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Diagnosis, screening, and follow-up of patients with familial interstitial lung disease: Results from an international survey

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Abstract

Background Advances in the field of genetics of interstitial lung diseases (ILDs) have led to the recent consensus statements made by expert groups. International standards for genetic testing in ILD have not yet been established. We aimed to examine current real-world strategies employed by pulmonologists working with familial ILD.

Methods A panel of pulmonologists with expertise in ILD developed an international survey aimed at clinicians working with ILD. The survey consisted of 74 questions divided into eight topics: characteristics of respondents, diagnosis, screening of first-degree relatives, screening tools, genetic testing methods, lung transplantation, ethical concerns, and future needs.

Results Overall, 237 pulmonologists from 50 countries participated. A family history of ILD was asked for by 91% of respondents while fewer asked for symptoms related to telomere disorders. Respondents stated that 59% had access to genetic testing, and 30% to a genetic multidisciplinary team (MDT). Many respondents were unaware of specific genetic testing methods. Pathogenic genetic variants were seen as a potential contraindication for lung transplantation in 6–8% of respondents. Genetic screening of relatives was supported by 80% of respondents who indicated insufficient evidence and a lack of formal guidelines for genetics and ILD. Only 16% had a standardized program.

Conclusion Most pulmonologists ask for a family history of ILD and recommend genetic testing for ILD and screening in relatives but have limited knowledge of specific tests and access to genetic MDT. Evidence-based guidelines to inform patients, relatives, and physicians are still warranted.

Keywords Familial pulmonary fibrosis, Familial ILD, Genetic testing, Interstitial lung disease, Multidisciplinary team meetings, International survey

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Introduction

Interstitial lung disease (ILD) is a large and heterogeneous group of rare diseases characterized by inflammation and/or fibrosis of the lung parenchyma [1, 2]. The most severe form is idiopathic pulmonary fibrosis (IPF) [3, 4]. A genetic predisposition is identifiable in 10–15% of IPF patients and their relatives have a 9- to tenfold increased risk of developing ILD [5–7]. Genetic studies of familial ILD or familial pulmonary fibrosis (FPF) have increased the knowledge on genetic factors and the risk of developing ILD [6, 8]. A recent European Respiratory Society (ERS) statement defined FPF as any fibrotic ILD in at least two blood relative first- or second-degree family members [8].

The most commonly identified genetic variants in ILD are involved in telomere homeostasis (telomere-related genes (TRGs)) and surfactant homeostasis (surfactant-related genes (SRGs)) and are associated with a risk of developing fibrotic and progressive ILD, especially in young adults [6, 9]. A genetic polymorphism in the *MUC5B* promoter is associated with the risk of developing fibrotic ILD, including IPF, hypersensitivity pneumonitis, and rheumatoid arthritis-associated ILD [8, 10–12]. Pathologic variants in TRGs and SRGs are associated with specific ILD features [6, 9], prognosis [13, 14], and tolerance and efficacy of treatment [15]. Furthermore, patients with pathogenic TRG variants may have worse outcomes following lung transplantation, including higher prevalence of infections and greater risk of drug toxicity [13, 16–19].

Due to emerging evidence and advances in genetics and ILD, genetic testing for familial ILD has been adopted into clinical practice in some centres [8]. Although expert task forces have evaluated the need for a standardized approach [8, 20], implementation of genetic analysis is not widely incorporated in ILD centres. International consensus regarding how, who, and when to test in a clinical program has not been established [8]. Furthermore, the tests included in routine practice vary between the centres that have incorporated genetic evaluation.

A recent survey of physicians, patients, and relatives identified widespread support for the implementation of genetic testing for ILD [21]. Of note, ethical concerns were raised by physicians, patients, and their relatives, highlighting a need for greater exploration of these issues and development of a framework.

We developed an international survey on diagnosis, screening, and follow-up of patients with familial ILD, aiming to better understand the ongoing real-world strategies employed by physicians managing patients with these diseases. In this survey, we sought to generate an overview of worldwide diagnostic approaches and screening programs for this important group of patients and their families.

