European Heart Journal Supplements (2019) **21** (Supplement K), K54–K59
The Heart of the Matter
doi:10.1093/eurheartj/suz208

My life with pulmonary arterial hypertension: a patient perspective

Pisana Ferrari[1] and Hall Skåra[2]*

[1]*Italian PH Association AIPI, Associazione Ipertensione Polmonare Italiana Onlus, Via Enrico Mattei, 92 - 40138 Bologna, Italy; and*
[2]*Pulmonary Hypertension Association Europe, Wilhelmstraße 19, A – 1120 Vienna, Austria*

KEYWORDS
Pulmonary arterial hypertension;
Patient-centred treatment;
Patient experience;
Patient representatives;
Patient associations;
Rare disease awareness

In recent years, there has been an increase in therapeutic options and treatment strategies for pulmonary arterial hypertension (PAH). However, patients still report delays in receiving a diagnosis, which is a significant burden associated with the disease, and which shows a general lack of disease awareness. This review has been written by two PAH patients to describe the patient experience and explore the ways in which patients are increasingly being given a voice in developing approaches to treatment. As patients with PAH are living longer, it is important that they work with healthcare professionals to develop treatment strategies that improve and maintain quality of life. Healthcare professionals should consider a holistic approach to disease management, including dietary recommendations, individually adapted exercise, and options for counselling where available, alongside therapeutic treatments. The experiences of patients with PAH are important not just for individual patient treatment but should also be considered in clinical trial design and guideline development. Patient representatives and patient associations can play an influential role in improving the treatment and management of PAH. In this review, we use our experiences as patient representatives to describe the current situation of patients with PAH from first experiencing symptoms to receiving treatment, using two patient cases as examples. We also discuss the role of patient advocacy in improving PAH care and future roles for patient associations and patient representatives in the design of clinical trials and development of new treatment guidelines.

Introduction

The patient journey from first symptoms to diagnosis of pulmonary arterial hypertension (PAH) can often be prolonged and frustrating, as PAH is a rare disease with non-specific symptoms (e.g. fatigue and shortness of breath), which may be mistaken for other common, less serious, illnesses. The survival rates of PAH have greatly increased in recent years,[1] as patients with PAH now have multiple treatment options and, if treated correctly, can expect to be managing their condition over many years.[1,2] PAH is a chronic and often rapidly progressive disease, which negatively impacts upon a patient's quality of life (QoL) and day-to-day functioning.[3–5] A survey of patients and carers with PAH across Europe revealed a large emotional, social, and financial burden associated with the disease, with patients often requiring associated support.[4]

In rare-disease management, understanding the patient perspective is an important step in identifying areas of unmet need and ways to improve patient care. Patients who are informed and active in their own care can work with physicians to improve their self-management and enjoy a better QoL.[6] Patient associations can also help provide patient support, and improve patients' understanding of their disease. For healthcare professionals (HCPs), a

*Corresponding author. Tel: +47 93 403 002,
Email: hall_skaara@mac.com

deeper understanding of the patient experience helps to identify the needs of the patient and allows shared decision-making to tailor the management approach toward patients' end goals.[7]

It is also important for regulators and guideline development groups to appreciate and understand the experiences of patients with PAH. One way to achieve this is by including patient representatives in task forces and clinical trial steering committees. In this way, experienced patients can act as patient advocates, informing and educating other patients, communicating patient experiences to HCPs, and representing the patients' viewpoints and priorities in collaborations with industry representatives and legislators.[8] The increased use of patient-reported outcomes in clinical trials, and the inclusion of patient representatives on trial steering committees, can help to capture patient response in trials of new therapies.

The aim of this article is to provide an overview of the patients' perspective of PAH management and treatment, from the point of view of two authors who are patients and through the use of two patient cases. We would also like to highlight areas where we feel that patient representatives, patient advocates, and patient associations can help to improve the future treatment and management of PAH.

