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Management of idiopathic pulmonary fibrosis in France: A survey of 1244 pulmonologists

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Summary
Background: The present survey coordinated by the French expert centres for rare pulmonary diseases investigated French pulmonologists' current diagnostic and therapeutic practice for idiopathic pulmonary fibrosis (IPF).
Methods: From December 7, 2011 to February 18, 2012, all French pulmonologists ($n = 2608$) were contacted. Those who reported following up at least one IPF patient ($n = 509$) were administered a 26-item questionnaire by phone or e-mail.
Results: 509 pulmonologists (41% of responders, 20% of French pulmonologists) were involved in the management of IPF patients. Of those, 36% discussed the cases with radiologists and pathologists. Out of 406 community pulmonologists practicing outside of reference or

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competence (e.g. expert) centres, 141 (35%) indicated referring patients to those centres. The 2011 international guidelines for IPF were known by 67% of pulmonologists involved in IPF, 84% of whom considered them appropriate for practice. About 58% of patients were diagnosed with mild to moderate IPF as defined by percentage predicted forced vital capacity ≥50% and percentage predicted diffusing capacity of the lung for carbon monoxide ≥35%. Management resulted from multidisciplinary discussion in 36% of the cases. By the end of December 2011, 49% of patients with mild to moderately severe IPF were treated with oral corticosteroids, and 27% received no treatment.

Conclusions: Despite correct awareness of international IPF guidelines, modalities of multidisciplinary discussion and of early diagnosis and management need to be improved through the network of expert centres.

Statement demonstrating the originality and clinical relevance

The present survey is the first survey on the management of idiopathic pulmonary fibrosis (IPF) since the 2011 international guidelines for IPF. Coordinated by the French expert centres for rare pulmonary diseases from December 7, 2011 to February 18, 2012, it investigated French pulmonologists' current diagnostic and therapeutic practice for IPF in 509 pulmonologists (20% of all French pulmonologists) involved in the management of IPF patients. Management resulted from multidisciplinary discussion in only 36% of the cases; 35% of physicians referred patients to expert centres, and 67% knew the 2011 international guidelines for IPF. Overall, this study shows that despite awareness of international IPF guidelines, modalities of multidisciplinary discussion and of early diagnosis and management need to be improved through the network of expert centres.

Introduction

Idiopathic pulmonary fibrosis (IPF) is the most common form of chronic idiopathic interstitial pneumonia in adults. It is a fibroproliferative, irreversible disease of unknown cause, occurring mainly from age 60 onward and limited to the lungs [1]. IPF is a fatal lung disease with a variable natural history, usually gradual and progressive. Symptoms are not specific and consist mainly in chronic exertional dyspnoea and dry cough. Typically, inspiratory crackles are found at lung auscultation.

The diagnosis of IPF requires exclusion of other known causes of interstitial lung disease (ILD) and the presence of a usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT), or specific combinations of HRCT and surgical lung biopsy UIP pattern in patients subjected to surgical lung biopsy [2]. The accuracy of the diagnosis of IPF increases with multidisciplinary discussion between pulmonologists, radiologists, and pathologists experienced in the diagnosis of ILD [3].

Considered as an orphan disease due to the lack of treatment with proven efficacy until very recently [4], IPF is a rare disease whose estimated prevalence in the United States is between 14 and 28/100,000 and estimated incidence between 6.8 and 8.8/100,000 per year [5]. In France this would theoretically translate into at least 9000 patients affected, with a minimum of 4400 new patients per year.

As defined by the French national plan for rare diseases, IPF diagnosis and management are coordinated in France by a national Reference Centre (RC) and currently 9 regional Competence Centres (CC) for rare pulmonary diseases, which have expertise in IPF and active patient monitoring.

The latest international guidelines on IPF diagnosis and management were released in 2011 [2]. Since then, new data have been published on the efficacy and safety of treatments proposed to retard the course of the disease or alleviate its symptoms [6]. It is now acknowledged that most of these treatments (including oral anticoagulants, ambrisentan, and the combination of prednisone, azathioprine, and N-acetylcysteine) should not be used in IPF patients because of their lack of efficacy and/or harmful effects [7—9]. Several other treatments targeting the mild to moderate stages of the disease (defined as the concomitance of a forced vital capacity ≥50% and diffusing capacity for carbon monoxide ≥35% of their respective predicted value) were under investigation in 2011—2012 [10,11].

