



Palliative care in interstitial lung disease: living well

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Lancet Respir Med 2017;
5: 968–80

Published Online
October 12, 2017

[http://dx.doi.org/10.1016/S2213-2600\(17\)30383-1](http://dx.doi.org/10.1016/S2213-2600(17)30383-1)

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Progressive fibrotic interstitial lung diseases (ILDs) are characterised by major reductions in quality of life and survival and have similarities to certain malignancies. However, palliative care expertise is conspicuously inaccessible to many patients with ILD. Unmet patient and caregiver needs include effective pharmacological and psychosocial interventions to improve quality of life throughout the disease course, sensitive advanced care planning, and timely patient-centred end-of-life care. The incorrect perception that palliative care is synonymous with end-of-life care, with no role earlier in the course of ILD, has created a culture of neglect. Interventions that aim to improve life expectancy are often prioritised without rigorous assessment of the individual's health and psychosocial needs, thereby inadvertently reducing quality of life. As in malignant disorders, radical interventions to slow disease progression and palliative measures to improve quality of life should both be prioritised. Efficient patient-centred models of palliative care must be validated, taking into account religious and cultural differences, as well as variability of resources. Effective implementation of palliative care for ILD will require multidisciplinary participation from clinicians, specialist nurses, psychologists, social workers, and, in some countries, non-governmental faith and community-based organisations with access to palliative care expertise.

Introduction

Chronic interstitial lung disease (ILD) is a heterogeneous group of mainly fibrotic diseases including idiopathic pulmonary fibrosis (IPF), sarcoidosis, hypersensitivity

pneumonitis, and connective tissue disease-associated ILD. Although often perceived as rare, ILD is the 40th most common cause of death globally,¹ with a 52% increase in mortality during the past 10 years. Despite therapeutic advances, a cure is usually unattainable in fibrotic ILD and only a minority of patients meet eligibility criteria for lung transplantation. IPF, the most prevalent fibrotic ILD, has a worse outcome than most malignancies, with an average survival of roughly 3 years from diagnosis.² Fibrotic ILDs are characterised by cough, fatigue, anxiety and depression, and increasingly disabling dyspnoea, ultimately requiring supplemental oxygen. The psychosocial burden of IPF is substantial for both patients and caregivers.³ As the disease advances, the need for support often increases exponentially.

Patients with ILD need timely diagnosis, comprehensive information, early treatment access, and holistic and palliative care (figure 1), as advocated by patients and their treating physicians in the European IPF Charter.⁴ Given that the needs of patients and caregivers in progressive ILD are strikingly similar to those in malignant disease, it is surprising that palliative care in ILD remains in its infancy.

In view of the absence of clear national and international guidelines on palliative care in ILD, we established an international group working in different health services and political and socioeconomic environments made up of ILD specialists, palliative care specialists, ILD nurses, a patient, and a caregiver, from various cultural and religious backgrounds. The working group identified important topics regarding palliative care in patients with ILD and a consensus statement was generated.

Here, we discuss the urgent need for the involvement of palliative care in ILD, both earlier in the disease course and in end-stage disease. We share our perceptions of the most important questions of palliative

Key messages

- The main goal of palliative care for patients with interstitial lung disease (ILD) is to improve and maintain quality of life
- Palliation is holistic and includes all aspects of patient care in ILD
- A disease behaviour-based strategy might be helpful in identifying the patients' need for palliation because of the unpredictable course of most fibrotic ILDs
- Assessment of needs is an iterative and dynamic process throughout the disease course in ILD
- Training of ILD teams on palliative care and of palliative care teams on ILD must be improved
- Patients and caregivers should be realistically educated on all aspects of the disease from the moment of diagnosis depending on the individual patients' needs and preferences
- Palliation should be discussed and initiated early in the disease course depending on the individual patients' needs, preferences, culture, and religion
- Caregivers should be supported throughout the disease trajectory and bereavement
- Advanced care planning, including discussion of treatment limitations and preferences on dying should be offered to all patients with ILD in whom it is evident or likely that the disease will be progressive despite treatment
- Further research is needed to identify the most appropriate models for palliative care and discussions with patients, possible markers to guide care, and suitable outcome measures for clinical trials of palliative care for ILD

care in ILD, and consider the religious and cultural differences that might affect decisions around palliative care, obstacles to implementing a palliative approach to care, and future research considerations.

What does palliative care and living well with ILD mean?

In general, palliative care is synonymous with comfort care, supportive care, and symptom management and aims to improve quality of life throughout the whole disease course for patients and caregivers⁵⁻⁷ (figure 2).^{8,9} Unfortunately, the incorrect view that palliative care consists solely of end-of-life care^{10,11} continues to be reinforced by some health-care professionals, the public, and, therefore not surprisingly, by patients themselves (panel 1).^{10,12-16} The negative connotations of end-of-life care are an important reason for delayed access to palliative care in patients with oncological disorders^{13,17,18} and might explain the underuse of palliative care expertise for patients with ILD in particular.^{19,20} WHO confronts this major failure of communication, recommending early palliative care to “improve the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual”.²¹ This standpoint underpins the European Declaration on Palliative Care.²²

In our view, living well with ILD requires the type of care that allows the recipient not only to improve their quality of life and control symptoms, but also to feel respected, confident, and able to make decisions in accord with their values and sense of self-worth (appendix p 1). The goal of promoting living well with ILD requires health-care teams to offer hope whenever possible, despite worsening of disease and loss of quality of life, and provide information, with sufficient time for discussion to allow informed and autonomous decisions to be made by patients and caregivers throughout the disease course, driven by individual values. Furthermore, prompt and effective measures should be taken to address symptoms that have a major effect on quality of life, and easy access to palliative care expertise is needed. Symptomatic interventions should be viewed as a separate treatment pathway from interventions directed to improving life expectancy. Finally, it is important to confront key psychological issues that detract from quality of life. A proactive approach is required to strengthen dignity and to minimise unease. In this regard, patients need to be able to confront the need for oxygen therapy and other potentially psychologically distressing issues on their own terms, without loss of self-respect and autonomy. This is a particularly important problem, given the poor understanding of fibrotic ILD by most patients and many non-specialist medical staff.