The pulmonary arterial hypertension patient's journey

From symptoms to diagnosis

There is very little published research regarding the experiences of patients with PAH prior to diagnosis; however, evidence from qualitative reports and patient surveys indicates a considerable physical, emotional, and economic burden of dealing with the symptoms of PAH without a diagnosis.[9] Prior to receiving a diagnosis, patients often increasingly struggle with QoL, attempting to continue with family life and/or work, and frequently report being frustrated or stressed at being unable to understand the cause of their symptoms.[10] Without a diagnosis, patients are also unable to access social care or benefits, despite struggling with the effects of the disease. As PAH is a rare disease, patients are often not aware of it, and therefore, do not always associate the initial symptoms of breathlessness with a potentially fatal disease.[10] In a large UK questionnaire survey, over 15% of patients subsequently diagnosed with PAH experienced symptoms for over a year before going to visit their doctor.[3] A lack of knowledge concerning PAH among both the general public and HCPs has been identified by several pulmonary hypertension patient associations as a cause for concern in the pre-diagnostic phase of the disease.[9]

Once they have initially reported their symptoms to primary HCPs, patients can still struggle,[3,11,12] with many patients visiting multiple doctors prior to receiving the correct diagnosis of PAH.[3] In qualitative surveys, patients report incorrect initial diagnosis, such as asthma or chest infection to explain their breathlessness.[3,10] In our experience, some patients—particularly female patients—are also dismissed by their doctor and told they are unfit or anxious, or that their symptoms are psychosomatic and should be treated with antidepressants.[3,10] It was noted in the REVEAL registry that patients who were younger or who had a history of common respiratory disorders were most likely to receive a delayed diagnosis,[11] which suggests that these patients are in some cases incorrectly diagnosed with, and treated for, respiratory conditions to explain their symptoms of breathlessness. In older patients (over the age of 65 years), symptoms of PAH may be mistaken for normal signs of ageing.[13] Early detection and diagnosis is important for improving patient outcomes in PAH,[14] because the earlier the disease is identified, the sooner the patient can be appropriately treated and the better the patient prognosis for outcome and QoL.[15]

From conversations with other patients, we have heard that there are a wide range of emotional responses to receiving the PAH diagnosis. Sometimes the diagnosis prompts relief that a reason for their previously unexplained symptoms has finally been found; however, at the same time, it can also cause emotions such as anger, confusion, anxiety, or worry about the future. Diagnosis can also change the relationships between the patient and their family members, placing the patient into the sudden position of having an incurable disease and family members into the position of full-time carers.[16] It is important that HCPs consider the impact a diagnosis can have on a patient and their carer, and that they make sure that the patient is

Patient Case 1: Path from symptoms to pulmonary arterial hypertension diagnosis

My general practitioner did everything right when he sent me to the local hospital for further tests after I complained about shortness of breath. All my blood tests had been normal. At the hospital, I did a test on a stationary bicycle, while my heart and blood pressure were monitored. To my great surprise, the test came out normal. I had the exercise capacity expected for a man my age; however, for me, this did not feel normal, as I had been in much better shape before I fell sick. When I told the nurse that this was a surprise, she commented that maybe my expectations of what I could achieve were too high. Later, I realized that her comment was one of the reasons why I waited 2 years before I next went to my doctor with symptoms, even though I was gradually getting worse. By this time, my symptoms were obvious, as I had problems walking up two to three flights of stairs.

This time, I saw a pulmonologist at the hospital. He performed a simple test: putting an oxygen meter on my finger and asking me to walk quickly up some flights of stairs at the hospital. The sudden drop in my oxygen saturation convinced him that something was wrong. I was sent to the national hospital in Oslo and was quickly diagnosed with idiopathic PAH.

I have since met and talked with many PAH patients. Based on what they have told me, it seems like 2 years between the onset of symptoms and a final diagnosis is typical. Hopefully, awareness campaigns among both HCPs and the general population will improve this.

aware of any support services available, including patient associations, for further questions or counselling.

