Improving Diagnosis, Treatment and Healthcare Security for Pulmonary Fibrosis to Advance Healthy China 2030

Boehringer Ingelheim

Executive Summary

Socio-economic development, the aging population, and the impact of the COVID-19 pandemic have compounded the increasing prevalence of respiratory diseases. As a major set of respiratory conditions, pulmonary fibrosis (PF) has caused **significant disease and economic burdens** on Chinese patients, families and society, **and its prognosis is poor**. Although PF is defined as a rare disease, the number of patients worldwide with idiopathic pulmonary fibrosis (IPF) alone has reached 3 million. According to the latest data from *the 2024 Survey Report on the Diagnosis, Treatment, and Quality of Life of Chinese Patients with IPF and Progressive Pulmonary Fibrosis (PPF)* published by the Chinese Organization for Rare Disorders (CORD), there may be up to 126,000 new PF cases each year in China if calculated at an annual incidence rate of 9.7 per 100,000. The number is expected to further increase as the population ages and the incidence rate rises. Economically, the average annual direct expenditure of Chinese PF patients and their families accounts for 70.2% of household income, far exceeding the 40% threshold set by the World Health Organization as catastrophic health expenditure. Moreover, 32.4% of patient families became indebted due to the disease, further exacerbating their already fragile financial status. Moreover, there is no cure available for PF, and its prognosis compared with other rare diseases is very poor. For example, for IPF patients, the median survival is only 2-3 years from diagnosis, and the five-year survival rate is lower than 30%.

In recent years, China has attached great importance to the diagnosis, treatment, and healthcare security of PF. However, there remains challenges in the following three aspects:

1. **Low awareness of PF,** low attention paid to the diseases, late diagnosis and treatment, and poor disease management.
2. **Immature PF diagnosis and treatment system,** unnecessary patient referrals, long diagnosis time, and high misdiagnosis rate.

3. **Limited treatment options for PF,** high unmet clinical needs, and poor patient survival status.

The grim situation requires coordinated efforts of multiple parties across the entire industry chain, including medical institutions, government authorities, industry, universities, research institutes, and patients. The aims are to jointly improve patients' sense of gain, disease diagnosis and treatment level, and industrial innovation capability. To do this, we propose the following recommendations:

1. **Strengthen awareness campaigns and patient education to enhance public awareness of PF, and promote early diagnosis and treatment.** Rely on medical experts and primary medical institutions to improve public education. Conduct education activities through various channels (such as online platforms, community lectures, etc.) to cover the general public and high-risk groups. Encourage people with suspected symptoms to seek professional medical assistance as early as possible. Strengthen patient and family education together with medical experts and patient support organizations to introduce basic disease knowledge, the importance of long-term treatment plans, self-care techniques, and emergency response measures. Establish a continuous follow-up care mechanism.
2. **Optimize IPF diagnosis and treatment network, strengthen the basic diagnosis and treatment capabilities of PPF, and improve the quality of diagnosis and treatment and patients' sense of gain.** Optimize the network by promoting the building and certification of national interstitial lung disease diagnosis and treatment centers, enhancing the IPF diagnosis and treatment capabilities of local core hospitals, and publishing a diagnosis and treatment map to optimize patient care pathways. Strengthen training in lower-tier cities and primary hospitals, improve the disease awareness and early identification capabilities of primary doctors, and establish a two-way referral system to ensure timely and effective management and treatment for patients. Strengthen the groundwork to improve PPF diagnosis and treatment capabilities, including organizing experts to compile clinical guidelines for the diagnosis and treatment of PPF, standardizing diagnosis and treatment processes, and improving the level of care. Enhance the screening and early diagnosis capabilities of rheumatologists for PPF patients, especially high-risk patients. Adopt a multidisciplinary team model to develop personalized treatment plans for PPF patients, and ensure timely initiation of anti-fibrosis treatment and long-term management of the primary disease.
3. **Accelerate the market access of innovative therapies for PF, improve medical insurance policies, and enhance the accessibility and affordability**

of drugs. Promote the approval and launch of innovative PF drugs as soon as possible, include PF drugs approved overseas into China's list of drugs with urgent clinical needs, and grant priority review and approval to PF drugs to shorten the approval time. Optimize the NRDL negotiation and adjustment mechanism, prioritize the inclusion of innovative PF drugs into the NRDL, optimize the comparator selection mechanism (not selecting volume-based procurement drugs as comparators), and evaluate the value of PF drugs in comprehensive ways to fully reflect their innovative and clinical value. Improve the existing medical insurance policies for PF, continue the current policies for specialty drugs such as dual channels and separate payment, improve the reimbursement level of outpatient chronic and special diseases, and improve the medical insurance payment policies for hospitalized patients.