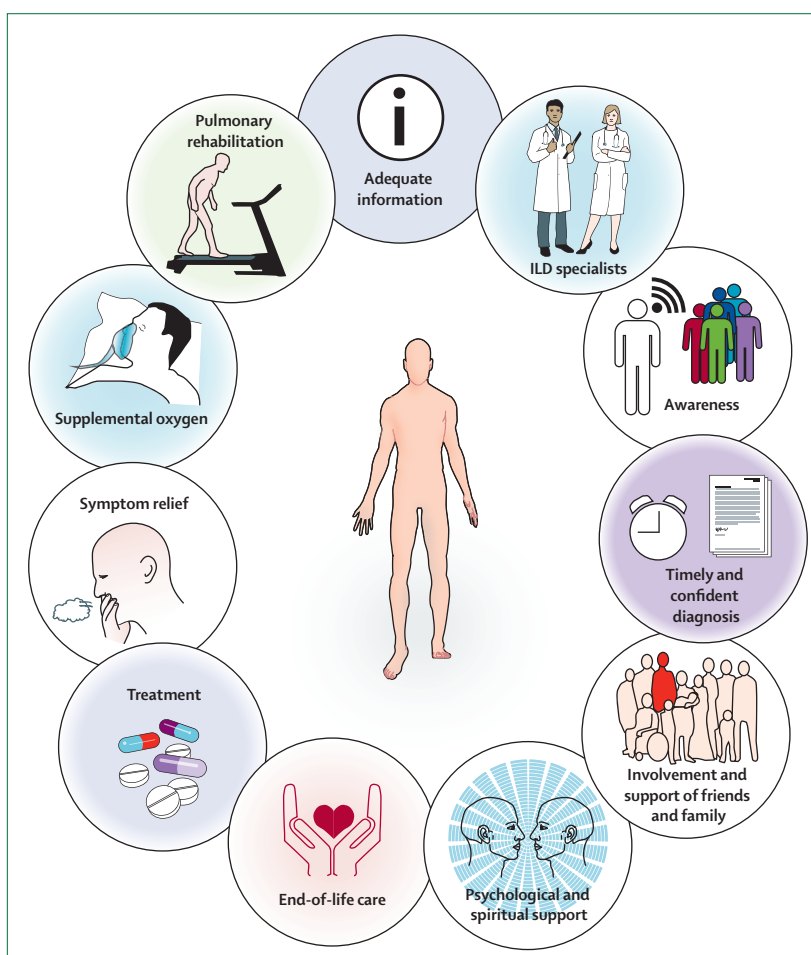


Figure 1: Needs of patients with interstitial lung disease
ILD=interstitial lung disease.

Why and in whom do we need palliative care in ILD?

Chronic ILD is associated with a high burden of disease and symptoms, substantial loss of quality of life, and shortened survival.^{2,23} Irrespective of the cause or histological pattern, chronic ILD is characterised by cough, dyspnoea, fatigue, and risks to reduced emotional wellbeing, resulting in severely impaired quality of life.^{3,24-29} As the disease progresses, the burden of symptoms increases; compared with patients with end-stage lung cancer, patients with advanced ILD face even more severe and frequent dyspnoea.^{30,31}

The need for immediate palliative care in symptomatic patients with ILD is self-evident. A greater challenge for clinicians is to identify those patients with ILD in whom progression of irreversible disease despite treatment is likely to occur, even if disease is not severe at presentation. In IPF, a progressive course is the rule, justifying consideration of palliative care from the time of first diagnosis. By contrast, when long-term stabilisation is likely to be achievable, as in many patients with fibrotic

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See Online for appendix

sarcoidosis or when chronic symptoms are minimal, palliative care initiatives might be less relevant. The group for whom identification of a future need for palliative care might be most difficult is patients with non-IPF fibrotic ILDs with irreversible fibrosis; in these patients, disease stabilisation is likely to be achievable, but progression despite treatment is equally likely.

The unpredictable course of ILD often induces psychological distress for patients and caregivers, who

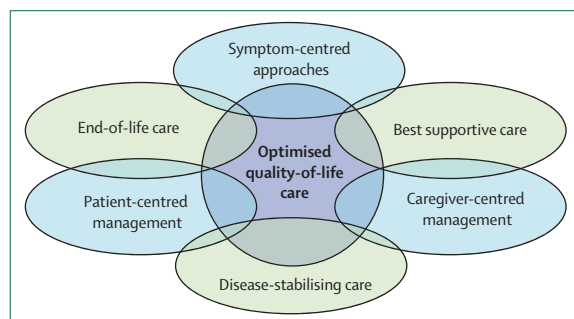


Figure 2: Living well with interstitial lung disease

To overcome the misunderstanding of palliative care as end-of-life care, a holistic approach to the treatment of interstitial lung disease is essential to encompass its different features. The central aim is to optimise quality of life at any stage of the disease. Disease-stabilising care consists of pharmacological and non-pharmacological therapies, including treatment of comorbidities. Symptom-centred approaches should consider quality-of-life-debilitating symptoms, but also depression and anxiety as well as fatigue and deconditioning. Patient-centred and caregiver-centred management include education and assistance for self-management, and end-of-life strategies include advanced care planning. Best supportive care includes interventions and multiprofessional approaches not covered in the other areas. Based on Lindell⁸ and Lee et al.⁹

Panel 1: Voices of patients receiving palliative care for ILD

Patients were asked "What does palliative care mean to you?"

- "...I fear it to some extent because I don't know exactly what it means..."
- "It's a bit scary—having someone explain might help"
- "...I would appreciate if somebody would talk to me about it..."
- "...Is palliative care not solely a euphemism for dying soon..."
- "...Before I was sent to the palliative care ward I was frightened to be demoted for dying but at the same time frightened to suffocate. Palliative care took away my breathlessness and my fears..."
- "...My main goal of therapy for my chronic disease is to maintain quality of life at the best achievable level for the time I have left..."
- "...I did not know that palliative care is reimbursed, many people think they have to pay for it themselves..."
- "...I do not want to be labelled as a doomed man - that's why I do not like to be sent to palliative care..."
- "...Professional carers that understand the needs of patients with fibrosis and administer help that make patients feel better..."
- "...I would not like it but if I need it, I would take it..."
- "...Dignity, pain free and of great benefit to patients and families..."
- "Palliative care always meant end of life to me but if it helps my quality of life for whatever time I have left, I would be happy to look into it"

ILD=interstitial lung disease.

must live with the looming possibility that their situation will worsen. We argue that if an IPF-like—ie, progressive—course becomes apparent, despite optimal medical management, and overt distress is present or symptoms are burdensome, early palliative care should be implemented. A disease behaviour-based algorithm could be a helpful guide for the clinician to decide when palliative care intervention is needed (figure 3).

