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Genetic testing in interstitial lung disease: An international survey

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Abstract

Background and objective: Genetic analysis is emerging for interstitial lung diseases (ILDs); however, ILD practices are not yet standardized. We surveyed patients', relatives' and pulmonologists' experiences and needs on genetic testing in ILD to evaluate the current situation and identify future needs.

Methods: A clinical epidemiologist (MT) together with members of the ERS taskforce and representatives of the European Idiopathic Pulmonary Fibrosis and related disorders Federation (EU-IPFF) patient organisation developed a survey for patients, relatives and pulmonologists. Online surveys consisted of questions on five main topics: awareness of hereditary ILD, the provision of information, genetic testing, screening of asymptomatic relatives and clinical impact of genetic analysis in ILD.

Results: Survey respondents consisted of 458 patients with ILD, 181 patients' relatives and 352 pulmonologists. Most respondents think genetic testing can be useful, particularly for explaining the cause of disease, predicting its course, determining risk for

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developing disease and the need to test relatives. Informing patients and relatives on genetic analysis is primarily performed by the pulmonologist, but 88% (218) of pulmonologists identify a need for more information and 96% (240) ask for guidelines on genetic testing in ILD. A third of the pulmonologists who would offer genetic testing currently do not offer a genetic test, primarily because they have limited access to genetic tests. Following genetic testing, 72% (171) of pulmonologists may change the diagnostic work-up and 57% (137) may change the therapeutic approach.

Conclusion: This survey shows that there is wide support for implementation of genetic testing in ILD and a high need for information, guidelines and access to testing among patients, their relatives and pulmonologists.

KEYWORDS

experience, familial ILD, familial pulmonary fibrosis, genetic testing, international survey, interstitial lung disease, needs, patient, perceptions, pulmonologist, relative

INTRODUCTION

Recent advances in medical science have increased our understanding of the role of genetic factors in interstitial lung diseases (ILDs).[1] Genetic mutations with high penetrance have been identified, most notably with progressive pulmonary fibrosis, often affecting multiple members of a single family.[2,3] It has been shown that genetic testing in hereditary forms of pulmonary fibrosis aids diagnosis,[2–6] influences clinical management[2,3,7–9] and may predict prognosis.[10,11]

With evidence accumulating, both patients and pulmonologists are increasingly aware of the possibility of a strong genetic component of disease and the possible implications for a subgroup of patients and their relatives. As a result, several specialized ILD centres have started implementation of genetic testing in clinical practice.

As with all new developments, there is little harmonization in the implementation of genetic analysis; its availability is limited and it is not yet clear how to identify the patients who are likely to benefit from testing. ILD clinics select patients eligible for genetic testing on an ad hoc basis, such as patients with familial pulmonary fibrosis, those with early age of disease onset or with evidence suggesting a genetic clinical syndrome, that is, extra-pulmonary features.[2,3] Furthermore, when available, tests are based on local gene panels, which may provide different results to members of a single family when visiting different clinics. Genetic analysis provides not only information about the patient, but also about the disease risk in their relatives. First screening studies have shown that early signs of ILD can be detected in asymptomatic relatives of patients with familial or genetic disease,[12–17] underlining the potential for early diagnosis and treatment of relatives. However, as developments continue, the perceptions and needs for genetic testing from pulmonologists, patients and relatives concerned with familial ILD have not been explored. The understanding of local clinicians, other professionals, patients and relatives, as well as the perception of the clinical impact of genetic analysis in ILD may vary widely.

SUMMARY AT A GLANCE

This survey on genetic testing in interstitial lung disease (ILD) was completed by 458 ILD patients, 181 patients' relatives and 352 pulmonologists. Overall, respondents supported the usefulness of genetic testing in ILD, but pulmonologists' eligibility criteria for patients and tests varied. Reported needs were guidelines, information and access to testing.

Therefore, we developed a parallel survey for pulmonologists, patients and relatives. As a group of doctors, researchers and patient representatives, we aimed to explore the views of pulmonologists, patients and their relatives on genetic testing in ILD in order to review the current situation and identify future needs based on the survey outcome.

METHODS

Survey design

A clinical epidemiologist (MT) together with members of the ERS taskforce and representatives of the European Idiopathic Pulmonary Fibrosis and related disorders Federation (EU-IPFF) patient organization developed a survey for patients, relatives and pulmonologists. In addition to demographic characteristics, the survey included several questions on five main survey topics divided into sections adapted to the target group; patients (five sections with 4–9 questions each), relatives of patients (five sections with 1–9 questions each) or pulmonologists (five sections with 2–15 questions each), as shown in the Supporting Information survey files. We included mainly questions with multiple choice answers and added additional branching logic for answers that raised specific questions not relevant to those who did not give those answers. Study data were collected and managed using

REDCap electronic data capture tools hosted at St Antonius Hospital, Nieuwegein, the Netherlands.[18,19] The survey was open from July 2020 till March 2021.