4. **Promote the development of patient organizations and strengthen the role of patients and patient organizations in decision-makings across the PF industry chain.** Continuously promote the development of PF patient organizations, support their growth with policies, funding and capacity building, enhance their capabilities in public education, information sharing, community support and resource assistance, and provide better services for PF patients. Give patients and patient organizations more voice in medical decision-making, actively and increasingly involve them in decision-making processes such as review and approval, NRDL inclusion and clinical use of PF drugs, and understand patient needs and fully incorporate them into the medical decision-making process to achieve "patient centricity".

1. Background

Idiopathic Pulmonary Fibrosis (IPF) and Progressive Pulmonary Fibrosis (PPF) are major types of pulmonary fibrosis (PF) that pose severe public health challenges in China. IPF is a chronic, progressive fibrotic interstitial pneumonia of unknown cause[1], occurring primarily in middle-aged and elderly individuals with higher prevalence in men. The median survival of IPF is only 2-3 years from diagnosis[2] and the five-year survival rate is lower than 30%[3]. The prognosis is poor and there is no current cure. PPF is not one specific disease but a set of conditions with similar clinical symptoms, chest imaging, and respiratory physiological changes[4].

In China, PF brings a heavy disease and economic burden on patients, families, and society. Since there is no epidemiological data in China, the Code Rare Disease Center (CORD)[5] draws data from epidemiological studies on the Korean population similar to the Chinese population, and estimates that there may be up to 126,000 new PF cases each year in China if calculated at an annual incidence rate of 9.7 per 100,000[6]. The number is expected to further increase as the population ages and the incidence rate rises. The diseases not only jeopardize the health and quality of life of patients but also place enormous psychological and mental stress on their families. Economically, the average annual direct expenditure of Chinese PF patients and their families accounts for 70.2% of household income, far exceeding the 40% threshold set by the World Health Organization as catastrophic health expenditure[7]. Moreover, 32.4% of patient families became indebted due to the disease, further exacerbating their already fragile financial status[4]. Moreover, PF patients often require long-term care, including medication, oxygen therapy, and rehabilitation, which are costly and often not covered by basic medical insurance.

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1 Interstitial Pulmonary Disease Group, Respiratory Branch, Chinese Medical Association et al. Chinese expert consensus on the diagnosis and treatment of acute exacerbation of idiopathic pulmonary fibrosis [J]. 2019.

2 Raghu G, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med. 2011;183(6):788-824

3 Vancheri C, du Bois RM. A progression-free end-point for idiopathic pulmonary fibrosis trials: lessons from cancer. Eur Respir J. 2013;41(2):262-269. doi:10.1183/09031936.00115112

4 Raghu G, et al. Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults: An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. Am J Respir Crit Care Med. 2022;205(9):e18-e47.

5 The Code Rare Disease Center (CORD) is a non-profit organization focusing on rare diseases. It was founded by Mr. Huang Rufang in June 2013. It is the largest, most influential, most international and most professional rare disease patient organization in China.

6 Chinese Organization for Rare Disorders. 2024 Survey Report on the Diagnosis, Treatment, and Quality of Life of Chinese Patients with IPF and PPF.

7 World Health Organization. Definition and measurement of catastrophic health expenditure. 2010.

In recent years, China has attached great importance to the diagnosis, treatment, and medical insurance of PF, incorporating IPF and Progressive Fibrosing Interstitial Lung Diseases (PF-ILD) into the first and second versions of the rare disease catalog, and including relevant medications in the National Reimbursement Drug List (NRDL). However, many challenges remain, including low disease awareness, an inadequate diagnosis and treatment system, high unmet clinical needs, and an inappropriate medical insurance evaluation mechanism. There is an urgent need for coordinated efforts across the entire industry chain, including medical institutions, government authorities, industry, universities, research institutes, and patients, to jointly improve patients' sense of gain, disease diagnosis and treatment level, and industrial innovation capability.