The availability of disease-modifying treatments in IPF^{32,33} has provided great hope for the ILD community. However, although antifibrotic drugs delay the loss of pulmonary function, they do not reverse pulmonary fibrosis or improve many outcomes meaningful to patients, such as exercise tolerance, symptoms, or quality of life. In fact, in some cases, side-effects can result in a net reduction in quality of life. Exactly the same considerations apply to the use of traditional therapies (eg, prednisolone or immunosuppressive agents) in other fibrotic ILDs. Management of side-effects and symptoms in irreversible disease requires expertise in both pharmacological and non-pharmacological treatments. The focus on disease-modifying strategies might result in the under-recognition of palliative care needs of patients and families.

In recent years, many insights have been gained into the needs of patients with ILD and their caregivers.^{3,4,20,24–27,34–42} Common denominators that have emerged for patients with ILD are the need for better information about the disease in general, better symptom relief, and better access to palliative and end-of-life care (figure 1). Individual patients with ILD differ greatly in their needs and preferences, which might fluctuate throughout the disease trajectory.³⁸ A patient-centred approach to care in ILD is essential. It has been argued that the delivery of palliative care should be based on need, not diagnosis or prognosis.^{43–45} Thus, although we do not advocate the routine initiation of palliative care for every patient with ILD, ongoing surveillance and discussion should be an integral part of long-term management, so that the implementation of palliative approaches to care is not unnecessarily delayed (figure 3). In ILDs with an unfavourable prognosis (eg, IPF or an ILD with idiopathic pulmonary fibrosis-like behaviour), palliative interventions can aid in the delivery of bad news and provide immediate reassurance that holistic support will be provided throughout the course of the disease.

The assessment of needs is an iterative process done throughout the disease course (figure 4).⁴⁶ Validated tools that identify palliative needs can be used to systematically assess requirements (appendix p 2).^{47,48} However, such tools cannot stand alone or replace conversations with patients and caregivers about informed planning of care (figure 4). Validated and clinically usable tools that easily identify symptom burden in ILD are scarce. The chronic obstructive pulmonary disease (COPD) assessment test (CAT) has been shown to be valid for the assessment

of dyspnoea, oxygenation, and anxiety in IPF,⁴⁹ but communication between care providers and patients with ILD might be complicated by an often unpredictable disease course, with acute changes in symptoms and oxygen needs.^{37,50,51} This unpredictability and lack of tools could lead to neglect of timely initiation of palliation early in the disease course or to the inappropriate use of health-care resources, medically futile interventions, loss of patient and caregiver autonomy, and denial of a dignified death at a chosen place at the end stage of the disease.^{19,20,52,53}

Holistic palliative care in ILD addresses not only the needs of patients, but also those of caregivers.^{19,20} Caregivers are usually family members, but for patients living alone, this role might be taken up by friends.⁵⁴ The delivery of holistic palliative care requires the clinician to identify and include the patient's support network. Living with and caring for an individual with symptomatic chronic ILD affects caregivers. Caregivers are at increased risk for physical and psychological illness and have increased mortality.⁵⁵ Like the caregivers of patients with other chronic illnesses, caregivers of patients with ILD face a significant burden and stress⁵⁶ that is magnified if caregivers are ill themselves or under financial pressure.⁵⁷ The understanding of the stresses faced by patients and caregivers has grown exponentially in the past decade.^{3,4,20,24–27,34–42}

What specific problems require palliative intervention and how to deliver them in ILD?

Key considerations for palliative care in ILD include symptom management, general issues to improve quality of life, management of end-stage disease, improving quality of dying and help for caregivers, considerations on comorbid disorders, and discussion of who to involve in the provision of palliative care. Some evidence exists to guide symptom management in patients with ILD (table).^{20,50,58–80}

Dyspnoea is a common and distressing symptom that can lead to inactivity, muscle mass deterioration, and deconditioning that, in turn, results in increased dyspnoea.⁸¹ Oxygen supplementation is regarded as the standard of care in patients with hypoxaemia and dyspnoea. A systematic review recommends oxygen (either on exertion or at rest) for relief of dyspnoea for patients with advanced lung disease.⁸² Results from a randomised controlled trial of supplemental oxygen use during routine daily activities showed an improvement in the quality of life in patients with fibrotic ILD.⁸³ In routine practice, barriers to optimal oxygen usage include inability to meet the high-dose oxygen demands of patients with advanced ILD and physician concerns about hypercapnia or progression of fibrosis due to oxidative stress. In ILD, neither concern has a sound basis. We believe that relief of dyspnoea should take precedence over these theoretical concerns, especially in advanced or end-stage disease with no realistic possibility

