

“It’s that invisible illness”: Patient and clinician perspectives on outcomes in pulmonary arterial hypertension treatment

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Abstract

Knowledge of what outcomes are most meaningful to pulmonary arterial hypertension (PAH) stakeholders is limited. In this qualitative study, patients and clinicians endorsed personalized physical activity, symptoms, and psychosocial well-being as key outcomes to assess PAH treatment response, yet few are routinely measured in PAH clinical trials.

KEYWORDS

outcomes, pulmonary hypertension, qualitative research

INTRODUCTION

There have been significant advancements in treatment of pulmonary arterial hypertension (PAH)¹ and therapeutic decisions have become increasingly complex.² Hemodynamics and six-minute walk distance (6MWD) have traditionally been used as outcomes in randomized clinical trials of PAH,³ yet these endpoints may not capture what truly matters to patients. Investigations into outcomes important to patients with PAH remain scant.⁴

More recent efforts have sought to develop PAH disease-specific measures of health-related quality of life (HRQoL)^{5–8} and the composite endpoint of time to clinical worsening.^{9,10} HRQoL has only been included as a secondary outcome and is commonly plagued by

informative data missingness.¹¹ Clinical worsening has been used as a primary outcome, however with varying components and without clear or consistent impact on patients.¹²

To inform optimization of patient-centered outcomes in PAH, we conducted a qualitative study among patients and clinicians to explore treatment priorities for these key stakeholders.

METHODS

We recruited physicians and nurse practitioners from eight US Pulmonary Hypertension Care Centers (PHCCs) and adults with PAH receiving care at a PHCC

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in Philadelphia, PA. Demographics and disease characteristics informed purposeful sampling of patients and clinicians.¹³ We conducted individual, semistructured interviews to explore perspectives on PAH treatment response and trial outcomes. The interview guide was developed using existing literature and consultation with experts in PAH and serious illness survivorship and piloted before data collection. Video interviews were conducted by trained research coordinators (R. B., T. L.). Interviews were audio-recorded and professionally transcribed.

We conducted separate analyses among patients and clinicians using a combined deductive and inductive approach for codebook development and content analysis to identify themes related to existing outcomes used in current PAH studies and newly emergent themes.¹⁴ The study team jointly reviewed transcripts to expand the codebook inductively. Deidentified transcripts were uploaded to NVivo v12 (QSR International Corp.) for data management. All transcripts were dual-coded (R. B., T. L.) with disagreements resolved by team consensus. We compared final themes between patients and clinicians. Recruitment and interviews were conducted concurrently until reaching thematic saturation in each group. The University of Pennsylvania Institutional Review Board approved this study. This study is reported in accordance with the Consolidated Reporting of Qualitative Research check-list.¹⁵

RESULTS

We interviewed 11 patients and eight clinicians; interviews ranged 20–40 min in duration. Thematic saturation was reached after eight interviews in each group. Patients' median age was 60 years (interquartile range [IQR: 51–65]). Eight patients identified as women (73%), nine as white (82%), and two as Black. Patients' PAH etiologies included connective tissue disease (33%), heritable or idiopathic (17%), drug or toxin induced (8%), HIV-related (8%), portopulmonary (8%), and congenital heart disease (8%). Half of patients (54%) had WHO functional class 3 disease. The median age of clinician participants was 45 years (IQR: 42–49). Most clinicians identified as men (62%) and white (88%), and years in practice ranged from five to more than 15.

Patient-identified outcomes

Patients prioritized the impact of PAH on their daily lives through physical activity tolerance, symptoms, and psychosocial well-being. Patients felt that PAH therapy

should improve or at least maintain daily activity tolerance by addressing fatigue and breathlessness.

If I could just go to the store and look...If I could just do that without having to take a rest.

While symptoms were important, the ability to accomplish specific activity goals (e.g., household tasks, participation in leisure activities) was paramount.

Being able to live on my own, take care of my day-to-day needs without needing help from others.

Physical activity impairment negatively impacted psychosocial well-being. Patients reported feeling burdensome when activities required assistance, yet also felt socially isolated if they chose to forego such activities.