Population of respondents

Pulmonologists, ILD patients and relatives of patients accessed the survey link via international and national patient and professional organizations. For patients, information and links were posted on the EU-IPFF website and the websites from national European sister organizations specifically in the UK, the Netherlands, Austria, Belgium, Bulgaria, France, Germany, Greece, Ireland, Italy, Norway, Poland, Portugal, Romania and Spain. The information and links were also spread via the World Association of Sarcoidosis and other Granulomatous disease (WASOG) website. Pulmonologists who were members of a specific ILD section received email calls, including the survey link, and information via WASOG and the European Respiratory Society (ERS) ILD section and via national ILD section by the authors and ILD heads of international respiratory societies who were informed on the survey and asked to distribute the information. The survey link was accompanied by a short text with information about the survey, including the reason for the initiation of the study and its aim. Awareness of the survey was increased through newsletters, social media and short texts at the websites of the collaborating organizations. Not any respondent identifiers were collected. When the survey was completed via the survey link, each response was recorded with a record number. Furthermore, the respondents were free to skip questions. The survey for pulmonologists was provided only in the English language. For patients and relatives, the survey was translated into seven languages: English, Dutch, French, German, Italian, Spanish and Greek. The survey outcome is presented for all pulmonologists and responding patients who self-reported an ILD and their relatives. Relatives were not necessarily related to a responding patient, and there was no restriction to first-degree biological relatives. However, a question for relative type was included. If relatives were patient themselves, they were only asked to complete the patient survey.

Data analysis

The data are presented as the number and percentage of respondents to the question. In case of multiple answers, the percentages of given answers should be viewed independent of each other. In the analysis of the results, parallel questions from the survey chapters for pulmonologists, patients and relatives were evaluated together, and presented in the order of the main survey topics: awareness of hereditary ILD, the provision of information, genetic testing, screening of asymptomatic relatives and clinical impact of genetic analysis in ILD.

RESULTS

Respondents

Survey respondents included 352 pulmonologists from 59 different countries and 639 predominantly European (94%) patients and relatives from 14 European and eight non-European countries. Self-reported disease was predominantly idiopathic pulmonary fibrosis (IPF) and nearly half of the responding relatives were children of patients (Table 1).

Awareness of hereditary ILD

Nearly all responding pulmonologists have been asked if the disease is hereditary (95%). They indicate that the diagnosis of these patients is most often IPF and least often exposure-related ILD (Figure 1).

Nearly all pulmonologists (275, 99%) ask their patients if they have relatives with similar disease. The question is asked at first visit (236, 87%), or when the diagnosis is established (59, 22%) or at each visit (17, 6%).

Patients' experiences

A little more than half of the patients (257, 63%) and relatives (107, 65%) reported to have asked a doctor if their disease could be hereditary. Over half of the responding patients (209, 51%) and almost three quarter of the responding relatives (119, 73%) worried about the possibility that other relatives will develop severe ILD, with no difference between patient diagnostic groups.

Provision of information

The vast majority of ILD patients and relatives reported not having received information (81%–83%) on genetic testing and having unanswered questions (68%–77%). Of the responding pulmonologists, 90% reported providing the information, 88% reported a need for education and 96% a need for guidelines (Figure 2).

We asked who should be informed about the presence of familial/heritable disease. Pulmonologists reported that this may depend on the family, but first-degree relatives (parents, siblings and children) were chosen by 35%–41%. Patients and relatives reported that children (50%–57%) should be informed, as well as siblings (37%–38%) and grandchildren (29%–30%), but did not often report that parents should be informed (8%–19%). The majority of patients (74%) and pulmonologists (64%) agreed that the patient should inform his/her relatives (Table S1 in the Supporting Information).

