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REVIEW

The Role of Palliative Care in Reducing Symptoms and Improving Quality of Life for Patients with Idiopathic Pulmonary Fibrosis: A Review

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ABSTRACT

Idiopathic pulmonary fibrosis (IPF) is a progressive fibrotic lung disease with a median survival of 3–4 years from time of initial diagnosis, similar to the time course of many malignancies. A hallmark of IPF is its unpredictable disease course, ranging from long periods of clinical stability to acute exacerbations with rapid decompensation. As the disease progresses, patients with chronic cough and progressive exertional dyspnea become oxygen dependent. They may experience significant distress due to concurrent depression, anxiety, and fatigue, which often lead to increased symptom burden and decreased quality of life. Despite these complications, palliative care is an underutilized, and often underappreciated, resource before end-of-life care in this population. While there is growing recognition about early palliative care in IPF, current data suggest referral patterns vary widely based on institutional practices. In addition to focusing on symptom management, there is emphasis on supplemental oxygen use, pulmonary rehabilitation, quality of life, and end-of-life care. Importantly, increased use of support groups and national foundation forums have served as venues for further disease education, communication, and advanced care planning outside of the hospital settings. The purpose of this review article is to discuss the clinical features of IPF, the role of palliative care in chronic disease management, current data supporting benefits of palliative care in IPF, its role in symptom management, and practices to help patients and their caregivers achieve their best quality of life.

Keywords: Idiopathic pulmonary fibrosis; Palliative care; Quality of life

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Key Summary Points

IPF is an unpredictable, progressive, and life-limiting disease where patients and caregivers experience significant stress, symptom burden, poor quality of life, and inadequate preparedness for end-of-life planning.

In patients with oncologic diseases who carry poor prognosis similar to IPF, early palliative care has been shown to improve quality of life and symptom control, reduce aggressive and inappropriate end-of-life care that do not align with patients' wishes, and decrease caregiver burden.

While beneficial in other patient populations, the benefits of early palliative care intervention have not been replicated in the IPF population.

Palliative care may be delivered by a member of the clinical care team, referred to as primary palliative care, or an interdisciplinary team, referred to as secondary, or specialty, palliative care.

Due to the unpredictable nature of IPF, early palliative care intervention, which includes pharmacologic and nonpharmacologic therapies, can address symptom burden and improve quality of life for patients with IPF and their caregivers.

INTRODUCTION

Our understanding of idiopathic pulmonary fibrosis (IPF) has increased tremendously in recent years due to advances in pathobiology, greater knowledge of non-genetic and genetic risk factors, and increased disease awareness [1, 2]. IPF carries a poor prognosis with a median survival of 3–4 years from initial diagnosis [3]. Patients often experience continued decline in quality of life as their disease advances. While antifibrotic therapies offer new therapeutic options, these medications delay, rather than prevent, disease progression [4]. With disease progression, patients and caregivers experience significant stress, symptom burden, poor quality of life, and inadequate preparedness for end-of-life planning. There is increasing data and appreciation for early palliative care intervention in this population. However, despite the life-limiting complications of IPF, palliative care is underutilized and rarely instituted before end-of-life care [5, 6]. We have found that patients and caregivers often fail to perceive the consequences of this diagnosis and therefore avoid discussions that can lessen their stress and reduce symptom burden [7]. In this review article, we aim to discuss the clinical features of IPF, the role of palliative care in chronic disease management, current data supporting benefits of palliative care in IPF, its role in symptom management, and practices to help patients and their caregivers achieve their best quality of life. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

WHAT IS IDIOPATHIC PULMONARY FIBROSIS?

Idiopathic pulmonary fibrosis is a chronic, progressive fibrotic lung disease of unknown etiology [1, 8]. Current reports estimate an incidence of 3–9 cases per 100,000 person-years in North America and Europe, with increasing prevalence over the past decade [9–11]. The incidence increases with age, from 1.1 new cases per 100,000 person-years in adults ages 18–34 to 19.3 new cases per 100,000 person-years in adults ages 55–64 [11]. Initial symptoms are often non-specific, such as non-productive cough and progressive exertional dyspnea, which may lead to delays in diagnosis and targeted management. Recent studies report an approximate 2-year delay from initial diagnosis to evaluation at a specialty referral center [5, 12, 13]. IPF occurs most commonly in men, with onset in the sixth or seventh decades [2]. It carries a poor prognosis, with a median survival of 3–4 years from diagnosis, similar to the clinical disease course of many malignancies

[14, 15]. While improved disease understanding and clinical trials have led to advancements in pharmacotherapeutic management [16, 17], lung transplantation remains the only definitive treatment [18].

