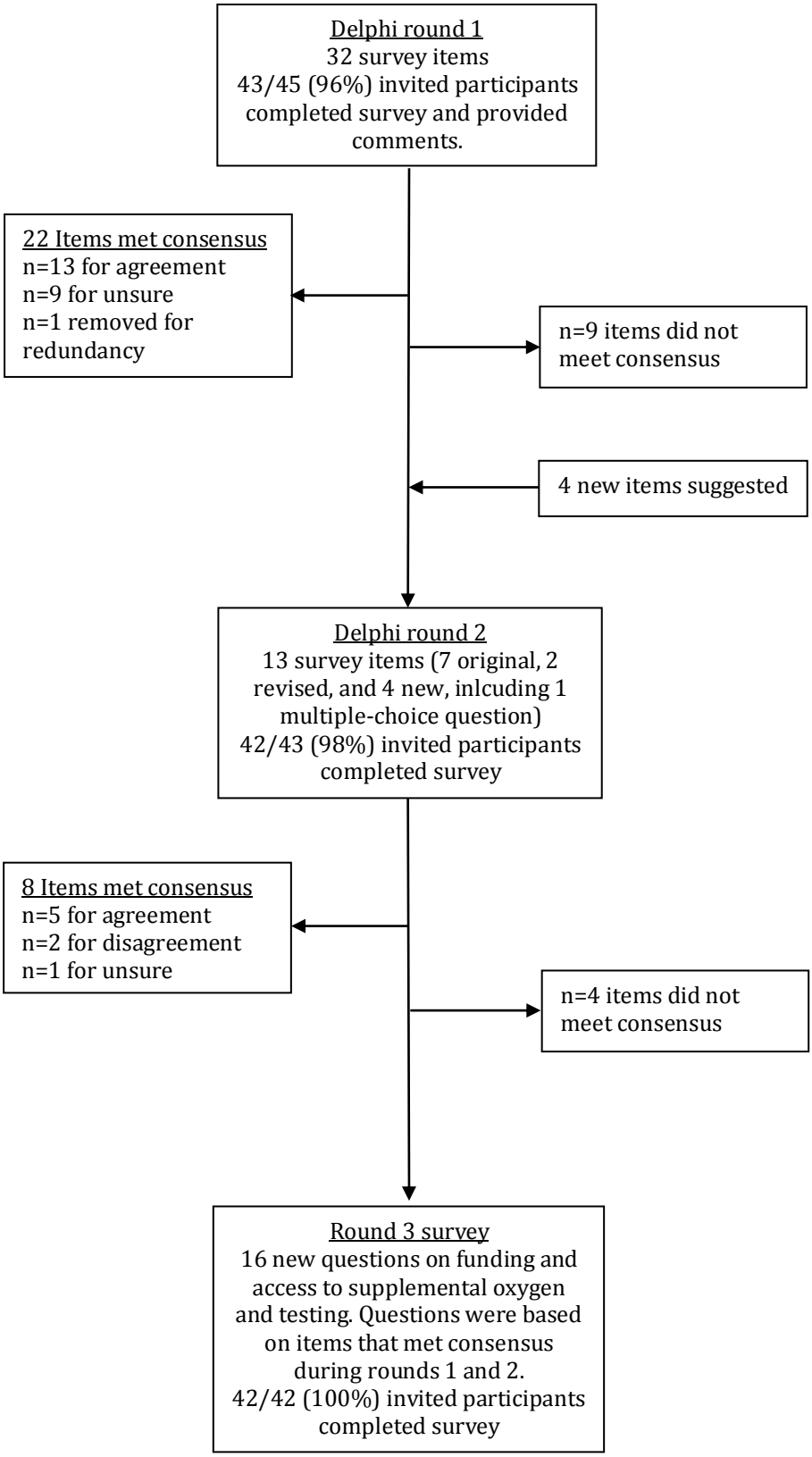
Figure Legend

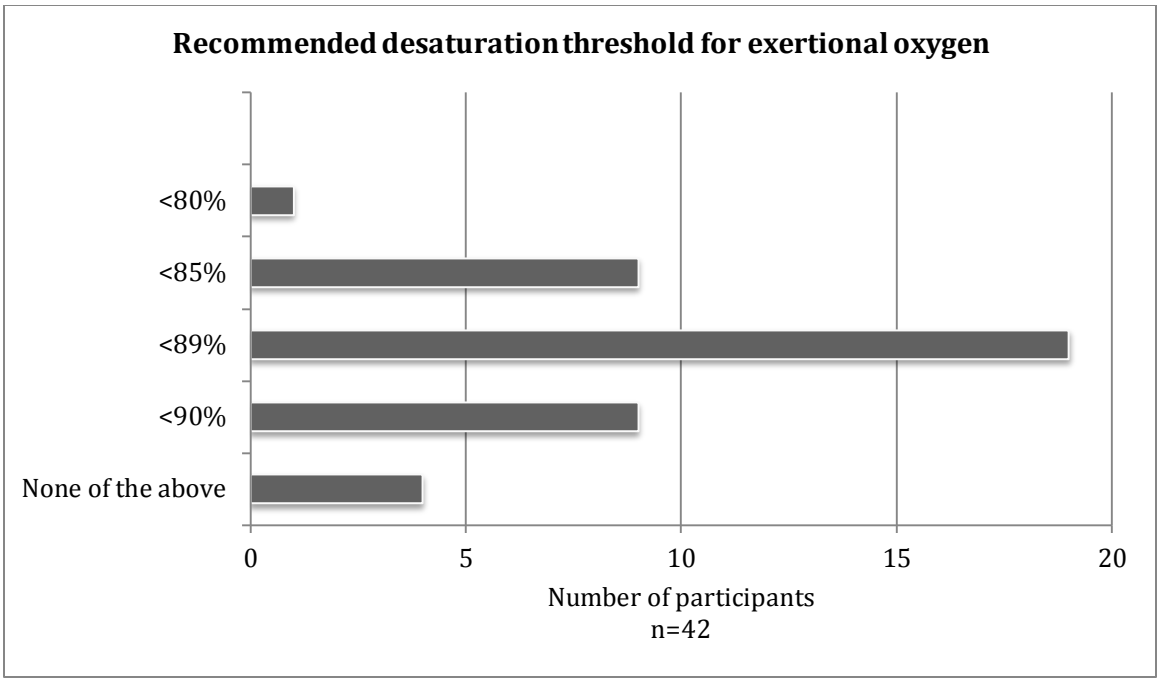
Figure 1: Flow diagram of the Delphi Survey.

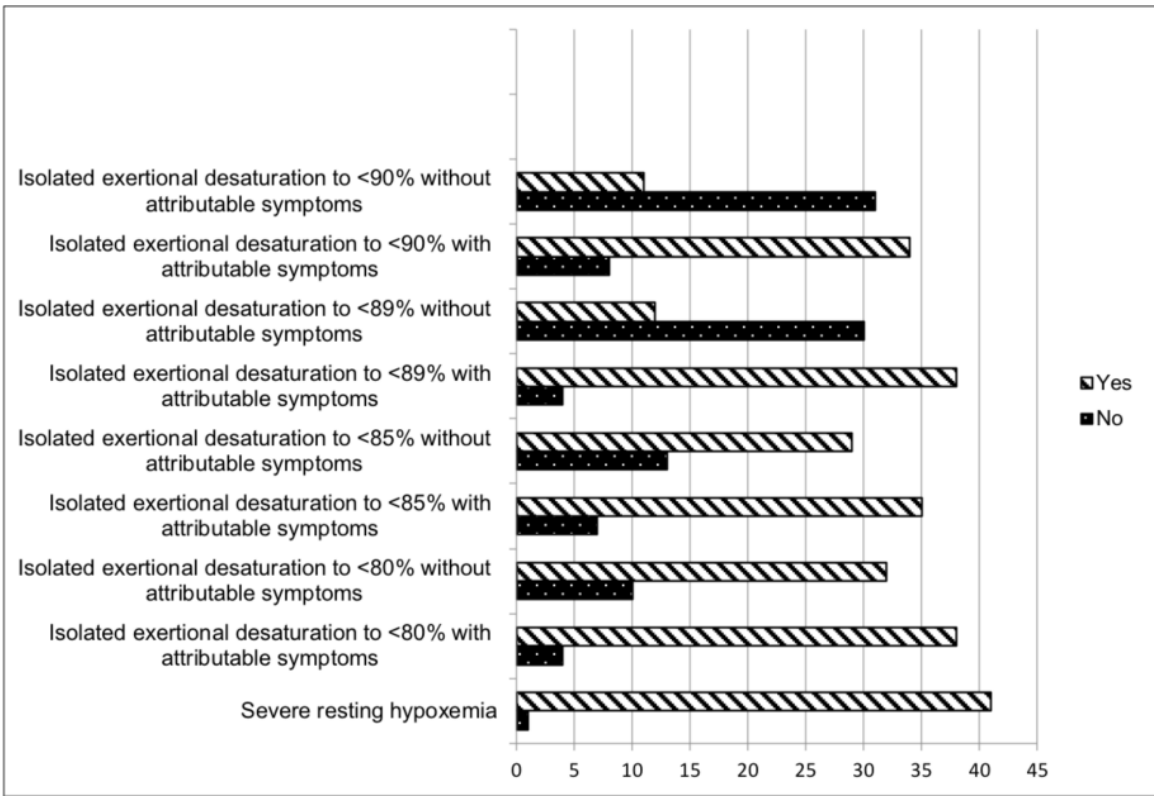
Figure 2: Expert-recommended exertional desaturation thresholds for supplemental oxygen use in patients with fibrotic interstitial lung disease.

