

Gaps in care of patients living with pulmonary fibrosis: An Expert Statement on the results of a Europe-wide survey.

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ABSTRACT

Background: Pulmonary fibrosis (PF) and its most common form, idiopathic pulmonary fibrosis (IPF), are chronic, progressive diseases resulting in increasing loss of lung function, impaired quality of life and survival. The aim of this joint Expert and Patient Statement was to highlight the most pressing common unmet needs of patients with PF and IPF, putting forward recommendations to improve the quality of life and health outcomes throughout the patient journey.

Methods: Two online surveys for patients and healthcare providers were conducted by the European Idiopathic Pulmonary Fibrosis and Related Disorders Federation (EU-IPFF) in 14 European countries.

Results: The surveys were answered by 286 patients and 69 healthcare professionals, including physicians and nurses. Delays in diagnosis and timely access to ILD specialists and pharmacological treatment have been identified as important gaps in care. Additionally, patients and healthcare professionals reported that a greater focus on symptom-centred management, adequate information, trial information, and increasing awareness of PF/IPF was required.

Conclusion: The surveys offer important insights into the current unmet needs of PF/IPF patients. Interventions at different points of the care pathway are needed to improve patient experience.

Key words

IPF; Pulmonary Fibrosis; Interstitial Lung Diseases; Doctor-Patient Relationship; Early Diagnosis; Access to Treatment.

INTRODUCTION

Interstitial lung diseases (ILDs) comprise a diverse collection of more than 200 lung disorders, affecting the interstitium of the lung (1). A large subgroup of patients with ILD have pulmonary fibrosis (PF); most forms of PF are characterised by a progressive phenotype, are associated with a high burden of disease and have devastating consequences for patients and their families (2-4). Idiopathic pulmonary fibrosis (IPF) is the most frequent form and accounts for 17-37% of all ILDs (5). A cure for IPF does not currently exist, although there are two drugs approved that slow disease progression (6, 7). Non-pharmacological treatment options include lung transplantation to prolong life and measures such as pulmonary rehabilitation and supplemental oxygen to ameliorate exercise tolerance and quality of life (8-10).

In 2016, a collaborative effort of patient associations and healthcare providers was undertaken to gain insights in the needs of patients with IPF, which led to a European IPF Charter (11). This charter was presented at the European Parliament to improve awareness and equal access to care around Europe for patients with IPF. The aim of the current project was to take a further step in improving care for patients with IPF, but also with other forms of pulmonary fibrosis. To do so, we aimed to identify the most pressing common unmet needs of patients with PF and IPF throughout Europe and to put forward recommendations in an Expert Statement to improve quality of life and health outcomes throughout the patient journey.

PARTICIPANTS AND METHODS

The study was conducted by the European Idiopathic Pulmonary Fibrosis and Related Disorders Federation (EU-IPFF) in association with the European Reference Network on Rare Lung Diseases (ERN-Lung). This Expert Statement is a result of the collaboration between patient representatives and medical experts.

Two online surveys were developed: one for PF/IPF patients and one for practising pulmonologists and nurses with ILD expertise. The questions for the surveys were developed by the EU-IPFF working group, consisting of four patient representatives and 14 ILD experts. The group met in person to discuss the topics of the surveys and to reach consensus on the questions. Both surveys contained 62 questions and were circulated between 29 June 2018 and 8 September 2018 in 14 countries. The survey for healthcare professionals (HCPs) was distributed through the ERN-LUNG network and the patient survey through the EU-IPFF's 17 member organisations. Caregivers were allowed to respond to the survey on behalf of the patient. The surveys are available as supplemental material (**Figure S1 and S2**).

Results have been divided into four geographical sub-regions: Northern Europe (Denmark, Ireland and UK), Eastern Europe (Bulgaria, Czech Republic and Poland), Southern Europe (Greece, Italy and Spain), and Western Europe (Austria, Belgium, France, Germany, and the Netherlands) (12).

In addition, a literature search was conducted for original articles and reviews about the care pathway and unmet needs of patients with PF/IPF. PubMed was searched for articles published between January 2010 and March 2018, using the (Mesh) terms "idiopathic pulmonary fibrosis", "pulmonary fibrosis", "interstitial lung disease" or "diffuse parenchymal lung disease" in combination with "care pathway", "unmet needs", and/or "barriers". The search was limited to adults and articles published in English. The reference lists of articles were manually screened for additional relevant publications.