A hallmark of IPF is its unpredictable disease course, ranging from periods of clinical stability to acute exacerbations with rapid decompensation. Patients typically follow one of three clinical trajectories: subclinical IPF with radiographic findings of disease prior to clinical symptomatology and/or diagnosis, slowly progressive IPF with progressive clinical deterioration over several years, or rapidly progressive IPF with shortened survival and death shortly after diagnosis [8, 19]. Many patients experience acute or subacute deterioration in the months prior to death [20]. In addition to common respiratory symptoms of dyspnea and non-productive cough, patients are often burdened by other symptoms. Prior studies estimate high prevalence of concomitant depression (10–49%) [7, 21, 22], anxiety (33–58%) [15, 23], heartburn (29–55%) [24, 25], sleep difficulties, including insomnia (47%), [26] and fatigue [27]. In many patients, comorbidities contribute to increased symptom burden and decreased quality of life [28, 29].

In light of its unpredictable disease course, delayed diagnosis, and high symptom burden, clinicians are challenged to provide supportive care in limited, and often brief, clinical encounters. After an initial encounter to establish a confident diagnosis, there are multiple therapeutic options to consider: symptom management, pulmonary rehabilitation, oxygen therapy, lung transplantation, research opportunities, and, importantly, decisions regarding end-of-life care [30]. Each encounter can therefore become lengthy.

WHAT IS PALLIATIVE CARE?

Palliative care is a multimodal service and approach aimed to improve quality of life, provide relief from pain and suffering, and offer support for patients living with chronic life-limiting conditions [31]. Of importance to those diagnosed with IPF, palliative care can assist patients and families through the process of advance care planning for end-of-life. The main goal of palliative care is to improve and maintain quality of life. The misconception that palliative care is synonymous with hospice has unfortunately led to delayed access to services and general underuse of palliative care expertise [32, 33]. Palliative care differs from hospice in several important ways: there is no timeline or prognostic limitation necessary for its introduction and there is growing evidence of its benefits at any stage of illness. For this reason, recent guidelines recommend that palliative care should be offered to all patients diagnosed with a serious life-limiting illness (see Fig. 1) [34, 35].

Historically, palliative care has been most closely associated with the oncologic population, with strong data supporting improvements in morbidity and mortality [36, 37]. In patients with metastatic non-small cell lung cancer, early palliative care integration was associated with enhanced quality of life, less aggressive end-of-life care, and decreased mortality [37]. A Belgian study evaluating general practitioner referral rates to palliative care reported substantially higher frequencies in malignancy (60%) compared to dementia (37%), congestive heart failure (34%), and chronic obstructive pulmonary disease (20%) [38]. A recent population-based study in England using death registration data estimated that 69–82% of decedents needed palliative care support [39]. Early palliative care implementation has been shown to improve quality of life and symptom control, reduce aggressive and inappropriate end-of-life care that do not align with patients' wishes [37], and decrease caregiver burden [40].

Reasons for fewer and/or late referrals identified from patient and provider interviews include uncertainty regarding disease prognosis (i.e., when to begin the discussion), lack of provider skill to initiate discussions (i.e., confidence in ability to guide the discussion in ways that explore beliefs without causing more distress), and fear of prescribing opioids for patients with chronic lung diseases [41]. In some countries, economic resources may limit access to specialty or secondary palliative care

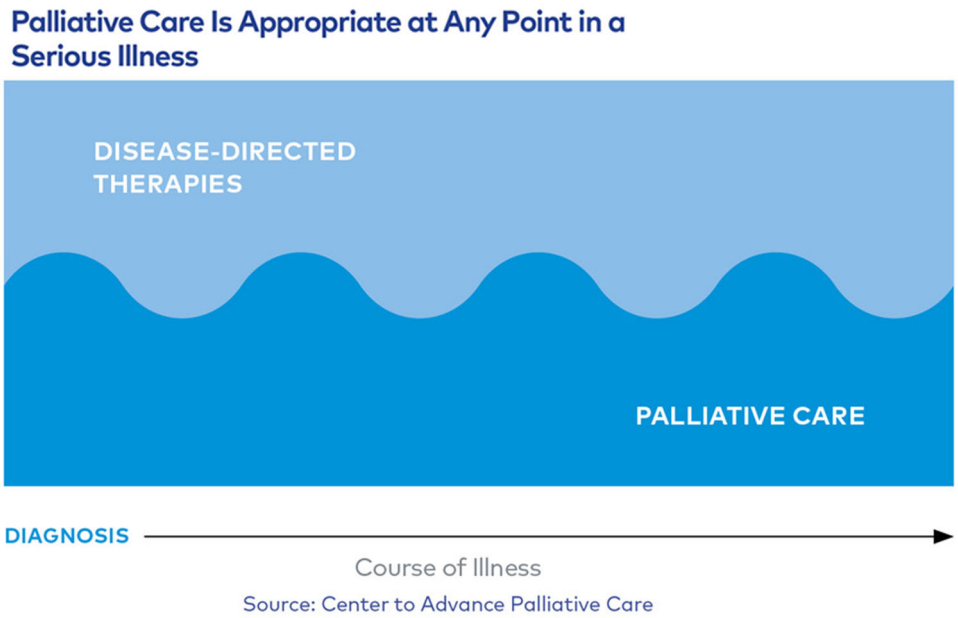

Fig. 1 Palliative care's place in serious illness. This figure was reused with permission from Center to Advance Palliative Care

services. An additional, and often cited, concern relates to fear that referral will diminish hope [37]. Findings from patients diagnosed with other terminal illnesses suggest this concern may be unfounded. When informed of this consequence during palliative care consultation, patients with terminal illnesses did not experience a loss of hope but, instead, reframed their goals [42]. This observation may relate to content of palliative care discussions [43]. During palliative care consultations, the initial visit focused on rapport building and understanding prognosis rather than immediately on resuscitation preferences. Led by an oncologist, this focus was also a part of discussions that were more likely to emphasize psychosocial elements, such as coping, as opposed to treatment and management of morbidity and complications [43].

