# MEETING THE NEEDS OF PEOPLE WITH PULMONARY ARTERIAL HYPERTENSION (PAH)

**Policy toolkit**

The Health Policy Partnership

This report was drafted by The Health Policy Partnership, who held editorial control under the guidance of the Steering Committee. The content is based on desk research and interviews with experts in the field of pulmonary arterial hypertension. The development of this report was initiated and funded by Merck Sharp & Dohme LLC. Experts provided their time for free.

## About this policy toolkit

The policy toolkit has been developed under the guidance of the Steering Committee through individual interviews, group workshops and written feedback. This was complemented by targeted desk research and semi-structured interviews with key experts in pulmonary hypertension and related areas of policy work. Research, drafting and stakeholder coordination were led by Karolay Lorenty, Ed Harding and Ismail Sattaoui at The Health Policy Partnership. The development of this report was initiated and funded by Merck Sharp & Dohme, who provided input into the document at key draft stages, prior to final validation by the Steering Committee.

The document aims to support multidisciplinary stakeholders to engage decision-makers and instigate policy change. The information in this resource is not intended for use in clinical decision-making or education; it is for advocacy purposes only.

# CONTENTS

# FOREWORD AND ENDORSEMENTS

Pulmonary arterial hypertension (PAH) is a rare progressive disease that, only a few decades ago, remained unnamed and unstoppable. While there is still no cure for PAH, now there is hope. Scientific advances have opened possibilities; there are new treatments available that prolong the lives of people with PAH and improve their quality of life.

But we still have so much more to do. Depending on where they live and their socioeconomic position, people with PAH may not have access to the care and treatment they need. This includes life-saving treatment, diagnostic tests and the fully equipped expert centres and teams that are so vital to effective management. Low awareness of the condition among healthcare professionals and poor implementation of diagnostic tests cause many people with PAH to wait years for a diagnosis – and to suffer irreversibly worsened health as a result. This, in turn, can drive the need for complex healthcare interventions and avoidable costs.

As a community, we have come very far in a short time. But now we need to change the conversation with our decision-makers as well as among the mainstream of healthcare professionals.

This policy toolkit aims to help PAH advocates communicate with a wider, non-specialist audience. It should help to ensure that others understand the importance of PAH and what we want to see in practice, clearly outlining the key actions we need policymakers to take. The toolkit includes core arguments for decision-makers, summarises the crucial aspects of high-quality care that people with PAH should receive, and highlights where health systems are falling short.

We have come together as a joint group from patient advocacy, clinical practice and research to guide this work. We hope these efforts help to ensure a future where nobody with PAH is left behind. But now we need you – and the PAH community – to help us communicate this work and take action where you can.

**Signed by the members of the Steering Committee, and endorsed by:**

afph ALLIANCE FOR PULMONARY HYPERTENSION

HTaPFrance ASSOCIATION DES MALADES, AIDANTS & TRANSPLANTÉS HYPERTENSION PULMONAIRE

AIPI ASSOCIAZIONE IPERTENSIONE POLMONARE ITALIANA ODV

PULMONARY HYPERTENSION ASSOCIATION OF CANADA
L'ASSOCIATION D'HYPERTENSION PULMONAIRE DU CANADA

PHA EUROPE PULMONARY HYPERTENSION ASSOCIATION

Fundación Contra la Hipertensión Pulmonar

PHA UK Pulmonary Hypertension Association UK

CORD Canadian Organization for Rare Disorders

## Steering Committee:

**Dr María Pilar Escribano Subías**
Director, Pulmonary Hypertension Reference Centre, Cardiology Department CIBERCV, Instituto de Investigación del Hospital Universitario 12 de Octubre, Universidad Complutense Madrid, Spain

**Pisana Ferrari**
President, Italian Pulmonary Hypertension Association (AIPI); Secretary General, Alliance for Pulmonary Hypertension, Italy

**Melanie Gallant**
Director, Association of pulmonary arterial hypertension patients, carers and transplant receivers (Association des malades, aidants & transplantés hypertension pulmonaire, HTaPFrance), France

