BMC Pulmonary Medicine

RESEARCH

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Perspectives of people living with idiopathic pulmonary fibrosis: a qualitative and quantitative study

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Abstract

Background The antifibrotic therapies, pirfenidone and nintedanib, have been approved since 2014 for idiopathic pulmonary fibrosis (IPF), but in the United States only a quarter of people living with IPF have ever been exposed to an antifibrotic. Understanding the burden and consequences of the disease and its treatment from the perspective of people living with IPF may facilitate improved education and outreach for them and their providers.

Methods Qualitative interviews with people living with IPF explored perspectives on the diagnosis and management of IPF. Transcripts were analyzed to derive themes and topics, and illustrative quotes were selected for presentation. Data were developed into a 74-item on-line survey taken by additional people living with IPF. Quantitative survey data were analyzed with 95% confidence intervals and Z tests.

Results Sixteen people living with IPF underwent qualitative interviews. Direct quotes were used to derive and support themes, and survey stimuli are presented. Ninety additional people living with IPF responded to the on-line survey. 52% of survey participants were male, 54% used supplemental oxygen, and 34% had never been exposed to an antifibrotic. Top sources of information about their IPF diagnosis were their healthcare provider, the internet, and support groups. Most participants had one or more of shortness of breath, fatigue, or cough and over 40% described these symptoms as very burdensome. The most common reason for not starting an antifibrotic was, "I am waiting to start treatment until my symptoms worsen." For those treated with antifibrotics, (78%) agreed with a statement that their antifibrotic gives them hope even though around 90% had at least one side effect.

Conclusions Most individuals living with IPF experienced significant challenges due to their disease and its treatment, that substantially impacted their quality of life. A better understanding of these challenges can facilitate patient-centered and shared decision-making, ultimately enhancing outcomes and satisfaction for people living with IPF.

Keywords Idiopathic pulmonary fibrosis, Quality of life, Qualitative research, Antifibrotic therapy, Oxygen therapy

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Background

October 2024 marked the first decade since antifibrotic therapy became available in the United States following the 2014 approvals of pirfenidone and nintedanib by the US Food and Drug Administration (FDA) for the treatment of idiopathic pulmonary fibrosis (IPF). These medications have been shown to slow the decline in lung

function, as measured by changes in forced vital capacity (FVC), in pivotal trials [1–3]. Pooled analyses of clinical trials demonstrated improvements in all-cause survival as well [4, 5]. Despite the availability of these medications, the overall prognosis for people living with IPF remains poor [6].

Following the first decade of antifibrotic therapy, one surprising finding has been the relatively low antifibrotic treatment rates for patients with IPF in the US. Several studies that focused on Interstitial Lung Disease (ILD) expert centers reported antifibrotic treatment rates of around 70%, while broader datasets point to much lower antifibrotic treatment rates across the US health care system. For example, registries that primarily derived patients with IPF from US academic medical centers found high treatment rates, including the IPF Prospective Outcomes Registry [551 of 782 (70.5%)] and Pulmonary Fibrosis Foundation Registry (PFFR), [742 of 1230 (60%)] were treated with an antifibrotic around the time of registry enrollment [7]. By contrast, an analysis of a US claims database from a national payer that included 10,996 patients with IPF, demonstrated that only 26.4% had ever been exposed to an antifibrotic [8]. An additional claims analysis from the TriNetX network of 76 healthcare organizations in the US showed that only 16% of patients received an antifibrotic within the first year after initial diagnosis [9]. Likewise, a Veterans Administration claims-based study that looked at 14,792 veterans with IPF showed that only 17% had ever received an antifibrotic [10].

Although the adoption of antifibrotic therapy has been limited, IPF treatment has changed the experiences of people living with IPF. For those on treatment, antifibrotics can potentially slow their lung disease progression, yet people living with IPF also have to contend with side effects and the financial cost of treatment [8]. The disease itself, as well as the treatments for it, can impact the experiences of individuals in ways that may not be known or well understood by prescribing providers. This study sought to better understand the experiences of people in the US who were diagnosed with IPF, including how antifibrotics used to treat this disease, in addition to the burden of the disease itself, can impact their quality of life. Our goal was to gather key insights into the opportunities and challenges in the diagnosis, management, and education of people living with IPF.

Methods

Participant recruitment

Participants for the qualitative interviews were recruited from IPF-specific patient panels. The participants for the quantitative survey were recruited from IPF-specific patient panels or from awareness campaigns through pulmonary fibrosis-focused patient advocacy and support groups from the United States. Throughout the process, the Sponsor was blinded to all participants' personal identifying information.

Inclusion and exclusion criteria

For both the qualitative and quantitative studies, all participants had to demonstrate a willingness to engage in a survey of experiences living with IPF, provide informed consent prior to any survey procedures, reside in the United States, and be age 40 or older at the time of consent. The qualitative interview required medical documentation of an IPF diagnosis or a healthcare provider attestation of an IPF diagnosis. The quantitative survey required that a participant self-identify as having IPF and deny having any other non-IPF fibrotic pulmonary diseases during a pre-screener questionnaire. Medical documentation of an IPF diagnosis was optional for the participants in the quantitative survey.

Individuals considering the qualitative interview study were excluded if they were unable to participate in a one-hour qualitative interview or if they were currently participating in any form of clinical trial. Individuals considering the quantitative survey were excluded if they were unable to participate in a 30-min on-line survey, were currently participating in a clinical trial for a new therapeutic agent or had previously undergone lung transplantation. Participants received modest financial compensation for their time.

Qualitative interviews

A professional medical interviewer conducted one-hour, semi-structured interviews to explore participant experiences in the following areas: symptoms and care prior to IPF diagnosis; professional and procedural actions to diagnose IPF; participant understanding of the IPF diagnosis; treatment received including oxygen therapy, pulmonary rehabilitation, and antifibrotic use; understanding of the role of antifibrotic treatment; experience with antifibrotic treatment; and—for those naïve to antifibrotics – the reasons for not being treated. The interview guide is available (Additional file 1).

Quantitative on-line survey development and implementation

Two authors (B.B. and C.G.) independently reviewed transcripts of qualitative interviews and extracted quotes. These quotes guided the development of topics and themes for the quantitative survey. Illustrative quotes that were used to design survey stimuli were selected for presentation. Interested individuals were provided

a link to a pre-screener that facilitated a determination that they had IPF and met inclusion criteria. Those that met the inclusion criteria were invited to participate in a 74-question, computer-based survey that was intended to take no longer than 30–40 min. A third-party vendor provided initial study outreach to those who responded to survey awareness campaigns, administered informed consent documents and all surveys, analyzed data for anomalous trends that could suggest a non-IPF diagnosis or duplication of survey participation, and arranged participant compensation. The survey questionnaire is available (Additional file 2).

Presentation of data

For each section of this analysis, all quantitative data come from the results of the on-line survey. All participant quotes shown in this analysis are derived directly, verbatim from the qualitative interviews. For the quantitative study, themes extracted from the qualitative interviews were presented as topics for rank order of importance, as statements of agreement accompanied by 7-point Likert scales where values of 5 through 7 were classified as "agree", or as statements of burden accompanied by 7-point Likert scales where values of 6 through 7 were classified as "very burdensome."

Ethics approval and consent to participate

Both the qualitative and quantitative protocols were submitted to the Institutional Review Board Western-Copernicus Group (Puyallup, WA; references 1–1,669,153-1 and 1–1,719,988-1), and this study was determined exempt under 45 CFR § 46.104(d)(2). The study was conducted in accordance with the principles of the Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects). A third party vendor described risks to participation and obtained consent to participate in the qualitative interviews. For the on-line survey, consent was also obtained prior to participation (Additional File 2 Survey Questionnaire).

Analyses

A thematic analysis of the qualitative interview transcripts was conducted by authors (BB and CG). Transcribed interviews were reviewed for themes, both pre-identified through the semi-structured interview guide and those that emerged *de novo*. Quotes were extracted from the most common themes to illustrate key concepts and experiences. Common responses were used to develop stimuli for the quantitative on-line survey. The quantitative survey results were analyzed as a whole, and then divided into key subgroups of interest to identify any statistically significant differences, including: 1) male versus female identifying participants, 2) participants who reported care in academic ILD centers versus community pulmonary practices (CPP), and 3) participants who had ever been treated with an antifibrotic medication versus not. For univariable comparisons between groups, 95% confidence intervals and a Z test were used with no correction for multiple comparisons.

Results

Sixteen participants underwent qualitative interviews, and 90 participants completed the on-line survey. The demographics and characteristics of the participants are listed in Table 1. Questions pertaining to the type of area they lived in (e.g., rural or urban/suburban), smoking status, race, and education were not asked in the qualitative interviews but were asked in the on-line survey. The on-line survey participants had a higher percentage of male participants compared to those in the qualitative interview. Male participants (77%) were significantly more likely to have an educational degree higher than a high school diploma (or equivalent) than females (56%).

Initial symptoms that led to a diagnosis of IPF

For the on-line survey participants, the median time from initial onset of symptoms to an IPF diagnosis was 0.5 years, with a wide range (0 to 14 years). Similarly, the time from the first discussion about lung problems to an IPF diagnosis was a median of 0.5 years (range 0 to 10 years).

When interview participants described the symptoms that led to a diagnosis of IPF, many described undergoing evaluations for other conditions prior to a diagnosis of IPF.