WHO SHOULD DELIVER PALLIATIVE CARE?

Palliative care may be delivered by a member of the clinical care team, referred to as primary palliative care, or an interdisciplinary team, referred to as secondary, or specialty, palliative care. Optimal palliative care for patients with chronic lung diseases such as IPF should incorporate both primary and specialty palliative care services [44]. In 2006, palliative care became officially recognized as a medicine subspecialty by the American Board of Medical Specialties (ABMS) and American Osteopathic Association (AOA). Physicians become board-certified in palliative care through the completion of a 12-month fellowship at an accredited institution. The main purposes of this training are to expose physicians to a variety of patient populations, focusing on symptom management, communication techniques, advanced care planning, hospice and end-of-life care, medical ethics, and cultural competence, among others. Additionally, advanced practice providers, nurses, and allied health providers are central to health care provision and are highly valued by patients and caregivers [45]. Currently, there exist certificate and graduate programs as training pathways for nurses, advanced care providers, and social workers to become involved in palliative care practices [46]. Although the number of palliative care programs in the United States has increased dramatically in recent years, the workforce required to provide appropriate palliative care

remains somewhat limited and is not uniformly available [47]. Therefore, clinicians need to be proactive in initiating discussions using available resources and prior training experiences.

PALLIATIVE CARE IN IDIOPATHIC PULMONARY FIBROSIS

There is growing recognition and emphasis about the benefits of early palliative care integration in multidisciplinary IPF care. The 2011 American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association (ATS/ERS/JRS/ALAT) clinical guidelines advise palliative care alongside disease-directed therapies [2]. However, its introduction is often late in the patient's clinical disease course. Palliative care referral patterns are institution dependent, with literature citing ranges between 3 and 14% [5, 6, 48, 49]. A recent study reported 71% of IPF decedents had their initial referral within 30 days of death, with the majority evaluated in the intensive care unit during acute exacerbations with respiratory failure [5]. Similarly, another study noted that 76% of IPF decedents died in the hospital setting [50].

Patients with progressive idiopathic fibrotic interstitial lung disease, such as IPF, often suffer unmet physical and psychological needs [51]. Qualitative descriptions of patient and caregiver perspectives describe the high supportive needs of this population. One study described that patients with IPF have a good understanding of their overall disease prognosis, but difficulty translating what is available options for management and; they frequently compared their situation unfavorably compared with oncologic patients who had "help coming from every direction" [52]. Patients also reported overwhelming symptom burden and frustrations with physical limitations, oxygen therapy, and caregiver burden [53].

A recent study evaluating patient-specific factors associated with palliative care referral and its impact on mortality found that recipients were older at diagnosis with more advanced lung disease, resided closer to the specialty referral center, and had higher frequency of outpatient visits [54]. Additionally, there were observable increases in the frequency of individual provider and institutional palliative care referral practices with the introduction of an outpatient palliative care clinic affiliated with the specialty referral center. These findings highlight the importance of the patient–-provider relationship in palliative care evaluation and end-of-life discussions [54]. In another study, patients reported the importance of family and caregiver inclusion in this provision of knowledge [55].

Support groups have been utilized in the IPF population as a venue for disease education, patient and caregiver communication, oxygen therapy management, emotional well-being, and advanced care planning [45, 55]. These meetings provide patients and caregivers with additional opportunities to interact with clinicians and improve disease awareness outside of the hospital setting. Participation at two specialty referral centers has been associated with improved psychological well-being, higher frequency of palliative care referral, and lower adjusted mortality [56, 57]. An ongoing IPF clinical trial includes an intervention focused on disease information, self-management strategies, and introduction to advanced care planning in a format with enhanced content available across multiple domains (i.e., face-to-face, printed material, digital) delivered by a nurse interventionist [58]. In one specialty referral center in Canada, a multidisciplinary collaborative model to deliver early integrated palliative care led to improvement in dyspnea management, greater engagement in advance care planning, reduced end-of-life hospitalization, reduced hospital deaths, greater adherence to patient wishes for care and place of death, and improved patient and caregiver experience. However, this center has faced hurdles on sustainability and continued organizational and leadership support [59].

ROLE OF PALLIATIVE CARE IN SYMPTOM MANAGEMENT

Patients with IPF experience tremendous symptom burden with disease progression.

