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COMMENTARY

Why Living with Pulmonary Arterial Hypertension Requires a Holistic Approach: A Patient and Clinician Perspective

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ABSTRACT

Pulmonary arterial hypertension (PAH) is a rare disease caused by high pressure in the blood vessels leading from the heart to the lung. PAH affects many parts of a patient's life, which means that patients should be managed by a clinical team of different specialists, including doctors, advance practice providers, nurses, social workers, and therapists. This article is co-authored by a patient living with PAH and an acute care nurse practitioner specializing in the management of patients with pulmonary hypertension. In the first section of this commentary, the patient describes her experience of living with PAH. The specialist nurse practitioner then discusses the management of PAH, to provide a clinician perspective in the context of the patient's experiences.

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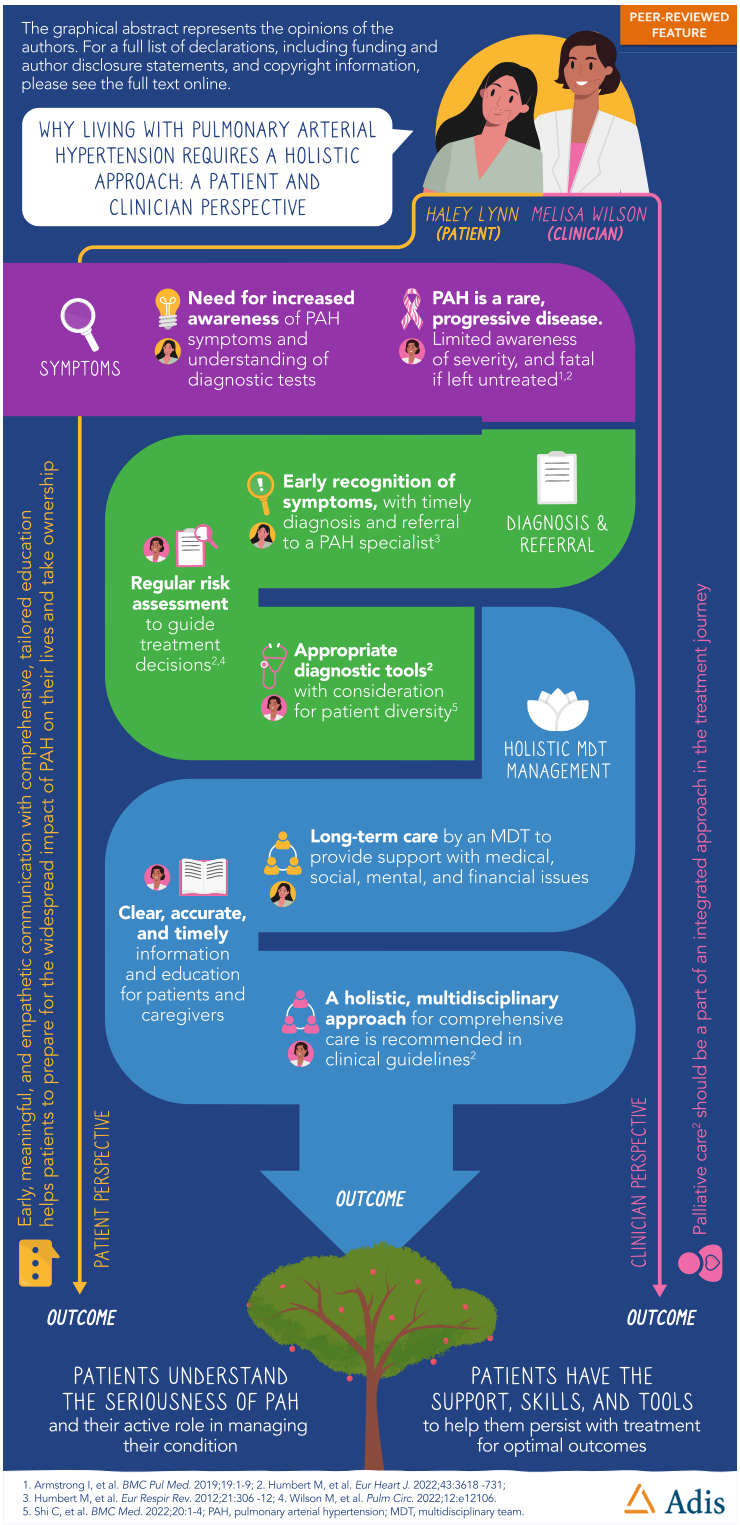
Graphical Abstract:



PLAIN LANGUAGE SUMMARY

This article describes the experience of a young patient with pulmonary arterial hypertension, or PAH, as well as the point of view of a PAH specialist nurse practitioner. PAH is a rare disease caused by high pressure in the blood vessels leading from the heart to the lung. This means the right side of the heart needs to work harder to pump blood through the lungs, which can make it weaker and eventually cause right heart failure and death. Although PAH cannot be cured and gets worse over time, effective treatment can delay worsening, reduce symptoms, and improve quality of life. Recognizing symptoms and diagnosing PAH early is important so that patients can be referred to specialists who understand PAH and can provide the most appropriate treatment. A patient's risk status shows the chance of the disease getting worse and the patient dying. The aim is to treat patients so that they stay low risk and improve their chance of living longer. Clinical guidelines give specialists advice on treating patients with PAH and say that regular risk assessment is important to guide treatment decisions. Because PAH affects many parts of a patient's life, the guidelines also say that patients should be managed by a clinical team of different specialists including doctors, advance practice providers, nurses, social workers, and therapists. Making sure that patients and carers understand PAH and the benefit of treatment is also important to help patients follow their treatment plan and actively help to manage their disease.

Keywords: Pulmonary arterial hypertension; Patient perspectives; Clinician perspectives

Key Summary Points

Pulmonary arterial hypertension (PAH) is a rare and progressive disease that can lead to fatal right heart failure.

Early diagnosis and referral to PAH specialists allows optimal management of patients with PAH.

Clinical guidelines recommend that there be regular risk assessment to inform treatment decisions and that patients are managed by a holistic, multidisciplinary team.

Understanding the benefits of PAH treatment can help patients follow their recommended treatment plan.

DIGITAL FEATURES

This article is published with digital features, including a graphical abstract, to facilitate understanding of the article. To view digital features for this article, go to https://doi.org/10.6084/m9.figshare.21732365.

PATIENT PERSPECTIVE BY HALEY

How It All Began

I experienced my first symptoms of pulmonary arterial hypertension (PAH) when I was 11 years old and running in my gym class; I nearly passed out. For the next 7 years, I struggled through middle school and high school while the adults around me thought nothing more of it than "just asthma". Carrying out normal

physical activities was challenging, such as climbing the stairs and walking to class. It was also difficult not having an explanation when friends and teachers asked why I was struggling to breathe. At the end of high school, I passed out during rehearsals for graduation and told my dad that I was having anxiety about climbing the many stairs to collect my diploma. My parents had been largely unaware of how bad I was, as most symptomatic episodes were happening at school where I was active; at home, I would just mask my struggles. As a child, I did not know how serious my symptoms were, and neither did my parents; this made it easier for us all to downplay the situation—no-one in my family had experienced anything like this before. This period in my life also coincided with changes at home and starting middle school, and I think that some of my symptoms were seen as a reaction to upheaval.

My PAH Diagnosis Experience

Finally, just before my high school graduation, my father witnessed a painful episode of my breathlessness, brought on simply by walking through a parking lot, which had me struggling to keep up with him. The severity of this incident prompted him to advocate for a cardiology appointment; he had to persevere to get the appointment because the cardiologist's office was hesitant to schedule a patient as young as me. At the consultation, the atmosphere seemed rather blasé to me, until my oxygen saturation test results came back measuring 85%. Rather than feeling concern, I felt validated at hearing what most people would consider troubling news. The cardiologist originally thought I had an atrial septal defect because of the echocardiogram and bubble test results. A right heart catheterization procedure was scheduled a couple of weeks after the original consultation (and 2 weeks after I turned 18 years of age, in 2010), to get measurements for the hospital that was going to patch the suspected defect. As staff cleared away equipment in the laboratory after the right heart catheterization, and the overhead lights came back on, the cardiologist told me there was no hole in my heart and revealed the more serious diagnosis of PAH. He simply stated the diagnosis, said that there was no cure, and explained that we had to start treatment immediately or I would not make it to 20 years of age.