Relevant articles were included in order to create an overview on the current state of knowledge on the care pathway and unmet needs of patients with PF/IPF.

Results

The patient survey was completed by 286 individuals from 14 different countries, of whom 79% were patients and 21% were caregivers (**Figure 1**). The majority of patients had IPF (86%) and 14% of respondents had another type of PF. The mean age of patients was 66 years, and 70% were male. One fifth of respondents (21%) reported a history of PF/IPF in their families.

The questionnaire for HCPs was completed by 69 respondents: 56 physicians (81%) and 13 specialist nurses (19%). Most HCPs (87%) were specialised in ILD and worked at recognised centres of expertise. There was a large variation in the reported number of patients with PF/IPF treated per centre (range 5-3000). The estimated total number of patients managed per year amongst all participating centres collectively was 10,000-11,000 for IPF and 27,000-28,000 for other forms of PF.

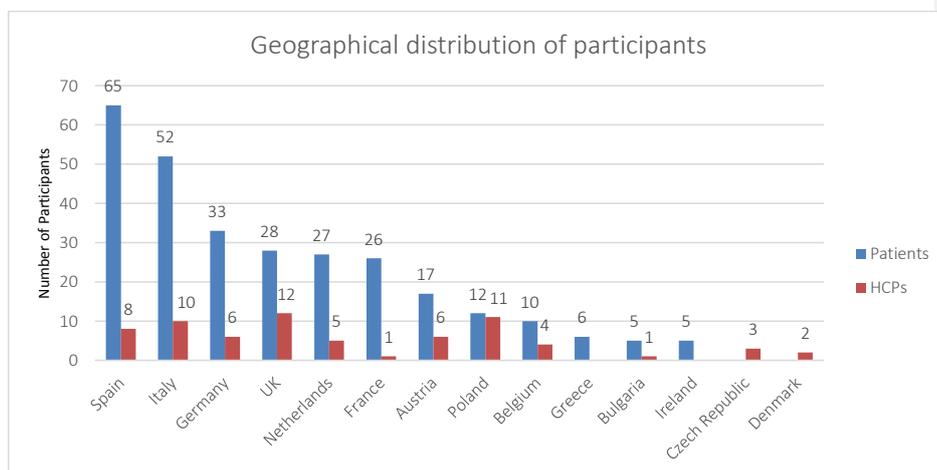


Figure 1. Number of participants (patients and HCPs) per country. HCP = healthcare professional

Referral pathways and access to ILD specialist care

In order to assess the delay in access to a pulmonary physician, patients were asked to indicate how much time passed before their general practitioner referred them to a respiratory specialist. Almost half of patients (45%) reported that referral took place within a month. In contrast, time to referral was more than a year for 16% of patients. No evident differences in referral time were found across Europe (**Figure 2**). Further to this, 33% of patients reported that their referral to a specialist centre took less than one month, with 20% reporting more than a year-long wait. Fewer than half of patients (47%) reported that a referral to a specialist centre was (very) easy to obtain, whereas 20% considered it a (very) difficult process.