These considerations prompted us to conduct a national survey in order to investigate the practical modalities of IPF diagnosis and management (including care settings and treatment) in France, describe the actual functioning of the IPF management network, broadly estimate the national prevalence and incidence of IPF, in particular in its mild to moderately severe form, and assess the expectations of pulmonologists related to IPF management.

Methods: organisation of the national survey

A national survey coordinated by the French national RC and the regional CC for rare pulmonary diseases was conducted between December 7, 2011 and February 18, 2012. The 2608 pulmonologists working in metropolitan France were asked by phone or e-mail if they were involved in the management of at least one patient with IPF. Repeated

phone calls and e-mail reminders were used if needed to maximise the response rate.

A 26-item questionnaire was then administered to pulmonologists who declared they were following up at least one patient with IPF. They were asked to report the type of care settings in which they were working and the number of IPF patients they were currently following up. The other questions were related to the practical modalities of diagnosis, management, and follow-up of patients with a mildly to moderately severe form of IPF.

Descriptive statistics were performed using Excel, Microsoft Office 2010. Incidence and prevalence were estimated based on the number of different IPF patients followed up per physician participating in the survey (new patients per year for calculation of incidence, and active files for prevalence), with corrections for the number of participating physicians out of the total number of respiratory physicians in France, by type of practice (RC or CC, university hospital, general hospital, private practice, mixed practice).

Results

Survey participants

Among the 2608 French pulmonologists, 1244 (48%) responded to the initial query. The 509 pulmonologists (41% of responders, 20% of all French pulmonologists, evenly distributed within France) (Figs. 1 and 2) who declared being involved in the management of at least one patient with IPF agreed to participate in the survey.

A majority (69%) of the survey participants worked in hospitals (58 in the RC or the CC, 101 in other university hospitals, and 190 in general hospitals); 116 (23%) had a private practice and 44 (9%)had a mixed type of medical practice (private practice + hospital). Distribution by clinical practice setting was not different from those in all French pulmonologists: 59% in hospitals, 24% in private practice, and 17% with a mixed type of medical practice. Sixty-nine percent of participants were male, with a median age of 49.8 years, and 31% were female with a median age of 42.5 years.

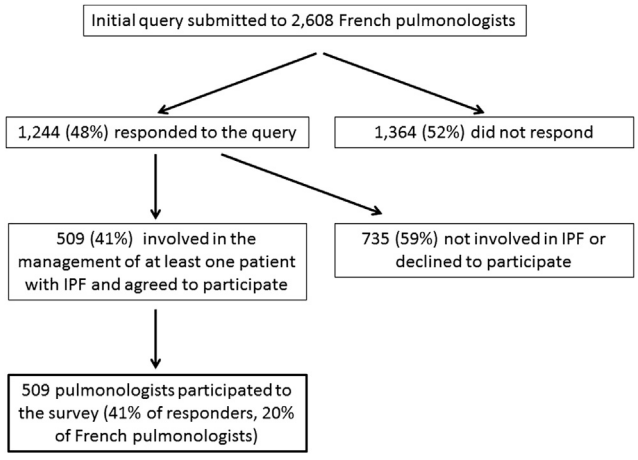

Figure 1 Proportion of French pulmonologists who answered the query and who participated to the survey.

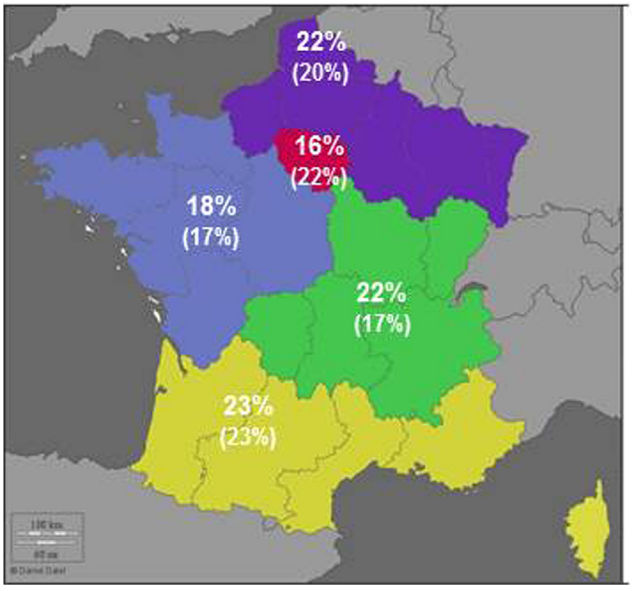

Figure 2 Distribution of survey participants (and of all pulmonologists) in metropolitan France.