"Just cough. It was just constant, and it was annoying." (65, F)

"Being short of breath and coughing. They originally attributed it to asthma, and they treated it as asthma… I was out of breath a lot. I always attributed it to the fact that I was out of shape, a little bit overweight and that's why I was out of breath when I was trying to keep up with people." (74, F)

"Shortness of breath. I always climb the back stairway up to my office. One day after climbing I thought,"I'm not the fat lady in the circus. I'm a little overweight, but it shouldn't be this short of breath." (74, F)

"I'd quit smoking back in 2012 or 2013. Any other time that I'd get winded. I just figured well, it's just because I'm a previous smoker and it's just part of life. But the time when I finally went in was whenever it took me a while, I kept breathing heavily trying to get enough air and I wasn't getting enough air." (58, F)

Table 1 Demographic characteristics of participants in qualitative interviews and on-line survey

Characteristics	Qualitative Phase (*n* = 16)	Quantitative Phase (*n* = 90)
Recruitment source (*n*, %)		
IPF panels	16 (100)	46 (51)
Advocacy/Support Groups	0 (0)	44 (49)
Sex (*n*, %)		
Male	6 (38)	47 (52)
Female	10 (62)	43 (48)
Age		
Median (Range)	69 (48–76)	72 (41–91)
Years since IPF diagnosis		
Median (Range)	5 (12)	4 (13)
Site of Care (*n*, %)		
Expert IPF or interstitial lung disease (ILD) center of excellence (i.e., affiliated with a university)	NA	45 (50)
Community private practice/ doctors'office	NA	41 (46)
Unsure	NA	4 (4)
Area of residence (*n*, %)		
Urban/Suburban	NA	64 (71)
Rural	NA	26 (29)
Geographic region (*n*, %)		
Northeast	4 (25)	14 (16)
Mid-Atlantic or Southeast	5 (31)	27 (30)
Midwest	3 (19)	24 (27)
Western US	4 (25)	25 (27)
Smoking status (*n*, %)		
Current smoker	NA	4 (4)
Previous smoker	NA	49 (54)
Never smoker	NA	37 (41)
Antifibrotic exposure (*n*, %)		
Pirfenidone alone	6 (38)	21 (23)
Nintedanib alone	5 (31)	29 (32)
Both pirfenidone and nintedanib via switch	3 (19)	9 (10)
Never on antifibrotic	2 (13)	31 (34)
Insurance (*n*, %)		
Medicare	12 (75)	62 (69)
Medicaid	0 (0)	5 (6)
Commercial	4 (25)	17 (19)
Veterans Administration/TriCare	0 (0)	2 (2)
Ethnicity (*n*, %)		
White or Caucasian	NA	80 (89)
Black or African American	NA	3 (3)
Native American/American Indian or Alaskan Native	NA	2 (2)
Asian, Native Hawaiian or Other Pacific Islander	NA	1 (1)
Hispanic	NA	2 (2)
More than one race/ethnicity	NA	2 (2)
Education (*n*, %)		
No high school diploma	NA	1 (1)
High school/Equivalent	NA	30 (33)
College degree	NA	36 (40)
Advanced degree	NA	23 (26)
Supplemental oxygen use (*n*, %)		
Yes	14 (88)	49 (54)
No	2 (13)	41 (46)

"I had had a persistent cough for many years. I had acid reflux and GERD and… The coughing that I was doing seemed to be related to that. Coughing was getting worse, and I was pursuing that in early 2021 with a gastroenterologist, and he concluded it wasn't the GERD causing the chronic cough. He sent me to an allergy doctor, pulmonologist in an allergy clinic." (73, F)

"I had symptoms for at least six months, maybe longer and I ignored them. My worst symptom was I was coughing all the time. I just coughed and coughed, but I had no other symptom that I was aware of. I couldn't figure it out. Well, I got on the internet, and I started reading and it said that your blood pressure medicine could cause that. I went to the doctor, and…we changed blood pressure medicines." (63, F)

"I had been seeing a doctor since 2013 just saying, 'I just don't feel good, and I just feel tired.' I can't dance through a whole song and just something's not right. I just kept getting prescribed antidepressants and being told to exercise more and I'm like, 'I'm trying to exercise, but my body's not cooperating.'"(48, F)

Communication with healthcare professionals about an IPF diagnosis

Participants visited a median of two healthcare professionals (HCP) before receiving a diagnosis of IPF. 40% of participants received their IPF diagnosis from a pulmonologist at an ILD center, 40% from a pulmonologist at a CPP, and 12% from a primary care physician. Significantly more female participants received their IPF diagnosis from a pulmonologist at an ILD center (51%) than male participants (30%). At the time of the survey, 50% of participants were receiving care at an ILD center, 46% at a community pulmonary practice, and 4% were unsure (for analysis purposes, responses from participants who were unsure how to characterize their type of medical practice were excluded from comparisons). 67% of participants receiving care at ILD centers reported that they were very satisfied with the communication and information they received about their IPF diagnosis compared to 59% of those receiving care at CPPs.

"He confirmed the diagnosis that I had been given was IPF. He wanted to do some more testing. We talked about how I had looked at Google and what Google said is the lifespan of somebody with IPF being three to five years. He said, 'Don't pay any attention to that.'"(65, F)

"Well, she really shocked me because she said the prognosis was three to five years. Again, I had no symptoms, so I almost fell off the examining table. I don't know that I heard anything else she had to say except she wanted me to be on medication, one of the two medications. I said, 'No, I'm not taking medication that doesn't promise a cure. It just slows progression when I have absolutely no symptoms.'"(66, M)

"That it was terminal. That they had medicines that can slow down the progress and that he wanted to start me on one. He asked me, which one I wanted to start on, and I told him that that's why they paid him the big bucks, so I let him pick it." (58, F)

"...she explained to me, gave me a lot of brochures to go through and told me to go home, and she tried to come up with a plan to slow it down. You can't stop it, I guess. The first thing I said is, 'You're kidding,' and she said, 'No.' I asked if it will kill me and she said, 'Well, eventually you may die from it.' She didn't say I would, but she said I may. Make sure you get along with your daughter. You don't get much longer. She was very compassionate about it." (70, M)

"She [primary care] sent me to a pulmonologist and he basically – I walked in the door, and he says, 'You need a lung transplant.' That's what it felt like. It felt like, 'What?'...'This is IPF. It shows up in your CAT scan.' They did a more thorough series of CAT scans. I looked it up on Dr. Google and was convinced I was going to die tomorrow." (71, F)

Use of social media/internet and support groups for information

Descriptions of where participants in the qualitative interviews found information about IPF were presented as options to participants in the quantitative interviews in order to rank each source by importance. Although only 14% of participants ranked the internet as their most useful source of information about an IPF diagnosis, 68% ranked the internet in the top three sources of information. Similarly, 64% of participants ranked IPF support groups as one of their top three sources for information (Fig. 1).

"I Googled everything I could find and read everything I could find. Through the support group on Facebook, I ask questions of people. I was like a sponge just taking in everything that I could read about it." (65, F)

"I was told, in fact, to stay away from the websites, and I can't remember if it's the first one or just the second. He said the information out there on websites is not really that accurate. I never looked it up on the Internet." (64, M)

"I'd read. Yes, I was absolutely prepared and that's what she said. She goes, 'You know so much.' I said, 'I've been a captive audience for a year reading and reading.' I belong to several groups online. Of course, I'm gleaning a lot of information from that, Pulmonary Fibrosis Foundation." (74, F)

"There're several Facebook support groups. I joined those and they do monthly or whatever, but one of them even weekly online phone calls. Just support and let people ask questions like stuff either they hear about it or learn from their doctors. It's good to have some of that other information too." (69, M)

"Yes, I joined a support group. It's amazing how much I had to learn through that. People from all over the world are in it. They all tell their stories. They tell what they're taking, and they discuss what can be done and what is being done." (63, F)

Perspectives on receiving a diagnosis of IPF

"Early on, you're waiting to die and then, afterward you then get to a point where you just want to hurry up and live." (58, F)

"I don't know. It was all just so shocking. It's pretty shocking when you're fine and then, you're told you have a life-threatening disease. Not life threatening, it's a fatal disease." (71, F)

"We're both Christians. We feel like that is our main support. We're accepting. It's not like we're in denial of it. We're just doing what we can and looking at other options." (69, M)

Comorbid conditions

For nearly all participants, IPF was not the only condition they had to manage (Table 2). 88% of participants had at least one additional comorbidity from a list of selected diseases. Female participants were significantly more likely to report obesity (35%) than male participants (15%), but otherwise comorbid conditions were similarly reported between female and male participants. Polypharmacy was common; 83% of participants took three or more prescription medications and 16% took more than ten.