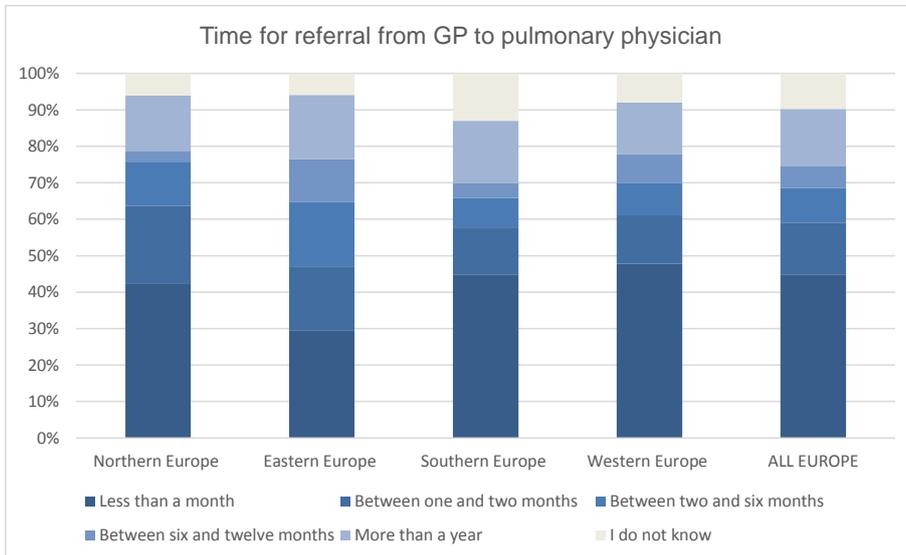


Figure 2. Time for referral from general practitioner (GP) to a pulmonary physician (patient survey)

More than one third of PF/IPF patients (37%) reported at least one misdiagnosis before they received a correct diagnosis. Half of these patients indicated that more than a year passed before they were correctly diagnosed (Figure 3).

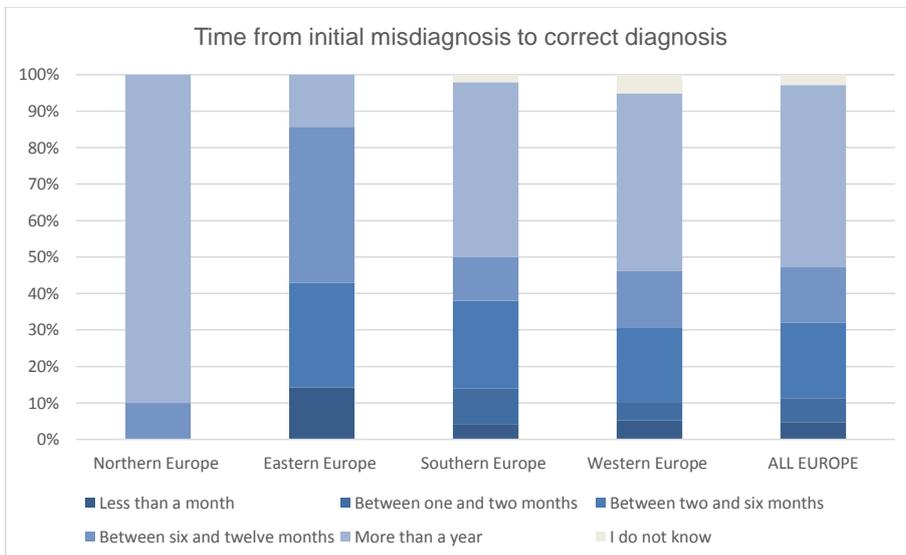


Figure 3. Time from initial misdiagnosis to correct diagnosis of PF/IPF (patient survey)

The vast majority of HCPs (94%) reported that in their centre they had access to a multidisciplinary team (MDT) for all IPF/PF patients, but composition of the MDT varied greatly. In the patient survey,

58% of respondents confirmed that they had access to an MDT. However, it is unknown if all patients were aware that their case was evaluated in an MDT. Around two-third of HCPs (65%) answered that ILD specialist nurses were available in their centre, whilst 52% of PF/IPF patients responded that they had access to specialist nurses.

Reported access to genetic screening differed across Europe. Half of the participating HCPs (49%) stated that genetic screening was offered, either in their own centre or via referral to another centre. In total, 16% of surveyed patients underwent genetic testing; of these 45 patients, 42% stated that they did not receive enough information about their results of the genetic tests.

Access to pharmacological treatment for IPF patients

Both approved treatments for IPF, nintedanib and pirfenidone, were available in all participating countries. Almost all HCPs (93%) confirmed that anti-fibrotic drugs could be prescribed in their centres. The majority of respondents with IPF (82%) were treated with either nintedanib or pirfenidone at the time of the survey.

The time from diagnosis to initiation of treatment varied greatly, and this was reflected throughout Europe (Figure 4). Although anti-fibrotic treatment was initiated within a month after diagnosis in 31% of patients, more than a quarter of patients (26%) reported that they had to wait more than six months before anti-fibrotic treatment was started.

In many European countries, reimbursement restrictions exist for prescription of anti-fibrotic treatment; this was confirmed by 78% of respondents in the HCP survey. In some countries, anti-fibrotic drugs are only reimbursed when patients are diagnosed in an ILD specialist centre, and in others lung function and/or age criteria exist. Specific lung function criteria were identified as the main barrier for prescription of anti-fibrotic medication by 70% of HCPs.