Several of the main benefits of palliative care include addressing symptom burden and managing symptoms as patients progress in their illnesses. Patients with IPF typically experience symptoms of dyspnea, cough, fatigue, anxiety, and depression. It is recognized that poor symptom control and psychosocial support lead to a poorer quality of life [60]. A variety of pharmacologic and nonpharmacologic therapies are available to help reduce symptom burden and improve quality of life. A recent study from Denmark demonstrated that opioids and benzodiazepines can play important roles in symptom management in this population [61]. Opiates and benzodiazepines have been shown to improve dyspnea and are suggested for debilitating symptoms and end-of-life care [60–62]. Additionally, in pooled cohort studies, sildenafil improves resting dyspnea without serious adverse events, but not without serious adverse events [63].

Chronic cough is a particularly distressing symptom of IPF and often challenging to treat. It is associated with poor sleep quality, limited exercise capacity, and decreased social interactions [53, 60]. Treatment options vary, from hot tea, honey, and menthol lozenges to the treatment of comorbidities such as gastroesophageal reflux disease, upper airway cough syndrome, and chronic sinusitis to opiate-containing formulations [64]. Opiates have modest effects and are suggested for debilitating cough refractory to alternative therapies [60, 65]. A recent multicenter prospective observational study of pirfenidone reported decreased objective cough without significant changes in quality of life [66]. In a proof of concept study, nebulized sodium cromoglycate has shown promising effect on cough in patients with IPF [67]. A randomized trial of thalidomide, an immunomodulator with anti-inflammatory effects, was studied for intractable cough with reported improvement in cough and quality of life in a small sample, but with adverse events of constipation, dizziness, and malaise. Recommendations were suggested to study this in a larger population [68].

Depression and anxiety have been found to be relatively common in patients with IPF and impacts health-related quality of life and overall health status [69–71]. Dyspnea was found to be associated with depression score, functional status, and disease severity in patients with fibrotic lung disease [23]. Despite the high prevalence in this population, there are currently no recommendations or guidelines for the routine use of nonpharmacologic or pharmacologic therapy.

Currently, pulmonary rehabilitation is one of the main interventions shown to improve quality of life for patients with IPF [4]. It is widely utilized to improve dyspnea, exercise capacity, physical activity, and quality of life in patients with chronic obstructive pulmonary disease, and benefits have been shown to also impact those with IPF [72, 73]. Patients with fibrotic lung disease experience reduced functional capacity, dyspnea, and exercise-induced hypoxia [74]. In a study performed at three pulmonary rehabilitation centers in North America, there were reported improvements in functional capacity and quality of life in patients with interstitial lung disease (ILD), with benefits lasting for at least 6 months [73]. They reported that the "consistency and magnitude of benefit across endpoints is substantial and markedly better than pharmacological interventions that have been studied in these diseases" and suggest that pulmonary rehabilitation should be the first-line therapy for patients with ILD [73]. Barriers for participation include distance from patient's residence and financial reimbursement for attendance. Reimbursement may involve obtaining authorization from the patient's payor source. While the specific intent differs between cardiac and pulmonary rehabilitation, both have similar emphasis on supervised and safe exercise to improve functional capacity [75]. In another study of patients with ILD attending pulmonary rehabilitation, patients wanted ILD-specific content and wanted information about end-of-life planning and most were happy to discuss it in a group [76]. In that same study, clinicians supported discussion of advanced care planning but not necessarily in the pulmonary rehabilitation setting [76]. Communication with patients about goals of care is crucial, and continued research in this area is needed. Patients with IPF should undergo formal pulmonary

rehabilitation, regardless of their disease severity or course.

One of the most important non-pharmacologic therapies in IPF is supplemental oxygen therapy. The 2011 ATS/ERS/JRS/ALAT clinical guidelines recommend prompt initiation of supplemental oxygen in patients with clinically significant resting hypoxemia [2]. A recent prospective randomized trial of oxygen therapy in patients with fibrotic ILD and exercise-induced desaturations without resting hypoxemia reported small improvements in several health-related quality of life measures [77]. While oxygen administration is associated with decreased exertional dyspnea and improved exercise tolerance [78], barriers to therapy initiation and compliance include cost, societal perceptions, and lack of subjective symptomatic relief [79, 80]. Exertional hypoxemia is more severe for patients with fibrotic lung disease with increased supplemental oxygen requirements due to the greater desaturation, and this may result in higher reported levels of stress and anxiety [7, 81].

Provision of high-flow supplemental oxygen, as commonly required by patients with IPF, is associated with numerous problems [82]. Responses to an online survey of oxygen-dependent patients identified that education regarding oxygen use is often not provided by clinicians, and if provided by durable medical equipment companies, may only be provided by the driver tasked with oxygen delivery. Most notably, this occurred in those with high-flow supplemental oxygen therapy who also experienced difficulty because the delivery needs of high-flow supplemental oxygen are difficult with the available technology [79]. Due to the rapid respiratory rate which often accompanies exercise in IPF and device technology, few, if any, oxygen-conserving, pulse-dose devices can fully meet patient needs [83]. Therefore, it has been suggested that high-flow continuous oxygen delivery via liquid oxygen devices is the most optimal option [84]. This option, however, is more costly and not always available through providers in the patient's geographic area. Clinicians should be aware of these potential problems and work collaboratively with durable medical equipment companies to provide equipment that matches patient needs [85].