After my PAH diagnosis, I was referred to a pulmonologist for PAH management, which included chest X-rays every 3 months, regular lung function tests and blood work, as well as occasional 6-min walking distance tests. I also saw the cardiologist for cardiology-related issues, including having an annual echocardiogram. My pulmonologist was great, but he did not feel it was appropriate for him to handle the long-term management of my condition; he wanted me to be managed by a PAH specialist. However, I was living in a small part of Texas at the time, and the nearest specialist willing to see me was 13 h away, in Houston. Therefore, my pulmonologist continued to treat me and did the best he could.

Being young and newly diagnosed, I failed to understand the severity of my PAH diagnosis. I was in denial as I watched my friends move on to attend college, go hiking in canyons, get engaged, and have babies, while I sat through scans and walked laps in hallways. Seeing my friends achieve their societal expectations, I felt slighted, and I was angry that my life did not resemble theirs. It was like waking up one day in a new, dark world where nothing made sense, and life could not continue as it had before; it was a monumental and desperate mental struggle. Instead of showing how I really felt, and asking for the support I needed, I projected a convincing image of a "strong survivor" and "advocate" for PAH; I did this while barely taking my medication, rejecting PAH therapies, cancelling appointments, and resisting doctors' advice.

Turning a Corner

I was referred to the University of New Mexico's PH Specialty Team in 2016. I came in not even able to remember when my last echocardiogram or walk test had taken place, and I tried, but failed, to hide from my new team that I took my medications only when I felt I needed them or

had the time. My doctor introduced herself with a sheet of paper in her hand, drawing out each type of pulmonary hypertension (PH) and circling the category my diagnosis belonged in. This was the first time I had a specialist talk to me with no assumptions of my prior knowledge and really explain, from the ground up, what PAH was and what to expect. For the first time since my diagnosis, a doctor made sure I understood that PAH was progressive, and that this meant it would get worse. She then brought my new team in one by one, explaining each of their roles. These included two nurse practitioners—one nurse case manager handling clinical aspects and one handling insurance specifically. I was also assigned a social worker who spent 30 min with me asking questions I did not even know were relevant, including whether I was in therapy (which I was not) and how I was coping emotionally. My social worker became an essential partner in my treatment, recommending therapists and encouraging me to face and deal with my brain health issues.

For me, this was the first facility where communication was not coming at me in an incomprehensible speed, but was instead an empathetic group experience. My PH team explained everything clearly, checking to make sure that I understood everything we discussed and providing educational materials on PAH for me to take away. I remember one leaflet focused on things to avoid unless you had first consulted your doctor, such as having anesthesia, flu medication, or dental work. This highlighted for me the wider impact of PAH on many different areas of my life, which was something I had not thought much about until then. My increased understanding was transformative; it was like a whole new world where PAH had a history, an explanation, and rules. My role as "just a patient" fell away as I began to realize that I needed to be an active participant in my own healthcare; this was not a job only for my doctors. I still left the consultation room as a non-adherent patient, but a seed had been planted in my mind—my new team had expectations and they actively wanted and needed me to help them, help me. When a new therapy was added to my treatment plan that required a monthly pregnancy test, I protested heavily that I would have to do this every month before receiving my prescription. My doctor called to discuss why this step was necessary, and ended the call with, "I know, you feel as though this disease is taking over your life." That was all it took in that moment because my doctor could hear and see what I was struggling with as a young woman, and I felt that I was finally being listened to and understood.

Researching Effective Patient Care

I feel that when patients have a lack of awareness of PAH (which is a rare disease), authentic communication, and empathy from healthcare workers can be the beginning of, and also the biggest missing piece in, a patient's new world and can help patients to grasp their changed reality. In my experience, initial communication was rather bare. I was told the name of my condition and what I had to do to stay alive; I do not feel that it was clearly explained from the beginning that this disease was going to bleed into every part of my life, causing a domino effect of consequences that would need to be addressed. When I did my own research, I found an article by Dr. Helen Riess [1] highlighting the importance of empathy in clinician–patient interactions, and describing the consequences of lack of empathy, including the resulting lack of trust, non-adherence, and, consequently, poor health outcomes.