Patient attendance by care setting

A majority of IPF patients were followed up by pulmonologists working in general hospitals or in private/mixed practice; fewer were followed up in university hospitals, and fewer still by the RC/CC (Table 1). The distribution among care settings of the mean number of newly diagnosed IPF patients seen per year had a similar pattern. This was consistent with the rate of direct recruitment of IPF patients (seen for the first time by a pulmonologist), which decreased steadily from private/mixed practice to general hospitals, university hospitals, and RC/CC.

IPF incidence in France and prevalence

Extrapolation of data from this survey suggests that IPF incidence was approximately 4.7/100,000/year and prevalence 8.7/100,000 in France.

Severity of the disease was reported as mild to moderate in about 58% of patients. This proportion was higher in private/mixed practice than in the university hospitals and in the RC/CC (Table 1).

IPF diagnosis

The IPF diagnosis algorithm defined in the international recommendations of 2011 (Fig. 3) was known by 67% of the 493 survey participants who answered this question, 84% of whom found it suitable for their practice. This proportion was lower, however, among pulmonologists who worked exclusively in private practice than among their colleagues who worked at least part-time in a hospital (Table 2).

Table 1 Number of IPF patients currently attended per type of physician practice.

Type of physician practice	RC/CC	University hospitals	General hospitals	Private or mixed practice	All practices
Number of IPF patients currently attended	556 (12%)	1112 (24%)	1877 (40%)	1135 (24%)	4680 (100%)
Proportion of attended IPF patients with mild to moderately severe disease	261 (47%)	600 (54%)	1070 (57%)	726 (64%)	2714 (58%)
Number of IPF patients seen per year	286 (12%)	454 (19%)	966 (41%)	665 (28%)	2371 (100%)
Direct recruitment of patients with mild to moderate IPF per year	120 (42%)	250 (55%)	618 (64%)	665 (100%)	1653 (70%)

RC/CC, Reference Centre/Competence Centre.

In most cases, the diagnosis of mildly to moderately severe IPF was made after a multidisciplinary discussion, with the help of a radiologist in 78% of cases, and a pathologist in 49% of cases with lung biopsy (Fig. 4). A majority (74%) of the pulmonologists practicing outside of the RC/CC referred their IPF patients to RC or CC (53%, including 32% of patients referred to the RC), or to a university hospital (47%).

Access to experienced radiologists and pathologists working outside of the RC/CC was possible for only 37% and 34% of respiratory physicians, respectively.

Management of mild to moderate IPF

Among the pulmonologists working outside of the RC/CC, 40% declared that management of their IPF patients was devised in cooperation with one of those centres. In 36% of cases, the management plan resulted from a multidisciplinary discussion involving other pulmonologists, radiologists, and pathologists. Management was discussed with other pulmonologists in only 40% of cases. Fourteen percent of pulmonologists devised the management on their own.

Regarding the selection of pharmacological treatment, 74% of the survey participants relied on a hospital centre, which was the RC or a CC for 60% of the physicians and a university hospital for 40% of the physicians.

By the end of December 2011, 27% of patients with mildly to moderately severe IPF received no treatment; 49% were treated with oral corticosteroids (27% with corticosteroids alone and 22% with corticosteroids associated with immunosuppressive therapy or N-acetyl-cysteine). Nine percent of patients were included in a clinical trial.