Management and ongoing treatment of pulmonary arterial hypertension

There are currently a range of approved treatment options for PAH suggested by the European Society of Cardiology (ESC)/European Respiratory Society (ERS) guidelines and the World Symposium on Pulmonary Hypertension recommendations for the diagnosis and treatment of pulmonary hypertension.[17,18] With proper management and treatment, today, many patients with PAH can continue to live relatively normal lives with appropriate lifestyle adaptations. A multidisciplinary review of how best to acknowledge and embrace the patient perspective of pulmonary hypertension (which included two patients as authors) suggested that HCPs should work with the patient through shared decision-making to understand and implement the patient's goals for treatment.[7] Patients often have a broader view of the impact of PAH on their overall lives than HCPs, including social, identity, financial, and emotional concerns.[19]

To address the full impact of PAH on the life of the patient, there are important management considerations beyond medical treatment of the underlying disease. Many patients report feeling insecure, isolated, and as if they are living with an invisible disease.[16] We believe that patients require time within their regular assessments to discuss not only symptoms but also the full experience of their illness in terms of the burden on their life. Depending on available resources for treatment, it may be appropriate for a nurse practitioner or counsellor to cover this aspect of patient care. In countries where access to PAH medication is still limited, or where patients are unable to afford medication, strategies to improve patient QoL beyond medical treatment are of particular importance as they may be the only treatment the patient is able to access.

Healthcare professionals should consider a holistic approach to PAH management to improve their patients' QoL, including dietary modification, exercise training, relaxation therapies, and pulmonary rehabilitation. Improvements to diet can help improve patient QoL, with PAH-related nutritional deficiencies linked to increased fatigue and exercise intolerance.[20] It is also important for patients to manage their sodium and fluid intake, and HCPs should ensure that patients receive suitable information and/or counselling concerning sodium and fluid restriction to help reduce the instance of peripheral oedema.[21] Supervised exercise training, specially adapted for patients, has been shown to improve peak oxygen consumption and haemodynamics in patients with severe PAH,[22] while lack of exercise or movement is associated with worse patient outcomes, including haemodynamic impairment and reduced survival in PH patients.[23]

As QoL is of particular importance to patients,[3] it is imperative that this outcome is captured in the design of clinical trials of new treatments. Validated pulmonary hypertension QoL questionnaires such as the emPHasis-10[24] and CAMPHOR[25] scores can be used in clinical trials to qualitatively measure patient response to treatment. The PAH-SYMPACT questionnaire is a PAH-specific QoL measure that has been developed and validated according to US Food and Drug Administration guidance.[26] The TRACE study,[27] which was designed to measure the effect of treatment on physical activity of patients with PAH using an active wearable wrist device, used the PAH-SYMPACT questionnaire as a major secondary study endpoint. In the TRACE study, a patient was included as part of the steering committee, attending all steering committee meetings, and, for instance, shared experience of how patients were likely to respond to the wrist device and suggested frequency of answering the PAH-SYMPACT questionnaire. To our knowledge, this is the first time such an approach, which ensures that the patient view point is fully captured and represented in study design, has been taken in PAH.

Healthcare professionals should also make sure that any specific patient concerns are addressed. We have found that patients are often concerned about their ability to travel with PAH, particularly at high altitudes, or to countries with a different climate. There are currently no data from randomized controlled trials regarding high-altitude safety for patients with PAH; although current guidelines recommend that patients bring extra oxygen for air travel, particularly if they are in World Health Organization functional class III or IV.[17,28] Patients should be counselled that they will need to ensure that they have enough medication supplies for their trip, and require facilities to keep medication on ice during the journey. In our experience, PAH patients should be cautious about prolonged stays at high altitude (above 1000 m) and should be especially cautious about physical activity at these altitudes, as patients have reported worsening of their illness in these conditions.