For me, the result of not having this deep understanding was that I was living in denial, being non-adherent, and reaching for ways of coping that were ultimately destructive. Eventually, with my PAH uncontrolled, intravenous therapy became my only option. I feel I lost many years—and caused irreparable damage to my heart and lungs—because of not having a strong foundation of knowledge from which to become competent at self-care and self-advocacy. Sadly, I believe that my experience is not unusual, and I have seen similar stories repeated in online forums.

Listening to podcasts introduced me to four core principles in patient care [2], all of which resonated with my experience: the patient's

dignity; the concept of suffering; the patient's independence; and the patient's dependence (the feeling of being a burden). As a non-adherent patient, I was not only battling my illness, but also facing confusion, grief, anger, poverty, and other issues. I was unable to participate in my own healthcare without first receiving help in dealing with these other issues. I went to therapy and was diagnosed with complex and recurring post-traumatic stress disorder. After I started on intravenous therapy, I watched as many of my friends died from their PAH. Learning how to cope with these losses and their emotional impact without resorting to unhelpful behaviors was an essential stage in my journey and understanding of how trauma was impacting my brain health. I undertook the hard work in coping with trauma, with support and consistent communication with my specialty team. Ultimately, I came to a deep understanding of my PAH, found relief with embracing that there is no "normal", and became the strictly adherent patient I am today (Fig. 1).

What About the Future?

Based on my experiences, I believe it is essential that patients have a strong foundation in education about their disease. There should be no assumptions as to what a patient already knows, especially with relatively young patients who likely have little real understanding of chronic or severe illness, or even their own mortality. Doctors should be aware of this and should consider whether patients are in the right mindset to absorb what can be a deluge of complex and frightening information. Discussions and explanations should happen right from the start, ensuring at all times that the patient has a full understanding of the disease, what treatment is recommended for it and why, and what the natural course is likely to be—including the importance of adherence to treatment and the potential consequences of non-adherence. I also think that disease education should be addressed as early as possible, so that patients can begin to grasp their new reality. Finally, I believe that management of patients with PAH should be a holistic and integrative approach; it should acknowledge and address the substantial mental health impact that being diagnosed with a rare, life-limiting, and life-threatening disease can have, regardless of whether or not the patient realizes there will be such an impact. Armed with this support, patients with PAH will have the tools to be active participants in managing their disease, and to be effective advocates for themselves and others.

CLINICIAN PERSPECTIVE

Diagnosing PAH

Haley's journey with PAH began in the pediatric setting where, in more recent years, pulse oximetry has been recommended for improved and early detection of congenital heart defects [3–5]). Pulse oximetry is a simple, non-invasive tool, making it particularly suited to primary care and pediatric settings. It may have helped to discover Haley's diagnosis sooner, when seen alongside hypoxia and other signs and symptoms of PAH. Normal values for oxygen saturation tests using pulse oximeters are considered to be 95% or higher. However, in the pediatric setting, it has been suggested that the normal range (at standard altitude) should be considered to be between 97 and 100%, with values of 95% and 96% prompting further investigation to assess whether there is an underlying cause [6, 7]. With regards to analyzing pulse oximeter test results, healthcare professionals should be aware that readings may be less accurate in people with dark skin versus light skin. This can lead to an overestimation of oxygen saturation, and, potentially, a missed diagnosis [8, 9]. Similarly, the impact of darker skin tones on the appearance of cyanosis, a classic symptom of PAH, should be considered [10]. Cyanosis presents as a relatively dark blue tint on light skin but may be whitish or gray on dark skin. It may therefore be more accurate to assess mucous membranes and nailbeds for signs of cyanosis in patients with darker skin. For cases in which PH is suspected in a child or young adult, guidelines advise that electrocardiogram and