Methods

Survey design

Prior to survey development, we conducted a literature search to identify areas relevant to the diagnosis, screening, and genetic testing of patients with familial ILD. Thereafter, an expert panel of pulmonologists with expertise in ILD was formed (Additional file 1). Questions for the survey were discussed until agreement was reached. The survey was provided by the online survey tool SurveyMonkey from May 2023 to October 2023. A network of ILD physicians identified by the expert panel were invited to participate in the study with study information, consent form, and confidentiality agreement. To ensure anonymity, participants were issued a code number and limited demographic data were collected. On the introductory page to the survey, participants gave consent to participate when choosing to participate in the survey.

The survey encompassed 74 questions grouped into 8 topics:

1. *Respondent demographics*
2. *Diagnosis of familial ILD (patient history and availability of genetic testing)*
3. *Diagnosis and screening of first-degree relatives*
4. *Screening tools*
5. *Genetic testing*
6. *Lung transplantation*
7. *Treatment related to genetic testing (antifibrotic treatment and management following transplantation)*
8. *Ethical concerns*

Survey questions were structured in different formats including closed (multiple-choice) and open-ended questions. All questions provided the possibility to elaborate an answer in free writing. The respondents were also permitted to skip any question.

Data analysis

Results are presented as the number and percentage of respondents to each question. Continuous variables are reported as means and standard deviation (SD) or median and interquartile range (IQR) as appropriate.

Results

Respondents

A total of 870 were invited and 244 (28%) physicians from 50 different countries responded to the survey. Seven respondents were excluded (six respondents did not work with ILD, one respondent did not answer this question), resulting in 237 pulmonologists included in the analysis.

From Europe, there were 119 respondents (50.2%), 44 (18.6%) from South America, 33 (13.9%) from Asia, 30 (12.7%) from North America, 10 (4.2%) from Oceania including Australia, and 1 (0.4%) from Africa.

Respondents could provide multiple answers and many respondents had more than one workplace. Of the respondents, 32% worked in a specialized ILD center/university hospital, 15% in general pulmonology departments/non-university centers, and 3% in an intensive care unit. Sixty-five percent worked in a public academic center, 8% in a public non-academic center, 15% in a private academic center, and 15% in a private non-academic center. Respondents had a median experience as an ILD physician of 13 years (IQR 9–20 years). The median number of ILD patients per center was 400 (IQR 160–1000) and the median number of new referrals per year was 100 (IQR 40–200). The respondents estimated that a median of 10% (IQR 5–15%) of their patients had a history of familial ILD.

Diagnosis and awareness of familial ILD

Components of the diagnostic process pertaining to a potential genetic predisposition are summarized in Fig. 1. A family history of ILD was requested by 91% of respondents when interviewing newly referred ILD patients. Specific questions relating to extrapulmonary diseases or telomeric traits associated with TRG variants (such as a family history of early grey hair), were routinely posed by 48% of the respondents. Fewer respondents asked for a family history of liver cirrhosis or bone marrow disease. Even fewer drew a pedigree when interviewing newly referred patients. If a family history was present or the patient was diagnosed with idiopathic ILD before the age of 50 years, the respondent more often asked for symptoms or diseases associated with TRG variants.

Genetic testing for familial ILD was available to 59% of the respondents. Half of those who performed genetic testing had access to a genetic multidisciplinary team (MDT) meeting (Table 1). Participating specialties in the MDT were pulmonologist 96%, clinical geneticist 46%, genetic counselor 28%, hepatologist 11%, and hematologist 18%. Furthermore, 54% mentioned participation of other medical specialties such as rheumatologists, radiologists, pathologists, thoracic surgeons, pediatricians, and immunologists.

A variety of responses were seen with respect to age of patients with recognized familial ILD and referral for genetic testing (Fig. 2). Only 34% of respondents would refer patients with a family history of ILD for genetic testing at any age, 9% in patients < 60 years, and 24% answered that age of patient prompting such a referral depended on an individual or family history of liver cirrhosis or bone marrow disease. For fibrotic ILD patients without a family history, 33% would refer for genetic testing in patients < 50 years, and 23% in patients < 60 years.