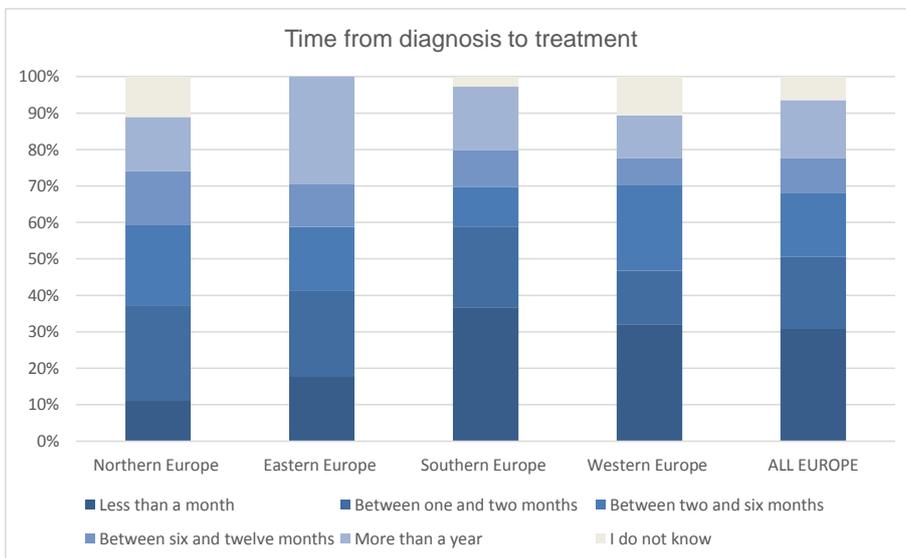


Figure 4. Time between diagnosis to start of anti-fibrotic treatment (patient survey)

Access to non-pharmacological treatment

Almost all HCPs (97%) were able to prescribe oxygen therapy for PF/IPF patients. More than three quarters of patients (78%) reported full coverage for the costs of ambulatory oxygen therapy, and two-thirds of patients (64%) for the costs of oxygen at home.

The vast majority of HCPs (88%) could refer patients for pulmonary rehabilitation (PR). One-third of HCPs answered that PR was not fully reimbursed in their country. Fewer than half of patients (42%) stated that they had access to outpatient PR; 11% of patients also had access to inpatient pulmonary rehabilitation. Just over half of HCPs (58%) reported that their patients had access to psychological support at their centre, with full reimbursement for 70% of patients. Patients were not specifically questioned about access to psychological support, however, 10% of patients spontaneously reported the need for (better) psychological support throughout their disease course.

No apparent differences in eligibility criteria for lung transplantation were found across Europe. Most HCPs (96%) reported that all eligible patients were referred for lung transplant. In one of the surveyed countries, lung transplantation was not possible at the moment of the survey.

Access to palliative care

Of the surveyed patients, 29% confirmed access to palliative care and 36% answered that they were involved in palliative care decisions. The majority of HCPs (88%) stated that they discuss possibilities for end-of-life care with patients, and almost all HCPs (93%) could prescribe (palliative) medication for symptom relief.

HCPs were asked to explain at which point in the disease course they initiate palliative care for their patients. Around one third answered that palliative care was started at an early stage of the disease if desired by patients. Most HCPs reported that palliative care is initiated in more advanced stages of PF/IPF. One fifth stated that palliative care was only initiated at the end-of-life.

Communication and education

The majority of patients (60%) had a positive experience whilst discussing their diagnosis with the pulmonary physician. However, one-fifth of patients answered that they did not receive any information about their disease at the time of diagnosis. Three out of four patients (73%) and 60% of HCPs felt that there was enough time to discuss diagnosis and treatment options. Only 39% of HCPs reported that they received training on how to effectively communicate information on diagnosis and treatment of PF/IPF with their patients.

Three quarters of patients received a treatment plan following their diagnosis, which was clearly explained in 73% of cases. Less than one-third of patients (31%) were involved in development of their treatment plan; this involvement was mostly related to the selection and dosage of anti-fibrotic medication, initiation of non-pharmacological management and participation in clinical trials.