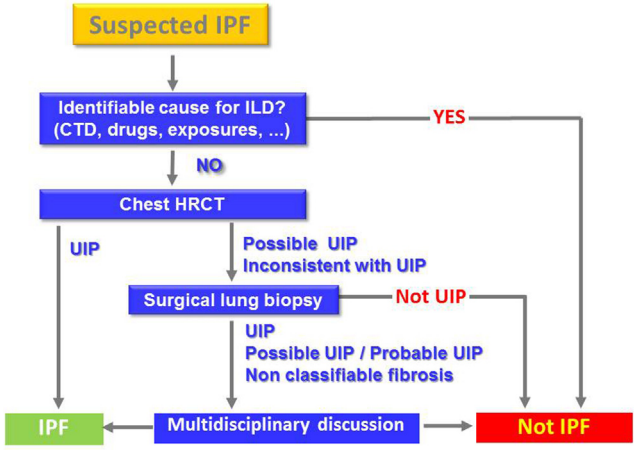

Figure 3 Diagnosis algorithm for idiopathic pulmonary fibrosis defined by the international recommendations published in 2011. Abbreviations: CTD, connective tissue disease; ILD, interstitial lung disease; HRCT, high-resolution computed tomography; IPF, idiopathic pulmonary fibrosis; MDD, multidisciplinary discussion; UIP, usual interstitial pneumonia (From Raghu G., et al. Am J Respir Crit Care Med 2011; 183:788—824).

Current follow-up of patients with mild to moderate IPF

Shared care was the rule for 56% of patients with mild to moderate IPF. Shared care involved other pulmonologists in 91% of cases and radiologists in 14% of cases.

Overall, 35% of pulmonologists followed up their patients in the context of a coordinated care network. Such care networks were more frequently used for patients followed up at the RC/CC and university hospitals than for those in the other care settings (Table 3). Involvement of general practitioners within the coordinated care networks was lower in the RC/CC than in the other care settings (Table 4).

Expectations and needs of pulmonologists regarding the diagnosis and management of mild to moderate IPF

The main expectations of the survey participants regarding improvements that could be proposed by the RC and CC were related to an improved cooperation between the different stakeholders of IPF management, recommendations to facilitate early diagnosis of the disease, a definition of the patient care trajectory, the need for a treatment with proven efficacy in IPF, and a publication in French of

Table 2 Proportions of pulmonologists who find international recommendations on the management of IPF suitable for their practice.

Care setting	Number of respondents	Finding recommendations suitable
Reference centre or competence centre	$N = 42$	86%
University hospital	$N = 77$	90%
General hospital	$N = 108$	87%
Private practice	$N = 65$	72%
Mixed practice	$N = 22$	86%

Table 3 Proportions of pulmonologists following up their IPF patients in the context of a coordinated care network.

Care setting	Number of respondents	Use of a coordinated care network
Reference centre or competence centre	$N = 45$	42%
University hospitals	$N = 65$	46%
General hospitals	$N = 95$	28%
Private practice	$N = 44$	30%
Mixed practice	$N = 17$	24%

well-described IPF diagnostic criteria and practice-oriented management recommendations (Fig. 5).

Discussion

This survey represents the first large-scale assessment of clinical practice patterns regarding the diagnosis and management of IPF by respiratory physicians in a European country, regardless of type of practice conditions. The results reflect a strong interest of French pulmonologists in the diagnosis and management of IPF. Nearly half of them answered the initial question regarding their involvement in the management of IPF patients. More than 40% of the respondents (representing 20% of all French pulmonologists) attended at least one patient with IPF and volunteered to participate in the survey despite the absence of financial or other incentive. Their interest in IPF was reflected by expectation of more practical recommendations on its diagnosis and management, written in the local language, including in particular a better definition of the patient care pathway.

The number of IPF patients attended and the proportion of those with a mild to moderate form of the disease decreased steadily from private/mixed practice and general hospitals to the RC/CC, with intermediate numbers and proportions being reported from the university hospitals.

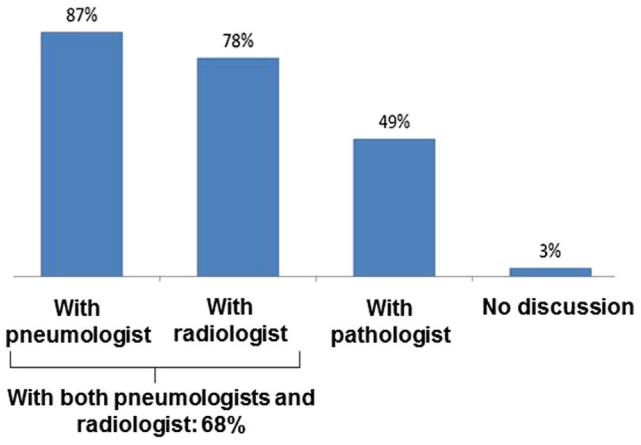

Figure 4 Proportion of pulmonologists discussing the diagnosis of mild to moderately severe IPF with other specialists.