"I do have Barrett's esophagus because I had a really, really, really, really, really bad heartburn like really bad. That was, I think, probably the catalyst or the injury that started my IPF journey...." (48, F)

"[I have] COPD because we were all smokers." (70, M)

"That GERD definitely played a big role in this flashback into the lungs. Well, I have pulmonary hypertension and that's due to the IPF. Just in the last two months, I was diagnosed with adult-onset diabetes so I'm taking metformin. (74, F)

"...the real concern is the IPF. But emphysema is also there. I can't tell the difference. I have no idea. (64, M)

"It's evolved and now I also have pulmonary hypertension, which I guess as I understand it in and of itself can be fatal." (58, F)

Impact of IPF on quality of life

Symptoms participants associated with IPF

All participants described symptoms associated with IPF, although symptoms varied in terms of how burdensome they were perceived to be. Figure 2 shows the percentage of participants who reported having one or more of a list of symptoms derived from the qualitative interviews. If a participant reported a symptom, they were asked how burdensome it was. Those who reported scores of 6 or 7 on a 1 to 7 scale are shown as "very burdensome." For example, 87% of participants reported having

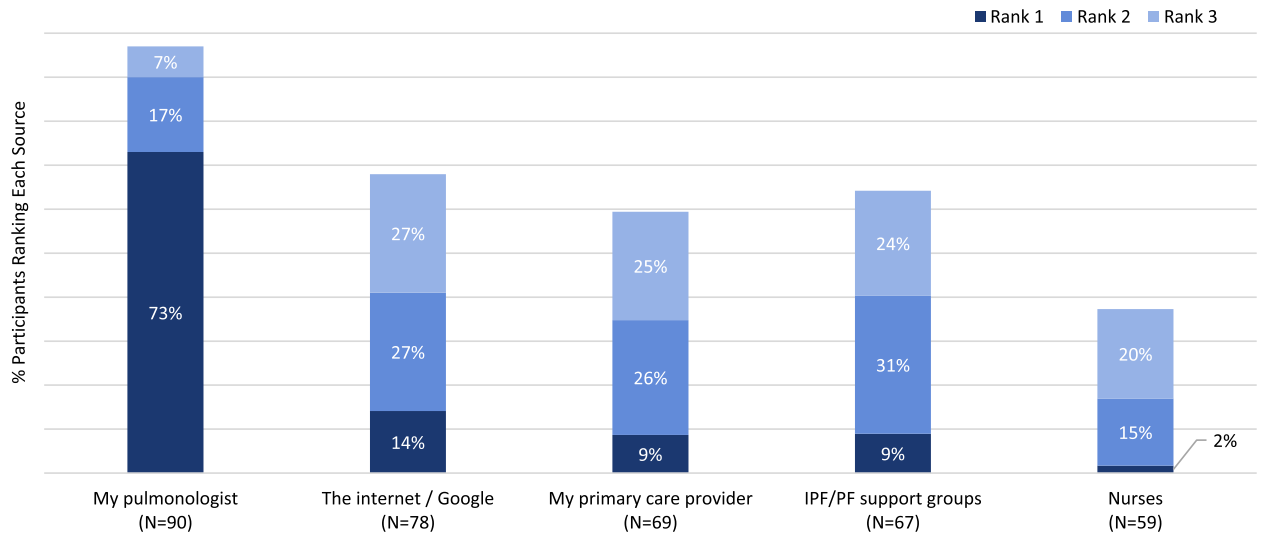

Fig. 1 Top Sources of Information about IPF. Legend 1: All *N*=90 participants were asked to rank avenues of information, from the most useful for discovering information about their IPF diagnosis (Rank 1) to the least useful (Rank 5). Survey participants were only required to rank 1 of the options. This figure shows the proportion of all participants who ranked each source of information as one of their top 3 most useful sources

shortness of breath or trouble breathing, and of those, 41% described this symptom as very burdensome.

"My worst symptom was I was coughing all the time. I just coughed and coughed, but I had no other symptom that I was aware of." (63, F)

"I cough a lot, I notice that. When I'm with other people, they're always like, 'Wow, you're really coughing.' I try to suppress it as much as I can, but sometimes you can't. I can sense that people go looking at each other go, 'Wow, he's really coughing,' whether or not they know I have an illness." (64, M)

"Now I do have a problem if I talk a lot and you're probably going to notice it at some point in this interview I start coughing. I was teaching school on the Zoom thing. I was teaching engineering classes over Zoom, and I got to the point where I couldn't lecture the students anymore because I couldn't stop coughing. I had to give up my teaching position." (76, M)

"My lungs are really sad. You do anything to them, and I just cough and cough and cough." (72, F)

Table 2 Reported comorbid conditions

Comorbid Conditions	Total ($n = 90$)
Gastroesophageal reflux disease (GERD)/Acid reflux	42%
Heart condition (congestive heart failure, high blood pressure, previous heart attack, etc.)	38%
Anxiety/depression	31%
Obstructive sleep apnea (OSA)	26%
Obesity	24%
Chronic obstructive pulmonary disease (COPD)/Emphysema	14%
Diabetes	14%
Pulmonary hypertension	13%
Asthma	11%
Cancer	8%
Pulmonary infection	2%
Pulmonary embolism	2%
None of the above	12%

Impact of symptoms associated with IPF on life activities

Based on responses received from the qualitative interviews, survey participants were presented with a set of statements about various common activities and asked whether they agreed with each statement. All statements were phrased in the negative for consistency. 64% of participants agreed with at least one of the quality-of-life statements that are shown in Table 3. When male participants and female participants were compared, the only statistically significant difference was in responses to the statement, "My IPF has negatively impacted my relationships with my partner;" 28% of male participants agreed compared to 7% of female participants. There were no other numerical trends in responses to these challenging scenarios by sex. There were more striking differences in responses by people who received care in CPPs versus in ILD centers. Numerically, higher numbers of participants receiving care in CPP agreed with these negative statements on quality of life compared to those in ILD centers, with a significantly higher number of participants agreeing with the statements "I have trouble keeping up with my family, friends, children and/or grandchildren because of my IPF" and " My IPF has impacted my basic personal hygiene (showering, brushing teeth)."

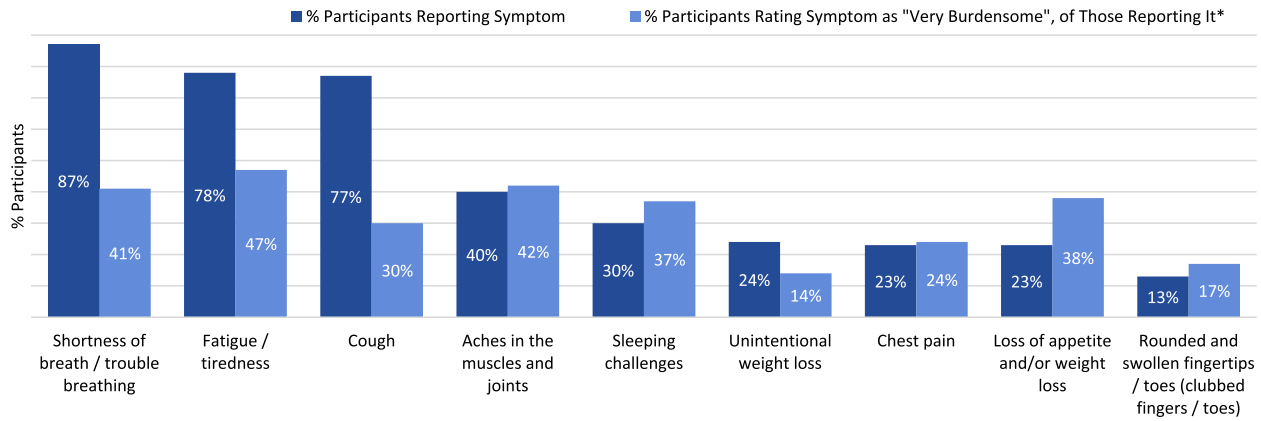

Fig. 2 Participants Reporting Symptoms and Burden Associated with IPF. Legend 2: All *N*=90 participants were asked to select which symptoms of IPF they have experienced. Only participants who reported experiencing a given symptom were asked about its burden.*"Very burdensome"= Percent of participants who rated each symptom a score of 6 or 7 on a 7-point scale of burden

"Everything changed when I got sick.... I can't go swimming anymore. Just walking to the car takes me completely out of breath. I'd walk them [dogs] over to the grocery store and now I can't. I can barely walk to the car. It's really impacted my quality of life." (63, F)

"The physical symptoms now I notice even just doing simple work around the house, sweeping the floor, I'll notice I get breathless. If I am trying to keep up with my dogs on a walk, they walk faster than I do sometimes, and I get winded. I was surprised the other day, I volunteered at a local wildlife refuge. I had to return a driver's license to a bird-watcher. The birdwatcher was walking with his 80-something-year-old mother, who was using a cane, and I couldn't catch up with them. That was trouble. I can't walk as fast as a person who's 80-year-old and walking with a cane. That bothered me." (68, M)

"I've tried to play golf and by the time I get out of the cart and go hit the ball and get back in the cart, my oxygen drops to 70. Even on oxygen. I can't do much." (71, F)

"I have taken to heart what several doctors said to me is don't give up my lifestyle. Don't give up socializing. Don't give up going places." (73, F)

"I can't do things that I used to do. I have to watch my wife do the yard work that I always love doing. All I can do now is watch and I hate it. I taught her well though." (70, M)

"Well, last year I went out and got a handicap pass for my car, which I never thought I would do, but again, when I'm out and about in the summer, I definitely take advantage of that. I'm in the gym three times a week. I'm never not going to not do that because I think it's important and I think it helps slow the progression. I have noticed some breathlessness when I'm going up or down the stairs. With New York City subways, if there's a station, I get off at that has an elevator, I'm more inclined to take an elevator than I ever was." (66, M)

"Well, at this point in time I can't do very much at all. Even with 3 antifibrotic of oxygen, I can't walk 25 steps outside to the garbage can without getting out of breath. Just going out to the mailbox at the curb is a major thing…I got a woodworking shop that's probably worth $100,000 to be able to [build pipe organs] and the pulmonologist has told me now,"Do not do woodworking."" (76, M)

Impact of participants' IPF on their caregivers

In the qualitative interviews, participants shared perspectives on how they thought their IPF diagnosis impacted their caregivers. Participants perceived the

Table 3 Agreement with quality-of-life statements

	Total ($n = 90$)	ILD ($n = 45$)	CPP ($n = 41$)
I have trouble keeping up with my family, friends, children, and/or grandchildren because of my IPF	49%	38%	63%*
I struggle to complete basic housework tasks because of my IPF	47%	36%	56%
I am no longer able to do hobbies and activities I enjoy because of my IPF	44%	38%	56%
My IPF has negatively impacted my independence	39%	31%	49%
I can no longer travel because of my IPF	33%	31%	39%
I chose not to go to a major family event in the past 12 months because of my IPF	30%	31%	29%
I had to stop working earlier than I planned because of my IPF	27%	24%	29%
My IPF has impacted my basic personal hygiene (showering, brushing teeth)	19%	11%	29%*
My IPF has negatively impacted my relationships with my closest family and friends	19%	13%	24%
My IPF has negatively impacted my relationships with my partner	18%	11%	27%

"Agreement" = Percents of participants who responded to agreement statements with a score of 5 through 7 on a 7-point scale

*Statistically significant compared to those treated at ILD centers

mental and physical tolls of taking care of a person with IPF. In the survey, almost 20% of participants agreed with the statements "My IPF has negatively impacted my relationships with my closest family and friends" and "My IPF has negatively impacted my relationships with my partner."