Just not being able to do normal things that I have to do every day. I'm always in pain or tired. And I try not to take advantage of people. It makes me feel guilty that they have to do more than I do.

Patients described guilt about physical limitations and the perception that PAH-associated symptoms were invisible to and poorly understood by loved ones.

It's that invisible illness that people can't physically see what's going on, so they think that you're exaggerating your symptoms and what you're going through.

Patients hoped their psychosocial well-being would improve if PAH treatment enabled them to walk further, breathe easier, or have more energy. Importantly, some patients highlighted burdens of PAH therapy itself, citing impediments to travel, employment, and socializing, though most were willing to endure treatment burdens to meet physical activity goals.

It was hard carrying my equipment...and I don't really wanna go to the office because carrying everything gets you tired...It's just a pain.

Clinician-identified outcomes

Clinicians listed clinical parameters as the most important PAH outcomes, such as assessments of right

ventricular function, 6MWD, hospitalization, and PAH risk prediction scores.¹⁶

The ideal [outcome] would be a low-risk status based off our risk calculations.

Clinicians noted that these endpoints failed to capture what they perceived as patients' priorities of functionality and HRQoL, identifying a distinction between "clinician outcomes" and "patient outcomes."

Frequently, I will see improvements on the physician's side of it. But, in reality, they don't feel any better. All these objective tests we do are what the physician wants to see. The quality of life is what the patient wants to see.

Clinicians suggested using personalized physical activity assessments to better bridge the divide between "clinician" and "patient" outcomes.

There are some really individual differences and it varies by demographic and type of patient. For younger people, functional means being able to work and take care of their family or go to school. Older people being able to enjoy a more peaceful less taxing life and retirement. Everybody's definition of functional is different.

They described opportunities to use personalized patient-centered approaches, accounting for an individual's baseline activity level and goals.

People who are feeling better do more...So by putting a Fitbit on them we can track [activity] more reliably in terms of their functional capacity.

Notably, while quality of life was acknowledged as an essential outcome in concept, there was no consensus on how quality of life should be measured.

We're not very good at applying [standardized measure of quality of life], but I think those are really, really important...It's just that we haven't had a chance to implement it...As a physician, I feel like I'm pretty quick to know if they're happy or not, or if they feel like their quality of life is good. But I think that that's something that we haven't done – establish a standardized matrix.

Clinicians considered survival important, but most emphasized limitations to its usefulness in randomized clinical trials.

Obviously mortality is [important]. But it's not viable for us to design morbidity and mortality trials in a rare disease...I don't think it's viable for us in the field to think about those as endpoints going forward.

DISCUSSION

Patients and clinicians identified distinct outcomes to assess PAH treatment response, few of which are measured in PAH clinical trials or routinely included as components of the composite outcome time to clinical worsening⁹ (Figure 1). Both patients and clinicians prioritized personalized physical activity tolerance, symptom burden, and psychosocial well-being, domains in which PAH patients are known to experience impairments.^{5,8,10} Patients highlighted burdens of therapies themselves, while clinicians emphasized clinical markers of disease severity. These results suggest that current clinical trial endpoints do not fully capture outcomes that are meaningful to both patients and clinicians.

There were important distinctions, however, in how patients and clinicians conceptualized the impact of physical activity intolerance and symptomatology. Patients described the importance of physical activity tolerance and symptoms through the lens of their daily lives. Standard measures to assess exercise capacity were less important than individualized goals, such as ability to perform one's social or occupational roles. Clinicians prioritized objective personalized assessments of physical activity. Wearable devices, such as accelerometers, can accurately monitor daily activity levels,¹⁷ and might also be utilized to serially collect patient reported outcomes and measures of psychosocial well-being. Future work is needed to operationalize and validate outcomes obtained using these methods and to incorporate personalized physical activity goals as a way to potentially bridge the divide between how patients and clinicians conceive of these outcomes.