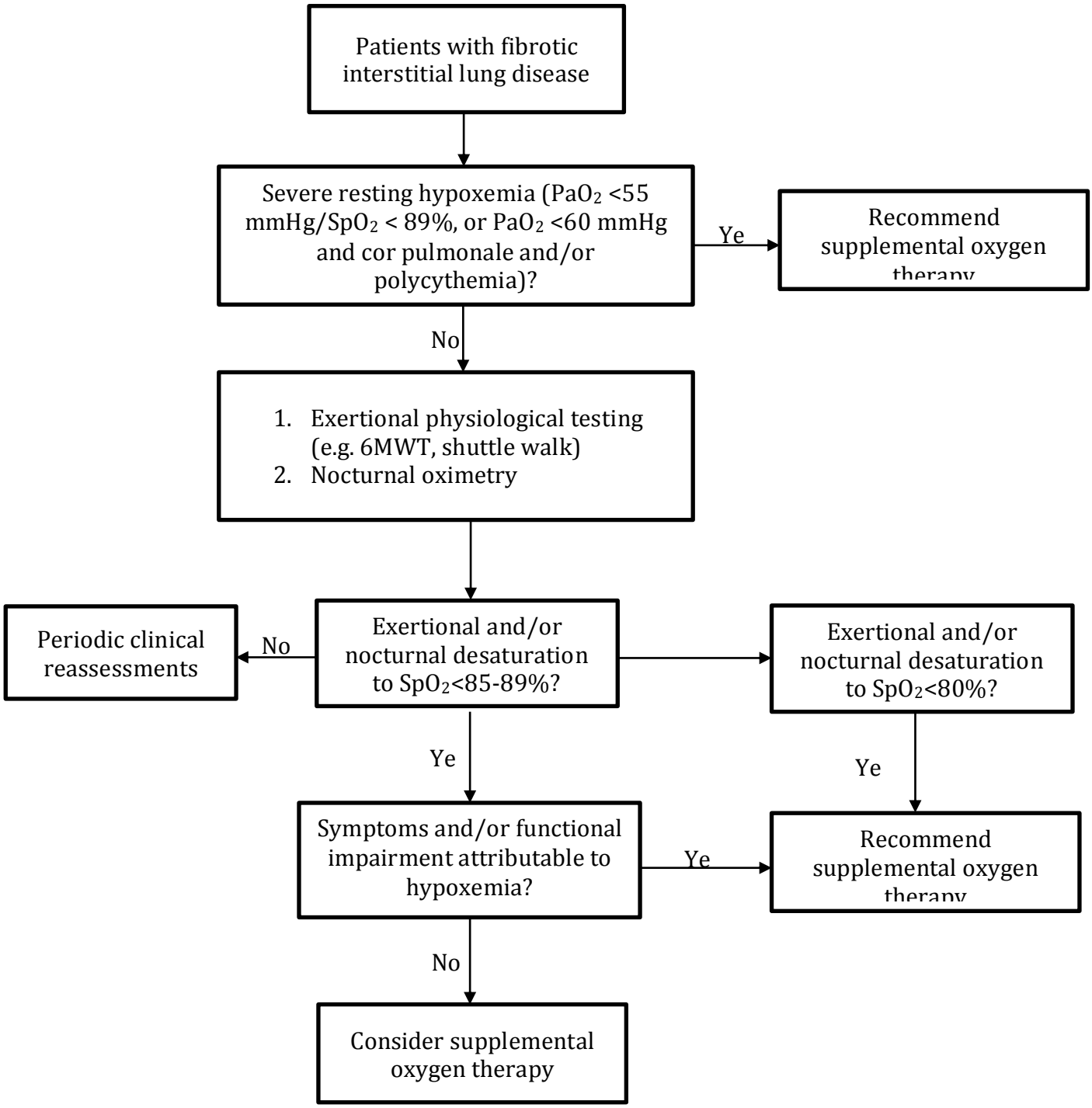
Figure 3: Regional oxygen funding coverage for patients with fibrotic interstitial lung disease, based on specific exertional desaturation criteria.