TABLE 1 Characteristics of respondents

	Pulmonologists *n* (%)[a]	ILD patients *n* (%)[a]	Relatives *n* (%)[a]
N	352	458	181
Sex, male/female	186 (53)/163 (46)	308 (68)/147 (32)	38 (21)/142 (79)
Age in years			
<20	1 (0)	1 (0)	0 (0)
20–30	8 (2)	0 (0)	10 (6)
30–40	104 (30)	5 (1)	33 (18)
40–50	121 (34)	27 (6)	51 (28)
50–60	68 (19)	94 (21)	39 (22)
60–70	42 (12)	116 (25)	30 (17)
>70	8 (2)	214 (47)	18 (10)
Clinical centre			
General hospital	82 (30)	222 (54)	N/A
Tertiary care centre	205 (74)	200 (49)	N/A
Group-specific details	**Residence**	**Diagnosis**	**Relative type**
	Europe 223 (63)	IPF 255 (61)	Partner 41 (23)
	North America 48 (14)	Sarcoidosis 96 (23)	Parent 17 (9)
	Asia 36 (10)	HP 19 (5)	Sibling 12 (7)
	South America 32 (9)	iNSIP 18 (4)	Child 83 (46)
	Africa 7 (2)	CTD-ILD 11 (3)	Grandchild 1 (1)
	Oceania 6 (2)	Other IP 7 (2)	Nephew or niece 2 (1)
		uILD 6 (1)	Another relative 24 (13)
		Other ILD 39 (9)	

Note: ILD diagnosis reported by patients: IPF, HP, iNSIP, ILD and IP, including: 1 desquamative interstitial pneumonia, 4 cryptogenic organizing pneumonia, 1 lymphoid interstitial pneumonia and 1 pleuroparenchymal fibroelastosis; uILD; CTD-ILD, including: 9 rheumatoid arthritis-related ILD and 2 systemic sclerosis-associated ILD, other ILD included: 9 rare ILD, 25 other and 5 unknown. Residence of the patients and relatives for each language version of the survey: English: 95 Great Britain, 25 United States, 6 Canada, 1 Bulgaria, 1 Spain, 2 France, 2 Germany, 3 Greece, 1 Italy, 1 South Africa, 1 Zambia; Dutch: 219 the Netherlands, 2 Belgium; French: 7 France, 1 Greece; German: 3 Germany, 2 Austria, 1 Greece; Italian: 30 Italy, 1 England; Spanish: 13 Spain, 5 Mexico, 2 South America, 1 Israel; Greek: 213 Greece, 2 Germany, 1 United States.
Abbreviations: CTD-ILD, connective tissue disease-associated ILD; HP, hypersensitivity pneumonitis; ILD, interstitial lung disease; iNSIP, idiopathic non-specific interstitial pneumonia; IP, interstitial pneumonia; IPF, idiopathic pulmonary fibrosis; uILD, unclassifiable ILD.
[a]Not all responders answered all questions.

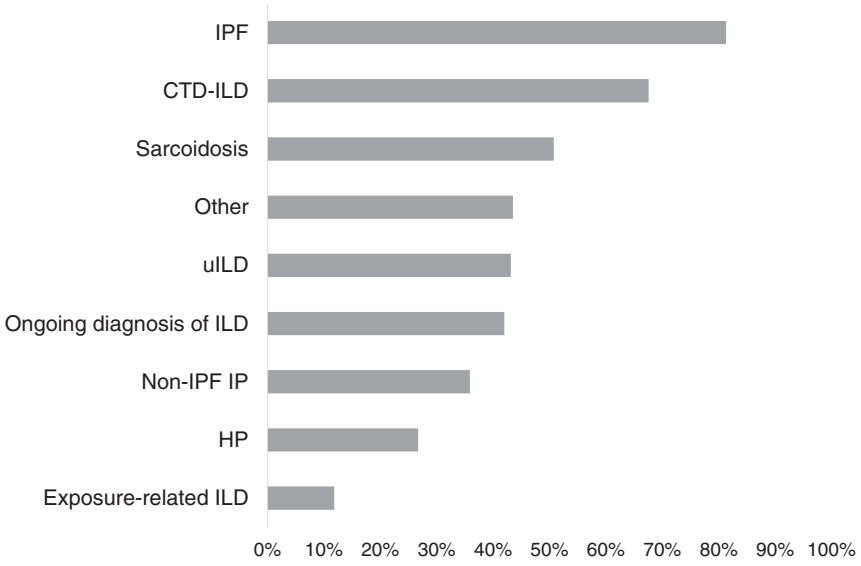

FIGURE 1 'What is the diagnosis of patients who ask if they have a hereditary disease?' The percentages represent pulmonologists indicating the diagnoses of patients asking this question. CTD-ILD, connective tissue disease-associated ILD; HP, hypersensitivity pneumonitis; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; non-IPF IP, non-IPF interstitial pneumonia; uILD, unclassifiable ILD.