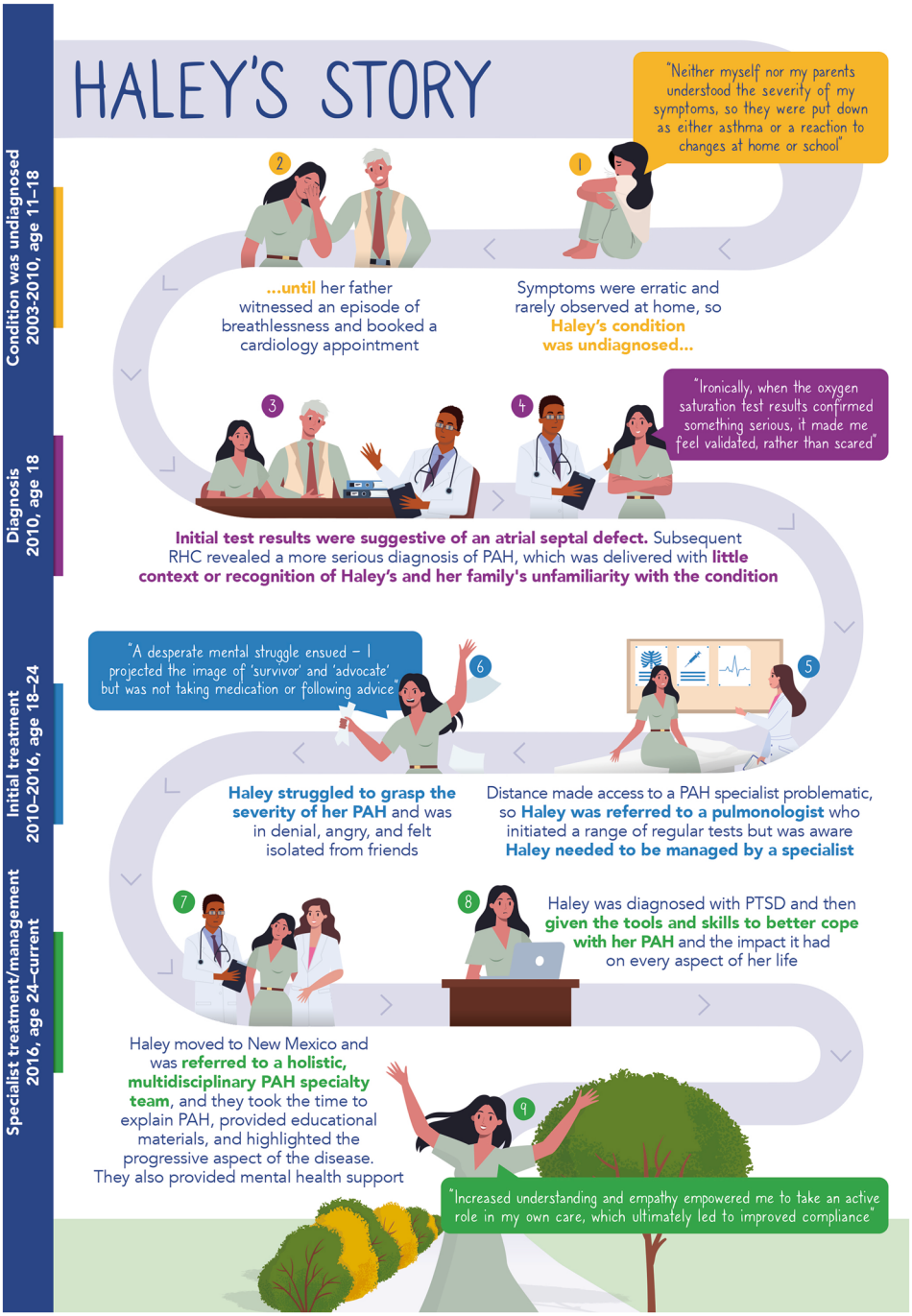


Fig. 1 Haley's patient journey with PAH. *PAH* pulmonary arterial hypertension, *PTSD* post-traumatic stress disorder, *RHC* right heart catheterization

echocardiography be conducted for screening. If the results of these analyses suggest PH, a chest computed tomography and/or chest X-ray is indicated, with cardiac catheterization, to confirm a PH diagnosis [5].