2. Status quo and challenges

2.1 Low awareness of PF, low attention paid to the diseases, late diagnosis and treatment, and poor disease management.

The first international consensus on IPF diagnosis and treatment was published by the American Thoracic Society and the European Respiratory Society in 2000. In comparison, the clinical concept of PPF was established much later, with the first international guidelines introduced only in 2022 and no Chinese guidelines yet, leading to low awareness of PPF among patients and the general public. In 2018, V. Cottin et al.[8] first proposed the concept of PF-ILD. In 2022, the American Thoracic Society released clinical practice guidelines that formally defined PPF and replaced the term PF-ILD[9]. In China, the Chinese Society of Respiratory Diseases of the Chinese Medical Association formulated the *Chinese Experts' Consensus on the Diagnosis and Treatment of IPF* in 2016, and later updated the section on acute exacerbation in 2019. For PPF, there are no formal expert consensus or clinical guidelines yet in China.

Due to low awareness of and low attention to the diseases, late diagnosis and treatment are common. From the patients' perspective, early symptoms of PF, such as dry cough and mild shortness of breath, are often subtle and similar to other respiratory diseases, leading patients to overlook them and delay seeking medical attention. Research indicates that about 70% of IPF patients are already in the late stages of the disease at diagnosis, significantly affecting treatment

8 Cottin V., et al. (2018). Progressive fibrosing interstitial lung disease: a new entity. European Respiratory Journal, 52(5), 1800795.
9 Raghu G., et al. (2022). An official ATS/ERS/JRS/ALAT clinical practice guideline: treatment of idiopathic pulmonary fibrosis. An update of the 2011 clinical practice guideline. American Journal of Respiratory and Critical Care Medicine, 206(1), e1-e70.

outcomes and prognosis[10]. Moreover, as patients are unaware of the diseases' severity, even when they experience noticeable symptoms like severe shortness of breath, they may choose to self-medicate or wait until their symptoms become unbearable before seeking medical help. This unmindful attitude towards the diseases accelerates progression and makes them harder and more costly to treat. Additionally, low public awareness of the diseases is also a significant factor in delayed diagnosis and treatment. According to a 2015 survey of IPF patients by the Pulmonary Fibrosis Foundation, fewer than 30% of respondents have heard of IPF, and even fewer could accurately describe its symptoms and caveats[11].

Meanwhile, patients have poor disease management awareness, do not pay attention to follow-up care and treatment, and lack education on self-management. Many patients lack sufficient understanding of long-term disease management after diagnosis and fail to follow medical advice for regular follow-up checkups. Reports indicate that 16.5% of PPF patients only get follow-up checks once a year or irregularly, and this proportion rises to 22.7% for IPF patients[4]. Additionally, the proportion of patients undergoing long-term standardized treatment is low. Studies show that only about 50% of IPF patients adhere to long-term anti-fibrosis therapy, while the rest discontinue treatment due to various concerns such as side effects, financial burden, or doubts about treatment efficacy. Furthermore, patient education on disease self-management is lacking. Many patients are unaware of useful tips, such as smoking less, reducing exposure to pollutants, maintaining a healthy diet, and exercising appropriately, all of which are crucial for slowing disease progression.

2.2 Inadequate PF diagnosis and treatment system, unnecessary patient referrals, long diagnosis time, and high misdiagnosis rate.

Thanks to the network built by the "Interstitial Lung Disease Center" in China, a basic diagnostic and treatment system for IPF has been established. However, in primary hospitals, IPF diagnosis and treatment needs to be standardized and the ability to manage complex cases needs to be improved. For one thing, the clinical symptoms of IPF are complex and varied. Early symptoms can be general and easily confused with other respiratory diseases. Therefore, without sufficient professional knowledge and experience, doctors in primary hospitals may miss the early symptoms of IPF. For another thing, IPF diagnosis relies on a series of complex examinations, such as high-resolution CT scans. Such tools and technologies are not universally available in primary hospitals, hindering

10 Martinez FJ, et al. Diagnosis and treatment of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. Am J Respir Crit Care Med. 2018.
11 Pulmonary Fibrosis Foundation. Public awareness of IPF survey results. 2015.

diagnosis of complex IPF cases.