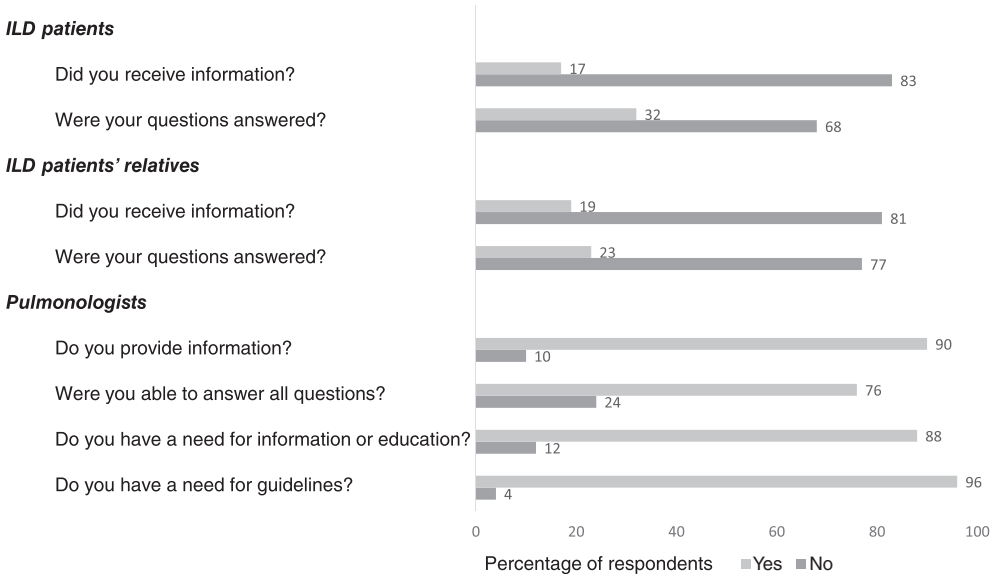

FIGURE 2 Needs regarding information on genetic testing in clinical practice

TABLE 2 Usefulness of genetic testing

In what ways do you think genetic testing can be useful? *N* (%)	Pulmonologists ($n = 277$)	ILD patients without sarcoidosis ($n = 306$)	Sarcoidosis patients ($n = 92$)	Relatives ($n = 160$)
In determining the necessity to test relatives	199 (72)	144 (47)	40 (43)	77 (48)
In explaining the cause of the disease	194 (70)	168 (55)	62 (67)	91 (57)
In determining the risk for developing disease	190 (69)	110 (36)	48 (52)	104 (65)
In predicting the course of the disease	190 (69)	137 (45)	53 (58)	86 (54)
In explaining other health problems besides the ILD	144 (52)	98 (32)	38 (41)	58 (36)
In decision-making concerning life course	141 (51)	57 (19)	19 (21)	53 (33)
In the evaluation of lung transplantation	135 (49)	71 (23)	11 (12)	NA
In the choice for drugs	119 (43)	112 (37)	41 (45)	NA
In another way	8 (3)	8 (3)	3 (3)	8 (5)
Not in any way	3 (1)	11 (4)	3 (3)	5 (3)
I do not know	3 (1)	52 (17)	9 (10)	13 (8)
I have objections against genetic testing	2 (1)	7 (2)	4 (4)	1 (1)

Abbreviation: ILD, interstitial lung disease.

Genetic testing

Usefulness

We then asked in what way genetic testing might be useful. Over two thirds of pulmonologists thought genetic testing may help explain the cause of ILD, assess the risk for developing disease, predict the disease course and determine the necessity to test relatives. Relatives especially thought genetic testing can be useful in determining the risk for developing disease (Table 2). Approximately half of the patients and relatives thought that genetic testing can explain the cause of the disease, predict disease course and determine the necessity to test relatives (Table 2). Interestingly, sarcoidosis patients in general rated the usefulness of genetic tests more highly than those with any other ILD.

If genetic tests are provided, most patients (73%), relatives (43%) and pulmonologists (78%) report that these are offered by the pulmonologist. Other persons who offer genetic tests include: a clinical geneticist (patients 28%; relatives 29%; pulmonologists 33%) or a genetic counsellor (patients 6%; relatives 21%; pulmonologists 24%). A third (91, 33%) of the pulmonologists answered that testing is not offered to their patients. It is mostly not offered because there is no access to genetic testing (76, 84%), it is not paid for by insurance (25, 28%) or it is not known how the results would influence clinical practice (29, 32%).