On the methods used for genetic testing, 32% used next-generation sequencing (NGS), 24% whole exome sequencing (WES), and 22% measurement of peripheral blood leukocyte telomere length. Many of the respondents did not have specific knowledge of the form of genetic tests used (Table 1). Regarding specific genetic variants, 40% of respondents tested for surfactant protein gene mutations and 44% for mutations in telomere-related genes. A minority also tested for *MUC5B*

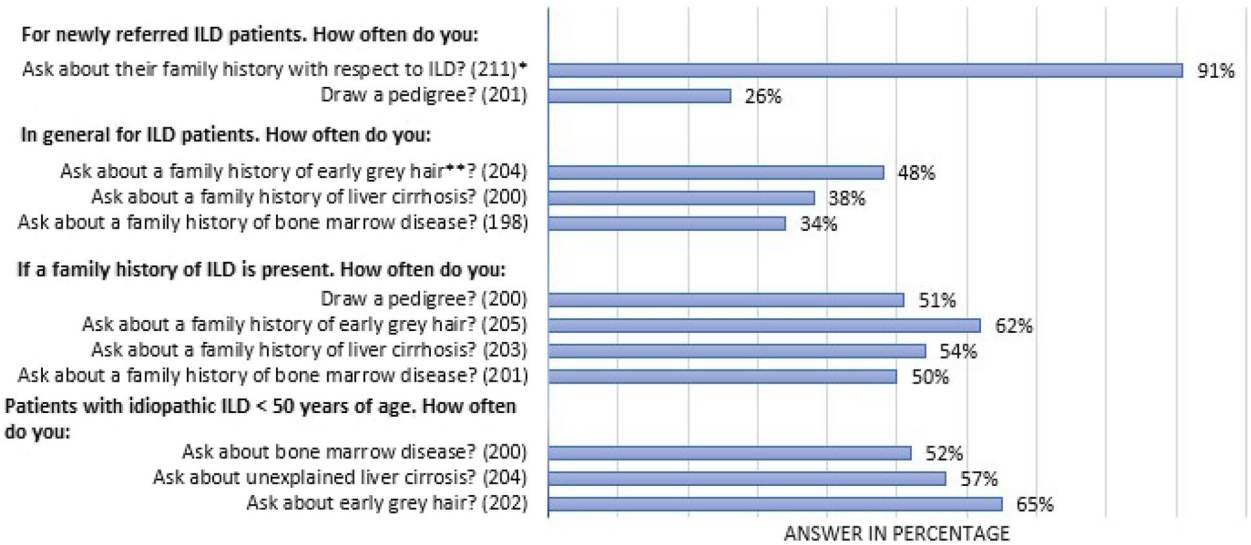

Fig. 1 Awareness of the possibility of hereditary ILD or extrapulmonary symptoms associated with telomerase complex mutations. *(n) = Number of respondents for the individual question ** Early grey hair: Before the age of 30

Table 1 Questions addressing genetic testing and genetic multidisciplinary team meetings (MDT)

Access to genetic testing and MDT (n)*	**Yes**	**No**	
Do you have access to genetic testing (209)?	59%	41%	
Do you have access to genetic MDT (210)?	30%	70%	
Does your local Department of Clinical Genetics use/measure:	**Yes**	**No**	**Don't know**
Next-generation sequencing (NGS) for genetic testing (200)?	32%	20%	48%
Whole genome sequencing (WES) for genetic testing (199)?	24%	26%	50%
Peripheral blood leukocyte telomere length (199)?	22%	40%	38%
Does your local Department of Clinical Genetics test for:	**Yes**	**No**	**Don't know**
Pathogenic gene variants in SRGs (197)	40%	23%	37%
Pathogenic gene variants in TRGs (198)?	44%	24%	32%
MUC5B promotor polymorphisms (198)?	36%	30%	34%

Note: *(n) = number of respondents for the individual question. TRG (telomere-related genes) SRG (surfactant-related genes)