QUALITY OF LIFE

While patients with IPF described impaired quality of life across multiple domains, the most commonly affected were related to physical health, including functional status, energy level, and independence [86]. Certain chronic and unrelenting symptoms, such as progressive dyspnea, exercise intolerance, non-productive cough, and psychosocial burden, are associated with decreased health-related quality of life. Current therapies aim to provide comprehensive and patient-centered care through early palliative care integration, support group participation, and symptom management. Among the many quality of life scores and metrics currently in existence, the A Tool to Assess Quality of Life in Idiopathic Pulmonary Fibrosis (ATAQ-IPF) is well validated and reliable as a measure of quality of life in this population [87]. Importantly, family members and caregivers should be assessed for excessive burden and fatigue given their heavy involvement in patient care.

LESSONS LEARNED

Despite the increasing prevalence of IPF and its growing recognition among providers, there remains a significant lag time between initial diagnosis and multidisciplinary evaluation [88]. This has contributed to delays in management, as well as patient and caregiver confusion and frustration over the natural disease course. Disease progression is associated with functional decline and varying symptom burden, ultimately affecting quality of life of both the patient and their caregiver(s) [89]. While beneficial in other patient populations, the benefits of palliative care have not been replicated in this patient population. It may be misconstrued as hospice and end-of-life care, resulting in delayed evaluation often far too late in a patient's disease course to have meaningful symptomatic benefit.

CONCLUSIONS

Idiopathic pulmonary fibrosis is an unpredictable, progressive, and life-limiting disease where patients and their caregiver(s) would benefit from early palliative care intervention. Disease education, communication, symptom management, and supportive care are essential in multidisciplinary IPF care. Early initiation and integration of palliative care is essential in optimizing symptom management while building patient-provider relationships to address advanced care planning and end-of-life discussions. Non-pharmacologic interventions, such as pulmonary rehabilitation and supplemental oxygen therapy, remain the cornerstone for symptomatic management. Pharmacologic therapies can provide relief of burdensome symptoms. Patients with ILD experience a wide range of diagnoses and may benefit most from early evaluation at a center with ILD expertise, such as the Pulmonary Fibrosis Foundation (PFF) Care Center Network [90]. Connecting patients with access to clinical trials can provide additional benefit to participate in research studies to advance knowledge and treatment of ILD, provide accurate information about their disease, and participation in support groups help to connect with other patients with similar needs. These measures can help to improve social support, emotional well-being, and help the patient and caregiver avoid social isolation, ultimately improving their quality of life.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

REFERENCES

1. Lederer DJ, Martinez FJ. Idiopathic pulmonary fibrosis. N Engl J Med. 2018;378(19):1811–23.

2. Raghu G, Collard HR, Egan JJ, Martinez FJ, et al. ATS/ERS/JRS/ALAT Committee on Idiopathic Pulmonary Fibrosis. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med. 2011;183(6):788–824.

3. Richards TJ, Kaminski N, Baribaud F, et al. Peripheral blood proteins predict mortality in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med. 2012;185(1):67–76.

4. Graney BA, Joyce L. Impact of novel antifibrotic therapy on patient outcomes in idiopathic pulmonary fibrosis: patient selection and perspectives. Patient Relat Outcomes Meas. 2018;9:321–8.

5. Lindell K, Liang Z, Hoffman L, Rosenzweig M, et al. Palliative care and location of death in decedents with idiopathic pulmonary fibrosis. Chest. 2015;147(2):423–9.

6. Liang Z, Hoffman LA, Nouraie N, et al. Referral to palliative care unit infrequent in patients with idiopathic pulmonary fibrosis (IPF) admitted to an intensive care unit. J Palliat Med. 2017;20(2): 134–40.

7. Lindell KO, Olshansky E, Song M, et al. Impact of a disease-management program on symptom burden and health-related quality of life in patients with idiopathic pulmonary fibrosis and their care partners. Heart Lung J Acute Crit Care. 2010;39(4): 302–13.

8. Ley B, Collard HR, King TE Jr. Clinical course and prediction of survival in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med. 2011;183(4): 431–40.

9. Hutchinson J, Fogarty AW, Hubbard R, et al. Global incidence and mortality of idiopathic pulmonary fibrosis: a systematic review. Eur Respir J. 2015;46(3):795–806.

10. Espositio D, Lanes S, Donneyong M, et al. Idiopathic pulmonary fibrosis in United States automated claims: incidence, prevalence, and algorithm validation. Am J Respir Crit Care Med. 2015;192: 1200–7.

11. Raghu G, Chen SY, Hou Q, et al. Incidence and prevalence of idiopathic pulmonary fibrosis in US adults 18-64 years old. Eur Respir J. 2016;48:179–86.

12. King T Jr, Tooze JA, Schwarz MI, et al. Predicting survival in idiopathic pulmonary fibrosis: scoring system and survival model. Am J Respir Crit Care Med. 2001;164:1171–81.