Finally, HCPs should consider the psychological aspects of a chronic illness experienced by patients with PAH.[29] A high incidence of mental health conditions, such as anxiety and depression, has been reported in patients with PH,[30,31] with between 20% and 35% of patients with PAH in the REVEAL registry diagnosed with depression.[32] As anxiety and depression in patients with PAH are often associated with an impaired QoL,[33] HCPs should make sure to address these conditions as part of patients' ongoing care.

In our experience, while patients globally report a delay in diagnosis of PAH, the treatment and management experiences of patients with PAH vary greatly both between and within countries. This is due to the differing availability of treatments worldwide, and different international healthcare systems and social services. Depending on the patient's nationality and local geography, even identifying a suitable medical facility for treatment may be challenging.[7] Differing healthcare systems between countries may lead to patients facing significant financial barriers to treatment, and, subsequently, having an increased burden of worry about managing the financial impact of the disease.[5]

Patient Case 2: Improving QoL through a holistic approach to treatment

Being diagnosed with a deadly disease at 32 years old, while 5 months pregnant with my first (and only) child, was devastating. At first, I went into total denial and even thought I had been misdiagnosed. Then came the realization, and with it fear and anxiety and many questions. How long did I have? Would I ever live to see my daughter grow up? Would I become a burden for my family? With time I found ways to cope, not only with the symptoms and physical limitations but also the psychological aspects of the disease. That is why it is so important for PH care to be holistic and take into account the overall impact of the disease. For me, yoga was very useful, especially the respiratory exercises, and helped give me some peace of mind. A few years later, I also started to practice meditation. I always made a point of having a healthy lifestyle: good food, lots of sleep, and outdoor walks surrounded by nature. I also kept myself very disciplined and organized. These measures helped me in managing reasonably well for about 12 years, after which I had to be listed for a double lung transplant. I am now 17 years post-transplant and, not only is my daughter a grown adult, but I'm a grandmother! I'm doing well and still sticking to the meditation and lifestyle routines that have worked so well for me up to now.

Patient advocacy and patient representatives

Patients who are willing to act as informed representatives have a vital role to play; from supporting other patients and caregivers living with the disease to involvement in research, drug development, and treatment guidelines. This is particularly important in the case of rare diseases where patient representatives can improve the understanding of the patient experience for HCPs, regulatory bodies, political associations, and research sponsors.[34] While we have experienced improvements in recent years in the role of the patient voice, there are still gaps in terms of real-life data to understand the patient experience, and we feel that greater focus needs to be placed on the process of shared decision-making and the role of patient associations.

The current clinical guidelines (ESC/ERS) for PAH recommend that expert referral centres should consider having a link to local PH patient associations.[17] There are a number of organizations worldwide that help PAH patient communities receive treatment and support, and provide a voice to patients and represent their interests at a political level. Patient-centred organizations can also provide opportunities for patients and carers to advocate for their own needs, and support them to participate in dialogue with HCPs, engage in policy discussions, propose solutions, and contribute to research and drug development.[7] Many patients are keen to find out more about PAH following their diagnosis and often use the internet to search for information. A quantitative survey revealed that 66% of patients used patient organizations to find further information about their disease; however, they were not regularly directed to this information by their HCPs.[4] Experienced patients can, therefore, act as an important source of information for new patients through support groups, online social media, and directing new patients to patient associations and reliable sources of information.

At a wider level, patients are collaborating with HCPs, medical registries, guideline bodies, and clinical trial sponsors to improve treatment and management guidelines. The patient association PHA Europe has effectively developed different forms of collaboration/participation with the following: EU institutions; regulatory bodies such as the European Medicines Agency; scientific societies including ESC, ERS, and the European Society for Organ Transplant; the European rare disease community (EURORDIS); leading European public health non-governmental organizations; and other PH associations around the world. In 2012, PHA Europe presented its call to action document to the European Parliament to raise awareness of the urgent needs in health policy and resources regarding treatment of pulmonary hypertension, and to explore the possibilities of EU- and national-level action to improve the QoL of patients with PAH.[35] A further call to action in 2016 on organ donation was also very successful, involving collaboration at a European level for a range of diseases for which organ donation was required, and including a PAH patient among the speakers.[36] Evidence-based on patient experience can affect guideline recommendations. For example, as a result of the large-scale European survey on the impact of PAH,[4] the ESC/ERS guidelines for PAH treatment gave a higher degree of recommendation for psychosocial support in the updated 2015 guidelines.[17]

