Pulmonary Hypertension: Your objective measures aren't telling the whole story

Written by The Life Science Feed Editorial Team · Published 6 September 2026 · Edited by Mara Voss

Pulmonary arterial hypertension (PAH) remains a debilitating condition, characterized by progressive remodeling of the pulmonary vasculature leading to increased pulmonary vascular resistance and right heart failure. Despite advances in targeted therapies, patients continue to experience significant symptom burden and impaired quality of life. The clinical picture, traditionally dominated by hemodynamic measurements and exercise capacity, often misses the granular impact on daily living that matters most to patients.
Integrating patient-reported outcomes (PROs) into routine clinical assessment and trial design offers a critical lens, moving beyond objective physiological markers to capture the lived experience of PAH. This shift acknowledges that how a patient feels and functions is as vital as their pulmonary artery pressure.

KEY TAKEAWAYS

- The Pivot: PROs provide a necessary complement to objective measures in PAH, offering a holistic view of disease impact.
- The Data: PROs consistently highlight the profound effect of PAH on daily activities, emotional well-being, and social function.
- The Action: Clinicians should routinely incorporate validated PRO tools to personalize treatment goals and assess therapeutic efficacy beyond hemodynamic parameters.

Pulmonary arterial hypertension is a rare, progressive disorder defined by elevated pulmonary artery pressure and pulmonary vascular resistance, ultimately leading to right ventricular failure and premature death. The disease mechanism involves complex interactions of vasoconstriction, vascular remodeling, and thrombosis, driven by endothelial dysfunction and smooth muscle cell proliferation. This pathological cascade narrows the pulmonary arteries, increasing the workload on the right ventricle, which eventually hypertrophies and dilates, losing its ability to pump blood effectively to the lungs. The clinical presentation is often insidious, with symptoms like dyspnea, fatigue, chest pain, and syncope gradually worsening, frequently leading to diagnostic delays.
Standard diagnostic workup for PAH includes right heart catheterization to confirm hemodynamic criteria, along with echocardiography, computed tomography, and ventilation-perfusion scans to identify underlying causes and assess disease severity. Current management strategies focus on targeted therapies that modulate pathways involved in vasoconstriction and vascular remodeling, such as endothelin receptor antagonists, phosphodiesterase-5 inhibitors, soluble guanylate cyclase stimulators, and prostacyclin analogues. These agents aim to improve hemodynamics, exercise

capacity, and clinical worsening events. But while these objective measures are essential for diagnosis and prognosis, they do not fully encapsulate the patient's experience.

The Limits of Objective Measures

For decades, the efficacy of PAH treatments has been primarily evaluated using endpoints like six-minute walk distance (6MWD), changes in pulmonary vascular resistance, and time to clinical worsening. These are quantifiable and reproducible metrics, providing a clear snapshot of physiological function. But a patient's ability to walk further in a clinic corridor does not always translate directly into an improved ability to perform daily tasks, engage in social activities, or experience a better quality of life. A patient might show a modest improvement in 6MWD, yet still report severe limitations in their ability to climb stairs, carry groceries, or maintain employment. This disconnect highlights a significant gap in how treatment success is traditionally defined and measured.

The focus on objective measures, while understandable from a regulatory and trial design perspective, risks overlooking the very aspects of health that patients prioritize. Patients with PAH frequently report profound fatigue, breathlessness, and limitations in physical activity, but also significant psychological distress, including anxiety and depression, and social isolation. These subjective experiences are not adequately captured by a right heart catheterization report or a treadmill test. The adaptive study programmes for PAH are beginning to acknowledge this complexity.

What Patient-Reported Outcomes Capture

Patient-reported outcomes are direct reports from patients about their health status, functional status, and quality of life, without interpretation by a clinician or anyone else. In PAH, PROs can encompass a wide range of domains, including physical function, emotional well-being, social function, fatigue, pain, and overall health perception. Validated PRO instruments, such as the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR), the Minnesota Living with Heart Failure Questionnaire (MLHFQ), or the SF-36 Health Survey, offer standardized ways to quantify these subjective experiences. These tools allow for consistent measurement across different patients and over time, providing a more comprehensive picture of disease burden and treatment impact.

The CAMPHOR questionnaire, for instance, specifically designed for PAH, assesses symptoms, activity limitations, and quality of life. It provides scores across these domains, allowing clinicians to track changes in a patient's subjective experience. The MLHFQ, while originally developed for heart failure, is also relevant given the right ventricular dysfunction inherent in PAH, capturing how symptoms affect daily life. These instruments move beyond simply asking if a patient feels better; they quantify how much better, and in which specific aspects of their life. This level of detail is invaluable for tailoring care plans and setting realistic patient-centered goals.

Integrating PROs into Clinical Practice

Incorporating PROs into routine clinical practice requires a systematic approach. This involves selecting appropriate, validated PRO instruments, ensuring consistent administration, and developing clear methods for interpreting the results. For example, a patient reporting a significant decline in their CAMPHOR activity score, even with stable hemodynamics, warrants further investigation into their functional limitations and potential interventions beyond drug titration. This might include pulmonary rehabilitation, psychological support, or adjustments to their daily routine. The advancements discussed at ATS 2026 highlight the growing recognition of holistic patient care.

The practical application of PROs can also inform shared decision-making. When a clinician presents treatment options,

discussing not only the potential impact on 6MWD but also the expected improvements in fatigue or social engagement, empowers patients to make choices aligned with their personal priorities. This collaborative approach fosters greater patient engagement and adherence to therapy. For clinicians managing complex conditions like PAH, a comprehensive reference such as the Oxford Handbook of Cardiology can be invaluable for integrating these aspects of care.