Thus, the general hospital appears to be the primary care setting for most patients newly diagnosed with IPF, with the university hospitals and the RC/CC being ultimately assigned the role of secondary and tertiary care settings, respectively.

In the absence of a recommended, well-defined patient pathway, cooperation between the pulmonologists and others involved in IPF management seemed to vary with local opportunities. Structured care networks were used by only 35% of the respondents. Thus, one lesson of this survey is that structured care networks developed by expert centres are needed and should aim to fulfil two primary objectives. First, multidisciplinary discussions should be generalised to facilitate earlier diagnosis and make appropriate decisions regarding the initial treatment. Second, care networks should be used to ensure proper management of acute exacerbations of IPF and of progressive worsening of symptoms, which unfortunately characterise the course of the disease. It can further be anticipated that care networks will steadily improve education and expertise of participating physicians, as well as foster collaboration and clinical research.

Regarding the treatment of IPF, the frequent use of corticosteroids alone (27%) or in combination with immunosuppressive therapy and/or N-acetyl-cysteine (none of them being approved for IPF) (22%) must be interpreted in light of the state of knowledge in 2011—2012. The international recommendations published in 2011 [2] were based on a low level of evidence for most of these treatments. The few studies suggesting that some improvements could be derived from corticosteroid-based therapies were

Table 4 Proportions of pulmonologists following up their IPF patients in the context of a coordinated care network involving a general practitioner.

Care setting	Number of respondents	General practitioner involvement
Reference centre or competence centre	$N = 37$	68%
University hospitals	$N = 57$	75%
General hospitals	$N = 92$	83%
Private practice	$N = 39$	79%
Mixed practice	$N = 16$	88%

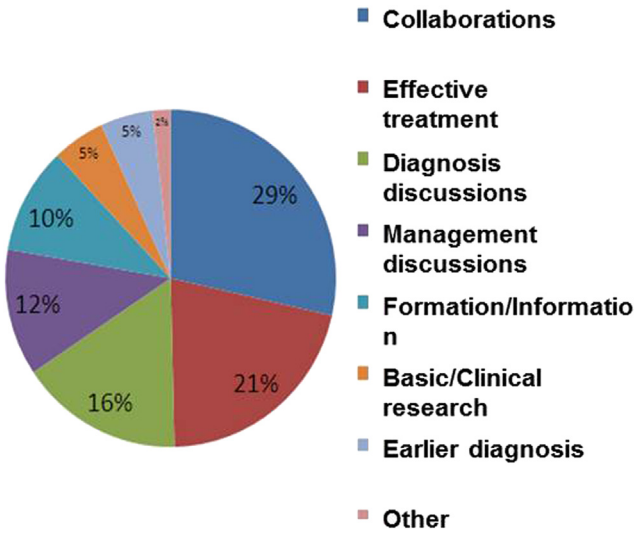

Figure 5 Main needs expressed by the survey participants.

not methodologically sound and no randomised clinical trial with a full placebo group had been published. Accordingly, there was a "strong" recommendation not to use those treatments in the majority of IPF patients, but to "consider" them in a minority prepared to accept the risk of long-term adverse effects in the hope of "hypothetical" improvements [9]. The IFIGENIA study [12] reported a lower decline of forced vital capacity in patients treated with N-acetylcysteine versus placebo, in combination with prednisone and azathioprine, but did not include a full placebo group. Results of the PANTHER trial [7], reporting an increase of hospitalisation and mortality in IPF patients treated with the triple therapy as compared with placebo, were released several months after the end of the present survey. On the other hand, pirfenidone, the first drug with efficacy demonstrated in phase III trials in the treatment of patients with mild to moderate IPF (i.e. with forced vital capacity $\geq$50% and carbon monoxide transfer capacity $\geq$35% of predicted value) [6,13], was granted a marketing authorisation just at the end of the survey (February 2012) and became available in France in October 2012. Pirfenidone was therefore not yet commercially available in France when the present survey was conducted, and it is likely that some change in the management of IPF has occurred since (this will be evaluated in a follow-up survey).