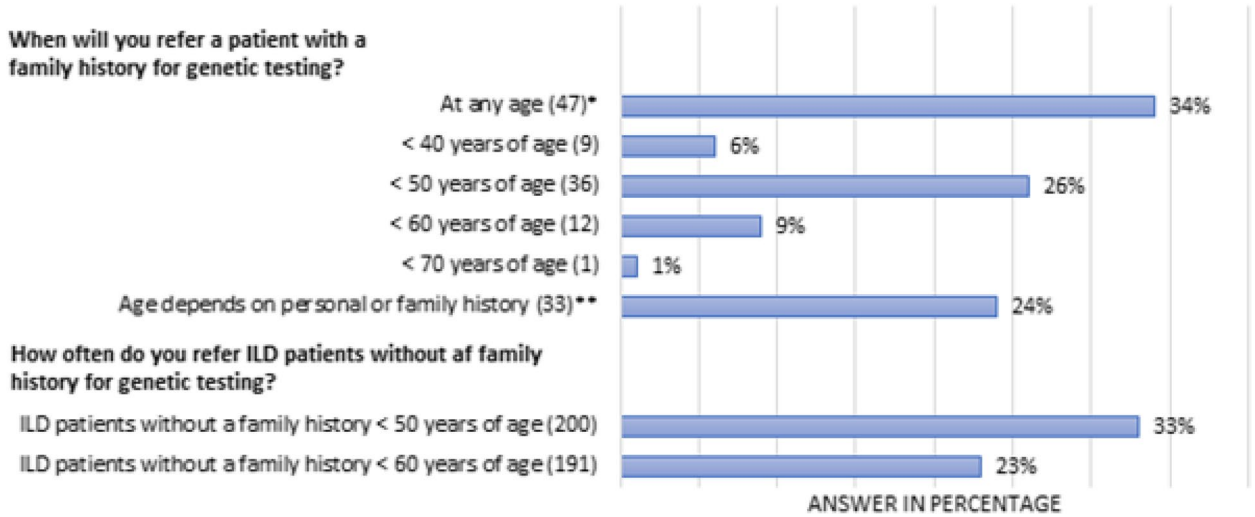

Fig. 2 Questions addressing timing for referral for genetic testing *(n) = Number of respondents for the individual question ** Age depends on personal or family history of liver cirrhosis or bone marrow disease

promotor polymorphisms (Table 1). Respondents answered that only a minority of patients with ILD asked for genetic testing.

Genetic testing and lung transplantation considerations

Only 12% of respondents routinely measured peripheral blood leukocyte telomere length during lung transplantation work-up in patients with familial ILD. The majority had no knowledge of whether it was measured at the transplant centre (Table 2). In patients with familial ILD, 29% referred patients for genetic testing as a part of their lung transplantation work-up program (Table 2). Interestingly, some physicians considered telomere- or surfactant-related gene variants and short telomeres as contraindications for lung transplantation. However, most of the respondents answered that identification of these gene variants would not prevent transplantation (Table 2). In patients with telomere length below the 10th percentile or TRG variants, 33% of respondents would modify their treatment protocol for lung transplant recipients (Table 2).

Regarding disease-modifying treatment before transplant evaluation, many answered that they would not use immunomodulatory therapy in non-IPF fibrotic ILD patients with pathogenic TRG variants (Table 2).

Screening and genetic testing of first-degree relatives and potential ethical concerns

If a pathogenic gene variant was proven in a first-degree relative, 80% recommended screening of relatives (Table 3). On the timing of screening initiation, 28% of respondents answered at 40 years of age and 15% answered 10 years before the index patient, to take genetic anticipation into account. If a pathogenic TRG

Table 2 Clinical genetic and questions addressing lung transplantation

In patients with familial ILD undergoing lung transplant work up do you (n)*:	**Yes**	**No**	**Don't know**
Measure peripheral blood leukocyte telomere length (196)?	12%	41%	47%
Refer patients for genetic testing (193)?	29%	25%	46%
At your transplant centre, will identification of:	**Yes**	**No**	**Don't know**
A telomere-related gene variant prevent transplantation (176)?	6%	73%	21%
A telomere length < the 10th percentile prevent transplantation (176)?	8%	72%	20%
A surfactant protein variant prevent transplantation (177)?	6%	77%	17%
Treatment protocol following lung transplantation Will identification of:	**Yes**	**No**	
A telomere length < 10th percentile modify treatment protocol (173)?	33%	67%	
A telomere related gene variant modify treatment protocol (173)?	33%	67%	
If a patient is known with a pathogenic variant in telomere related genes. Will you:	**Yes**	**No**	**Sometimes**
Offer the patient treatment with immunomodulatory drugs (183)?	11%	56%	33%

Note: *Number of responses for each question

Table 3 Questions addressing screening and screening programs for relatives

If a first degree relative has a proven pathogenic variant in telomere-related gene or surfactant protein gene, do you (n)*:	**Yes**	**No**
Recommend screening for ILD among their relatives (200)?	80%	20%
If a pathogenic variant in telomere-related gene is found in a first degree relative, do you recommend:	**Yes**	**No**
Screening for liver disease in this individual (196)?	66%	34%
Screening for bone marrow in this individual (196)?	61%	39%
Screening for other organ involvement in this individual (197)?	25%	75%
Screening program for first degree relatives. Do you:	**Yes**	**No**
Have a standardized screening program for first degree relative with a pathogenic mutation (203)?	16%	84%
Perform a somatic evaluation as part of this program (195)?**	57%	43%
Recommend HRCT as part of this program (199)?	84%	16%
Recommend pulmonary function tests as part of this program (198)?	85%	15%