"I don't think I could have another husband. I have honestly, the best husband I could probably have as somebody living with IPF. His love language is acts of service so that is so helpful...He probably gets really frustrated because I get so frustrated with my own body and how it's like turned on me...I feel sorry for him because he didn't sign up for this, but I have good qualities. I try to think that I make up for it in other ways." (48, F)

"[My husband] takes care of appointments. He basically just takes care of everything. Keeps my oxygen going. I'm sure this isn't what he wanted to do in his retirement, but he's not resentful at all. He takes care of me. He's taken over most of the cooking. The thing that's getting us through is we both have a pretty good sense of humor and that's really helped. Because if you don't, you're going to just crawl up in a corner and turn into a raisin." (71, F)

"My wife's always worried constantly. With her working and me being home alone she always worries that I'm going to fall or lose my breath and not get it back. There's a lot of worry. My daughter worries. My granddaughter worries. My grandson worries. They check on me a lot." (70, M)

"When I bring home groceries, he [husband] knows to come help because making trips back and forth to the car and carrying groceries – and to carry anything with weight to it, it uses my oxygen that quicker." (58, F)

"[My husband] is very involved. I'm really private and so, he likes to go with me in my appointments because he feels like I won't tell him stuff unless he goes and hears it himself...He likes to know what's going on. He doesn't like to read anything about IPF because he thinks that it's all too depressing." (72, F)

"My husband's way of coping with that was – we came home, and he started booking trips. I'm like,"I know what you're doing."He's going to take us to all the bucket list places before I die in three years, which is what Dr. Google says." (71, F)

Use of supplemental oxygen

Supplemental oxygen use was reported by 54% of survey participants and 27% of this group reported using it all the time. Supplemental oxygen was perceived to be helpful in improving IPF symptoms but also contributed to the burden of IPF (Table 4).

"I'm prescribed 2 litres. Sitting down, watching TV, I don't use any. If I'm cleaning the house and stuff like that, then I use 2 to 3 to 5. If I go to town, I leave it dead set on 2 to 3. At home, I don't use it very much." (58, F)

"I can't keep up with my daughters and their kids like going hiking on the trails and stuff we have around here... It takes too much oxygen for me to have a portable to go. My little concentrator, the portable one, doesn't provide enough for me to be very active." (63, F)

"I was on oxygen for about a year, and I hated it. I hated putting it on. I hated wearing it. I was only on oxygen for a year. It was awful. It was cumbersome and it was embarrassing." (48, F)

"Well, I'm an amateur radio operator. Ham radio, as they call it. I do a lot of that now because I can't get out the house very much. I'm confined now with oxygen. I'm on 3 antifibrotic of oxygen and while have a portable concentrator, they can put out 3 antifibrotic. It's almost as big as the one I have in my house. Very hard to travel with so I don't spend a lot of time out in the street." (76, M)

"If I don't have oxygen, I'm done. I just don't get enough air in. Oh, it's terrible. I got to have a hose wound on my neck. Only good part is my wife can always find me. Just follow my hose. When I sleep if I roll over, I get tied up in it. My cats like to play with it. Easy to trip over so a pain in the ass. Yes, I wouldn't recommend it." (70, M)

"I go to pulmonary rehab, and they do the intake, and they say, 'You need oxygen.' I'm going, 'No, I don't need oxygen.' It turns out I was happily hypoxic." (74, F)

"Well, it's very limiting on what I can do. Plus, I have to worry about whether my battery is going to go dead. My oxygen company will either let you have the portable or bring out those bigger tanks. If I can't use the little portable anymore, then I can't fly to see my daughter. You constantly have to worry about tripping over the tubing and the grandkids when they come over getting tangled up in it or falling. I wish they'd come up with a higher concentration portable oxygen thing. I couldn't understand why they can't if we can put people in outer space." (63, F)

"Well, every time I get out of the car, I put on the backpack or get out the cart and go somewhere with the oxygen. I've been embarrassed by having it. I am old, but I don't feel that old. I've always tried to take care of myself, so I feel less of a man...Now I got the handicap sticker, the whole bit. People look at you a little different...It's like, 'Don't forget.'...It does affect your life, and it crushes your self-confidence." (64, M)

"I use oxygen whenever I'm out and about. Usually at home, it's not necessary unless I get up and get busy sweeping my family room because I don't have any carpet in my house. That's exhausting. Every few minutes I have to stop and go breathe on my oxygen tank for a few minutes and then go back to what I'm doing." (58, F)

Participation in pulmonary rehabilitation or independent exercise

In the qualitative interviews, participants often expressed a desire to be active and a belief that physical activity was beneficial to their health. In the survey, 34% of respondents participated in pulmonary rehabilitation and 64% engaged in exercise. Participants receiving care in ILD centers were numerically more likely to have participated in pulmonary rehabilitation (42% versus 24%) and exercise (73% versus 56%) compared to those receiving care in CPP, although these differences were not statistically significant.

"I'm in the exercise clinical study, and I'm exercising and it's improving my lung function. I did a yoga clinical study as well. We did these breathing techniques and that made a huge difference. Huge. I think the yoga might have even made a bigger difference than the exercise." (68, M)

"One of the other reasons that I swim every day is because both my pulmonologist and my PCP have said to me that they think that I'm still alive because of swimming. I don't know if you were ever a swimmer or not. When you swim you take deep breaths, which expand your lungs as much as you can. You hold it and then, you blow it out through pursed lips the same way you do during a pulmonary function test or when you go to pulmonary rehab. I'm doing that every single day. I'm not sure that it is the swimming that's making me stay healthy." (72, F)

Table 4 Agreement with statements for participants who used supplemental oxygen

	Total (*n* = 49)
Oxygen helps improve my IPF symptoms a lot	78%
I can no longer participate in my hobbies and things I love because of my need for supplemental oxygen	53%
I am embarrassed that I need to bring my oxygen with me when I leave my home	33%
I rarely leave my home because of my need for supplemental oxygen	27%
I often struggle with accessing enough oxygen	14%

"Agreement" = Percents of participants who responded to agreement statements with a score of 5 through 7 on a 7-point scale

"I stay fit in pulmonary rehab. I still have an athletic build. I'm very positive." (74, F)

"Right now, I feel so good because I'm not doing anything. I'm just doing oxygen and doing the best I can to stay fit in pulmonary rehab." (74, F)

"I'm learning breathing techniques and physical therapy and the things I can do to be stronger for this." (48, F)

Provider-patient communication for participants who had never initiated antifibrotic therapy

Thirty-one survey participants (34%) had never been exposed to pirfenidone or nintedanib (Table 1). There were no significant differences between those receiving care at ILD centers versus CPPs. Female participants were significantly more likely never to have been treated with an antifibrotic than male participants (51% vs 19%).

Thirty-two percent of those who had never been treated with antifibrotics reported that their doctor never talked to them about antifibrotic treatments, while 48% reported that their doctor mentioned both treatment options and 19% reported only having one treatment option mentioned. Of the participants who had discussed antifibrotics but not yet started one, 35% reported that this was the physician's decision or recommendation, 23% stated that it was their decision or preference, and 42% reported it was a combined decision between the participant and their physician. Participants ranked reasons for not starting an antifibrotic from a list derived from qualitative interviews and the most common reason selected was "I am waiting to start treatment until my symptoms worsen" (Fig. 3).

"'I want to see if I can tolerate the two drugs that might have an impact.' He said, 'No, I won't prescribe that for you because it'll make you sick. Don't sacrifice your lifestyle while you still have real good lung function. Wait until it gets worse.'"(73, F)

"It rather surprised me. He said, 'You can go with no medication although these two medications had been shown to slow up IPF.' Since, at that time, I wasn't showing much symptoms other than a cough, I turned down taking either medication and I called him back two or three months later and said, 'That was a silly choice of mine. Let's talk about it.' Next time I saw him, we talked about it, and he literally gave me the choice of either one. He said, 'The research has shown that both can be effective depending on the person and we don't know which one will be best for you. Just choose and here are the side effects.'" (68, M)

"I don't know that I heard anything else she had to say except she wanted me to be on medication, one of the two medications. I said, 'No, I'm not taking medication that doesn't promise a cure. It just slows progression when I have absolutely no symptoms.'"(66, M)

"My local [pulmonologist] did not want to put me on any antifibrotic. Because number one, you're going to have a lot of side effects. I thought, 'Well, okay.' He goes, 'I've had people that have lost a lot of weight.' I think, 'Okay, well, I could stand to lose weight.' He says, 'No, I'm not going to put you on it.' I go up there to [a second pulmonologist] …and it's the first thing out of her mouth. 'We're going to start you on an antifibrotic.' I was talking to my daughter about it. I said, 'This is a deal. If I cannot tolerate it, I'll go off it. I least owe it to myself to try it.'"(74, F)

"I went to another pulmonologist in early 2021, who agreed with the allergy doctor that my lung function was so high. He told me, 'The only thing to do for this disease is start taking one of two drugs that are so intolerable. I have never, ever had a patient be able to tolerate them and I refuse to prescribe that for you. Just wait until your lung function decreases and then, come back to see me.'" (73, F)

Provider-patient communication for participants who initiated antifibrotic therapy

Fifty-nine survey participants (66%) had ever been exposed to one or more antifibrotic (Table 1). 23% of survey participants had only ever taken pirfenidone, 32% had only taken nintedanib, and 10% had taken both via switch. Sources of information about each antifibrotic are shown in Table 5.