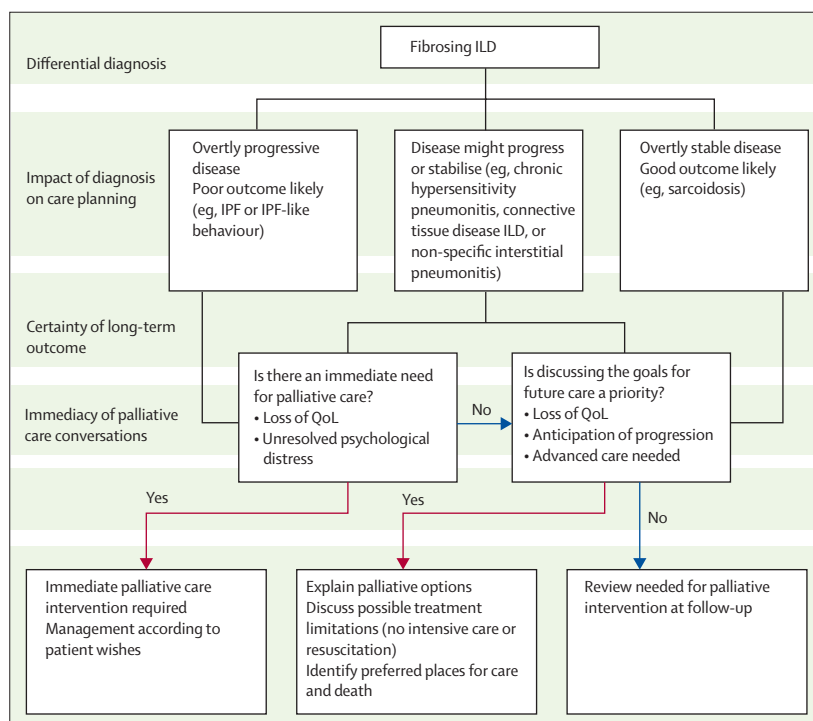


Figure 3: Disease behaviour-based algorithm

The algorithm is designed to help clinicians to assess the immediacy of a current palliative care need for patients with interstitial lung disease. ILD=interstitial lung disease. IPF=idiopathic pulmonary fibrosis. QoL=quality of life.

of the prolongation of survival. In some parts of the world, there are logistical limitations for oxygen use: patients might not have electricity in the home or be able to afford oxygen equipment or the increased electricity usage associated with a home oxygen concentrator.

Opioids are often prescribed to relieve dyspnoea.⁸⁴ Some patients might be reluctant to use opioids because of the side-effect profile, whereas others might fear opioid dependency. Physicians might also be dissuaded from prescribing opioids by a perceived risk of respiratory drive depression. Data on the role of opioid treatment in fibrotic ILD are scarce and the findings are variable.⁵⁹ There is no evidence of effectiveness for inhaled or nebulised opioids, and only low-quality evidence for the benefit of oral or parenteral opioids in the relief of dyspnoea in ILD.⁵⁹ No respiratory depression, as judged by desaturation and reduced ventilation, has been reported with the low doses of opioids used to treat dyspnoea, and our clinical experience suggests that they are effective.⁵⁹ Non-pharmacological interventions such as air fans⁶⁷ and pulmonary rehabilitation might also have a beneficial effect on dyspnoea.^{68,85}

Relentless cough can be distressing and a major source of loss of quality of life in patients with ILD. No medical therapies for cough are uniformly effective in ILD, but opioids, low-dose prednisolone, and neuromodulators such as gabapentin might be helpful in some patients and can reasonably be considered empirically.⁸⁶ One small

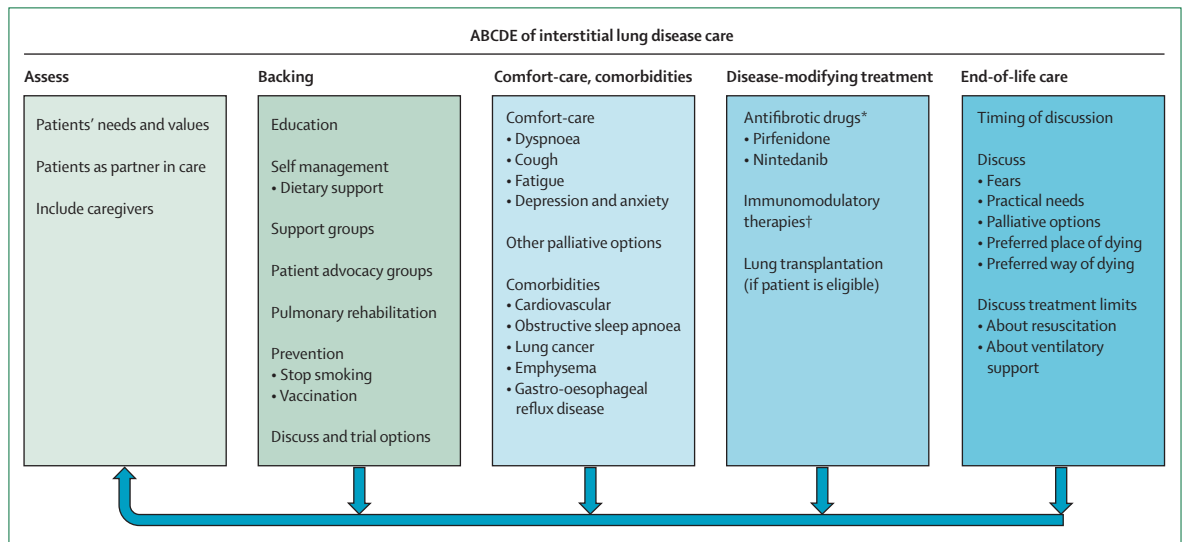


Figure 4: The ABCDE of interstitial lung disease care

The ABCDE model shows a possible structured approach to comprehensive care, including palliative care throughout the disease course. *Idiopathic pulmonary fibrosis. †Non-idiopathic pulmonary fibrosis interstitial lung diseases. Based on van Manen et al⁴⁶ by permission of the authors.

study reported that thalidomide was beneficial for cough in idiopathic pulmonary fibrosis,⁸⁷ but its use has not been widely adopted. Results from an observational trial showed a benefit from pirfenidone, which reduced objective 24-h cough counts and improved cough-related quality of life, but these reports have yet to be confirmed in randomised clinical trials.⁸⁰ The effect of nintedanib on cough has yet to be studied. In a safety and efficacy study of a novel formulation of sodium cromoglicate (PA101), a 31% reduction of chronic cough was seen in idiopathic patients with pulmonary fibrosis, which warrants further investigation.⁸⁸ Other potential causes of cough, such as gastro-oesophageal reflux, angiotensin-converting-enzyme inhibitors, and postnasal drip, should be identified and adequately addressed (table).