Patients' selection

The selection of patients eligible for genetic testing and characteristics of hereditary ILD was evaluated in survey questions for pulmonologists, as summarized in Figure 3. Familial disease was most frequently chosen as indication for offering genetic testing, although there is little consensus on the criteria for familial disease, and the type of genetic analysis that should be offered. Disease affecting two first-degree relatives is the mostly used criterion to define familial interstitial pneumonia and was reported by 62% of pulmonologists, but disease is not necessarily chronic, fibrotic or idiopathic. A majority of pulmonologists also found patients with a familial or personal telomere syndrome eligible for genetic testing, with haematological and liver abnormalities and early hair greying most frequently chosen as suggestive of telomere syndrome. Most pulmonologists also found that patients with early onset of disease or genetic disorders of surfactant are eligible for genetic testing (Figure 3).

Patients and relatives were asked about their experience with genetic testing. In total, 74 patients (19%) and 14 relatives (9%) were offered genetic testing for ILD. Furthermore, of the 66 patients (17%) and 14 relatives (9%) who reported to have had genetic tests, more than half (56% of patients and 69% of relatives) did not know the outcome of the test. Patients who reported to have had genetic tests were mainly responders to the English (14%) and Dutch surveys (23%). Of the patients who completed the survey in one of the other available languages, 4% reported to have had genetic tests.

Clinical consultation with asymptomatic relatives

We investigated the experiences of clinical consultation with asymptomatic relatives.

Patients and relatives were asked who should receive screening and the majority prioritize children. About one

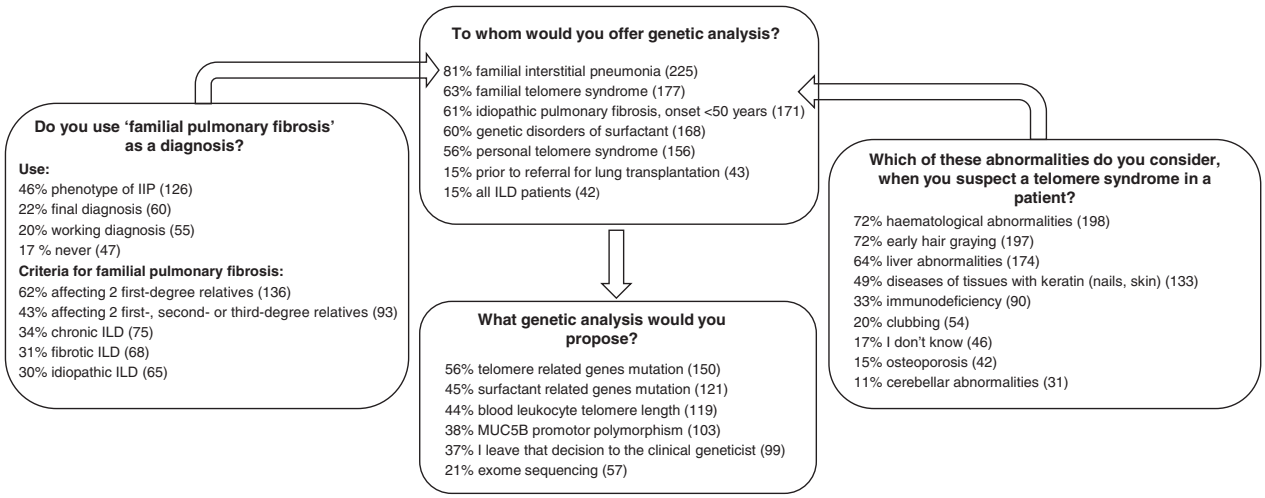

FIGURE 3 Patients eligible for genetic testing in interstitial lung disease according to pulmonologists. Familial pulmonary fibrosis was written as familial interstitial pneumonia/familial pulmonary fibrosis in the questions.