As for PPF, a progressive form of PF, there are even greater challenges in clinical management. Currently, there are no formal clinical treatment consensus or guidelines in China, leading to a lack of standardized protocols and guidance for doctors. The more complex pathophysiological mechanisms, diverse clinical manifestations, and rapid disease progression of PPF make it more demanding for doctors to diagnose and treat. In clinical practice, treatment methods may vary significantly depending on regions, hospital levels, and the professional background and experience of the doctors. This inconsistency affects patient outcomes, potentially leading to poor disease control and accelerating progression. It also increases uncertainty and causes anxiety, making patients lose confidence of treatment plans or feel confused and frustrated by their frequent changes. Additionally, the lack of standardized diagnostic and treatment protocols can lead to wasted medical resources and increased financial burden.

Patients face numerous challenges in seeking medical care, including unnecessary referrals, long diagnosis times and high misdiagnosis rates. Data show that up to 84.4% of IPF patients and 74.1% of PPF patients are referred to multiple hospitals before receiving a final diagnosis[4]. This process is not only time- and money-consuming but may also delay the optimal time-window for treatment. More concerning is that 11.4% of IPF patients take more than a year to be diagnosed, and 15.4% of PPF patients take more than three years to be diagnosed[4], which increases the risk of disease progression. Misdiagnosis is also an alarming issue, with 22.4% of PPF patients having been misdiagnosed with pneumonia[4]. This not only affects the treatment outcomes but can also bring additional psychological and financial burden to patients. Misdiagnosis may also lead to unnecessary treatments and potentially worsen the condition due to incorrect treatment.

2.3 Limited treatment options for PF, high unmet clinical needs, and poor patient survival status.

Currently, the primary treatment for PF involves anti-fibrosis drugs. However, their clinical options are limited, with only two drugs ever approved globally, and their accessibility remains challenging. In China, the two drugs were included in the NRDL in 2017 and 2022[12]. Despite their inclusions, patients in some regions still face accessibility hurdles in the last mile. Such issues not only affect treatment outcomes but also increase the financial burden on patients.

Although the available drugs have been widely used in clinical practice, their

12 Official website of the National Healthcare Security Administration. https://www.nhsa.gov.cn/

efficacy and safety still have room for improvement. Nintedanib and pirfenidone do not improve lung function but only slow the progression. Additionally, their side effects are common, leading some patients to discontinue treatment due to intolerance. Data show that 62.3% and 60.7% of PPF patients believe their treatment is ineffective or experience significant side effects respectively, and the proportions are both 56.6% for IPF patients[4].

Besides treatment issues, the survival status of IPF and PPF patients is also concerning. IPF typically affects middle-aged and elderly individuals, while PPF has a broader age distribution. Most patients can only receive diagnosis after multiple referrals. Patients commonly experience anxiety, depression, and pain which severely jeopardize their quality of life. According to *the 2024 Survey Report on the Diagnosis, Treatment, and Quality of Life of Chinese Patients with IPF and PPF*, the average health utility values for IPF and PPF patients are 0.62 and 0.53 respectively, significantly lower than the value of 0.95 for the healthy Chinese population[4], reflecting the poor survival status and poor quality of life of those patients.

3. Policy Recommendations

3.1 Strengthen public and patient education to enhance awareness of PF and promote early diagnosis and treatment.

- **Enhance public education:** We recommend building a multi-layered, multi-channel education network with medical experts and primary medical institutions as core pillars. Online platforms with wide reach and fast speed can be the main channel to publish disease knowledge, symptom recognition tips, and diagnostic and treatment processes. Additionally, offline community lectures and health consultation activities can be organized to reach community levels, answering common questions and improving the effectiveness of public education. For high-risk groups, such as long-term smokers and people with a family history, specialized education plans should be developed, including regular health reminders and special screenings to enhance their self-protection awareness. Moreover, media collaboration in the form of public service advertisements and special reports can further spread knowledge about PF to a broader audience, encouraging the whole society to pay attention to and take part in the care of PF. Strive for early detection and treatment by encouraging individuals with suspected symptoms like cough and shortness of breath to seek medical attention promptly.
- **Strengthen education for patients and families:** We recommend collaborating with medical experts and patient organizations to jointly