Looking more broadly at interventions to improve symptoms and quality of life for patients with ILD, pulmonary rehabilitation and sildenafil have both been reported to have a beneficial effect on dyspnoea and quality of life in patients with IPF.^{68,89} Evidence also suggests that education and peer support might improve emotional wellbeing in this population of patients.⁹⁰

While all the considerations discussed apply to a wide spectrum of ILD severities, the needs of patients with advanced or end-stage ILD are also highly variable. Dignified end-of-life care and death is synonymous with the avoidance of futile interventions such as invasive ventilation, extracorporeal membrane oxygenation, and resuscitation in patients who are dying. However, the religious and cultural values, as well as the judgments and expectations of patients with end-stage disease and their caregivers must be recognised and considered. Spiritual needs are complex, often overlapping with social or psychological needs.⁹¹ Although a patient's religious denomination might be recorded for administrative

purposes, it will not necessarily be discussed in the consultation. To enable joint decisions on the involvement of a spiritual leader in palliative care, clinicians should discuss their patients' religious affiliations (appendix p 3).⁹²

Quality of dying also needs to be improved for patients with ILD and provisions need to be made for their caregivers. In advanced malignant disease, palliative care at home reduces the need for hospital admission in patients with cancer.⁹³ This finding is highly relevant to ILDs, especially IPF, given the malignant outcome in that disease. Insufficient palliative care involvement is associated with failure to take into account the patient's wishes on their preferred place of death.⁵⁰ Despite the fact that most patients with IPF prefer to be treated and die at home or in a hospice,^{94,95} at least half die in hospital.^{19,52,95} Palliative care intervention has been shown to increase the proportion of patients with ILD who die outside hospital, at home in a peaceful, familiar environment, surrounded by loved ones.⁵⁰ In patients with cancer, involvement of a palliative care team increased the proportion of patients dying at home and was associated with longer survival.^{50,96} Importantly, palliative care does not stop after the death of patients. A complicated sorrow reaction, which can manifest as various significant psychological problems, occurs in up to 15% of caregivers after the death of a loved one.⁹⁷ No known risk factors exist that allow this response to be anticipated. Health-care teams should therefore establish a relationship with caregivers before death, as this allows improved and more effective bereavement follow-up, as in the case of other fatal diseases.

Patients with ILD are often affected by comorbid conditions, including cardiovascular disease, pulmonary hypertension, emphysema, sleep disorders, lung cancer, and disorders in emotional health, such as anxiety and

depression.^{98–100} These comorbidities can reduce life expectancy and quality of life by increasing the severity of dyspnoea or generating their own unique symptoms. They complicate the already challenging clinical management of patients with ILD.¹⁰⁰ Assessing and treating comorbid conditions might not be indicated at the end of life. However, earlier in the course of disease, the identification and treatment of comorbidities might result in major improvements in symptoms and quality of life.

The multiple goals of palliative care require a broad range of skills. Any member of the clinical team with skills in compassionate care can take the lead on palliative care for ILD. However, ILD specialists might not always recognise palliative care needs because they have not been trained in this area or have insufficient time to devote to these issues. Conversely, palliative care specialists might be unfamiliar with ILDs. Thus, an integrated team approach could best address the needs of patients and their families. If available, an ILD nurse specialist might play an important part in palliative care in ILD. Results from one study have showed the benefits of a nurse-led advanced care programme in ILD and underscore the beneficial participation of specialised ILD and palliative care nurses.¹⁰¹ Access to an ILD nurse specialist could improve the delivery of the care pathway and result in major improvements in quality of life for the patient and caregiver.^{37,102}

However, specialist nurse and palliative care expertise is not always available. In some parts of the world, patients and caregivers are supported by various professional carers, including physicians, nurses, physiotherapists, dieticians, psychologists, and social workers. Some programmes also include general practitioners, general or community palliative care nurses, and other allied health professionals.⁵⁰ The optimal composition of such a team for patients with ILDs has not been defined and will be determined by local resources, cultural factors, and the religious beliefs of patients and caregivers (appendix p 3). In many cultures, care might be largely provided by family, community workers, and traditional healers, supported by health-care professionals where possible.

When should palliative care be initiated in ILD?

There is a rapidly growing consensus that palliative care input in ILD should be initiated early and not delayed until disease is advanced, thus avoiding the misconception that palliation is a euphemism for imminent death. Early palliation is particularly important when advanced care planning is discussed because in some cultures the preservation of life over-rides all other considerations, irrespective of the futility of interventions.¹⁰³ The need for a sensitive approach to the management of IPF has been highlighted in a survey of the patients' perspectives.¹⁰⁴ In some cases, patients and caregivers prefer to delay discussions of end-of-life management until the disease is advanced.^{35,37} However, many patients with pulmonary fibrosis value discussions on end-of-life management shortly after diagnosis.²⁶

In-depth qualitative interviews of patients with ILD with a range of disease severity and caregivers identified a uniform unmet wish: they wanted more information from clinicians, provided earlier in the course of disease, on palliative measures in advanced disease and coordination of end-stage care.⁴⁰ Quotes collected from around the world iterate this message (panel 1). Furthermore, discussion of comfort measures while still continuing disease-modifying care might be confusing for patients and their families.¹⁰⁵

Clinicians must strive to correctly interpret the wishes of patients and caregivers, providing adverse prognostic information and discussing management of advanced disease when this is needed (figure 4). A common

	Pharmacological management	Non-pharmacological management
Dyspnoea	Treat any reversible causes, eg, infection or pulmonary hypertension Low-dose opioids ^{38–40} Benzodiazepines if anxiety-related breathlessness present ^{61–63} Supplemental oxygen ^{64–66} Bronchodilators if airflow limitation present	Cool air fan ⁶⁷ Relaxation and breathing exercises ⁶⁷ Pulmonary rehabilitation ⁶⁸ Positioning ⁶⁷ Reassurance ⁶⁷ Cognitive behavioural therapy or psychotherapy ⁶⁷ Energy conservation or pacing activities Loose clothing Mouth care Breathlessness intervention service ⁶⁹
Cough	Treat any reversible causes or comorbidities, eg, infection, COPD, or angiotensin-converting-enzyme inhibitors Low-dose opioids, including codeine ^{70–72} Gabapentin ⁷³ Low-dose prednisolone ⁷⁴ Thalidomide Antifibrotic treatment* Rhinitis therapy if indicated—oral antihistamine with or without decongestant ⁷⁵ Anti-reflux therapy (high-dose proton-pump inhibitor and H ₂ antagonists) ^{14,76,77} Prokinetic therapy, if oesophageal dysfunction suspected ⁷⁸ Simple linctus or codeine linctus	Lifestyle advice—eat small meals and earlier in day Speech therapy
Fatigue	Treat secondary underlying causes such as sleep apnoea, anaemia, venous thromboembolism, infection, dehydration, or hypothyroidism Supplemental oxygen	Pulmonary rehabilitation ^{58,68}
Depression and anxiety	Antidepressants ⁷⁹ Anxiolytics ⁷⁸	Provide good palliative care Assess any psychosocial concerns Assess quality of relationships with significant others Facilitate communication between family members Consider a guided self-help programme that consists of provision of appropriate written materials and support Consider a brief psychological intervention, problem-solving therapy, or counselling ⁷⁹ Pulmonary rehabilitation
Weight loss	Low-dose prednisolone	Dietary evaluation including protein supplementation Pulmonary rehabilitation ⁶⁸