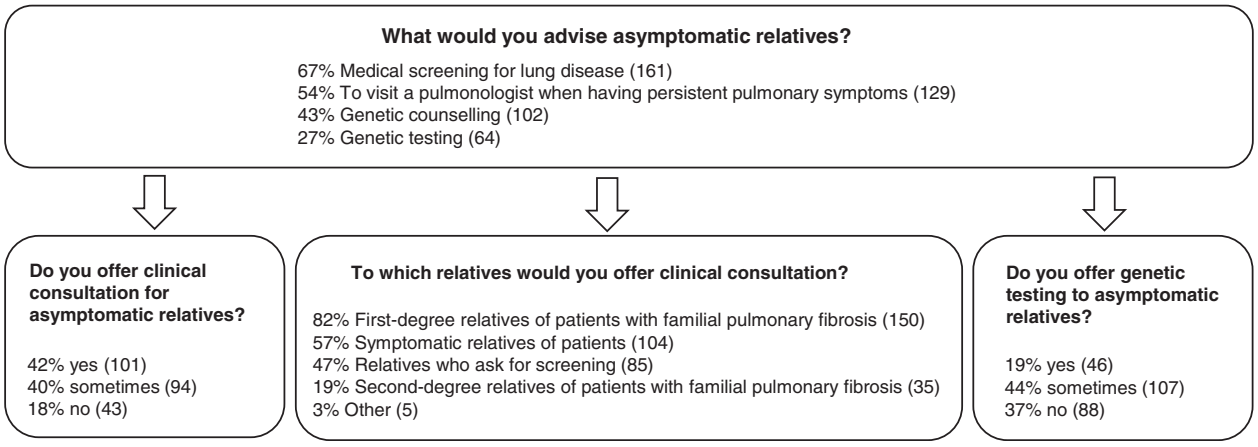

FIGURE 4 Pulmonologists' experiences with screening asymptomatic relatives

TABLE 3 Modification of clinical work-up by the pulmonologist ($n = 240$)

Do you modify your diagnostic work-up according to the results of the genetic analysis? *n* (%)	**Yes 76 (32)**	**Sometimes 95 (40)**	**No 69 (29)**
Reported modifications in diagnostic work-up	If yes or sometimes		
Postponement or exclusion of surgical lung biopsy	123 (78)		
Exclusion of BAL	36 (23)		
Use of haematological parameters	46 (29)		
Performing telomere length measurement	62 (39)		
Change of diagnosis	85 (54)		
Do you modify your therapeutic proposal according to the results of genetic analysis in a mutation carrier?	**Yes 43 (18)**	**Sometimes 94 (39)**	**No 103 (43)**
Reported changes of therapeutic proposal	If yes or sometimes		
Propose antifibrotic treatment	91 (74)		
Exclude lung transplantation	18 (15)		

Note: Additional remarks: telomere syndrome identification requires multisystem evaluation, specific medication and other treatment decisions, and referral to specialized transplant centres may be needed. Targeted treatments are possible for some specific gene mutations (e.g., anti-Jak for STING/COPA).
Abbreviation: BAL, bronchoalveolar lavage.

third of respondents were of the opinion that siblings and grandchildren should also be offered screening (Table S2 in the Supporting Information). The majority of pulmonologists advised relatives to have screening for lung disease and to visit a pulmonologist when having persistent pulmonary symptoms. Most of the pulmonologists offered a clinical consultation (82%) or genetic testing (63%) to asymptomatic relatives (Figure 4). This consultation would be offered to first-degree (82%) or sometimes also second-degree (19%) relatives of patients with familial pulmonary fibrosis, relatives with symptoms (57%) or relatives who ask for screening (47%). Reasons for not offering clinical consultation to asymptomatic relatives (open field answers) were a lack of expertise, high costs and limited availability of genetic tests.

Impact of genetic analysis in the management of ILD patients

This survey topic was only available for pulmonologists and involved questions on the clinical and financial aspects of genetic analysis in ILD. We asked if genetic analysis would change the management of ILD patients; not in what direction. There was an impact of genetic test results on the diagnostic work-up and therapeutic approach according to 72% and 57% of pulmonologists, respectively (Table 3). A majority reported to exclude a biopsy, change the diagnosis and propose antifibrotic treatment according to the genetic test results (Table 3).

Payment for genetic testing, counselling and screening is provided by the public system (according to half of the respondents) and by the patient (according to a third) (Table S3 in the Supporting Information). Our final survey question for pulmonologists was: 'Do you have worries about the impact of familial disease management, including genetic testing, counselling, and screening of asymptomatic relatives, with respect to the affordability of healthcare in your country?' Their answers were: yes ($n = 126$, 53%); sometimes ($n = 44$, 18%); and no ($n = 69$, 29%).

DISCUSSION

This study presents the results of a survey on current perceptions and needs of pulmonologists, ILD patients and their relatives on genetic testing in ILD.

A majority of ILD patients are aware of the possibility of hereditary disease, but according to the pulmonologists there is a predominance of IPF patients inquiring about it. It is known that having a family member with IPF increases the risk for relatives to develop pulmonary fibrosis.[20] Furthermore, familial disease is associated with a worse prognosis.[10,11,21,22] It is therefore encouraging that 99% of the responding pulmonologists do report that they ask their ILD patients if they have relatives with similar disease. Previous studies found that between 12% (non-IPF ILD) and 25% (IPF-ILD) of ILD patients reported having a relative with pulmonary fibrosis.[20,22] However, studies on familial ILD used varying inclusion criteria for their cohorts that differed in age, relative type, diagnosis and other characteristics. The lack of consensus definitions, particularly for what is familial pulmonary fibrosis, is reflected by the relatively low agreement among pulmonologists on how to use and define the term and this may also impact the rate and the population selected for genetic testing or screening. Eligibility criteria for genetic testing in ILD are not yet standardized across clinical practices, and indications for testing are not limited to familial disease. Relatively young patients or patients with evidence for short telomere syndromes or genetic disorders of surfactant are also considered eligible for testing. Most pulmonologists recognize the features 'haematological abnormalities', 'early hair greying' and 'liver disease' as suggestive for the presence of a telomere syndrome and

would offer analysis of 'telomere syndromes related mutation'.