* Number of responses for the individual question

** According to the nature of the mutation/syndrome (cutaneous examination, premature greying of hair, nail dystrophy, oral leukoplakia and abnormal skin pigmentation, signs of liver cirrhosis

gene variant was found, most recommended screening for liver (66%) and bone marrow disease (61%). Only 25% recommended screening for other organ involvement (Table 3). A standardized screening program was present at 16% of the respondents' hospitals for first-degree relatives with a pathogenic gene variant. Evaluation of first-degree relatives was recommended by 57% of respondents and 84% recommended a high-resolution-computed-tomography (HRCT) scan as part of the program. Most respondents (85%) recommended pulmonary function testing of first-degree relatives (Table 3), including spirometry and diffusing capacity as part of the screening program. Pulmonologist indicated that they experienced that 25% of first-degree relatives asked for HRCT and pulmonary function testing.

Ethical concerns regarding testing of first-degree relatives of affected patients was expressed by 33%. In free writing respondents mentioned potential impact on mental wellbeing, insurance coverage, the lack of genetic counsellors, and specific treatment options as reasons for not testing. Respondents estimated 15% of first-degree relatives asked for genetic testing and a further 19% declined genetic testing when suggested by their physician/genetic counselor. Reasons for first-degree relatives to decline genetic testing included cost of the test and fear of results could negatively affect either their mental wellbeing or insurance coverage.

Usefulness of genetic testing and future needs

When determining if familial screening was necessary, most respondents found genetic testing of ILD patients useful and many respondents found it useful to better evaluate the risk of extrapulmonary disease. Genetic testing was not considered useful by 9% of respondents (Fig. 3). As part of lung transplantation work-up, 45% of respondents found genetic testing useful and relevant for determining treatment options for ILD patients, and 54% found genetic testing to be diagnostically helpful.

Most respondents stated that the lack of evidence-based specific treatment options for familial ILD and the lack of guidelines for screening for familial ILD were the current major challenges regarding genetics and ILD. Many respondents stated lack of guidelines for diagnosis of patients with familial fibrosis and the lack of trials focusing on patients with familial fibrosis as the most important current challenges. Other challenges included low availability of genetic testing and lack of evidence to support genetic testing.

Discussion

Our survey results reveal the current differences in diagnostic, treatment, and screening strategies, highlighting the need for an evidence-based and pragmatic approach to standardization. The impact of pathogenic variants on transplant candidates and potential ethical concerns following genetic testing in patients and relatives were also areas requiring further evaluation and guidance. Although most respondents considered genetic testing in ILD useful, only 59% had access to these tests in clinical practice and solely one-third had access to a genetic MDT.

Several studies have proven that family aggregation and genetic predisposition are risk factors for familial ILD and worse prognosis [5, 6, 13, 14, 22]. Furthermore, the disease trajectory of an individual with familial ILD seems to be predictive of a worse prognosis for other affected family members [23]. Like Terwiel, most respondents in our study asked for a family history of ILD in newly referred patients [21]. This reassuringly indicates that ILD physicians are aware of familial ILD. Previous studies found familial ILD patients to be indistinguishable from sporadic IPF patients on several clinical parameters, however familial ILD patients tended to be younger with worse survival [8, 24–26]. Regarding extrapulmonary diseases associated with TRG gene variants, the answers were more variable; respondents more often looked for extrapulmonary features of telomere dysfunction if the patient had a known familial history or in sporadic fibrotic ILD younger than 50 years. Previous studies indicate that fibrotic ILD in young adults are more likely to represent monogenic TRG or SRG variant cases than in older ILD patients [8, 13, 14, 27–29]. Features such as early grey hair, hematological abnormalities, liver disease, or abnormal liver parameters may indicate a TRG variant [13, 14, 30–34]. Respondents most often asked about early grey hair in patients and relatives followed by questions of a family history of liver disease and bone marrow disease. Overall, there seems to be high awareness of the importance of a familial background in newly referred ILD patients, but less focus on extrapulmonary symptoms or findings.