13. Lamas DJ, Kawut SM, Bagiella E, et al. Delayed access and survival in idiopathic pulmonary fibrosis: a cohort study. Am J Respir Crit Care Med. 2011;184(7):842–7.

14. Vancheri C, Failla M, Crimi N, et al. Idiopathic pulmonary fibrosis: a disease with similarities and links to cancer biology. Eur Respir J. 2010;35: 496–504.

15. Carvajalino S, Reigada C, Johnson MJ, et al. Symptom prevalence of patients with fibrotic interstitial lung disease: a systematic literature review. BMC Pulm Med. 2018;18:78.

16. Richeldi L, du Bois RM, Raghu G, et al. For the INPULSIS trial investigators. Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. N Engl J Med. 2014;370:2071–82.

17. King T, Bradford WZ, Castro-Bernardini S, et al. A phase 3 trial of pirfenidone in patients with idiopathic pulmonary fibrosis. N Engl J Med. 2014;370: 2083–92.

18. Gottlieb J. Lung transplantation for interstitial lung diseases. Curr Opin Pulm Med. 2014;20:457–62.

19. Selman M, Carrillo G, Estrada A, et al. Accelerated variant of idiopathic pulmonary fibrosis: clinical behavior and gene expression pattern. PLoS One. 2007;2:e482.

20. Martinez FJ, Safrin S, Weycker D, et al. The clinical course of patients with idiopathic pulmonary fibrosis. Ann Intern Med. 2005;142(12 Pt 1):963–7.

21. Akhtar A, Ali MA, Smith RP. Depression in patients with idiopathic pulmonary fibrosis. Chronic Respir Dis. 2013;10:127–33.

22. Ryerson C, Arean PA, Berkley J, et al. Depression is a common and chronic comorbidity in patients with interstitial lung disease. Respirology. 2012;17(3): 525–32.

23. Ryerson C, Berkley J, Carrieri-Kohlman VL, et al. Depression and functional status are strongly associated with dyspnea in interstitial lung disease. Chest. 2011;139(3):609–16.

24. Patti M, Tedesco P, Golden J, et al. Idiopathic pulmonary fibrosis: how often is it really idiopathic? J Gastrointest Surg. 2005;9(8):1053–6.

25. Bandiera C, Rubin AS, Cardoso PF, et al. Prevalence of gastroesopagheal reflux disease in patients with idiopathic pulmonary fibrosis. J Bras Pneumol. 2009;35(12):1182–9.

26. Mermigkis C, Bouloukaki I, Antoniou KM, et al. Sleep as a new target for improving outcomes in idiopathic pulmonary fibrosis. Chest. 2017;152(6): 1327–38.

27. Schoenheit G, Becattelli I, Cohen AH. Living with idiopathic pulmonary fibrosis: an in-depth qualitative survey of European patients. Chronic Respir Dis. 2011;8:225–31.

28. Reinke LF, Vig E, Tartaglione EV, et al. Symptom burden and palliative care needs among high-risk

veterans with multimorbidity. J Pain Symptom Manage. 2019;57(5):880–9.

29. Swigris JJ, Stewart AL, Gould MK, et al. Patients' perspectives on how idiopathic pulmonary fibrosis affects the quality of their lives. Health Qual Life Outcomes [electronic resource]. 2005;3:61.

30. Kreuter M, Bendstrup E, Russell AM, et al. Palliative care in interstitial lung disease: living well. Lancet Respir Med. 2017;5:968–80.

31. Organization WH. Definition of palliative care. http://www.who.int/cancer/palliative/definition/en/. Accessed 21 Aug 2019.

32. Hanratty B, Hibbert D, Mair F, et al. Doctors' understanding of palliative care. Palliat Med. 2006;20(5):493–7.

33. McIlfatrick S, Noble H, McCorry NK, et al. Exploring public awareness and perceptions of palliative care: a qualitative study. Palliat Med. 2014;28(3):273–80.

34. NCP. National Consensus Project Clinical Practice Guidelines for Quality Palliative Care, 4th edition. 2018. https://www.nationalcoalitionpc.org/ncp/. Accessed 27 Dec 2019.

35. Ferrell B, Twaddle ML, Melnick A, et al. National consensus project clinical practice guidelines for quality palliative care guidelines, 4th edition. J Palliat Med. 2018;21:1684–9.

36. Rocque G, Cleary JF. Palliative care reduces morbidity and mortality in cancer. Nat Rev Clin Oncol. 2013;10(2):80–9.

37. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med. 2010;363(8):733–42.

38. Beernaert K, Cohen J, Deliens L, et al. Referral to palliative care in COPD and other chronic diseases: a population-based study. Respir Med. 2013;107(11):1731–9.

39. Murtaugh F, Bausewein C, Verne J, et al. How many people need palliative care? A study developing and comparing methods for population-based estimates. Palliat Med. 2014;28(1):49–58.

40. Wittenberg-Lyles E, Goldsmith J, Parker Oliver D, Demiris G, et al. Targeting communication interventions to decrease caregiver burden. Semin Oncol Nurs. 2012;28(4):262–70.