develop and implement systematic education programs. The content should comprehensively cover basic knowledge for PF, including causes, pathology, symptoms, and treatment methods, helping patients and their families understand the basics of the diseases. Meanwhile, education should highlight the importance of long-term treatment and explain the mechanisms, side effects, and precautions of medications, which may help improve patient adherence to treatment. Training in self-care techniques, such as breathing exercises, dietary adjustments, and psychological coping strategies, are also essential to help patients improve their quality of life and reduce complications. For emergency situations such as acute exacerbations, detailed response measures should be explained to ensure swift and effective response by patients and their families. Continuous follow-up mechanisms should also be established through regular phone calls, online consultations, and outpatient checkups to help monitor patients' progression and treatment needs and provide personalized guidance and advice. Last but not least, the content should be updated promptly to reflect the advances in medical research, ensuring that patients can receive the latest and most effective information and technical support.

3.2 Optimize the IPF diagnosis and treatment network, strengthen PPF diagnosis and treatment capabilities in primary hospitals, and improve patient care quality and sense of gain.

- **Build diagnosis and treatment centers for interstitial lung disease to improve the IPF medical care network:** Promote the building and certification of diagnosis and treatment centers for interstitial lung diseases nationwide. Ensure that the centers have advanced diagnostic equipment, professional medical teams, and standardized diagnostic and treatment processes, setting a benchmark for IPF treatment. Leverage those centers to enhance the IPF treatment capabilities of local core hospitals by transferring technology and providing expert guidance. Build regional treatment centers with the advanced diagnostic techniques and management experience. Moreover, publish an IPF diagnosis and treatment map, clearly marking the location, service scope, and specialties of each treatment center. Patients can choose suitable medical institutions based on their conditions according to the map, optimizing their medical care pathways. Strengthen training for lower-tier cities and primary hospitals to improve disease awareness and early identification capabilities among doctors. Regular training sessions, academic exchanges, and remote education should be held to share the latest IPF knowledge, diagnosis standards, and treatment plans with primary doctors, enabling them to promptly identify suspected cases and provide

initial treatment. Additionally, establish a two-way referral system, clarifying the roles and referral standards of hospitals at different levels. This ensures that patients can be referred to higher-level hospitals for necessary treatment, and later return to primary hospitals for rehabilitation and follow-up care once condition stabilizes, guaranteeing treatment continuity and realizing localized management of patients.

- **Strengthen the groundwork to improve PPF diagnosis and treatment capabilities:** Organize experts to compile clinical guidelines for the diagnosis and treatment of PPF that clearly defines the diagnostic criteria, treatment principles, and follow-up requirements, providing standardized references for doctors. Promote the application of the guidelines to improve diagnostic and treatment capabilities, reducing misdiagnosis and missed diagnosis. As rheumatic diseases are common causes of PPF, rheumatologists play a critical role in the early diagnosis of PPF. Therefore, improving the screening and early diagnosis capabilities of PPF among rheumatologists is crucial. Better training should be provided for rheumatologists to ensure they understand the clinical manifestations, diagnostic criteria, and key features of PPF. High-risk patients, such as those with systemic sclerosis, rheumatoid arthritis, and other rheumatic diseases, should be given lung examinations and assessments. Moreover, develop personalized treatment plans for PPF patients through a multidisciplinary team (MDT) approach. Consisting of experts from respiratory medicine, rheumatology, radiology and pathology, the MDT can discuss patients' condition and formulate comprehensive treatment plans. During treatment, ensure the timely initiation of anti-fibrosis therapy to slow disease progression, while also focusing on the long-term management of the underlying diseases to control their active periods and reduce complications.

3.3 Accelerate the approval and access of innovative therapies for PF, improve medical insurance policies, and ensure drug accessibility and affordability.

- **Accelerate the approval and launch of innovative PF drugs:** We recommend including PF drugs approved overseas in the list of drugs with urgent clinical needs. Simplify the import approval process through mechanisms like green channels and accelerate their entry into China to better meet patient needs. In practice, a cross-departmental coordination mechanism can be established to enhance communication and collaboration among drug regulatory authorities, research institutions, and drug manufacturing companies, so that issues encountered during approval can be addressed promptly. Additionally, encourage companies to increase R&D

investment and promote the discovery of new drugs to provide more treatment options for PF patients.