Figure 4: Proposed algorithm for assessment and prescription of oxygen. Decisions regarding supplemental oxygen use should be made with consideration of the benefits and risks, as well as patient values and preferences.


Delphi round 1
32 survey items
43/45 (96%) invited participants completed survey and provided comments.
22 Items met consensus
n=13 for agreement
n=9 for unsure
n=1 removed for redundancy
n=9 items did not meet consensus
4 new items suggested
Delphi round 2
13 survey items (7 original, 2 revised, and 4 new, inlcuding 1 multiple-choice question)
42/43 (98%) invited participants completed survey
8 Items met consensus
n=5 for agreement
n=2 for disagreement
n=1 for unsure
n=4 items did not meet consensus
Round 3 survey
16 new questions on funding and access to supplemental oxygen and testing. Questions were based on items that met consensus during rounds 1 and 2.
42/42 (100%) invited participants completed survey


Recommended desaturation threshold for exertional oxygen
<80%
<85%
<89%
<90%
None of the above
0
5
10
15
20
Number of participants
n=42


Isolated exertional desaturation to <90% without attributable symptoms
Isolated exertional desaturation to <90% with attributable symptoms
Isolated exertional desaturation to <89% without attributable symptoms
Isolated exertional desaturation to <89% with attributable symptoms
Isolated exertional desaturation to <85% without attributable symptoms
Isolated exertional desaturation to <85% with attributable symptoms
Isolated exertional desaturation to <80% without attributable symptoms
Isolated exertional desaturation to <80% with attributable symptoms
Severe resting hypoxemia
0
5
10
15
20
25
30
35
40
45
Yes
No


Patients with fibrotic interstitial lung disease
Severe resting hypoxemia (PaO_2 <55 mmHg/SpO_2 < 89%, or PaO_2 <60 mmHg and cor pulmonale and/or polycythemia)?
Ye
Recommend supplemental oxygen therapy
No
1. Exertional physiological testing (e.g. 6MWT, shuttle walk)
2. Nocturnal oximetry
Exertional and/or nocturnal desaturation to SpO_2<85-89%?
No
Periodic clinical reassessments
Exertional and/or nocturnal desaturation to SpO_2<80%?
Ye
Ye
Symptoms and/or functional impairment attributable to hypoxemia?
Ye
Recommend supplemental oxygen therapy
No
Consider supplemental oxygen therapy

Oxygen in Patients with Fibrotic Interstitial Lung Disease: An International Delphi Survey

Rachel K. Lim, Christopher Humphreys, Julie Morisset, Anne E. Holland, Kerri A. Johannson

Supplementary Material

Interview guide

Preamble: Questions are to be asked in the context of a hypothetical situation without geographic funding criteria, and we are specifically not addressing patient preference for the purposes of this survey. Like all therapeutic interventions, all decisions must be made considering evidence of potential benefit and patient preference and wishes.

1. Demographics:
    a. Age, gender, country of practice
    b. How long have you been in independent clinical practice as a pulmonologist or nurse clinician or health professional?
    c. What proportion of your clinical work is focused on ILD?