41. Brown C, Jecker NS, Curtis JR. Inadequate palliative care in chronic lung disease. AnnalsATS. 2016;13(3):311–6.

42. Coulourides Kogan A, Penido M, Enguidanos S. Does disclosure of terminal prognosis mean losing hope? Insights from exploring patient perspectives on their experience of palliative care consultations. J Palliat Med. 2015;18:1019–25.

43. Yoong J, Park ER, Greer JA, et al. Early palliative care in advanced lung cancer: a qualitative study. JAMA Intern Med. 2013;173(4):283–90.

44. Reinke L, Janssen D, Curtis JR. Palliative care issues in adults with nonmalignmant pulmonary disease. In: Hollingsworth D, ed. Up to Date. 2015.

45. Duck A, Spencer LG, Bailey S, et al. Perceptions, experiences and needs of patients with idiopathic pulmonary fibrosis. J Adv Nurs. 2015;71(5):1055–65.

46. https://advancingexpertcare.org/HPNA/Certification/HPCC/CertificationWeb/Certification.aspx?hkey=993a4764-2575-4c2e-ac38-203812fc7a0f. Accessed 27 Dec 2019.

47. http://aahpm.org/uploads/Program_Data_122718.pdf. Accessed 17 Sep 2019.

48. Ahmadi Z, Wysham NG, Lundstrom S, et al. End-of-life care in oxygen-dependent ILD compared with ILD: a national population-based study. Thorax. 2016;71(6):510–6.

49. Rush B, Berger L, Celi LA. Access to palliative care for patients undergoing mechanical ventilation with idiopathic pulmonary fibrosis in the United States. Am J Hosp Palliat Care. 2018;35(3):492–6.

50. Bajwah S, Higginson IJ, Ross JR, et al. Specialist palliative care is more than drugs: a retrospective study of ILD patients. Lung. 2012;190(2):215–20.

51. Bajwah S, Yorke J. Palliative care and interstitial lung disease. Curr Opin Support Palliat Care. 2017;11(3):141–6.

52. Sampson C, Gill BH, Harrison NK, et al. The care needs of patients with idiopathic pulmonary fibrosis and their carers (CaNoPy): results of a qualitative study. BMC Pulm Med. 2015;15:155.

53. Lindell K, Kavalieratos D, Gibson KF, et al. The palliative care needs of patients with Idiopathic Pulmonary Fibrosis: a qualitative study of patients and family caregivers. Heart Lung J Acute Crit Care. 2017;46(1):24–9.

54. Zou RH, Nouraie M, Klesen MJ, et al. Assessing patterns of palliative care referral and location of death in patients with idiopathic pulmonary fibrosis: a 16-year single-center retrospective cohort study. J Palliat Med. 2019;22(5):538–44.

55. Senanayake S, Harrison K, Lewis M, et al. Patients' experiences of coping with idiopathic pulmonary fibrosis and their recommendations for its clinical management. PLoS One. 2018;13(5):e0197660.

56. Magnani D, Lenoci G, Balduzzi S, et al. Effectiveness of support groups to improve the quality of life of people with idiopathic pulmonary fibrosis a pre-post test pilot study. Acta Biomed. 2017;88(5):5–12.

57. Zou RH, Nouraie, SM, Rosenzweig, MQ, et al. Evaluating the role of support group participation on palliative care referral and mortality in idiopathic pulmonary fibrosis. In: American thoracic society international conference; Dallas, TX. 2019.

58. Lindell KO, Nouraie M, Klesen MJ, et al. Randomised clinical trial of an early palliative care intervention (SUPPORT) for patients with idiopathic pulmonary fibrosis (IPF) and their caregivers: protocol and key design considerations. BMJ Open Respir Res. 2018;5:e000272.

59. Kalluri M, Richman-Eisenstat J. From consulting to caring: care redesign in idiopathic pulmonary fibrosis. NEJM Catalyst. 2019. https://catalyst.nejm.org/idiopathic-pulmonary-fibrosis-care/. Accessed 27 Dec 2019.

60. Booth S, Johnson MJ. Improving the quality of life of people with advanced respiratory disease and severe breathlessness. Breathe. 2019;15(3):199–215.

61. Bajwah S, Davies J, Tanash H, et al. Safety of benzodiazepines and opioids in interstitial lung disease: a national prospective study. ERJ. 2018;52:1801278.

62. Simon ST, Higginson IJ, Booth S, et al. Benzodiazepines for the relief of breathlessness in advanced malignant and non-malignant diseases in adults. Cochrane Database Syst Rev. 2016;2016(10):CD007354.

63. Zisman D, Swartz M, Anstrom KJ, et al. A controlled trial of sildenafil in advanced idiopathic pulmonary fibrosis. N Engl J Med. 2010;363(7):620–8.

64. Silhan LD. Nonpharmacologic therapy for idiopathic pulmonary fibrosis. Interstitial lung disease. Philadelphia: Elsevier; 2017.