- **Optimize the NRDL negotiation and adjustment mechanism:** During the adjustment of NRDL, we recommend prioritizing the timely inclusion of newly approved innovative PF drugs to reduce patient medication costs. Additionally, optimize the comparator drug selection mechanism, grant "drugs-without-comparators" designation to innovative drugs, and avoid selecting volume-based procurement products as comparators, ensuring that innovative drugs are reasonably priced to reflect their innovative and clinical value. As the NRDL adjusts and improves, we recommend formulating and publishing standards for comparator selection. NRDL negotiations should be based on a scientific, fair, and transparent evaluation system and consider factors such as drug efficacy, safety, innovativeness, and patient needs to assess the value of each innovative drug in a customized way. For PF drugs with significant clinical advantages and innovativeness, higher reimbursement level should be set to encourage continuous innovation and promote the healthy and sustainable development of the pharmaceutical industry.
- **Improve current medical insurance policies for PF:** We recommend continuing to implement specialty drug insurance policies such as dual channels and separate payment to ensure stable access and treatment for PF patients. Meanwhile, optimize the outpatient service system for special diseases and chronic diseases and enhance inpatient drug security to improve the healthcare security of patients. To address drug availability issues, we recommend that relevant authorities should develop regular procurement plans. Hospitals unable to procure on a regular basis should establish temporary procurement mechanisms, opening a green channel for rare disease drugs to meet patient needs and improve long-term accessibility. Additionally, strengthen communication and collaboration between health commissions and medical security authorities to ensure the alignment of disease diagnosis codes in medical institutions with disease names on the medical insurance platforms, resolving patient reimbursement issues.

3.4 Promote the development of patient organizations and strengthen their role in decision-making across the PF industry chain.

- **Continuously promote the development of PF patient organizations:** Policy-wise, we recommend formulating and improving policies and regulations to support the development of patient organizations and

clarifying their legal status and functions to provide them a conducive environment. Financially, establish special funds or provide financial subsidies to support patient organizations in conducting public welfare activities and service projects, and encourage donations and sponsorships to broaden sources of funding. In terms of capacity building, enhance the management and training of patient organizations, and improve their organizational development, project management, publicity and promotion capabilities, so that they can better provide education, information, community support, and resource assistance to patients. By supporting the development of patient organizations, a bridge can be built among patients, medical institutions and government authorities, which promotes information exchange and sharing, and improves patients' self-management and mutual assistance capabilities.

- **Strengthen the voice of patients and patient organizations in medical decision-making:** We recommend giving patients and patient organizations more voice in PF-related decision-making, and ensure their participation in the review and approval, NRDL access, and hospital use processes. During drug review and approval, we recommend establishing a patient consultation mechanism to hear patients' opinions on drug efficacy, safety and accessibility, and incorporating them into the decision-making process. In NRDL negotiations, invite patient representatives to take part and share patients' medication needs and affordability, promoting the optimization and adjustment of the NRDL. In hospital use, optimize patient participation mechanisms and invite patients' opinions and suggestions on medical services and drug availability to improve service quality. In this way, the principle of "patient-centricity" is honored and medical services of higher quality and efficiency can be provided.

4. Conclusion

In summary, improving disease awareness of PF, enhancing diagnostic and treatment capabilities, and ensuring the accessibility and affordability of anti-fibrosis drugs are critical topics related to the health and well-being of patients and the development of the healthcare sector.

Boehringer Ingelheim is a global leading biopharmaceutical company founded in Germany in 1885. With expertise and scientific leadership in various therapeutic areas over the past 140 years, the company has been dedicated to the principle of Sustainable Development for Generations (SD4G). Committed to patient-centric innovation, Boehringer focuses on the research and development of innovative drugs for PF, giving a ray of hope to the patients. As Boehringer celebrates the 30th anniversary of its presence in China in 2025, the company will continue to

work with the Chinese government, share international experiences, and foster collaborations to create a better future for PF patients, contributing to the realization of Healthy China 2030.