Seventy-five percent of participants treated with antifibrotics reported that their doctor had mentioned both antifibrotic treatment options, while 25% reported only one was mentioned. Significantly more participants treated at ILD centers reported that their doctor had mentioned both antifibrotic treatment options (93%) compared to those treated at CPPs (57%). Conversely, significantly more participants treated at CPPs said that their doctor just mentioned one option (43%), compared to those treated at ILD centers (7%). Of the participants treated with an antifibrotic and who reported that their doctor told them about both pirfenidone and nintedanib (n = 44), 23% reported that their doctor made the decision about which antifibrotic to start, 55% reported that they made the decision together with their doctor, and 23% reported that their doctor did not share a strong opinion and allowed the participant to make the decision. Table 6 lists the percent of

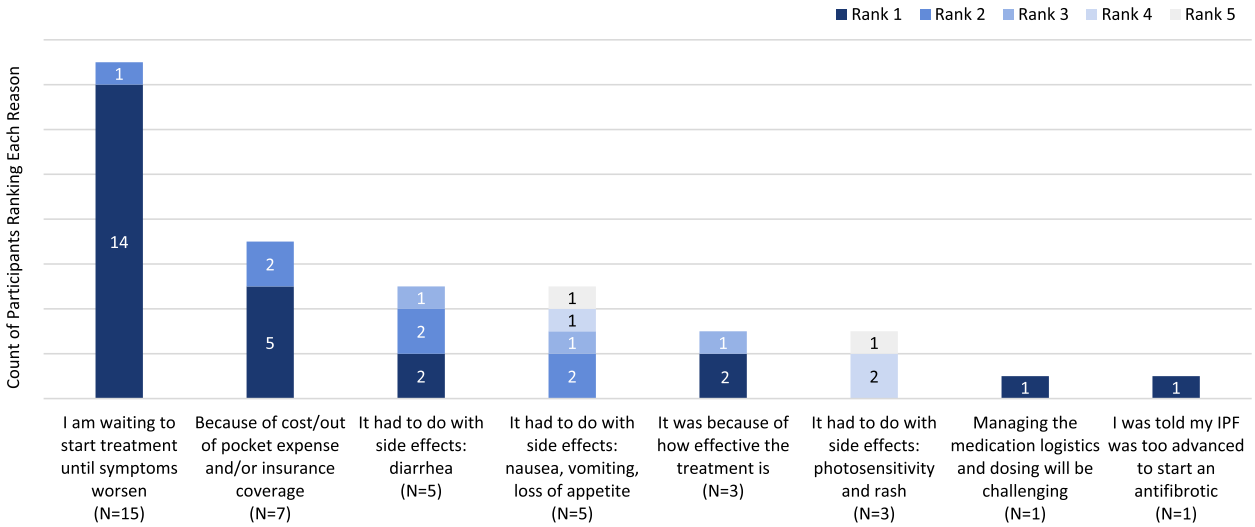

Fig. 3 Reasons for not Starting an Antifibrotic Medication, of Those Never Treated with an Antifibrotic. Legend 3: Participants who were never treated with an antifibrotic (*N*=31) were asked to rank reasons for not starting an antifibrotic, from the most relevant reason (Rank 1) to the least relevant reason (Rank 5). Survey participants were only required to rank one of the options. This figure shows all reasons that >1 participant selected

participants who agreed with various potential reasons for selecting a specific antifibrotic.

Significantly more male participants (82%) described feeling very confident in their understanding of antifibrotic treatment options, including dosing and side effects, compared to 57% of female participants. When recalling how their doctor discussed the timing of starting antifibrotic treatment, 78% of participants who started pirfenidone reported that their doctor wanted them to start treatment right away compared to 69% of those who started nintedanib. 15% of those starting pirfenidone reported that their doctor did not share a strong opinion and allowed the participant to make the decision about when to start, compared to 25% of those starting nintedanib. 78% of participants starting pirfenidone expressed that they wanted to start treatment right away compared to 84% of those who started nintedanib. A significantly higher percent of participants taking pirfenidone (77%) reported being very satisfied with their treatment compared to those taking nintedanib (45%).

"The way he brought [the antifibrotics] up was very unbiased. He brought them up both just, 'Here are your options. Here are the facts. This is what you can expect from this one. This is what you can expect from this one and pluses.' Just basically pluses, minuses, this is what you got. It was very unbiased and very much my choice." (48, F)

"It's like, 'We think that this might help slow the progression down. Some people it slows it down. Some people it actually stops it. We think.'" (71, F)

"As far as how they work, he told me they were about the same. It wasn't like, 'Oh, this one's a whole lot better than the other one.' It was like, 'You pick.' Here's the different side effects for me to pick. That's one reason I was disappointed with the doctor. His knowledge is what I wanted because I didn't have any." (69, M)

"Just that Esbriet or Ofev were the only two treatment options, and they were just to slow the progression, not to cure anything. That there were lots of potential side effects." (63, F)

"Well, he said, 'There's a medicine out there now, and I'd like you to try it.' Something like that.
I don't recall any other medicine being mentioned... What he had stated was, 'This certainly isn't a cure. This medicine is intended to slow it down. Slow down the effects of IPF.' That's the way I understand it. He told me it might make me nauseous, tired, body aches, muscle aches...I decided immediately that I'll put up with any side effects there are because I want something to help slow this disease down. I want to live like everybody." (64, M)

"That [IPF] was terminal. That they had medicines that can slow down the progress and that he wanted to start me on one. He asked me, which one I wanted to start on, and I told him that that's why they paid him the big bucks, so I let him pick it." (58, F)

Table 5 Sources of information about antifibrotics, among those treated with antifibrotics

	Pirfenidone (Esbriet) (*n* = 59)	**Nintedanib (Ofev) (*n* = 59)**
My doctor informed me	71%	75%
I discovered it from my own research	12%	14%
I heard about it from another person with IPF/support group	7%	3%
I am not aware of this medication	8%	8%
A family member or friend discovered it and informed me about it	2%	0%

"I got home and I told my daughter and my wife what was going on, my daughter decided she was going to get on the internet and try to figure out – she started joining groups and support groups and stuff and she came up with the idea that there was this drug called Ofev. The pulmonologist never recommended this or told us it was not available or anything. My daughter went to the pulmonologist, raised hell with her and said, 'Why aren't you giving my father Ofev?' She said, 'We can do that.' She said, 'It's got side effects and it's very expensive and insurance doesn't cover it.' They didn't cover it at the time.... Well, she said, 'That's a serious drug. You can have a lot of nasty side effects from it.'" (76, M)

Perceptions of the role of antifibrotics in IPF

Sixty-seven percent of participants taking pirfenidone and 61% of participants taking nintedanib agreed with a statement that their antifibrotic is slowing the progression of their IPF. The narratives suggested an acknowledgement that participants could not be sure that their antifibrotic was helping them since it did not cure the disease or make them feel significantly better.

"There's a magic eight ball when you're a kid. It's a little black ball and you turn it upside down. The little thing spins and gives you a reading. It's a mystery how it comes up. It's the same thing with Esbriet and Ofev. It is a mystery because how fast would my progression have been if I hadn't been on them? Who knows? How fast has it been? I can measure how fast it's been taking Ofev and then Esbriet because I take breathing tests. But how fast would it have been without them? Anybody's guess. I think there's no way for anyone to know if these medications are effective for them." (68, M)

"That [the antifibrotic] would give me some more time. There's nothing else I could do. You can't get a lung transplant. If it goes bad, I don't think they'll give you lungs. You either do this or you do nothing." (70, M)

"From what my doctor says, it's slowed it down a lot. But as far as I know, I haven't got no clue. I just feel like I can't catch my breath. If it's me all the time, I don't notice any big changes. It's always subtle. That I might get to live longer. My wife wants me around, so I guess I have to do what she says." (70, M)

"If it slows it down, I'm all for it. But I don't know how you prove that it's working...Of course, I don't like taking medicine, but I was all for it. If this is going to slow this illness down, I'll do it. That's a tough question to answer. I've got the illness. I've lasted a long time, which makes me think it's probably working...Certainly not curing it because I'm getting worse." (64, M)

"I really felt like I was preventing an acute exacerbation, and I worry about those a lot. Because I know that that's what kills people like me. It's those acute exacerbations. Even people that are stable like I am." (48, F)

"I've always felt that I won't go off of it because I'm doing really well for someone that was diagnosed with this disease. It's eight and a half years and I'm doing really well. I don't know if it's working or not, but I'm not about to give it up. I'm grateful for it. I'm really grateful that I have this medication." (72, F)

"…to my knowledge, all it does is prevent further scarring or slow down further scarring that it wasn't going to make anything any better. It seems to have stopped any progression of the disease." (65, F)

"You can't tell. They can't prove it to me one way or the other because I haven't gone without it since I've been diagnosed. I don't know. I know I didn't have any decrease for two years so I'm very thankful for that." (69, M)

Hope

The majority of participants taking antifibrotics (78%) agreed with a statement that their antifibrotic gives them hope.