Haley described having a bubble test, or bubble contrast echocardiography; these are

routinely conducted for diagnosis of congenital heart defects such as atrial septal defects [11]. In the normal heart, right and left chambers are separated but in people with atrial septal defects, the blood can flow from right to left, and bubbles injected into a vein will appear on the left side of the heart, rather than being confined to the right side. PAH is a rare disease, with a reported prevalence of around 10 per million individuals in the United States, although this may be an underestimation [12] due to the generally non-specific symptoms. However, the combination of congenital heart defects with PAH is not uncommon, with PAH occurring in 4–28% of patients with congenital heart defects [13]. Given the rarity of PAH, neither patients nor their parents/guardians are likely to be aware of this chronic condition or, as in Haley's case, have any family members with the disease. This highlights the importance of clear, accurate, and timely information and education for patients/caregivers, without making assumptions about what they may already know. The benefits and potential risks of treatment should be carefully explained, and patients should be signposted to quality self-education resources that they can access in their own way and time, especially as a diagnosis of PAH can be both devastating and difficult to comprehend all at once.

Tackling Treatment Non-adherence

In the real-world setting, non-adherence to PAH-specific medications has been reported in around 25–40% of patients across different studies, but these estimates may vary according to type of medication [14–16]. Reasons for non-adherence in PAH can be multifactorial and complex [16, 17], but non-adherence can be exacerbated if the severity and potential consequences of suboptimal PAH management are poorly explained by healthcare professionals and/or are not well understood by patients/caregivers. Haley's experience of non-adherence is not unusual. Younger patients in particular may feel "well" and may not understand the need for, or value of, following prescribed treatment or the substantial health risks associated with non-adherence. Irrespective of treatment type, patients who manage to adhere to their PAH treatment experience better outcomes than those who do not; the consequences for failing to take medication can be life-threatening [16, 18]. Given the potentially dire consequences of non-adherence, there is a growing number of programs and initiatives to facilitate treatment adherence, including implementation of self-care management contracts [19, 20] and integrated specialty pharmacy approaches [21]. Early, comprehensive, and ongoing education is critical to convey the seriousness of the disease and the importance of adhering to recommended treatment [22, 23].

There are also educational strategies for healthcare professionals who treat patients with PAH, to improve their competence in facilitating medication adherence [24]. Every healthcare professional on the patient's team has a role in enabling the patient's adherence, by providing information and support, and possessing a real understanding of what is driving non-adherence in individual patients. For example, if a patient is reluctant to use a pump-based medication delivery system, fearing that it would be large, noisy, intrusive, and embarrassing, showing them the size and discreteness of a real working pump could help to allay such concerns. It is also important to discuss with patients/caregivers the medication options and the different formulations. Many adherence issues are based around knowledge, so it is essential that patients/caregivers have a practical understanding of their treatments, and that they know what to expect and how to manage potential challenges that may arise.

The Changing Landscape of PAH Management

Outcomes for patients with PAH have improved with advances in disease management, including improved screening for earlier detection, risk assessment to guide treatment strategies, and increased effectiveness of therapeutic options. Over the past 40 years, 1-year survival rates have increased from 65% to between 86 and 90% [25]. Recent guidelines for PAH

highlight the utility of three-strata risk assessment tools for initial assessment at diagnosis, but now recommend use of four-strata risk-assessment tools at follow-up, which better discriminate within the intermediate-risk group to guide treatment decisions [26]. Using four-strata risk assessment, 1-year and 5-year survival rates range from 93 to 97% and 65 to 67%, respectively, for patients at intermediate–low risk, and from 86 to 91% and 44 to 47%, respectively, for patients at intermediate–high risk (Table 1) [27, 28]. Guidelines recommend that patients should be treated with the aim of attaining or maintaining low-risk status [26]. While PAH is a progressive and currently incurable disease, healthcare professionals should highlight to patients that the range of treatment options means achieving low-risk status to optimize survival is an attainable goal for many patients.