Patients were asked to give recommendations on how healthcare staff could work more effectively with them and their caregivers. Many patients answered that they would like to have more time allocated for their questions and concerns, and receive more information about PF/IPF including practical issues such as reimbursement. Furthermore, patients mentioned the need for timely referral to a specialist centre and more awareness of PF/IPF amongst general practitioners, nurses and

physicians in community hospitals. Around two-thirds of participating centres (65%) offered educational activities specifically for PF/IPF patients, such as nurse led education sessions, information meetings, eHealth programs and patient support groups. Amongst the surveyed patients, 39% attended educational sessions in their treating centre.

Involvement in research

The majority of HCPs (95%) reported that their centre participated in clinical trials and that they inform their PF/IPF patients on ongoing clinical trials. Half of patients (53%) were aware of ongoing clinical trials, 31% had been asked to participate and 25% had actually participated in a clinical trial. Patient registries for IPF and PF existed in 75% and 48% of centres respectively. A quarter of patients (27%) declared that they contributed to the collection of registry data.

General recommendations

In general, 61% of patients described that their experience with the healthcare system as either good or excellent. Both patients and HCPs were asked about suggestions to improve the patient experiences at different stages of the disease. Based on the answers on this question five recommendations by this expert panel were proposed (Figure 5).



Figure 5. General recommendations to improve the IPF/PF patient journey

Kommentiert [GW1]: 1.S. 7, Forderungen finde ich gut!
Unter Punkt 3 hinzufügen, nicht nur „fewer restriction..“, sondern allgemein formulieren „better access to pharma treatment“ hier spielen andere Kriterien auch eine Rolle, wie u.a. richtige Einordnung/Kriteriologie der IPF, komplizierte Antragsverfahren, etc.

Kommentiert [GW2R1]:

DISCUSSION

This is the first study investigating unmet needs of patients with pulmonary fibrosis in a Europe-wide survey. Despite recent advances in PF/IPF care and research, the unmet needs and gaps in care revealed in this study are in line with previous research (Table 1).

Table 1. Unmet needs of patients with PF/IPF reported by patients and caregivers	Reference(s)
Timely and accurate diagnosis	(11, 13-26)
More awareness of PF/IPF	(11, 13-15, 18-21, 23, 26, 27)
Adequate information and education	(11, 13-19, 22-24, 26-32)
Access to pharmacological treatment	(11, 14, 15, 19-21, 26)
ILD specialists	(11, 13-16, 18, 19, 22, 25-27)
Symptom relief	(17, 18, 20, 21, 23, 28, 30)
Psychological support	(11, 13-15, 17, 23, 26-28)
More involvement and support of partners	(14, 16, 17, 24, 28, 32, 33)
Non-pharmacological management (i.e. supplemental oxygen, pulmonary rehabilitation)	(11, 13, 15-17, 19, 21-23, 26, 30)
Access to a multidisciplinary team	(11, 16, 17)
End-of-life care	(11, 16, 19, 20, 22, 23, 26-30)

Referral pathways and access to specialist care

One of the major unmet needs in PF/IPF care is a timely and accurate diagnosis (13, 15, 19, 24, 25). In the current study, a significant number of patients were initially misdiagnosed; time from misdiagnosis to correct diagnosis was often more than a year. This is in agreement with previous studies, which showed that many patients receive at least one misdiagnosis, consult more than three physicians before receiving a final diagnosis, and have a delay in diagnosis of more than one year (15, 25, 26, 34). Although the current study shows less delay than some previous reports, one out of five patients in this study still had to wait more than a year for referral to an ILD specialist centre. It is of utmost importance to reduce delays in diagnosis and referral, since previous research indicated that a lengthy diagnostic trajectory can have an adverse effect on QoL, and that delayed access to tertiary referral centres is associated with a higher risk of death in IPF (13, 25, 35). In fact, access to ILD specialist centres may increase the perceived quality of care (15, 26). Access to MDTs appears to have increased in recent years. In contrast to the European IPF patient charter in 2016 (11), almost all HCPs in the current study reported access to an MDT, whilst the composition of the MDT still widely varies.