65. Kohberg C, Uggerhoj Andersen C, Bendstrup E. Opioids: an unexplored option for treatment of dyspnea in IPF. Eur Clin Respir J. 2016;3:30629.

66. van Manen MJG, Birring SS, Vancheri C, et al. Effect of pirfenidone on cough in patients with idiopathic pulmonary fibrosis. Eur Respir J. 2017;50:1701157.

67. van Manen MJG, Wisenbeek MS. Cough, an unresolved problem in interstitial lung disease. Curr Opin Support Palliat Care. 2019;13(3):143–51.

68. Horton M, Santopietro V, Mathew L, et al. Thalidomide for treatment of cough in idiopathic pulmonary fibrosis: a randomized trial. Ann Intern Med. 2012;157(6):398–406.

69. Matsuda T, Taniguchi H, Ando M, et al. Depression is significantly associated with the health status in patients with idiopathic pulmonary fibrosis. Intern Med. 2017;56(13):1637–44.

70. Chang JA, Curtis JR, Patrick DL, et al. Assessment of health-related quality of life in patients with interstitial lung disease. Chest. 1999;116(5):1175–82 **(see comment)**.

71. Lee Y, Choi SM, Lee Y, et al. Clinical impact of depression and anxiety in patients with idiopathic pulmonary fibrosis. PLoS One. 2017;12(9):e0184300.

72. Rochester C, Vogiatzis I, Holland AE, et al. An Official American Thoracic Society/European Respiratory Society Policy Statement: enhancing implementation, use, and delivery of pulmonary rehabilitation. Am J Respir Crit Care Med. 2015;192(11):1373–86.

73. Ryerson C, Cayou C, Topp F, et al. Pulmonary rehabilitation improves long-term outcomes in interstitial lung disease: a prospective cohort study. Respir Med. 2014;108(1):203–10.

74. Dowman L, Hill CJ, Holland AE. Pulmonary rehabilitation for interstitial lung disease. Cochrane Database Syst Rev. 2014;(10):CD006322.

75. Spruit M, Rochester C, Pitta F, et al. Pulmonary rehabilitation, physical activity, respiratory failure and palliative respiratory care. Thorax. 2019;0:1–7.

76. Holland A, Fiore JF, Goh N, et al. Be honest and help me prepare for the future: what people with interstitial lung disease want from education in pulmonary rehabilitation. Chronic Respir Dis. 2015;12(2):93–101.

77. Visca D, Mori L, Tsipouri V, et al. Effect of ambulatory oxygen on quality of life for patients with fibrotic lung disease (AmbOx): a prospective, open-label, mixed-method, crossover randomised controlled trial. Lancet Respir Med. 2018;6(10):759–70.

78. Ramadurai D, Riordan M, Graney B, et al. The impact of carrying supplemental oxygen on exercise capacity and dyspnea in patients with interstitial lung disease. Resp Med. 2018;138:32–7.

79. Jacobs S, Lindell KO, Collins EG, et al. Patient perceptions of the adequacy of supplemental oxygen therapy: results of the American Thoracic Society Nursing Assembly Oxygen Working Group Survey. Ann Am Thorac Soc. 2018;15:24–32.

80. Lindell KO, Catazanarite L, Collins EG, et al. Equipment, access and worry about running short of oxygen: key concerns in the Patient Supplemental Oxygen Survey. Heart Lung. 2019;48(3):245–9.

81. Du Plessis J, Fernandes S, Camp JR, et al. Exertional hypoxemia is more severe in fibrotic interstitial lung disease than in COPD. Respirology. 2018;23:392–8.

82. Swigris J. Supplemental oxygen for patients with interstitial lung disease: managing expectations. Ann Am Thorac Soc. 2017;14(6):831–2.

83. Christopher KL, Porte P. Long-term oxygen therapy. Chest. 2011;139(2):430–4.

84. Jacobs SS. Clinician strategies to improve the care of patients using supplemental oxygen. Chest. 2019;156(3):619–28.

85. Jacobs S, Lederer DJ, Garvey CM, et al. Optimizing home oxygen therapy; an official American Thoracic Society workshop report. Ann Am Thorac Soc. 2018;15(12):1369–81.

86. Olson A, Brown KK, Swigris JJ. Understanding and optimizing health-related quality of life and physical functional capacity in idiopathic pulmonary fibrosis. Patient Relat Outcomes Meas. 2015;7:29–35.

87. Swigris JJ, Wilson SR, Green KE, et al. Development of the ATAQ-IPF: a tool to assess quality of life in IPF. Health Qual Life Outcomes [Electron Resour]. 2010;8:77.

88. Cosgrove GP, Bianchi P, Danese S, et al. Barriers to timely diagnosis of interstitial lung disease in the real world: the INTENSITY survey. BMC Pulm Med. 2018;18(1):9.

89. Lindell KO. Nonpharmacologic therapies in interstitial lung disease. Curr Pulmonol Rep. 2018;7(4):126–32.

90. Pulmonary Fibrosis Foundation Care Center Network. http://www.pulmonaryfibrosis.org/medical-community/pff-care-center-network. Accessed 8 Mar 2019.