Many domains identified in this study are captured within disease-specific HRQoL scores,^{6,7} supporting their inclusion in future PAH trials.¹⁰ Lack of consensus around the optimal PAH specific HRQoL instrument demonstrates the need for future comparative assessments and refinement of existing tools.^{10,18} A composite endpoint of clinical worsening (or clinical improvement) could be enhanced by incorporating measures of daily activity, psychosocial well-being, and symptom burden.

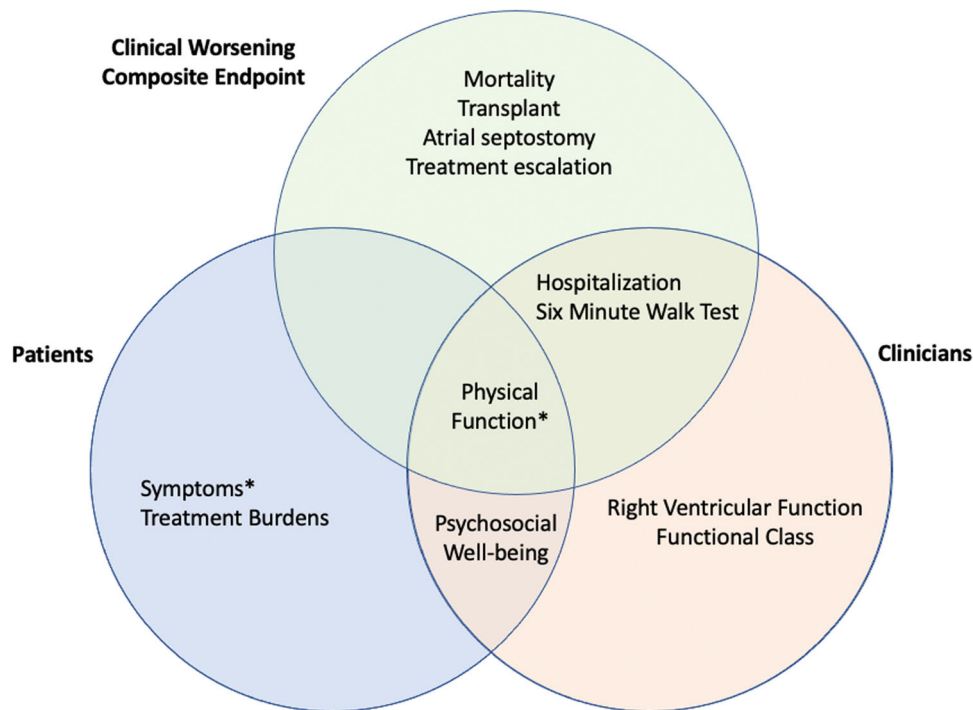


FIGURE 1 Similarities and differences in specific outcomes identified by patients, clinicians, and the components of the composite endpoint of clinical worsening. *For patients, physical function and symptoms were described primarily with regard to their impact on participation in daily life, leisure, and occupation. For clinicians, there was an emphasis on a need for standardized measures of symptoms and physical function.

Consistent with a growing literature in serious illness,^{19,20} patients with PAH may differentially value various health outcomes. Further work to quantify such valuations might allow for refinement of the clinical worsening endpoint in future trials.

The main limitation of this formative, hypothesis-generating work is its generalizability. We enrolled English-speaking and predominantly white patients from a single academic center and clinicians employed at PHCCs. Thus these perspectives may not sufficiently represent those of caregivers, PAH patients from racial and ethnic minorities, historically disadvantaged populations, or nonacademic PAH clinics. Though data saturation was achieved within both participant groups, enrolling a larger sample may have yielded additional themes.

This study's findings can inform efforts to align data collection and measurement of patient-centered outcomes in future PAH clinical trials with the priorities of patients and clinicians.

AUTHOR CONTRIBUTIONS

Randi Blue, Steven Kawut, and Katherine Courtright were involved in the conception and design of the study. Randi Blue and Tess Lapatra conducted data acquisition. All authors analyzed and interpreted the data, revised the

manuscript critically for important intellectual content, approved the final manuscript, and agreed to be accountable for its overall content.

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CONFLICTS OF INTEREST STATEMENT

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ETHICS STATEMENT

The University of Pennsylvania Institutional Review Board approved this study (#842958).

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