One of the reasons for delayed diagnosis is the lack of knowledge regarding PF/IPF amongst the general public, GPs and physicians in community hospitals (5, 11, 15, 26). Improving knowledge about IPF, through education and awareness campaigns, could facilitate earlier diagnosis and referral (11,

Kommentiert [GW3]:

1. Die „unmet needs“ auf Seite 7 sind sehr anschaulich formuliert, aber sie müssten hier im Verhältnis zur Einschätzung der Angehörigen/Patienten in Hinblick auf Lebensqualität und zur Lebensverlängerung/-verkürzung gesetzt werden -> Bei zu Tode führenden Krankheiten ist eben eine besonders gute Aufklärung ausschlaggebend! Wenn ich frühere Informationen und eine adäquate Diagnose frühzeitig erhalten hätte, hätte ich voraussichtlich um x Jahre länger gelebt. (Oder zumindest Klassifizierung und Wesentlichkeitseinschätzung pro unmet needs).

2. Generell: Die Form der Verschriftlichung ist kein Positionspapier, sondern ein wissenschaftlicher Abstract. Bei einem Positionspapier ist es wichtig, dass die politischen Forderungen und Handlungsempfehlungen an erster Stelle stehen und anschließend kurz und knapp begründet werden (nächste Mal „unmet needs“ und Forderungen hochziehen); die Lobbyisten haben nur wenig Zeit. Alles Ausführliche im Anschluss oder auf einen abstract verweisen.

3. Weitere Herausforderungen:

- Verbot der Behandlung mit „alter“ Medikation: keine falschen, alten Methodiken mehr, z.B. Azathioprin, etc.
- Umsetzbarkeit der Kommunikation mit Angehörigen, z.B. Vereinbarung von Terminen angestimmt auf die Angehörigen, psychologische Betreuung.
- Berücksichtigung des psychischen Impacts auf die Patienten.
- „All new technologies (as AI) need to be developed from a patient centric point of view. A data set of PF/IPF patients vitals signs/ values (thorax CT, lungue values) in order to feed AI systems to support faster medical diagnosis“.

4. Weitere Herausforderungen:

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- Verstärkte, unabhängige Grundlagenforschung, u.a. in Richtung „gender specific“ criteria of PF/IPF (warum ist die Rate an „male“ oftmals so hoch, ich habe darüber noch wenig gelesen, weiß man hierüber schon etwas, welche Angehörigen hatte aus der Familie bereits ähnliche Dianogse (20% waren das Väterlicherseits?)

13, 34). A prior study suggested to develop symptom-based algorithms for GPs, to help identify which patients should be referred for further analysis (19).

Pharmacological treatment

Although anti-fibrotic medication can be prescribed in all participating countries in this study, timely access to treatment has been highlighted as an issue by both patients and healthcare professionals. A recent study found that up to 40% of patients with a confirmed IPF diagnosis do not receive treatment with anti-fibrotic medication (36). Barriers to pharmacological treatment include delayed access to specialist care and reimbursement restrictions (36). Moreover, a watch-and-wait approach is sometimes preferred in patients with mild or relatively stable disease, despite the fact that the importance of early treatment initiation has been emphasised in recent years (5, 36-39).

Our results show that reimbursement restrictions continue to be an important cause of delayed access to anti-fibrotic treatment. Treatment delays vary between countries due to different prescription criteria. To ensure equal access to anti-fibrotic medication across Europe, fewer reimbursement restrictions and uniform criteria acknowledging the patient needs reported in this statement are imperative.

Non-pharmacological treatment

Non-pharmacological treatment options, such as pulmonary rehabilitation, oxygen therapy, psychological support, and lung transplantation are a vital part of holistic care for patients with PF/IPF (2, 40, 41). Previous studies demonstrated that non-pharmacological treatment options are not equally available for patients in different European countries (11, 19). In the current survey, the vast majority of HCPs indicated that they could refer patients for lung transplantation and PR as well as being able to prescribe oxygen therapy. In contrast, fewer than half of the patients reported that they had access to PR. This discrepancy could be due to the fact that PR is often not fully reimbursed, that many patients are unaware that PR programs exist for PF/IPF, and that patients often have to travel long distances for PR (11). The need for better emotional and psychological support for patients and caregivers has been frequently reported and is underlined by the findings from our study (11, 13, 14, 17-19, 21, 23, 28, 33). Nevertheless, reimbursement and access to psychological support for PF/IPF patients remains restricted. If referral to a psychologist is not possible, other options for emotional support should be explored. Previous work shows that many patients also benefit from psychological and emotional support through peer support groups, PR and ILD specialist nurses (11, 13, 14, 23, 30, 42, 43). Strikingly, only half of the surveyed patients in this study had access to ILD specialist nurses, demonstrating that more specialist nurses should be trained.