Patients have an official role in all European Reference Networks (ERNs), including two PH patients involved in the ERN-Lung patient advocacy group. The 2018 ERN fourth annual conference in Brussels, Belgium included patient representatives from all of the ERN advisory groups to address the current state of the ERNs, along with tools and resources for using them in clinical practice. Patients and patient organizations were involved in discussions of the challenges facing integration of ERNs into the healthcare system, and solutions for consolidating the EU political and institutional commitment to rare diseases.[37] Similarly the sixth World Symposium on Pulmonary Hypertension, also in 2018, included a newly created task force dedicated to patient perspectives, which involved representatives from patient associations worldwide,[38] with a patient acting as co-chair alongside a clinical expert.

Conclusions

While there has been an improvement over the last three decades in the availability of PAH therapies and in the life expectancy of patients with PAH, there are still delays in diagnosis and a lack of awareness of the disease among

both primary HCPs and the general population. Patient goals for treatment often prioritize QoL and, therefore, HCPs should consider a holistic approach to treatment, including dietary recommendations, individually adapted exercise, and options for counselling where required. These will most likely not only improve patients' QoL but also improve their condition. It is important to maintain an active partnership between patients and HCPs to work towards the patient's treatment goals. Patient associations play a vital role in raising awareness of the disease and advocating for patients and can support and empower patient representatives. The importance of patient representatives for future research, clinical trials, and guideline development is increasingly being recognized by professional societies and institutions, and, in the future, patient associations and patient representatives will have a large role to play in improving the treatment and management of PAH.

Funding

Medical writing and editorial support were provided by Shuna Gould and Richard McDonald of Watermeadow Medical, an Ashfield Company, funded by Actelion Pharmaceuticals Ltd (Allschwil, Switzerland).

Conflict of interest: P.F. has no conflict of interest to declare. H.S. has received steering committee member fees from Actelion Pharmaceuticals Ltd.