(Table continues on next page)

Pharmacological management		Non-pharmacological management
(Continued from previous page)		
Pain	Paracetamol Codeine Low-dose opioids ⁵⁸	Pulmonary rehabilitation ⁶⁸
Miscellaneous	..	Patient education ²⁰ Patient support groups ²⁰ Family reassurance ²⁰ Assess patients' coping strategies; where necessary, facilitate the development of new effective strategies to help patients regain a sense of control (eg, staying active, taking a walk, engaging in social relationships, finding meaning in events) Advise patients and their families where to seek financial and practical support (eg, advice on housing and employment issues, state benefits, mobility [eg, disabled parking], help with personal care, cleaning, and shopping); health professionals should be aware that some patients might have spiritual needs and arrange support from appropriate spiritual advisers (eg, chaplains) when necessary Participation in research programmes Individualised case conference model of care ⁵⁰

Symptom-based therapies should be balanced against potential adverse effects in a case-by-case discussion. COPD=chronic obstructive pulmonary disease. *Patient and expert opinion suggest that some antifibrotics might lessen cough.⁸⁰

Table: Potential symptom-based therapies

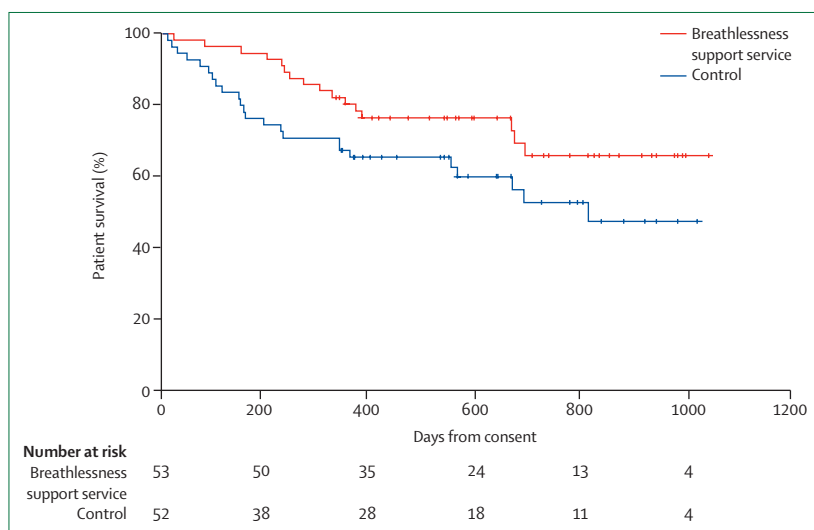


Figure 5: Effect on survival of a breathlessness support service

The breathlessness support service was an early palliative care approach integrated with respiratory services for patients with advanced disease and refractory dyspnoea. The intervention also resulted in significant improvements for patients with interstitial lung disease. Reproduced from Higginson et al by permission of the authors.¹¹¹

misconception is that active palliative care is incompatible with ongoing interventions aiming to improve life expectancy in IPF or other fibrosing ILDs, such as antifibrotic therapy or listing for lung transplantation. This view is strongly rejected by our working group: palliative care in ILD aims to relieve symptoms, improve quality of life, and fulfil vital needs in advanced disease and at the end of life, irrespective of other interventions.

Acute or subacute deterioration of ILD requires quick treatment decisions to be made, including the question of admission to the intensive care unit (ICU), in the knowledge of a high-risk of limited survival and the likely need to manage an end-of-life situation.¹⁰⁶ This challenge especially applies to acute exacerbations of IPF, which can occur in the early stage of disease,¹⁰⁷ are the most common cause of death in patients with IPF in Japan,¹⁰⁸ and have in-hospital mortality of 50–70% in patients admitted to the ICU.^{109,110} Because of the prognostic effect and variability of therapeutic responses in acute exacerbations, patients and caregivers are confronted with the need to participate in urgent decisions on treatment changes.

Where patients with ILD are admitted to the ICU, we advocate the routine involvement of palliative care professionals. Palliative care expertise facilitates symptom control and addresses caregiver needs at a time of great stress, given the major prognostic uncertainty associated with ICU admission. Palliative care input in the ICU will not, in most cases, change the likelihood that the patient will die in an acute care facility. As already discussed, the home or a hospice is the preferred place of death for most patients with ILD, and yet most patients die in hospital, often in the ICU.^{19,52} This situation reflects the fact that few patients with IPF are referred to palliative care before or during ICU admissions.⁵³ It also highlights the importance of a timely discussion of limitations of treatment to avoid futile medical interventions and allow patients to die among family and in their preferred place.¹⁰⁶

Does palliative care improve outcomes in patients with ILD?

Although there is a paucity of data on this question, the obvious parallels between progressive ILD and malignant disease provide helpful guidance. Patients with malignant disease benefit from early palliative care input, with improvements in quality of life and survival and benefits for family caregivers.^{96,111–115} Partly on the basis of data from the field of oncology, governmental and expert group guidance includes recommendations that palliative care input should be available to all patients with life-limiting disease and should be incorporated throughout the disease course.^{2,102,116} Data supporting these recommendations also exist in pulmonary disease. A randomised controlled trial of an integrated palliative and respiratory care service in 105 consecutive patients with chronic dyspnoea included 19 patients with ILD. Mastery of breathlessness and survival improved in both the comprehensive intervention group and the ILD group (although the small number of patients with ILD is a limitation; figure 5).¹¹¹ In a phase 2 randomised controlled feasibility study in 53 patients with ILD, the use of community palliative care case conferences in patients with advanced fibrotic disease was associated with improvements in symptoms and quality of life after