In recent years, genetic testing for familial ILD has been implemented in some, but not all specialized ILD centres [8, 35]. In our study, the majority considered genetic

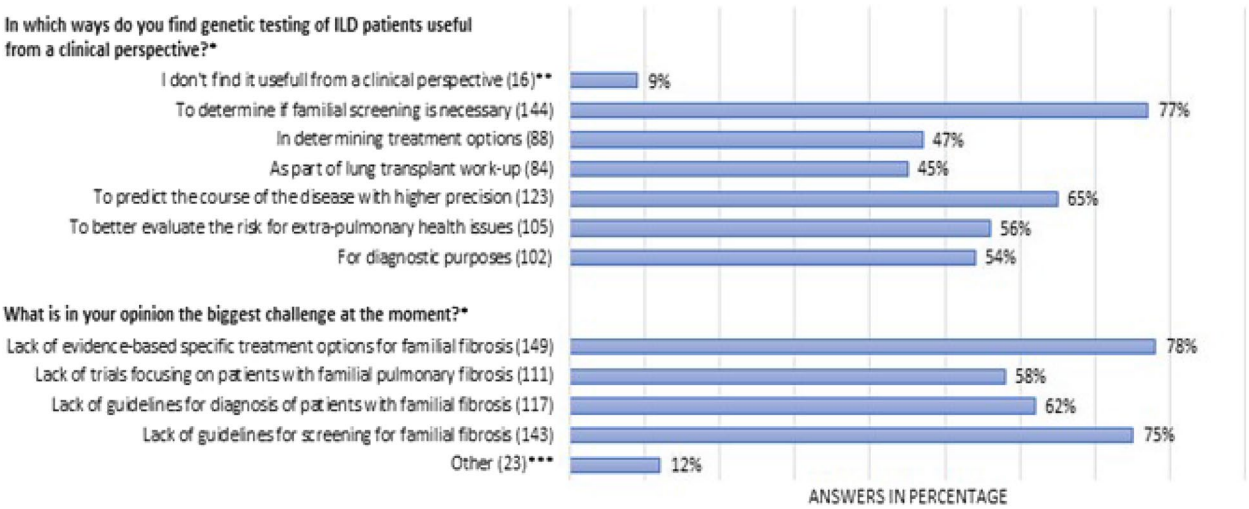

Fig. 3 Usefulness of genetic testing and current challenges. *Multiple answers were possible.**Number of respondents for the individual question. ***Respondents were able to elaborate in free writing

testing in ILD useful. Despite this, just over half of our respondents had access to genetic testing and one third did not offer genetic testing due to limited resources. This proportion is unchanged from the findings by Terwiel [21]. Our results regarding access to genetic testing may even be overestimated as we do not know if non-responders to this question choose not to answer due to limited access to genetic testing or because they had no knowledge of this topic. A recent ERS statement recommends genetic testing for any patient with an idiopathic fibrosing ILD before the age of 50 years, irrespective of family history [8]. In our survey, only 33% of respondents would refer an ILD patient without a family history under 50 years of age for genetic testing. Lack of availability might explain the limited incorporation of genetic evaluation, but other factors like lack of international consensus or awareness of the recommendation for genetic testing have been suggested [8]. Another explanation could be that some of the younger patients might have a connective tissue disease related ILD and thus not qualify for genetic testing. A recent study recommended genetic MDTs as standard care for patients with suspected or confirmed genetic ILD and found that the diagnosis was modified for 10% of the patients after an MDT evaluation [36]. The study recommended that the genetic MDT should include ILD specialists, a geneticist, pediatrician, chest radiologist, and other medical specialists such as hepatologist and hematologist, especially if the patients were carriers of TRG mutations [36]. Contrary to this, our study found that only a third of the respondents had access to genetic MDTs. Most respondents had pulmonologists in the genetic MDT, whereas a clinical geneticist was participating in less than half of the MDTs. Many mentioned radiologists and only few mentioned pediatricians as participants. These findings highlight the need for more research in genetic MDTs and consensus on the medical specialties involved when evaluating patients suspected and diagnosed with familial ILD.