"I'm hoping Esbriet is slowing my progression. I'm still progressing. I'm still getting worse over time. I'm hoping Esbriet is slowing that effect of what it would be without it." (68, M)

"It's what I had hoped for. A hope that I'm putting off the decline of the lung function even further by taking the medication." (73, F)

"That there was hope that maybe I might be able to prolong the effects of the pulmonary fibrosis." (63, F)

"Three times a day is a bit of a challenge, but I figured out how to do that. It makes me tired, but I'm at a stage in my life where it's okay to be tired and okay to kick back. It's what I had hoped for." (73, F)

Adverse effects associated with antifibrotic treatment

Similar percents of participants taking pirfenidone (87%, Fig. 4a) and nintedanib (92%, Fig. 4b) reported at least one side effect from a list derived from qualitative interviews. Side effects varied in terms of the perceived burden experienced by participants. For example, 50% of participants taking pirfenidone reported fatigue as a symptom, and more than half of those participants (53%)

Table 6 Decision to start with one antifibrotic treatment option and not the other

	Total ($n = 44$)	Pirfenidone First ($n = 21$)	Nintedanib First ($n = 23$)
It was because of how effective the treatment is	34%	33%	35%
It had to do with side effects: nausea, vomiting, loss of appetite	34%	38%	30%
It had to do with side effects: diarrhea	20%	24%	17%
It had to do with side effects: photosensitivity and rash	20%	10%	30%
Another reason (please specify)	18%	29%	9%
It had to do with dosing and managing the medication logistics	16%	5%	26%
Because of cost/out of pocket expense and/or insurance coverage	18%	24%	13%

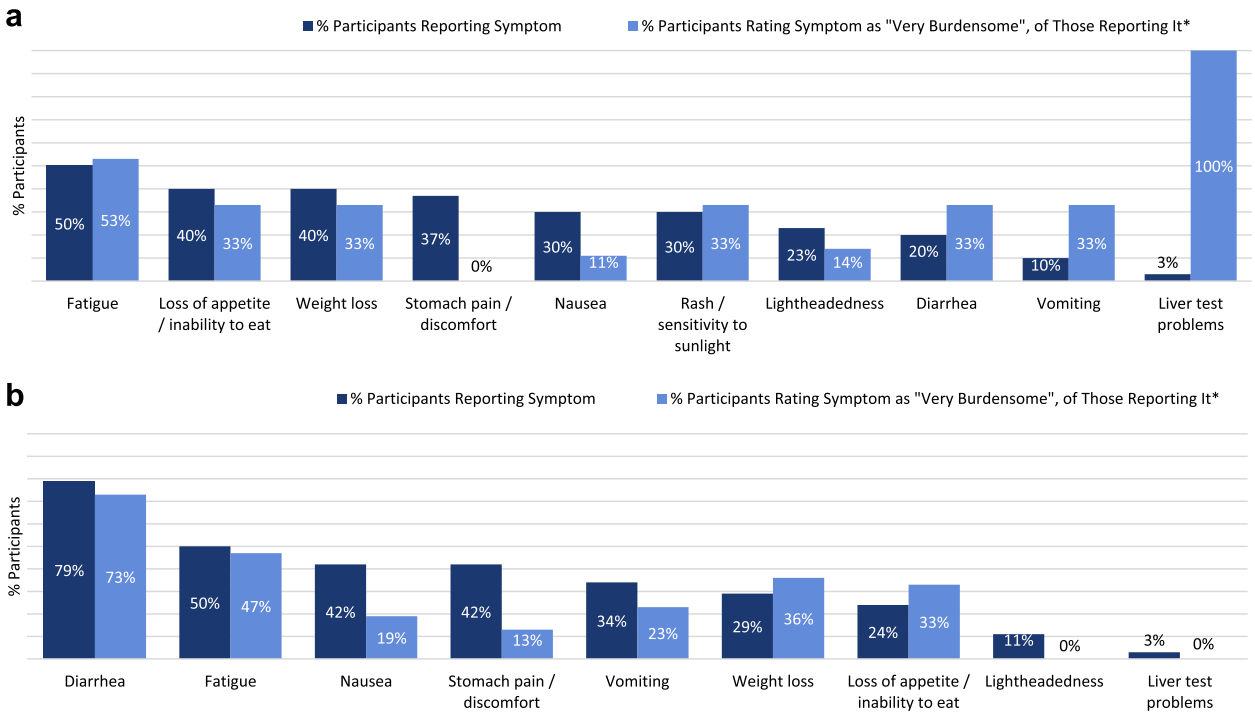

Fig. 4 **a** Side Effects and Burden Associated with Pirfenidone. Legend 4a: Participants who have ever taken pirfenidone to manage their IPF (*N*=30) were asked about the side effects they have experienced with that medication. Only participants who selected a given side effect were asked about its burden. *"Very burdensome"= Percent of participants who rated each side effect a score of 6 or 7 on a 7-point scale. **b** Side Effects and Burden Associated with Nintedanib. Legend 4b: Participants who have ever taken nintedanib to manage their IPF (*N*=38) were asked about the side effects they have experienced with that medication. Only participants who selected a given side effect were asked about its burden. *"Very burdensome"= Percent of participants who rated each side effect a score of 6 or 7 on a 7-point scale

reported it as very burdensome. On the other hand, 42% of participants on nintedanib reported stomach pain/discomfort as a symptom, while only 13% of those participants viewed it as very burdensome. When presented with a set of statements about the perceptions of their antifibrotic medications, 23% of participants taking pirfenidone and 53% of participants taking nintedanib agreed with a statement that they struggle to manage the side effects of their antifibrotic. 30% of participants taking pirfenidone and 55% of participants taking nintedanib agreed that the side effects of their antifibrotic significantly impacted their quality of life.

Dose modification, discontinuation and pausing antifibrotic treatment

Participants frequently took lower doses than the label-indicated full dose, skipped doses, paused their antifibrotic, and/or stopped their antifibrotic while prescribed pirfenidone (57%) or nintedanib (63%) (Table 7). The median number of times participants reported stopping pirfenidone was 2, similar to the median 2.5 times reported for nintedanib. Twenty-nine percent of participants taking pirfenidone and 46% of participants taking nintedanib reported that they had modified, skipped, paused, and/or stopped their antifibrotic due to side effects that included nausea, vomiting, or loss of appetite (Table 8). Twelve percent of participants taking pirfenidone and 58% of participants taking nintedanib reported that they had modified, skipped, paused, and/or stopped their antifibrotic due to diarrhea.

I often have trouble knowing what's a side effect and what's age. For instance, right now I'm getting tired during the day relative to my normal energy levels. Is that age? Is it lack of oxygen? Or is it Esbriet? I don't know if anyone knows." (68, M)

"The other side effect of the pirfenidone that I take is photosensitivity and needing sunscreen. In general, I used to be out in the sun a lot. Now, I have a fear of it and a hatred for sunscreens… Three times a day is rough. It's eight hours apart. I need to take it just before I go to sleep, and I need to take it right when I get up. That's not always eight hours. I just find that tough to do those eight-hour increments. It would be so much easier if it didn't have to be so precise. I ask the pharmacist, 'How much leeway can I give that?' She said, 'Well, try not to give it more than half an hour leeway at all.'" (73, F)

"Well, I couldn't go out in the sun. If the sun hit any place on my skin, it would almost blister up immediately. Like in the movies. I felt like I was a vampire. I had a lot of nausea in the beginning, but I just took another pill. When I'm in the sun, I just stayed out of the sun, wear long-sleeved shirts, big, floppy hat so it never got to my skin after the first time." (70, M)

"I would have diarrhea just out of the blue and couldn't hold it. I'd have to wear a Depend or something, and it was just real stressful." (63, F)

"I'm on Esbriet. I'm not on the full dose because I really can't take the full dose. It makes me very nauseous.

My current dose is three tabs b.i.d. and I can't go any further than that because to this day, I have nausea. I know the full dose is nine pills a day. I'm on six. Right now, I'm on Zofran, which helps. When I was working sometimes, I'd wake up in the morning and from the previous night's dose I'd be so nauseous I couldn't get on the bus to go to work. It doesn't happen so much to that extent, that intensity, but I still get nauseous." (66, M)

"Oh, yes. I have all the typical stuff. They're much less now than they were initially though. The nausea and dizziness and all that stuff. I medicate with other stuff to manage side effects. I take Nexium. I take Zofran. I take Pepcid. I take stuff so that I can function normally. I tried going off Zofran about a month ago and I didn't take it for a couple weeks and I lost 7 pounds because I just wasn't hungry. It's not like that I was so nauseated necessarily. I just completely lost my appetite, so I went back on it. When you first go on this medication, your side effects are remarkably worse than they are eight years later. I used to have two. When I first went on this medication, I'd have to lie down for 45 minutes after I took each dose. I couldn't even stand up because I was so dizzy and so nauseated. I can just take it now and go about my day. I can take it in the morning after breakfast and immediately go to the pool and swim. I don't have to accommodate for it the way I used to." (72, F)

"The Ofev didn't seem to work. I took it for a year, as I said. It didn't seem to do much except give me chronic diarrhea that I couldn't even go out the house for the most part. I was living between bathrooms at the time." (76, M)

"They started me on Ofev first. I tried to take it for a year, but I had severe diarrhea. I couldn't even go out in public hardly, or I would just bomb it spontaneously. It was really bad. We even tried lower doses of the Ofev, and it still affected me that way. It got to where the side effects were causing a terrible quality of life so I just decided I couldn't do it. Not knowing when the diarrhea was going to attack and when I would just spontaneously need to throw up. Without even having nausea sometimes it would just,"Okay. I've got to throw up."I have to stop on the side of the road and throw up. I was not able to hold the diarrhea to get to the bathroom in time sometimes and that was horrible." (63, F)