References

1. Benza RL, Miller DP, Barst RJ, Badesch DB, Frost AE, McGoon MD. An evaluation of long-term survival from time of diagnosis in pulmonary arterial hypertension from the REVEAL registry. *Chest* 2012;**142**: 448–456.
2. Gin-Sing W. Pulmonary arterial hypertension: a multidisciplinary approach to care. *Nurs Stand* 2010;**24**:40–47.
3. Armstrong I, Billings C, Kiely DG, Yorke J, Harries C, Clayton S, Gin-Sing W. The patient experience of pulmonary hypertension: a large cross-sectional study of UK patients. *BMC Pulm Med* 2019;**19**:67.
4. Guillevin L, Armstrong I, Aldrighetti R, Howard LS, Ryftenius H, Fischer A, Lombardi S, Studer S, Ferrari P. Understanding the impact of pulmonary arterial hypertension on patients' and carers' lives. *Eur Respir Rev* 2013;**22**:535–542.
5. Zhai Z, Zhou X, Zhang S, Xie W, Wan J, Kuang T, Yang Y, Huang H, Wang C. The impact and financial burden of pulmonary arterial hypertension on patients and caregivers: results from a national survey. *Medicine* 2017;**96**:e6783.
6. Vahdat S, Hamzehgardeshi L, Hessam S, Hamzehgardeshi Z. Patient involvement in health care decision making: a review. *Iran Red Crescent Med J* 2014;**16**:e12454.
7. McGoon MD, Ferrari P, Armstrong I, Denis M, Howard Luke S, Lowe G, Mehta S, Murakami N, Wong BA. The importance of patient perspectives in pulmonary hypertension. *Eur Respir J* 2019;**53**:1801919.
8. Dunkle M, Pines W, Saltonstall PL. Advocacy groups and their role in rare diseases research. *Adv Exp Med Biol* 2010;**686**:515–525.
9. Yorke J, Armstrong I, Bundock S. Impact of living with pulmonary hypertension: a qualitative exploration. *Nurs Health Sci* 2014;**16**:454–460.
10. Armstrong I, Rochnia N, Harries C, Bundock S, Yorke J. The trajectory to diagnosis with pulmonary arterial hypertension: a qualitative study. *BMJ Open* 2012;**2**:e000806.
11. Brown LM, Chen H, Halpern S, Taichman D, McGoon MD, Farber HW, Frost AE, Liou TG, Turner M, Feldkircher K, Miller DP, Elliott CG. Delay in recognition of pulmonary arterial hypertension: factors identified from the REVEAL registry. *Chest* 2011;**140**:19–26.
12. Strange G, Gabbay E, Kermeen F, Williams T, Carrington M, Stewart S, Keogh A. Time from symptoms to definitive diagnosis of idiopathic pulmonary arterial hypertension: the delay study. *Pulm Circ* 2013;**3**: 89–94.
13. Berra G, Noble S, Soccal PM, Beghetti M, Lador F. Pulmonary hypertension in the elderly: a different disease? *Breathe (Sheff)* 2016;**12**: 43–49.
14. Lau EM, Manes A, Celermajer DS, Galiè N. Early detection of pulmonary vascular disease in pulmonary arterial hypertension: time to move forward. *Eur Heart J* 2011;**32**:2489–2498.
15. Lau EM, Humbert M, Celermajer DS. Early detection of pulmonary arterial hypertension. *Nat Rev Cardiol* 2015;**12**:143–155.
16. Kingman M, Hinzmann B, Sweet O, Vachiéry J-L. Living with pulmonary hypertension: unique insights from an international ethnographic study. *BMJ Open* 2014;**4**:e004735.
17. Galiè N, Humbert M, Vachiéry JL, Gibbs S, Lang I, Torbicki A, Simonneau G, Peacock A, Vonk Noordegraaf A, Beghetti M, Ghofrani A, Gomez Sanchez MA, Hansmann G, Klepetko W, Lancellotti P, Matucci M, McDonagh T, Pierard LA, Trindade PT, Zompatori M, Hoeper M. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Heart J* 2016;**37**:67–119.
18. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, Williams PG, Souza R. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J* 2019;**53**:1801913.
19. Alami S, Cottin V, Mouthon L, Desjeux D, Quessette E, Poiraudeau S, Sitbon O. Patients', relatives', and practitioners' views of pulmonary arterial hypertension: a qualitative study. *Presse Med* 2016;**45**:e11–e27.
20. Vinke P, Jansen SM, Witkamp RF, van Norren K. Increasing quality of life in pulmonary arterial hypertension: is there a role for nutrition? *Heart Fail Rev* 2018;**23**:711–722.
21. Zeiger T, Cobo GC, Dillingham C, Burger CD. Prevalence of sodium and fluid restriction recommendations for patients with pulmonary hypertension. *Healthcare (Basel)* 2015;**3**:630–636.
22. Ehlken N, Lichtblau M, Klose H, Weidenhammer J, Fischer C, Nechwatal R, Uiker S, Halank M, Olsson K, Seeger W, Gall H, Rosenkranz S, Wilkens H, Mertens D, Seyfarth H-J, Opitz C, Ulrich S, Egenlauf B, Grünig E. Exercise training improves peak oxygen consumption and haemodynamics in patients with severe pulmonary arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, randomized, controlled trial. *Eur Heart J* 2016;**37**:35–44.
23. Ulrich S, Fischler M, Speich R, Bloch KE. Wrist actigraphy predicts outcome in patients with pulmonary hypertension. *Respiration* 2013; **86**:45–51.
24. Yorke J, Corris P, Gaine S, Gibbs JS, Kiely DG, Harries C, Pollock V, Armstrong I. emPHasis-10: development of a health-related quality of life measure in pulmonary hypertension. *Eur Respir J* 2014;**43**: 1106–1113.
25. McKenna SP, Doughty N, Meads DM, Doward LC, Pepke-Zaba J. The Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR): a measure of health-related quality of life and quality of life for patients with pulmonary hypertension. *Qual Life Res* 2006;**15**: 103–115.
26. McCollister D, Shaffer S, Badesch DB, Filusch A, Hunsche E, Schuler R, Wiklund I, Peacock A. Development of the Pulmonary Arterial Hypertension-Symptoms and Impact (PAH-SYMPACT(R)) questionnaire: a new patient-reported outcome instrument for PAH. *Respir Res* 2016;**17**:72.
27. Frantz R, Hemnes A, Rosenkranz S, Skaara H, Pfister T, Humbert M, Howard LS. Rationale and design of TRACE: a double-blind, placebo-controlled phase 4 study in pulmonary arterial hypertension to assess the effect of selexipag on physical activity, patient-reported symptoms and their impact, in daily life. *Am J Respir Crit Care Med* 2018; **197**:A5680.
28. Thamm M, Voswinckel R, Tiede H, Lendeckel F, Grimminger F, Seeger W, Ghofrani HA. Air travel can be safe and well tolerated in patients