4 weeks and in anxiety and depression in both patients and caregivers.⁵⁰

Although survival is a robust outcome marker, the assessment of change in symptoms and quality of life (in both patients and caregivers) is more complex (appendix p 2). Consensus on which tools to use in ILD is needed. In severely ill or dying patients, the use of multiple or long questionnaires should be avoided. There is extensive evidence on scores specifically developed for palliative care in cancer and other fields such as the Edmonton Symptom Assessment System-revised (ESAS-r)^{117,118} or the Palliative Care Outcome Scale (POS).¹¹⁹ However, validated outcome measures to assess efficacy and cost-effectiveness are scarce in some settings and patient groups,¹²⁰ including patients with ILD, and uncertainties exist on whether economic evaluations should use generic measures such as the EuroQol five-dimensional questionnaire (EQ-5D) to calculate cost per quality-adjusted life-year (QALY) gained. This approach emphasises patient function and might not be best suited to the assessment of health-related quality of life in palliative care.¹²¹ Thus, research is needed to validate or modify existing tools that meaningfully assess the effect of palliative care interventions in individual patients with ILD across the spectrum of disease severity, including advanced or end-stage disease.

What obstacles exist to effective ILD palliative care?

Many barriers to the provision of optimal palliative care exist, including various aspects that are affected by human, political, economic, social, religious, and cultural factors (panel 2). Palliative care is still at a nascent stage in many countries, especially for non-malignant conditions. In India, for example, the incidence of ILD is similar to that in Europe and the USA,¹²² yet there are no more than a handful of palliative care specialists in the country and just seven small hospices offering terminal end-of-life care;¹²³ only 0.4% of patients who are dying in India are estimated to have access to end-of-life care.¹²⁴ Although the amount of focus on palliative care and numbers of palliative care specialists are greater in developed countries, many patients are still not offered timely palliation and guidelines for palliative care in ILD are conspicuously absent.

What are the core research priorities in ILD palliative care?

Solutions to the problems discussed in this Review demand to be explored in future work and priorities for this research are shown in panel 3. The ideal model of palliative care delivery for ILD is unknown. The needs of patients with ILD and their caregivers might not be met by the cancer model of palliative care. Work is needed to develop and assess other models of palliative care that improve communication, coordination, and cohesion of the pathways shared by ILD and palliative care teams.

Panel 2: Barriers to effective palliative care for ILD

ILD-related factors

- Unpredictable course of the disease generating uncertainty
- Diagnostic uncertainty in some cases obscuring the pathway of care
- Little awareness of ILD in the general population
- Scarcity of evidence for palliative care in ILD
- Only a few established tools to identify the need for palliative care in patients with ILD
- Few established patient-related outcomes for palliative care in ILD

Misconceptions about palliative care in the general population

- Misinterpretation of palliative care as hospice care and end-of-life care by patients and health-care professionals
- Little knowledge of palliative care in the general population
- Cultural and religious restraints to palliative care
- Discussions to establish patient health beliefs and preferences left too late in the disease course

Barriers in health-care providers

- Little knowledge and lack of awareness of knowledge deficits relating to ILD and palliative care
- Insufficient time to initiate a potentially emotive conversation
- Personal barriers to raising the topic of palliative care in consultations with patients
- Absence of guidelines for palliative care in ILD
- Insufficient awareness of patient's culture, religion, or spirituality
- Denial of the patient as the expert of their own disease

Patient-related barriers

- Little understanding of the serious nature of the disease thus affecting acknowledgment of disease by patient and caregiver
- Personal beliefs, spirituality, ethnic, and cultural identity and traditions
- Communication impairments between patients, caregivers, and health-care providers
- Denial and desire to protect family and loved ones
- Fear of confronting mortality

Health-care system-related barriers

- Insufficient palliative care resources
- Limited access to symptom-based therapies (eg, lack of electricity in rural areas for oxygen concentrator for long-term oxygen therapy)
- Insufficient reimbursement for palliative care services
- Deficient collaboration between primary treatment team and palliative care team
- Overloaded and impractical hospital services

ILD=interstitial lung disease.

Without uniformity in disease definitions, endpoints and the description of cohort characteristics, a robust evidence base cannot be constructed. In other areas of research in ILD the lack of standardisation has made it necessary to start again after a decade of endeavour. Expert groups have had to be convened to provide consensus guidance in influential research statements.^{107,125} We call for a similar initiative to be taken for research into palliative care for ILD.

Validated endpoints have been scarce in trials of palliative care for ILD. The complex questionnaires used to quantify changes in symptoms and quality of life might not be appropriate in frail patients. Patient-reported outcome measures that have been validated in different cultures

For *The Lancet Commission on palliative care* see [http://dx.doi.org/10.1016/S2213-2600\(17\)30384-3](http://dx.doi.org/10.1016/S2213-2600(17)30384-3)

Panel 3: Recommended research focus points

- Development and assessment of different models of palliative care for ILD, including:
 - Early vs late models
 - Integrated palliative and respiratory care service
 - Nurse-led facilitated advanced care planning intervention
 - Differences of in-hospital and ambulatory palliative care
- Identification of optimal markers to predict and characterise end-stage disease and allow timely intensive discussion and initiation of end-of-life care
- Mixed methods studies to assess the most appropriate model to discuss end-of-life issues
- Mixed methods studies on how to overcome professional, cultural, and religious barriers to palliative care for ILD
- Formulation of an international consensus research statement for research on palliative care for ILD to standardise selection of outcomes and population baseline characteristics
- Amalgamation of research data from different cohorts, based on standardisation of research
- Validation of patient-reported outcome measures for use in trials of palliative care for ILD, including possible use as primary endpoints
- Further investigation into the role of oxygen, opioids, and breathlessness intervention services
- Further investigation into neuromodulatory agents for cough
- Exploration of cost-effectiveness of palliative care in ILD

ILD=interstitial lung disease.

Search strategy and selection criteria

We searched PubMed for articles published from Jan 1, 1971, to June 30, 2017, using the terms “palliative care and lung diseases”, “palliative care and interstitial lung diseases”, “palliative care and diffuse parenchymal lung disease”, “palliative care and pulmonary fibrosis”, “palliative care and lung fibrosis”, “palliative care and pulmonology”, “palliative care and pulmonary disease”, “palliative care and pneumology”, “palliative care and lung cancer”, and “chronic obstructive pulmonary disease and palliative care”. We also identified relevant articles published between Jan 1, 1990, and Jan 1, 2017, through searches of our personal files.