PROs in Clinical Trials and Regulatory Decisions

The role of PROs extends beyond individual patient care to the broader market of clinical research and regulatory approval. Increasingly, regulatory bodies recognize the importance of PROs as primary or secondary endpoints in clinical trials. This ensures that new therapies are not only physiologically effective but also meaningfully improve patients' lives. A drug that improves hemodynamics but leaves patients feeling just as fatigued or depressed may not offer a true clinical advantage. Trials that incorporate PROs provide a more complete picture of a therapy's benefit-risk profile.

Designing trials with PROs as key endpoints requires careful consideration of methodology. This includes selecting appropriate instruments, defining clinically meaningful change thresholds, and ensuring robust statistical analysis. The challenge lies in standardizing these measures across diverse patient populations and trial settings. But the investment is worthwhile, as it leads to a deeper understanding of treatment effects and ultimately, more patient-centered drug development. The ongoing discussions about pulmonary hypertension screening in scleroderma also highlight the need for early and comprehensive assessment, including PROs.

Challenges and Future Directions

Despite their clear utility, integrating PROs faces several challenges. One is the burden on patients, who may find lengthy questionnaires time-consuming, especially when already fatigued. Selecting concise, relevant instruments is important for patient adherence. Another challenge is the interpretation of PRO data. Clinicians need training on how to effectively use PRO scores to guide clinical decisions, moving beyond simply noting a score to understanding its implications for patient management. Electronic PRO (ePRO) systems can help streamline data collection and integration into electronic health records, reducing administrative burden and facilitating real-time monitoring.

Standardization across different centers and countries is also a hurdle. While validated instruments exist, variations in language, cultural context, and healthcare systems can affect how PROs are administered and interpreted. Developing international consensus on core PRO sets for PAH would facilitate broader adoption and comparability of data. Research is needed to establish clear correlations between PRO changes and objective clinical outcomes, strengthening the evidence base for their use. For instance, understanding how improvements in a fatigue PRO score relate to reductions in hospitalizations or mortality would further solidify their clinical relevance. The field must continue to refine how these subjective experiences are captured and utilized, ensuring that the patient's voice is not just heard, but acted upon.

> **CLINICAL IMPLICATIONS**
>
> The persistent reliance on hemodynamic metrics and 6MWD as primary indicators of success in pulmonary arterial hypertension trials misses the point for patients. While these objective measures are necessary for diagnosis and regulatory approval, they often fail to capture the profound, debilitating impact of the disease on daily life. Clinicians must recognize that a patient's subjective experience of breathlessness, fatigue, and emotional distress is not merely an adjunct to their pulmonary artery pressure, but a central component of

their illness.

Integrating validated patient-reported outcome tools into routine practice is no longer optional; it is a clinical imperative. These instruments provide a structured way to understand what truly matters to patients, allowing for more personalized treatment goals and a more holistic assessment of therapeutic efficacy. Ignoring these patient perspectives risks optimizing numbers on a chart while leaving the individual struggling with their quality of life.

The pharmaceutical industry, in turn, should prioritize PROs as primary or co-primary endpoints in future clinical trials. This shift would incentivize the development of therapies that not only improve physiological parameters but also deliver tangible, meaningful benefits to patients' lived experiences. Regulatory bodies are increasingly receptive to this, pushing for a more patient-centered approach to drug evaluation.

A comprehensive approach to PAH care demands that we listen to our patients. Their reports on how they feel and function should carry as much weight as any invasive hemodynamic measurement. This will lead to better-informed treatment decisions, improved patient satisfaction, and a more accurate understanding of what constitutes true clinical success in this challenging disease.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. 1. Luijten D, de Jong CMM, Ninaber MK, Spruit MA, Huisman MV, Klok FA. Post-Pulmonary Embolism Syndrome and Functional Outcomes after Acute Pulmonary Embolism. Semin Thromb Hemost. 2023;49(8):848-860. doi:10.1055/s-0042-1749659
2. 2. Patel SM, Kang YM, Im K, et al. Sodium-Glucose Cotransporter-2 Inhibitors and Major Adverse Cardiovascular Outcomes: A SMART-C Collaborative Meta-Analysis. Circulation. 2024;149(23):1789-1801. doi:10.1161/CIRCULATIONAHA.124.069568
3. 3. Casal Moura M, Merkel PA, Jayne D, et al. Challenges in the diagnosis, classification and prognosis of ANCA-associated vasculitis. Nat Rev Rheumatol. 2025;21(12):719-736. doi:10.1038/s41584-025-01306-w
4. 4. Patel R, Wadid M, Makwana B, et al. GLP-1 Receptor Agonists Among Patients With Overweight or Obesity, Diabetes, and HFpEF on SGLT2 Inhibitors. JACC Heart Fail. 2024;12(11):1814-1826. doi:10.1016/j.jchf.2024.07.006
5. 5. Middleton JT, Maulik A, Lewis R, et al. Arrhythmic Burden and Outcomes in Pulmonary Arterial Hypertension. Front Med (Lausanne). 2019;6:169. doi:10.3389/fmed.2019.00169
6. 6. Chen H, Taichman DB, Doyle RL. Health-related quality of life and patient-reported outcomes in pulmonary arterial hypertension. Proc Am Thorac Soc. 2008;5(5):623-30. doi:10.1513/pats.200802-020SK

LICENCE & RIGHTS

MEDICAL DISCLAIMER

This content is intended for healthcare professionals only and does not constitute medical advice. Clinical decisions must be made by qualified practitioners based on individual patient circumstances.