"The first year was awful. You have nausea and diarrhea all the time. It was a struggle to get out of the house. It's mellowed some and I've gotten the handle on it and figured out when I'm going to have Tums, when I'm not. I'm better recognizing it and preventing it." (58, F)

"They [pulmonologist] said, 'Well, it'd be okay if [the diarrhea] ever gets out of control to stop it for a few days and then, start back.' Because I did wonder how serious that would be because every now and then, it's not often, but some will come up where I miss a dose. If it's more than two hours after you would normally take it, they say don't take it. Just wait until the next one and start then... They said 'No, it wouldn't be that serious.''Well, am I losing a month of my life by missing a dose?' I didn't know what the effect would be. Nothing tells you that saying if you miss a dose or five doses, how big a deal is it? The doctor said it's not that big a deal. You just start back, but I don't really know." (69, M)

"I occasionally miss a dose just literally forget to take it even though I carry it with me all the time. It's not like, 'Oh, I left my bottle at home.' No, I carry three pills in my pocket at all times. I can take it during the day as I eat wherever I am. But sometimes I forget." (68, M)

"I never skip it on purpose, but it does happen by accident. It can easily happen. I've done this before... where I'm not really hungry, but it's almost time for that pill. I'll make a sandwich or something. I'll eat it and then I'll forget to take the pill. I go, 'I wasn't even hungry. I just ate a sandwich for nothing because I forgot to take the pill.'" (64, M)

"Lots of times I end up not getting all three doses in. Either not at home or just not able to eat something to alleviate not getting sick." (65, F)

Table 8 Reasons for dose modification, discontinuation and treatment pauses

	Pirfenidone (Esbriet) (*n* = 17)	**Nintedanib (Ofev) (*n* = 24)**
Side Effects		
Nausea, vomiting, loss of appetite	29%	46%
Photosensitivity and rash	18%	0%
Diarrhea	12%	58%
Clinical Efficacy		
Did not think the medication was working	12%	13%
My lung function declined/tests showed progression of IPF	0%	4%
Logistics & Access		
Logistics of managing/I forgot	41%	21%
Refills were delayed	6%	4%
Cost	6%	8%
Another reason*	24%	13%

*Other reasons listed as open-ended responses that fit into one of the provided categories were reassigned without duplication. Reasons listed as open-ended responses that did not fit into one of the provided categories for pirfenidone included surgery (12%), liver (6%), and unspecified physician recommendation (6%). Reasons that did not fit into one of the provided categories for nintedanib included liver (8%) and unspecified physician recommendation (4%)

Table 7 Dose modification, discontinuation and treatment pauses

	Pirfenidone (Esbriet) (*n* = 30)	**Nintedanib (Ofev) (*n* = 38)**
I have never stopped, paused, or taken fewer doses of my antifibrotic medication	43%	37%
I occasionally skip a dose or pill(s) or have in the past	33%	29%
I have paused my antifibrotic for a period of time before restarting	13%	26%
I have consistently taken a lower dose/fewer pills of my antifibrotic than the full dose	10%	16%
I stopped taking my antifibrotic and switched to the other antifibrotic	10%	5%
I stopped my antifibrotic and have not started taking it again	7%	16%

Role of food to help with side effects associated with antifibrotics

In the qualitative interviews, participants noted the importance of taking their medications with food, including the composition and timing of their diet. In the survey, 37% of participants taking pirfenidone and 37% of participants taking nintedanib agreed with the statement "I have to force myself to eat when I am not hungry to help with the side effects."

"I drink a 30-gram protein shake... Usually, that's sufficient. It would be great if they had one extended release or something like that. I would love it. Timing it 12 hours apart like that is tough. I don't wake up hungry for example so, I have to make myself drink one of those protein shakes so that I can take my meds." (58, F)

"I see the warnings about some of the side effects. They're real. You better take it with food or you're not going to feel good. It runs my life a little bit, because sometimes I'll wake up in the morning and I'm not hungry. I might not want to eat something until afternoon, but if I do that, I got to take three doses during the day with food...I'm being forced to eat sometimes when really I'm not hungry, but you got to stay on the clock and get this medicine in." (64, M)

"He said to take it with protein. Try to have a full stomach when you take it. Pretty much it. I had to make sure I ate especially with some protein, and sometimes I didn't want to. That was a little difficult sometimes." (63, F)

"If I don't eat the right things before I take the medicine, I feel nauseous...Well, I was concerned about [side effects], but I wasn't going to let it stop me from taking it. I just made sure that I stocked up on Imodium, sunscreen, and things that I would need to deal with it...Taking three pills three times a day. I think that it affects my appetite. I'm not really hungry because lots of times I don't really feel like eating, but the clock says it's time to take the meds... You have to eat to take it, so I have to force myself to eat something protein-based so that I don't feel sick. Suggestions that I picked up from the support group is that some people just eat a slice of bread with peanut butter on it and that seems to work to help me not feel sick." (65, F)

"I'm not a big breakfast eater. I eat the same thing every day. I eat a protein bar that is 10 grams of protein and fruit. That's how I take my first dosage... one of my favorite things to eat at night is apple slices and two scoops of peanut butter. Again, a protein bar if I don't feel like figuring out something else. Cheese, anything small that's not a big deal, but I look for something that has at least 10 grams of protein. Hard boiled-eggs sometimes...I tell you when I had a little bit of light nausea – and I had morning sickness. There's something called Preggie Pops, which is for morning sickness. I got some of those just in case I need it. That takes care of it immediately. You just suck on those." (74, F)

"I found early on that if I eat something, like I was urged to do, eat protein when you take the drug, apparently sometimes I just don't eat quite enough. I eat another few bites of something or some protein drink and the nausea seems to go away right away." (73, F)

"I read enough to know that and he did assure me, 'Yes, it's better with food,' and it is. I found that already with Ofev. If I took Ofev without any food, I get sick to my stomach. Really, within 15 minutes of taking it, I'd be nauseous and couldn't eat any food at that point, which was troublesome. I had to eat it in the middle of a meal. I found with Esbriet not so much. As long as it's around food, if I forget to take it right when I'm eating and I take it 15, 20 minutes later, that's fine. Or if I take it 10 minutes before I start my meal, that's fine. It's a little more forgiving in that sense." (68, M)

Financial constraints on access to IPF care and treatment

Twenty-four percent of all participants believed their financial resources limited their ability to access the care and treatments they needed for their IPF. Of those who had never received antifibriotic treatment, 26% reported that it was because of cost/out of pocket expenses and/or insurance coverage. Participants were asked about monthly costs associated with IPF as well as costs associated with other conditions or diseases. For the participants who had been treated with antifibrotics, median expenses were $120 in total healthcare costs per month. For those who had never received antifibrotic treatment, median expenses were $60 in total healthcare costs per month.

Discussion

This study was conducted to better understand the experiences of people living with IPF in the US and the types of interventions that could help them, their caregivers, and their medical teams improve their quality of life. This research was conducted in 2023–2024, roughly 10 years after the first approval of pharmaceutical treatments for IPF in the US. Our goal was to build on data such as rates of adverse events commonly presented in clinical trials or patient-reported outcomes using standardized instruments that may not have been developed for people living with IPF in order to explore the burden and consequences of living with IPF and its treatment [11]. We included extensive quotes from the qualitative interviews to provide context to the quantitative data generated from the survey.

We focused on people living with IPF living in the Unites States because there is a substantial discrepancy between rates of antifibrotic use in the US compared to other regions, such as Western Europe, and we thought that this discrepancy could be related to multiple barriers in the care journey. We examined insights from peoples' experiences of initial symptoms to a diagnosis of IPF, engagement in ILD-specific medical care, and decisions around initiation of antifibrotic therapy to better understand facilitators of and barriers to care at each step. Some of the themes that emerged from this study have not been extensively explored in the medical literature.

Lancaster et al. found that physicians under-reported patient symptoms compared to what patients with IPF reported in that study [12]. Our study found a similar pattern of common symptoms including shortness of breath/trouble breathing, fatigue/tiredness, and cough and 30% or more rated these symptoms as very burdensome on their quality of life. These symptoms had a major impact on people's ability to engage in activities that are important to them such as keeping up with family and

friends, completing basic housework tasks, doing hobbies or activities, or maintaining their independence. The physical and emotional strain of an IPF diagnosis is also borne by caregivers [13]. Here, illustrative quotes provide insight into how people perceived the impact that their IPF diagnoses had on their caregivers and other people in their lives. Our study highlights the importance of diminishing or abrogating intolerable symptoms for patients and suggests that members of medical teams can explore the burden and consequences of such symptoms to identify potential interventions and improve quality of life.

People living with IPF described the experience of being evaluated for other causes of their symptoms (i.e., medical conditions like asthma, obesity, depression, or GERD, medications, or a history of smoking) prior to being diagnosed with IPF, and quotes illustrated their perceptions of being misdiagnosed ("I just kept getting prescribed antidepressants…"). The participants in this study reported a high level of co-morbid conditions (88% with at least one comorbidity) which likely made the diagnosis of IPF more challenging. The presence of so many comorbid conditions, while not surprising in an older patient population, suggests that careful, coordinated diagnosis and treatment by the IPF-treating provider and the rest of the patient's care team will improve their overall care. Symptom education to help patients recognize the need for prompt evaluation and avoid attributing symptoms to aging, obesity, deconditioning, prior smoking, or other comorbidities is paramount to avoid delays in diagnosis and treatment.