Around 30% of patients with familial ILD are carriers of TRGs, SRGs, or other rare genes [6]. Terwiel found that nearly half of their respondents would analyze for TRG variants and that less than half would test for SRG mutations or measure peripheral blood leukocyte telomere length [21]. Thirty-seven percent would leave the decision to the clinical geneticist. In our study, fewer would test for mutations in TRGs and SRGs. Like Terwiel, we found that a significant proportion of the respondents suggested testing for *MUC5B* even though the *MUC5B* promoter variant is not especially associated with familial fibrotic ILD. This mutation may be seen in a minority of familial cases and some experts suggest testing for *MUC5B* especially if TRG or SRG mutations are not found [6, 8]. Many of the respondents did not know if their geneticist tested for these mutations and the majority were unaware of which methods were used for genetic testing [21]. These findings indicate an unmet need for further education as many pulmonologists are not fully aware of which genes and methods to use for genetic evaluation, perhaps partly due to their limited access to MDT expert geneticists and/or genetic counsellors.

In contrast to Terwiel, we found respondents more prone to refer for genetic testing when considering lung transplantation [21]. Studies have shown transplantation outcomes in patients with TRG mutations to be similar to patients without mutations [16, 18, 37, 38], whereas other studies indicate that short telomere length may affect transplant prognosis negatively [37, 39]. In our study, few respondents answered that TRG and SRG mutation or a telomere length below the 10th percentile would directly prevent transplantation. In the recent ERS statement, it was recommended that familial ILD patients be considered potential lung transplantation recipients, adjusting the immunosuppressive treatment regimen where short telomere syndrome was present, to minimize potential hematological and renal complications [8, 16–18]. Accordingly, many of our respondents would modify treatment following transplantation if short telomere or telomere-related gene mutations were identified. Although practice appeared to generally align with expert recommendations for transplant work-up and referral, some misconceptions and limited awareness of specific genetic screening highlight the need for more education in this area.

In the absence of formal guidelines on evidence-based practice for screening programs for first-degree relatives of familial ILD patients, recent expert statements endorsed by ERS [8] and the Pulmonary Fibrosis Foundation [20] seek to provide frameworks for clinical practice. The ERS statement suggests screening with chest CT and pulmonary function tests in symptomatic first-degree relatives, with less certainty and greater variation in practice for asymptomatic first-degree relatives [8]. As it is not uncommon for patients to have early CT findings and reduced lung function even without respiratory symptoms, a standardized practice of screening all first-degree relatives irrespective of symptoms may be prudent, and likely to be of high yield [20]. Antifibrotic treatment in early ILD is warranted and may result in better survival, thus emphasizing the importance of early diagnosis and potential need for screening in asymptomatic first-degree relatives. However, it is important to note that research on specific treatment strategies for familial ILDs and the benefit/burden balance of very early treatment is limited.

Given the high frequency of hematological and hepatic abnormalities in TRG disorders, screening with a complete blood count and liver function tests for relatives of

patients with short telomere syndrome is recommended by the ERS panel [8]. Due to the risk of liver cirrhosis in patients with TRG, it could be speculated if they had a higher risk of drug-induced hepatitis due to antifibrotic therapy. However, retrospective studies have shown a similar safety profile in these patients compared to patients with sporadic IPF and progressive pulmonary fibrosis [8]. Few of our respondents had standardized screening programs even though the majority supported screening for ILD among relatives. The majority recommended HRCT and pulmonary function test as screening methods with many respondents screening for liver- or bone marrow disease if a TRG mutation was found, similar to the findings by Terwiel [21]. Genetic testing or screening for ILD may have ethical considerations for physicians, patients, and their relatives. A recent study by Carmichael asking relatives of pulmonary fibrosis patients found that these were generally in support of screening for early disease, but as would be anticipated, receipt of abnormal test results were associated with more negative feelings [40]. Many of our respondents indicated ethical concerns for testing of first-degree relatives, often due to potential impact on insurance coverage, incomplete penetrance, and potential psychological consequences for patients and relatives. As indicated by Carmichael amongst relatives [40], the experience of our respondents was that only 19% of first-degree relatives declined genetic testing. These results indicate different views between physicians, patients, and relatives, underscoring the need for guidance concerning shared decision making.