The clinical impact may be substantial, as 72% of the pulmonologists consider that the results of the genetic testing may change the diagnostic work-up and 57% consider that the results may change the therapeutic approach. Associations between genetic test results and diagnosis, treatment, lung transplantation or disease prognosis have been reported.[2–11] However, evidence for implications of genetic test results for clinical management is limited. Examples of studies reporting such implications include the following. A study in children with ILD (age > 2 years) showed that genetic tests contributed to 15% of the diagnoses, which was slightly better than the contribution of lung biopsies (13.5%) to the diagnosis, without having the risk associated with the surgical procedure.[23] In a pilot study for multidisciplinary team discussion on inherited pulmonary fibrosis in 95 subjects, discussion of the combined clinical, familial and genetic findings of patients resulted in a modification of the diagnosis in 10% of cases. While histology was only available in 23% of patients, performing an additional surgical lung biopsy was only proposed for four patients. However, for nearly half of the cases, additional genetic tests were issued (to complete the patient's genetic test or test for segregation with disease in the family). The discussion mainly changed the status of the genetic findings into a (working diagnosis of) a damaging or pathogenic variant. These genetic results were found to provide important information for genetic counselling and to suggest specific therapeutic options.[24]

Genetic testing of patients may impact patient management, but also predicts disease risk of family members. Understanding the benefits and drawbacks of genetic testing and periodic screening of healthy individuals requires further research and optimization of screening protocols. HRCT is commonly used as a screening method for relatives of IPF patients, although the age at which screening should start and the frequency with which computed tomography and lung function should be repeated are not established. Two recent studies found that in around a quarter of IPF patients' first-degree relatives, interstitial lung abnormalities (ILAs) were found upon first screening visit.[25,26] Furthermore, it is interesting that potentially modifiable risk factors for ILA were detected as well, such as self-reported exposure to mould, birds, lead and aluminium smelting.[25] It has been shown that most relatives of patients with pulmonary fibrosis have no major concerns with screening for early disease by means of genetic testing.[27] However, if relatives received abnormal imaging or pulmonary function test results, more regret and other negative feelings were experienced.[27] Thus, appropriate counselling, but also expert medical advice are of crucial importance.

Population-specific differences regarding all aspects of genetic testing probably exist. Although the survey was not developed to specifically address these differences, we noticed that the number of patients who reported to have had genetic tests was much higher among the English (14%) and Dutch (23%) speaking, in comparison to the patients who completed the survey in another of the available languages (4%). Furthermore, pulmonologists provided us with the information that quite some of them (76, 84%) had no access to genetic tests. This may be due to factors involving the provision of information, ethics, costs and so on, and deserves further investigation. Strikingly, most patients and relatives indicated they do not know the outcome of the genetic screening tests. Findings of pathogenic highly penetrant genetic variants have a profound impact on the life of patients and their relatives, including life event choices, psychological well-being, family planning, insurance, profession and so on. Genetic test results of patients with highly penetrant genetic variants should therefore be clearly communicated, that is, hand out the written report, to the patient and the family so that they can make informed choices. A more complicated situation exists for variants conferring relatively low additional risk for disease, such as the MUC5B promoter polymorphism rs35705950. Testing MUC5B was proposed by 38% of the responding pulmonologists. The *MUC5B* risk allele is present in ~10% of the general Caucasian population[1] and has low disease penetrance. Even so, the risk allele is associated with worse or better survival depending on the disease entity, and may become a genetic marker outside the scope of hereditary disease.[28–31]

The current study has several limitations. We chose to secure the privacy of patients, relatives and pulmonologists by keeping their responses anonymous. It is thus not possible to verify the responding population, and we do not know whether the way of survey distribution has caused any selection bias in respondents. Second, the patient and relative surveys were only available in seven commonly used European languages. There are likely patients and relatives who were not reached due to a language barrier. Although we have succeeded in gathering an international survey response, we are thus aware that we have not reached all ILD patient populations across the world, particularly outside Europe. On the other hand, for relatives, there was no restriction to relative type. Only 62% of responding relatives were first-degree relatives for whom disease risk is highly increased in case of genetic ILD. Third, it is important to acknowledge that the pulmonologists who responded to this survey may be biased towards those interested and informed on recent data in this field and might not be representative of all pulmonologists who have patients with ILD. Furthermore, it is possible that recall bias is a general issue in this study.