Access to palliative care

As of yet, there are no (international) guidelines on palliative care in PF/IPF. This leads to underuse of and varying access to palliative care across Europe, which is also influenced by differences in local resources, cultural and religious beliefs, and misconceptions about the meaning of palliative care (2, 11). It is important to acknowledge that palliative care comprises more than just end-of-life care alone, and aims to improve quality of life during the whole disease course (2, 44, 45). Still, our results indicate that many HCPs in Europe start palliative care in more severe stages of PF/IPF. The majority of HCPs in this study stated that they discuss end-of-life care with all patients. However, the optimal timing of end-of-life discussions and referral to palliative care services remains difficult in PF/IPF (16, 19, 29) and depends on various factors including culture, religion etc. Prior reports suggest that early palliative care can potentially reduce symptom burden for patients with IPF, but needs to be tailored to the

preferences of individual patients (2, 28). Hence, palliative care should be an integral part of comprehensive care for patients with PF/IPF (2).

Communication and education

Education plays an important role in the management of PF/IPF. To enable shared-decision making and enhance communication, patients should be well-informed about their disease and its prospects (40, 46). Whilst our results show that three quarters of patients receive a treatment plan after their diagnosis, only one-third of patients are actually involved in developing this plan. Possible reasons are the lack of time to discuss treatment plans with patients and the fact that patients need to be better educated to become more involved (46). Adequate information about PF/IPF, more education and continuous counselling were amongst the frequently reported suggestions for improvement of the care pathway in the patient survey. The need for more information is in agreement with findings from previous surveys and interviews (11, 15-18, 23, 24, 27-29). Whereas two-thirds of centres in the current study offer education for patients, only a minority of patients attended any educational activity. This suggests that greater awareness of the educational activities amongst patients may be required, or that some patients might prefer to receive written information and/or use online resources (24, 31, 46). To improve experiences for patients and caregivers, educational material about PF/IPF should be easily accessible, understandable, updated frequently and adapted to individual patients' needs (14, 23, 24, 46).

Involvement in research

Results of this study highlight that patients should be better informed about clinical trials and patient registries. Only half of patients were aware of ongoing clinical trials and only a quarter actually participated in a trial. Previous research suggested that many patients wish to be informed about possibilities to participate in clinical trials and that patients treated in specialist centres were more likely to be participating in a clinical trial (13, 15, 27, 37). Moreover, one study reported that patients who participated in a clinical trial were more hopeful regarding treatment than other patients (13). Efforts should therefore be made to inform all PF/IPF patients about clinical trials, and to refer patients to specialist centres for participation in trials. Many countries have local or national registries for PF/IPF, however, only a quarter of patients indicated that they contribute data to a registry. Improved collaboration with patients and between countries is needed to collect data and establish a multinational registry. Such a registry will not only enhance understanding of disease behaviour, but may also provide insights to improve care and outcomes for patients with PF/IPF (47, 48).

LIMITATIONS

This study has several limitations. Firstly, the results are only representative of the situation in 14 EU-IPPF member countries; in particular newer EU Member States have been underrepresented. Further, the HCP survey was distributed through the ERN-lung network. This resulted in a high number of responses from physicians in ILD specialist centres, representing an important bias. Similarly, the patients who participated in the survey may have better access to information and specialist care, because they were recruited via support groups. There may also have been a bias towards less impaired patients amongst the respondents, which makes it difficult to compare answers of HCPs and patients.

CONCLUSIONS

This survey and literature search offers important insights into the current unmet needs of PF/IPF patients in Europe and should be considered for healthcare decisions. Recommendations set out in this statement could provide a useful tool to healthcare providers and policy makers to improve the patient journey and overall care of these rare diseases. Better international collaboration between clinicians, researchers, patients, caregivers, industry partners, and governments should be established to solve unmet needs, improve outcomes, and develop evidence-based multidisciplinary care for PF/IPF patients.

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