Only few studies have assessed pulmonologists and patients attitudes towards the use of genetic testing among familial ILD patients and their relatives [21, 40]. We found that pulmonologists were in favor of genetic testing of ILD patients and especially found testing useful for several indications, including to determine if familial screening was necessary, to evaluate extra-pulmonary health issues, as part of lung-transplant work-up, to inform treatment options, and to predict the course of the disease with higher precision. Respondents stated a need for evidence-based treatment options and formal guidelines for diagnosis and screening of familial ILD. Importantly, several of the respondents stated in free writing, that one of the biggest challenges was the lack of access to genetic testing and genetic counselling of ILD patients and relatives.

Our survey has several potential limitations. To secure the privacy and anonymization of the respondents, responses were de-identified; hence we could not verify the respondents. There were only few respondents from Oceania and Africa. Respondents were invited from a network of the authors and participation was voluntary which potentially may have caused selection bias with an over-representation of participants with a specific interest in familial ILD. Respondent answers may thus not reflect broader current practice. As a challenge for surveys in general, the response rate of our survey may have an impact when drawing definitive conclusions. Our study has several strengths. Since the survey was anonymous, the answers are anticipated to be less biased. Also, the survey was sent out world-wide and we received answers from most parts of the world with a significant number of responding pulmonologists.

Conclusions

In conclusion, we found a high awareness of the possibility of familial ILD in this international survey. Pulmonologists were open towards genetic testing and screening of ILD patients and relatives. Our findings strongly support further international collaborations between ILD specialists to develop this important area of research.

Abbreviations

ILD	Interstitial lung disease
MDT	Multidisciplinary team
IPF	Idiopathic pulmonary fibrosis
FPF	Familial pulmonary fibrosis
TRG	Telomere-related gene
SRG	Surfactant-related gene
NGS	Next generation sequencing
WES	Whole genome sequencing
HRCT	High resolution-computed-tomography

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-03532-0.

Supplementary Material 1.

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Authors' contributions

EVM: Conceptualization (lead); data curation (lead); project administration (lead); formal analysis (lead); investigation (lead); methodology (lead); visualization (lead); writing – original draft (lead); writing – review and editing (lead). TSP: Conceptualization (equal); data curation (lead); formal analysis (lead); methodology (equal); visualization (equal); writing – original draft (equal); writing – review and editing (equal). MK: Conceptualization (equal); formal analysis (equal); investigation (equal), methodology (equal); writing – review and editing (equal). WAW: Conceptualization (equal); formal analysis (equal); investigation (equal), methodology (equal); writing – review and editing (equal). MMM Conceptualization (equal); formal analysis (equal); investigation (equal), methodology (equal); writing – review and editing (equal). MW: Conceptualization (equal); formal analysis (equal); investigation (equal), methodology (equal); writing – review and editing (equal). AM: Investigation (equal), writing – review and editing (equal). AT: Investigation (equal), writing – review and editing (equal). CJR: Investigation (equal), writing – review and editing (equal). FC: Investigation (equal), writing – review and editing (equal). IB: Investigation (equal), writing – review and editing (equal). JM Investigation (equal), writing – review and editing (equal). JL: Investigation (equal), writing – review and editing (equal). JMO: Investigation (equal), writing – review and editing (equal). LKT: Investigation (equal), writing – review and editing (equal). MFC: Investigation (equal), writing – review and editing (equal).

MLA: Conceptualization (equal); formal analysis (equal); investigation (equal), methodology (equal); writing – review and editing (equal). RB: Investigation (equal), writing – review and editing (equal). SLW: Investigation (equal), writing – review and editing (equal). SR: Investigation (equal), writing – review and editing (equal). YK: Investigation (equal), writing – review and editing (equal). YHK: Investigation (equal), writing – review and editing (equal). EB: Conceptualization (lead); data curation (lead); supervision (lead); formal analysis (lead); investigation (lead); methodology (lead); visualization (lead); writing – original draft (lead); writing – review and editing (lead). All authors approved the final manuscript to be published and were involved in critically drafting or assessing the content of this paper.

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Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study, a health science survey questionnaire, was conducted in Denmark and was not subject to medical research involving human biological material. According to Danish Legislation no registration details were therefore required [41]. In this study, participants were not subject to procedures and participated voluntarily. To ensure the anonymity of the participants no email addresses were collected, participants were issued a code number and limited data were collected. It was therefore exempted from research ethics approval according to Danish legislation [41]. Prior to participating in the survey, the respondents were informed on the study, handling of the data and gave consent to participate when accepting to participate in the survey. All respondents were free to participate in the survey and skip any questions.

Consent for publication
Not applicable.

Competing interests
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