with clinically stable pulmonary hypertension. *Pulm Circ* 2011;**1**: 239–243.
29. Turner J, Kelly B. Emotional dimensions of chronic disease. *West J Med* 2000;**172**:124–128.
30. Bussotti M, Sommaruga M. Anxiety and depression in patients with pulmonary hypertension: impact and management challenges. *Vasc Health Risk Manag* 2018;**14**:349–360.
31. McCollister DH, Beutz M, McLaughlin V, Rumsfeld J, Masoudi FA, Tripputi M, Yaeger T, Weintraub P, Badesch DB. Depressive symptoms in pulmonary arterial hypertension: prevalence and association with functional status. *Psychosomatics* 2010;**51**:339–339.e8.
32. Badesch DB, Raskob GE, Elliott CG, Krichman AM, Farber HW, Frost AE, Barst RJ, Benza RL, Liou TG, Turner M, Giles S, Feldkircher K, Miller DP, McGoon MD. Pulmonary arterial hypertension: baseline characteristics from the REVEAL registry. *Chest* 2010;**137**:376–387.
33. Harzheim D, Klose H, Pinado FP, Ehlken N, Nagel C, Fischer C, Ghofrani A, Rosenkranz S, Seyfarth H-J, Halank M, Mayer E, Grünig E, Guth S. Anxiety and depression disorders in patients with pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension. *Respir Res* 2013;**14**:104.
34. Mavris M, Le Cam Y. Involvement of patient organisations in research and development of orphan drugs for rare diseases in Europe. *Mol Syndromol* 2012;**3**:237–243.
35. PHA Europe. *A Call to Action on Pulmonary Hypertension: The European Parliament Launch Event*. https://www.phaeurope.org/wp-content/uploads/PH-CTA-Launch-Summary-fin3.pdf (21 May 2019).
36. PHA Europe. *Event Report: Improving Organ Donation and Transplant Across the EU: A Cross-Condition Campaign*. https://www.phaeurope.org/wp-content/uploads/EP-event-ODT-report-final-3.11.2016.pdf (21 May 2019).
37. European Commission. *European Reference Networks: Conference Report*. https://ec.europa.eu/health/sites/health/files/ern/docs/ev_20181121_frep_en.pdf (21 May 2019).
38. Galiè N, McLaughlin VV, Rubin LJ, Simonneau G. An overview of the 6th World symposium on pulmonary hypertension. *Eur Respir J* 2019; **53**:1802148.