Part 1: Indications for oxygen

2. Thinking about your patient population with fibrotic/chronic ILD, which patients should be considered for supplemental oxygen therapy?
3. How do these specific situations influence your recommendation?
    a. Severe resting hypoxemia (ie. SpO2<88% or PaO2<55mmHg)
    b. Moderate resting hypoxemia (SpO2 88-92)
    c. Isolated exertional hypoxemia based on ambulatory oximetry during formal or informal walk test. What if desturates < 88% or < 80%
    d. Concomitant nocturnal hypoxemia
    e. Existing pulmonary hypertension
    f. Dyspnea, symptomatic, impaired functional capacity
    g. Different sub-types of fibrotic ILD. E.g. IPF vs HP vs. CTD-ILD
    h. Those being considered or awaiting lung transplant
    i. Palliation

Part 2: Goals of oxygen therapy

1. What are the main goals (or anticipated benefits) you aim to achieve with supplemental oxygen in those above situations?
   Prompts: prevent/minimize pulmonary hypertension, HRQoL, survival, reduce exacerbations/ hospitalizations, dyspnea, functional capacity, anxiety, deconditioning, cognitive function, improved sleep.
2. How do you navigate weighing the potential benefits of supplemental oxygen with patient preference re: usage?

Part 3: Practical use of oxygen

1. How should patients be assessed for supplemental oxygen? (prompts: should there be a threshold for oxygen saturation or PaO2 on ABG? At rest or on exertion with formal 6MWT?)

2. How frequently should patients be assessed for oxygen indication? (prompts: every visit, symptom-based, times of worsening)

3. What do you think are potential toxic effects or contraindications to supplemental O2 in ILD patients? Prompts: Falls, smoking, dementia. What general issues have you encountered with oxygen prescribing in ILD?

4. How do you recommend oxygen usage in your patients with fibrotic ILD, and how does that vary based on the indication for oxygen? (i.e. number of hours worn per day, titration with activity, baseline flow rate, wear if it improves symptoms)

5. What guides your recommendation on patient use of oxygen during sleep, (e.g in the absence of documented sleep-disordered breathing)?

6. Is there anything else you'd like to discuss? Are there items that you think are important to include in the Delphi survey?

Table S1: Items not achieving consensus for agreement or disagreement

Consensus for Unsure	Round
Supplemental oxygen may improve the survival of patients with fibrotic ILD and resting hypoxemia.	1
Supplemental oxygen may improve the survival of patients with fibrotic ILD and isolated exertional hypoxemia.	1
Supplemental oxygen prevents acute exacerbations due to fibrotic ILD.	1
Supplemental oxygen prevents hospitalizations due to fibrotic ILD.	1
Isolated exertional hypoxemia leads to the development of pulmonary hypertension in patients with fibrotic ILD.	1
Nocturnal hypoxemia leads to the development of pulmonary hypertension in patients with fibrotic ILD.	1
Supplemental oxygen use slows the progression of existing pulmonary hypertension in patients with fibrotic ILD and resting hypoxemia.	1
Supplemental oxygen use slows the progression of existing pulmonary hypertension in patients with fibrotic ILD and isolated exertional hypoxemia.	1
Supplemental oxygen use slows the progression of existing pulmonary hypertension in patients with fibrotic ILD and nocturnal hypoxemia.	1
Supplemental oxygen should be recommended for fibrotic ILD patients with isolated exertional desaturation to <89%, regardless of symptoms.	2
Non-consensus statements (after 2 rounds)	
Supplemental oxygen should be recommended for fibrotic ILD patients with isolated exertional desaturation to <89%, only if the patient reports symptoms and those symptoms improve with oxygen.	
For fibrotic ILD patients with exertional hypoxemia and symptoms, supplemental oxygen should be titrated to achieve symptom improvement.	
In patients with fibrotic ILD and exertional hypoxia, it is often difficult to titrate supplemental oxygen to maintain a specific target SpO_2 threshold, due to technical limitations of currently available oxygen delivery devices.	
In patients prescribed supplemental oxygen for isolated exertional hypoxemia, oxygen should be continued for physiologic benefit, regardless of the impact on patient symptoms or exercise capacity.	

Abbreviations: ILD=interstitial lung disease, SpO_2=peripheral oxygen saturation