With a number of PAH-specific medications now available, along with risk-profile guided management [26], there is an increasingly individualized treatment approach that considers the patient profile when selecting the most appropriate therapeutic options. Of note, recent guidelines have highlighted the importance of considering comorbidities during treatment decision making and acknowledged that in some cases achieving low-risk status may not be possible. For example, sleep apnea can contribute to PH and affect prognosis [26]. Health education should reflect this evolving treatment landscape and the natural history of PAH. For example, education should be tailored to ensure that patients/caregivers understand that while a simple approach may be

Table 1 Risk category and associated 1-, 3- and 5-year survival rates from two studies using a four-strata risk-assessment tool [26–28]

Determinants of prognosis	Low risk	Intermediate–low risk	Intermediate–high risk	High risk
Points assigned	1	2	3	4
WHO-FC[a]	I or II[b,c,d]	–	III[b,c,d]	IV[b,c,d]
6MWD, m	> 440[b,c,d]	440–320[b,c,d]	319–165[b,c,d]	< 165[b,c,d]
BNP, ng/l	< 50[b,c,d]	50–199[b,c,d]	200–800[b,c,d]	> 800[b,c,d]
NT-proBNP, ng/l	< 300[b,c,d]	300–649[b,c,d]	650–1100[b,c,d]	> 1100[b,c,d]
1-year survival rates, %[e]	99[b]	97[b]	91[b]	78[b]
	98[c]	93[c]	86[c]	75[c]
3-year survival rates, %[e]	91[b]	82[b]	63[b]	48[b]
	89[c]	81[c]	63[c]	45[c]
5-year survival rates, %[e]	83[b]	67[b]	47[b]	33[b]
	75[c]	65[c]	44[c]	31[c]

6MWD 6-min walking distance, *BNP* brain natriuretic peptide, *COMPERA* Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension, *ERS* European Respiratory Society, *ESC* European Society of Cardiology, *NT-proBNP* N-terminal pro-brain natriuretic peptide, *WHO-FC* World Health Organization functional class

[a]WHO-FC I and II are assigned 1 point as both are associated with good long-term survival

[b]Baseline data from COMPERA 2.0: a refined four-strata risk-assessment model for pulmonary arterial hypertension

[c]Baseline data from external validation of a refined four-strata risk-assessment score from the French Pulmonary Hypertension Registry

[d]2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

[e]$P < 0.001$ for between-group comparisons of 3- and 5-year Kaplan–Meier estimated survival rates

Fig. 2 A holistic, multidisciplinary approach to the support and management of patients with PAH. *PAH* pulmonary arterial hypertension [25, 26, 38, 39]

appropriate in early disease, parenteral or other treatment may be required as the disease progresses. Importantly, patients should not perceive, or be made to feel, that experiencing disease progression and requiring more aggressive treatment is a failure on their part, or a reason to lose hope. Treatment outcome is a team responsibility and patients should be encouraged to persevere, to improve outcomes.

The Importance of a Multidisciplinary Team Approach in PAH Management

The wide-ranging impact of PAH on diverse aspects of patients' and caregivers' lives is widely acknowledged [29–34]. In particular, and as Haley stressed, the effect of PAH on mental health and well-being should not be underestimated. Up to 50% of patients with PAH have reported symptoms of anxiety and/or depression

in European and United States studies [35], while studies in China have reported rates of around 66–70% [36, 37]. Consequently, a holistic, multidisciplinary team approach is essential for patient management (Fig. 2), as recommended in guidelines [26]. It is important to listen, have empathy and compassion, and show a willingness to collaborate on patient care. Healthcare professionals should connect with other relevant disciplines and invite their patients to be part of that connection, so that discussions about their health and disease management can be as a partnership, with shared responsibility and accountability.

Healthcare professionals should also consider themselves an active part of their patients' lives, and should address the more personal perspective of quality-of-life issues, and not just clinical outcomes. Palliative care aims to improve health-related quality of life for patients/caregivers; it should be seen as a crucial part of the multidisciplinary team approach, alongside medication and other interventions [38]. However, the perception of palliative care as being synonymous with end-of-life care can be a barrier that needs to be addressed [40] in order to raise understanding and acceptance that it is as an integral component of overall care and best practice. Recent consensus statements provide practical guidance to healthcare professionals on how and when to incorporate palliative care in patient management and they highlight its role as part of an integrated approach across the patient journey [41].

In conclusion, PAH is a debilitating and progressive disease with widespread impact on many aspects of patients' and caregivers' lives. Patients and healthcare professionals must work in partnership to identify and implement individualized and holistic management approaches for optimal outcomes that are meaningful for patients and their families.

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