Delivering news of a serious diagnosis such as IPF is difficult, and the results of these interviews and survey highlight the need for improved education at the training, postgraduate, and practicing physician level to provide accurate information in a compassionate and caring manner. People living with a terminal disease like IPF need time to process the news of their diagnosis while understanding that there are options for therapy to prolong lung function and survival. Without having time to process, critical information regarding antifibrotics that slow disease progression can be lost. This was eloquently stated by the participant who said, "I don't know that I heard anything else…" after receiving a diagnosis of IPF. At the least, scripts or examples can be provided by pulmonary societies and discussed at educational seminars in national and international meetings to guide providers on delivering difficult news compassionately while not destroying hope. Support and advocacy groups need to be empowered to challenge less than optimal care or communications and help people living with IPF and their caregivers understand what optimal care entails.

Most participants reported being satisfied with the communication and education they receive from their pulmonologists about IPF, but they also sought information from the internet and pulmonary fibrosis support groups. Valid and reliable internet resources represent a high unmet need in IPF [14]. An enormous amount of unvalidated, incorrect, or outdated information lives on the internet for people exploring information about IPF to access. Processes for validation of sites that share factual data, via a "seal of approval" from respected organizations, such as medical professional societies in collaboration with advocacy groups like the Pulmonary Fibrosis Foundation, could support high quality education efforts.

This study included a higher number of people currently taking antifibrotics relative to large, claims-based US samples that demonstrate low rates of exposure to antifibrotic treatment [8]. For those taking antifibrotics, the majority felt treatment was helping to slow their disease progression, although many recognized that it may not be possible to know how much they are benefiting as an individual. Participants on treatment reported frequent adverse events for pirfenidone (fatigue, loss of appetite, weight loss, stomach pain/discomfort, nausea, rash) and nintedanib (diarrhea, fatigue, nausea, stomach pain/discomfort, vomiting, weight loss) and many of these participants rated these adverse events as very burdensome. As described in other studies, participants self-managed their antifibrotic dosing [14]. Over half of participants reported adjusting their dose of antifibrotic (lowering a dose, skipping doses, interrupting dosing) in response to adverse events, highlighting that the currently approved antifibrotic therapies pose tolerability challenges for some people and improved management strategies may improve both efficacy and quality of life.

Studies have shown improvement in quality of life for people using supplemental oxygen. In a trial of ambulatory oxygen use, 21 participants underwent qualitative interviews and over half reported benefits in less breathlessness when walking or doing daily activities, not having to stop as much when doing activities, and improvement in their quality of life because they could do more [15]. In this study, participants also highlighted the burden of oxygen that included cumbersome and heavy equipment, tripping risks on tubing, difficulty with accessing portable tanks and oxygen resources, and limited activities and travel outside the home due to challenges with equipment. With patients noting symptom improvement in dyspnea with oxygen, titrating oxygen to the flow rate that provides adequate oxygen saturation with rest and with walking or exertion is important to consider at each clinic visit as needs can change over the course of days to weeks. Symptoms of dyspnea may not occur until oxygen levels are much lower than normal so regular screening

for patients at risk should be considered. Supplemental oxygen remains a physical and public sign of illness and debility that can create embarrassment for patients. Challenges noted by these participants emphasize the need for improved education and innovation for durable medical equipment companies, patients, and medical providers.

It is notable that 78% of participants taking an antifibrotic agreed with a statement that their antifibrotic gave them hope. A European study of patients taking pirfenidone also found that people described that their antifibrotic gave them a sense of hope, but this perception was limited to those who did not report adverse effects with their antifibrotic [16]. This perception of hope contrasts with the reason given by a majority of people who had never been treated with an antifibrotic for their lack of treatment - they were waiting to start until their symptoms worsened. It is also notable that women were significantly more likely to have never been treated with an antifibrotic than male participants (51% vs 19%). These results suggest an important healthcare disparity, although paired data with health providers would be needed to fully understand reasons for delays in antifibrotic treatment. Waiting for disease progression prior to starting antifibrotics suggests a misconception that a lack of symptoms or changes in tests means no progression has occurred. Although pulmonary function testing, symptom monitoring, and chest HRCT evaluation are part of our collection of tools for monitoring IPF disease progression, stability in these tests does not assure stability at the tissue or cellular level since disease is likely still progressing. This "watch-and-wait" rationale has not been supported by professional pulmonary societies and suggests that additional educational efforts directed to pulmonologists, people living with IPF, support groups, and internet resources on the risks and benefits of antifibrotics, and how to communicate these points, may be needed. In addition, opportunities exist to educate patients about treatments as well as providers about shared decision-making. Moving to a well-informed, patient-directed approach to treatment decisions can empower patients to be active participants in their care. Shared decision-making combines disease state education and education on antifibrotic treatment expectations and side effects to allow patients to make fully informed decisions for their care with their providers.

We found a few differences in reported care between people who attended ILD academic centers and those who received care with community-based pulmonologists. More participants treated at ILD centers reported that their doctor discussed both nintedanib and pirfenidone as potential treatment options for their IPF, whereas more participants treated at community pulmonary practices reported that their doctor mentioned just one option. More participants treated at community pulmonary practices agreed with statements that reflected a negative impact of IPF on their lives. Expert centers such as those in the Pulmonary Fibrosis Foundation Care Center Network provide services such as support groups and pharmacists to offer directed education on treatment and management of IPF, which may benefit a patient's quality of life.

Limitations of this study include enrolling some participants in the quantitative phase who did not have a documented confirmation of diagnosis of IPF. We required medical records that documented a diagnosis of IPF for qualitative interviews but did not require this for quantitative surveys. We took several steps to increase the likelihood that participants had a diagnosis of IPF. About a third of survey participants did provide optional documentation and their responses were not substantially different from those who did not (data not shown). The initial health screener did not indicate which health diagnosis we were seeking and people who provided responses that were not consistent with IPF such as autoimmune diseases or immunosuppressive medications were screened out. The third-party organization that facilitated recruitment has internal algorithms to reduce the risk that an individual would participate in more than one survey and looked for data anomalies that could suggest a participant that did not have IPF.

We used established patient panels and advocacy groups that provide services predominantly to people with pulmonary fibrosis to share the opportunity to participate in the survey. This may introduce participation bias and participants may not have been representative of the general population of people living with IPF in the US. The majority had been exposed to antifibrotics, while US claims-based data suggest only 26% of people with an IPF diagnosis have ever taken an antifibrotic [8]. The survey participants were relatively well educated, which may be a reflection of the recruitment process or the requirement to have access to the internet. For the on-line survey participants, the mean time between onset of symptoms that were likely related to IPF and a formal diagnosis, at 0.5 years, was shorter than described in a large survey of physicians and patients with IPF, where the median time from onset of symptoms to IPF diagnosis was 1.7 years in the US [12]. In addition, the themes derived from a small group of interviewees may not represent the full extent of the patient experience in the areas we explored in the online survey. For example, palliative care is an important part of the experience of people living with IPF, but this form of care was not brought up in interviews and was not explored in the survey.

Conclusions

We are thankful that 106 people shared their experiences living with IPF and gave insights into challenges they face, barriers to their quality of life, and the hope they hold on to. We believe this study could be useful in a number of ways: 1) provide recognition and context for the experiences of people living with IPF, 2) offer language to help people living with IPF better communicate their experiences to caregivers and providers, 3) allow caregivers a window into common experiences that may help them better support their loved ones, 4) improve healthcare provider awareness of factors that diminish patients' quality of life and help guide solutions, 5) provide guidance to support groups to help people living with IPF better advocate for themselves, 6) help raise awareness about symptoms that could lead to an earlier diagnosis of IPF, and 7) guide patient-reported outcomes research in clinical trials to ensure the needs and experiences of trial participants are captured and ultimately, inform novel drug therapy approvals.

Abbreviations

COPD	Chronic obstructive pulmonary disease
CPP	Community pulmonary practices
FDA	Food and Drug Administration
FVC	Forced vital capacity
GERD	Gastroesophageal reflux disease
HCP	Healthcare professionals
ILD	Interstitial lung disease
IPF	Idiopathic pulmonary fibrosis
IRB	Institutional Review Board
OSA	Obstructive sleep apnea
PH	Pulmonary hypertension

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-03689-8.

Additional file 1. Qualitative Study Interview Guide.

Additional file 2. Survey Questionnaire.

Acknowledgements

We want to sincerely thank all participants for sharing their time and experiences. Taleena Koch provided technical expertise and raised awareness about the survey opportunity through Breathe Support Network.

Authors' contributions

C.G. contributed in conceptualization, methodology, data analysis, and writing the original draft; B.B. contributed in conceptualization, methodology, and data analysis; F.S. contributed in conceptualization, methodology, data analysis, and writing the original draft; E.P. contributed in data analysis, figure preparation, and revising the original draft; J.S. contributed in methodology, data analysis and revising the original draft, L.L. contributed in conceptualization, methodology, data analysis, and writing the original draft; and T.K. contributed in conceptualization, methodology, data analysis, and revising the original draft. All authors had access to all data and reviewed and approved the final manuscript.

Funding

Support for this study was provided by PureTech Health.

Data availability

The datasets used for this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Both the qualitative and quantitative protocols were submitted to the Institutional Review Board Western-Copernicus Group (Puyallup, WA; references 1–1669153-1 and 1–1719988-1), and this study was determined exempt under 45 CFR § 46.104(d)(2). The study was conducted in accordance with the principles of the Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects). A third party vendor described risks to participation and obtained consent to participate in the qualitative interviews. For the on-line survey, consent was also obtained prior to participation (Additional file 2 Survey Questionnaire).

Consent for publication

Not applicable.

Competing interests

C.G., E.P, B.B. and F.S are current or former employees of PureTech Health and L.L and T.K are consultants to PureTech Health.

Received: 9 March 2025 Accepted: 28 April 2025
Published online: 08 May 2025

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