Of specific interest are developments in children's ILD (chILD),[4–6] which includes genetic mutations leading to ILD presenting at child age, and congenital multisystem disorders with the occurrence of ILD. This survey was not optimized for chILD, but its topic should be addressed as well, especially because anticipation[2,32] occurs in hereditary forms of pulmonary fibrosis. In the field of chILD,[4–6] specific gene test panels are available in some countries. Treatment decisions in chILD are based on the affected gene, with novel mutation targeting therapies under development. Informing in chILD is different from informing in adult ILD, and management of paediatric patients is traditionally a 'family-

centred medicine'.[33] Some of the most fundamental ideas behind the concept 'family-centred medicine' are mutual influence of the treatment process and family dynamics.[33] Altogether, and particularly when gene- or mutation-specific therapies are available, we think that adult ILD may learn from chILD, where genetic analysis is more common and medicine is more family-centred.

This study shows that the pulmonologists initiate care around genetic testing in ILD. However, they report a lack of information and guidelines in the care for familial or genetic ILD.

Based on the findings in this survey, we would suggest the following actions should be addressed to the main identified needs:

a. Develop educational material for patients, relatives and pulmonologists. Define the roles on provision of information; involve clinical geneticists, counsellors and specialized nurses.
b. Incorporate statements on genetic testing in guidelines and standardize the gene panel involved.
c. Assess gains and setbacks of genetic testing and screening programmes and its impact on patients, their relatives and the healthcare system.
d. Define the populations that could benefit from genetic testing.
e. Improve access to testing worldwide.

This international survey on pulmonologists', patients' and relatives' experiences and needs regarding genetic testing in ILD showed that implementation of genetics in ILD care is supported and information and guidelines are needed.

AUTHOR CONTRIBUTION

Michelle Terwiel: Conceptualization (lead); data curation (lead); formal analysis (lead); funding acquisition (lead); investigation (lead); methodology (lead); validation (lead); visualization (lead); writing – original draft (lead); writing – review and editing (lead). **Raphael Borie:** Conceptualization (equal); formal analysis (equal); investigation (equal); methodology (equal); writing – review and editing (equal). **Bruno Crestani:** Conceptualization (equal); formal analysis (equal); investigation (equal); methodology (equal); writing – review and editing (equal). **Liam Galvin:** Investigation (equal); project administration (equal); writing – review and editing (equal). **Francesco Bonella:** Investigation (equal); writing – review and editing (equal). **Aurelie Fabre:** Investigation (equal); writing – review and editing (equal). **Antoine Froidure:** Investigation (equal); writing – review and editing (equal). **Matthias Griese:** Investigation (equal); writing – review and editing (equal). **Jan C. Grutters:** Investigation (equal); supervision (equal); writing – review and editing (equal). **Kerri Johannson:** Investigation (equal); writing – review and editing (equal). **Caroline Kannengiesser:** Investigation (equal); writing – review and editing (equal). **Leticia Kawano-Dourado:** Investigation (equal); writing – review and editing (equal). **Maria Molina-Molina:** Investigation (equal); writing – review and editing (equal). **Antje Prasse:** Investigation (equal); writing – review and editing (equal). **Elisabetta A. Renzoni:** Investigation (equal); writing – review and editing (equal). **Jasper van der Smagt:** Investigation (equal); writing – review and editing (equal). **Venerino Poletti:** Investigation (equal); writing – review and editing (equal). **Katerina Antoniou:** Investigation (equal); writing – review and editing (equal). **Coline H. M. van Moorsel:** Conceptualization (lead); data curation (lead); formal analysis (lead); funding acquisition (lead); investigation (lead); methodology (lead); supervision (lead); validation (lead); visualization (lead); writing – original draft (lead); writing – review and editing (lead).

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CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings are included in the manuscript.

HUMAN ETHICS APPROVAL DECLARATION

This study was conducted in the Netherlands and was not subject to the Medical Research Involving Human Subjects Act (WMO). In this study, participants were not subject to procedures, they were not required to follow rules of behaviour and respondents were anonymous (no email addresses were collected). It was therefore exempted from research ethics approval. Respondents were informed on the study and handling of the data with an introduction to the survey. They were free to take the survey and to skip questions.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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