We manually reviewed the articles resulting from the search and relevant references cited in the articles found. We limited our searches to articles published in English and German.

and countries should be investigated as candidate primary and secondary endpoints; the role of such measures should be explored in patient care and in informing the organisation and delivery of palliative services. The creation of a hierarchy of endpoints specific to ILD palliative care research lies beyond the scope of this current work and might require a definitive Delphi exercise, as has been used to reach consensus on endpoints in the field of connective tissue disease-associated ILD.¹²⁶

More research is urgently needed on symptomatic interventions for ILD. The current reliance on data generated in other diseases such as COPD is unsatisfactory. Further investigation is needed into

approaches such as oxygen, opioids, alternative therapies (eg, singing, mindfulness, and yoga), pulmonary rehabilitation, and breathlessness intervention services for control of dyspnoea and neuromodulatory agents such as gabapentin for cough.

Further research is needed to identify the most appropriate model or models to discuss end-of-life issues with patients and caregivers. Mixed method studies of bereaved caregivers' experiences are likely to yield important information about their perception of the patients' needs. Future studies should address the information needs and psychological burden of patients and caregivers in the context of end-stage disease. Furthermore, research into the best way to support caregivers should be prioritised, including assessments of quality of life, disease burden, pre-bereavement and post-bereavement psychology, and level of functioning.

Conclusion

The main aims of palliative care in ILD are to improve quality of life by addressing symptom-related, psychological, social, and spiritual needs and to ensure that patients with ILD live well throughout the course of disease (figure 2). The unpredictable disease course of most fibrotic ILD makes it difficult to identify individual patients' need for palliation and a disease behaviour-based strategy might be helpful. Palliative care input must be individualised according to the needs of patients and caregivers. Effective communication is crucial to assess and adapt to the needs of the patient throughout the disease course. The over-riding consideration is that palliation should be patient-centred, with patient choice exercised on the optimal site and timing of palliative care input and decisions affected by symptom severity, difficulties in travelling, and location and availability of palliative care expertise.

Sadly, palliative care is often perceived as synonymous with hospice and end-of-life care. In our opinion, the widely practised dichotomous model, in which treatments that aim to improve life expectancy are pursued exclusively, with palliative care input only when these fail, is as inappropriate in patients with ILDs as it is in other chronic diseases. This model is driven by physician intent to prolong life expectancy in response to disease progression. It does not accommodate patients' wishes to be treated seamlessly in a trajectory in which the prognosis is often uncertain from the time of diagnosis. Many clinicians have an imperfect appreciation of the role of palliative care as an integral component of care for patients with ILDs (figure 4).

Optimal palliation requires various skills, provided by a team of health-care professionals, with the constituent elements of the team determined by local resources, cultural factors, and the religious beliefs of patients and caregivers. In this respect, the poor understanding of ILDs by many non-specialist clinicians is particularly challenging. Education of the public, health-care

professionals (directed towards improving communication strategies), and policy makers about the major benefits of palliative care for patients with ILD and their caregivers should be prioritised. Support groups for both patients and caregivers should also have an important role.

A multidisciplinary approach is needed to facilitate decision making and preparations for end-of-life care, including symptom management, medical decisions for the dying process, refusal of resuscitation when appropriate, and meeting patient wishes on the preferred place of care and death. Only by these means can we hope to address the unfortunate reality that most patients with ILDs continue to die in hospital after undergoing unrealistic attempts to prolong life until shortly before death and experience unacceptable delays in end-of-life decisions.

Contributors

MKr (pulmonologist and ILD specialist), EB (pulmonologist and ILD specialist), A-MR (Research fellow and ILD nurse consultant), AW (pulmonologist and ILD specialist), and MW (pulmonologist and ILD specialist) conceived the idea for this Review and contributed equally to the conception of this work, outlined the questions regarding palliative care in ILD in consensus with all authors, and drafted the report. MKr coordinated the outline and discussion on different attitudes achieving a consensus amongst all authors. Crucial intellectual content was contributed by SB, KL, and CEB from the perspective of specialists in palliative care for ILD; by YA, GC, TJC, AAH, KJ, RK, MKo, YK, SQ, JS and ZU as an international group of specialists on ILD with various cultural and religious backgrounds; and by NC as a caregiver and KG as a patient, with important associations with national and international patient support groups. All authors contributed to and approved the final version of the report.

Declarations of interests

NC reports grants from Boehringer Ingelheim and Roche Products Ireland, and other funding from Roche, provided to the Irish Lung Fibrosis Association. AW reports personal fees from Boehringer Ingelheim, Intermune/Roche, Bayer, and Chiesi. A-MR reports grants and personal fees from F Hoffman-La Roche. TJC reports grants and personal fees from Boehringer Ingelheim and Roche; grants from Bayer, BMS, Actelion, and Sanofi; and personal fees from AstraZeneca. KJ reports personal fees and non-financial support from F Hoffman-La Roche and Boehringer Ingelheim and grants from UCB Biotech. RK reports personal fees from Roche and Boehringer Ingelheim. MKo reports grants from Canadian Pulmonary Fibrosis Foundation and the Canadian Institute for Health Research; other funding from Roche, Sanofi, and Boehringer Ingelheim; grants and other funding from the Pulmonary Fibrosis Foundation; grants and personal fees from Roche Canada and Janssen; and personal fees from Boehringer Ingelheim, GlaxoSmithKline, AstraZeneca, Vertex, Genoa, Gilead, Prometic, and Alkermes. YK reports advisory board fees and personal fees from Asahi Kasei Pharma and personal fees from Boehringer Ingelheim, Eisai, Kyorin Pharmaceutical, Novartis Pharma, Shionogi & Co, and Teijin Pharma, outside of the work. MKr reports grants and personal fees from Boehringer Ingelheim and Roche/InterMune. SQ reports grants from Boehringer Ingelheim. MW reports grants and other funding from Boehringer Ingelheim and Intermune/F Hoffman-La Roche and other funding from Galapagos. All other authors declare no competing of interests.

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