A comparison with the results of a survey of 272 academic pulmonologists conducted in 2006 in the USA [14] shows that a similar proportion of pulmonologists prescribed a pharmacological therapy to their IPF patients (73% in France vs. 77% in the US), with little consensus regarding modalities of management, as in the current survey. The incorporation in the 2011 international guidelines of clinical studies suggesting a possible efficacy of certain therapies might explain these differences. However, corticosteroids were more frequently prescribed by the French pulmonologists. From the US survey data, it can be inferred that corticosteroid-based therapies were prescribed by 39% of the respondents [14], compared with 49% in our survey. This observation suggests that community respiratory physicians may need further education and regular updates regarding the management of IPF. Comparison with older surveys [15,16] is limited due to major changes in the definition of IPF and in its diagnosis and management over the last decades.

However, it must be stressed that 67% of respiratory physicians involved in IPF were aware of the 2011 international guidelines, and 84% of them considered the guidelines appropriate for practice. In a previous survey of 6443 pulmonary medicine board-certified fellows of the American College of Chest Physicians [17], 72% of all respondents were familiar with the ATS/ERS consensus statement and only 63% of them considered it clinically useful. This may reflect an improved suitability between the documents published in 2000 [18] and 2011 [2], as well as differences related to the countries surveyed (namely, the USA and France). Critical comments regarding the recommendations and the need for updates have been published [19]. However, elucidating the reasons for the underlying insufficient suitability of current guidelines and how this may have influenced IPF management by physicians who expressed this opinion is beyond the scope of this survey.

This survey has a number of limitations that must be taken into account when interpreting its results. Forty-eight percent of pulmonologists responded to the initial question asking whether they were following up at least one patient with IPF. This can be considered as a high response rate, comparing favourably with a prior survey with a response rate of 13% [17], yet pulmonogists participating to the present survey represented only 20% of all French pulmonologists, i.e. a rate not high enough to make use of the data reported here to write a comprehensive description of IPF diagnosis and management in France. It might be that the majority of non-responders were not motivated because they did not have to deal with IPF patients, but this is only speculative. Calculated incidence and prevalence were rough estimates, and the present survey should not be seen as a valid epidemiologic study. Furthermore, the results of the present survey may not apply to other European countries, in which organisation of care, national guidelines, and drug availability may vary. As with any survey, ours relied on a self-report method of data collection. It cannot be excluded that patients followed up by several physicians in several care settings may have been counted twice. In addition, imaging and pathology data were not centrally reviewed.

Overall, this survey should be considered as giving a broad picture, from which emerge several noteworthy trends and current practice patterns for the diagnosis and management of IPF in France. One major conclusion is that, despite correct awareness of international IPF guidelines by a majority of respiratory physicians, modalities of multidisciplinary discussion and of early diagnosis need to be improved through care networks to be developed by the expert centres. This survey has thus highlighted priorities and needs for the improvement of the care of patients with IPF.

The need to facilitate early diagnosis of the disease is illustrated by a survey of 45 IPF patients from 5 European countries [20], in which the reported time from initial presentation to confirmed diagnosis of IPF ranged from $<$1 week to 12 years (median: 1.5 years); 55% of patients

reported consulting at least 3 physicians before receiving an IPF diagnosis. In another prospective study of 129 adults [21], the delay in diagnosing IPF was evaluated as 2.2 years (interquartile range 1.0—3.8 years), with delayed access to a tertiary care centre being associated with a higher risk of death, independent of disease severity. As prompt treatment of IPF depends on early diagnosis, which is mandatory in improving the long-term outcome of this condition, we recently argued that this may be achieved through more attention being paid by general physicians to fine "Velcro" crackles at lung auscultation (triggering further investigation when present and especially HRCT of the chest), and through the use of current large-scale lung cancer screening strategies with low-dose HRCT in smokers for the incidental detection of subclinical ILD, and especially early IPF [22].

Major initiatives taken in France following this survey included the development, according to the method proposed by the *Haute Autorité de Santé* (HAS) and under the leadership of the Reference and Competence Centres, of national recommendations on the diagnosis and management of IPF [23]. While being an update of the international recommendations of 2011, this expert consensus will also aim to meet the needs expressed by French pulmonologists for clear and practical diagnostic criteria and treatment recommendations and summary. A tool for the multidisciplinary discussion has been made freely available to pulmonologists caring for patients with IPF (http://www.splf.fr/s/spip.php?article2225), educational meetings on IPF have been held at the national and regional levels, and a project has been initiated to organise care networks across the French regions. Future studies will be needed to evaluate the impact on IPF management of the initiatives listed above, and further surveys will be conducted once the results of several large clinical trials that are currently ongoing worldwide will have been made available.

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