**Professor Marc Humbert**
Director, Department of Respiratory and Intensive Care Medicine, Pulmonary Hypertension Reference Centre, Hôpital Bicêtre, France

**Elizabeth Joseloff**
Vice-President, Quality Care & Research, Pulmonary Hypertension Association (PHA) US

**Professor Nicholas Kolaitis**
Director of Bronchoscopy, Division of pulmonary, critical care, allergy and sleep Medicine, University of California San Francisco, US

**Jamie Myrah**
Executive Director, Pulmonary Hypertension Association (PHA) Canada

**Eva Otter**
Vice President, Pulmonary Hypertension Association (PHA) Europe, Austria

**Professor Jay Suntharalingam**
Clinical Lead, Pulmonary Hypertension Service, Royal United Hospitals Bath, UK

**Natalia Maeva**
President, Bulgarian Society of Patients with Pulmonary Hypertension, Bulgaria

## Other experts consulted:

**Barbara Bujar** Board Member, Polish Pulmonary Hypertension Association, Poland

**Hall Skaara** Advocacy Manager, PHA Europe, Norway

**Beth Slaunwhite** Board Director, PHA Canada, Canada

**Sean Taylor** Director of Science and Public Health, World Heart Federation, Switzerland

**Durhane Wong-Rieger** President, Canadian Organization for Rare Disorders, Canada

# EXECUTIVE SUMMARY

## WHAT IS PULMONARY ARTERIAL HYPERTENSION?

**Pulmonary arterial hypertension (PAH) is a rare – but treatable – form of pulmonary hypertension (PH),** which is defined as blood pressure of over 20 mmHg and vascular resistance over 2 WU in the pulmonary artery.[1] In people with PAH, this arises due to the narrowing of the pulmonary arteries.[2] PAH is a rare disease that:

| | | |
|---|---|---|
| presents with **non-specific symptoms**, such as shortness of breath and fatigue, which can hinder a person's ability to walk[3-5] | affects **every aspect of a person's daily life**, including their education, work, relationships, household tasks and mental health[6-12] | rapidly progresses to **right heart failure** if left untreated, leading to hospital admissions and eventually death.[2 13] |

## WHY DO DECISION-MAKERS NEED TO ACT NOW?

### Despite being a rare disease, PAH drives substantial costs for health systems

PAH is estimated to cost Spain's health system up to

**€100 million**

every year.[14]


Delays in access to a PAH diagnosis and treatment lead to costly hospitalisations and additional therapies.[15-18]

### There are unacceptable delays in access to PAH diagnosis and life-saving treatment

People with PAH typically wait years before receiving a diagnosis, seeing multiple healthcare professionals and being misdiagnosed with common conditions.[4 19 20]

By the time most people with PAH receive a diagnosis, their symptoms significantly affect their functioning and they are at a higher risk of death.[19 21 22]

### Delayed access to PAH care is a missed opportunity

Timely access to diagnosis and treatment of PAH can reduce the risk of disease progression and death.[23-25]

Earlier diagnosis of PAH could save up to

**$4,000**

per patient per month in the US.[16]

### People with PAH experience major inequities in access

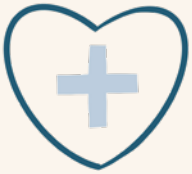
Expert centres are unequally distributed. For example, Italy has just seven main centres, resulting in long travel times and travel costs for many people with PAH.[26]

Some countries still do not reimburse life-saving medications for PAH.[26 27]

In the US, people with PAH have the lowest rate of lung transplantation and the highest rate of waiting-list mortality compared with people living with other diagnoses.[28]

## WHAT ARE THE KEY OPPORTUNITIES AND PRIORITY ACTIONS FOR PAH?

### OPPORTUNITIES

| 1 | 2 | 3 | 4 |
|---|---|---|---|
|  |  |  |  |
| **Increase awareness of PH and deliver more diagnostic tests to reduce time to a PAH diagnosis** | **Establish networks of accredited PH expert centres to ensure access to best-practice care** | **Increase PAH research to help address inequitable access to effective treatment** | **Improve decision-making and health-system design to prioritise the needs of people with PAH and their quality of life** |

### PRIORITY ACTIONS

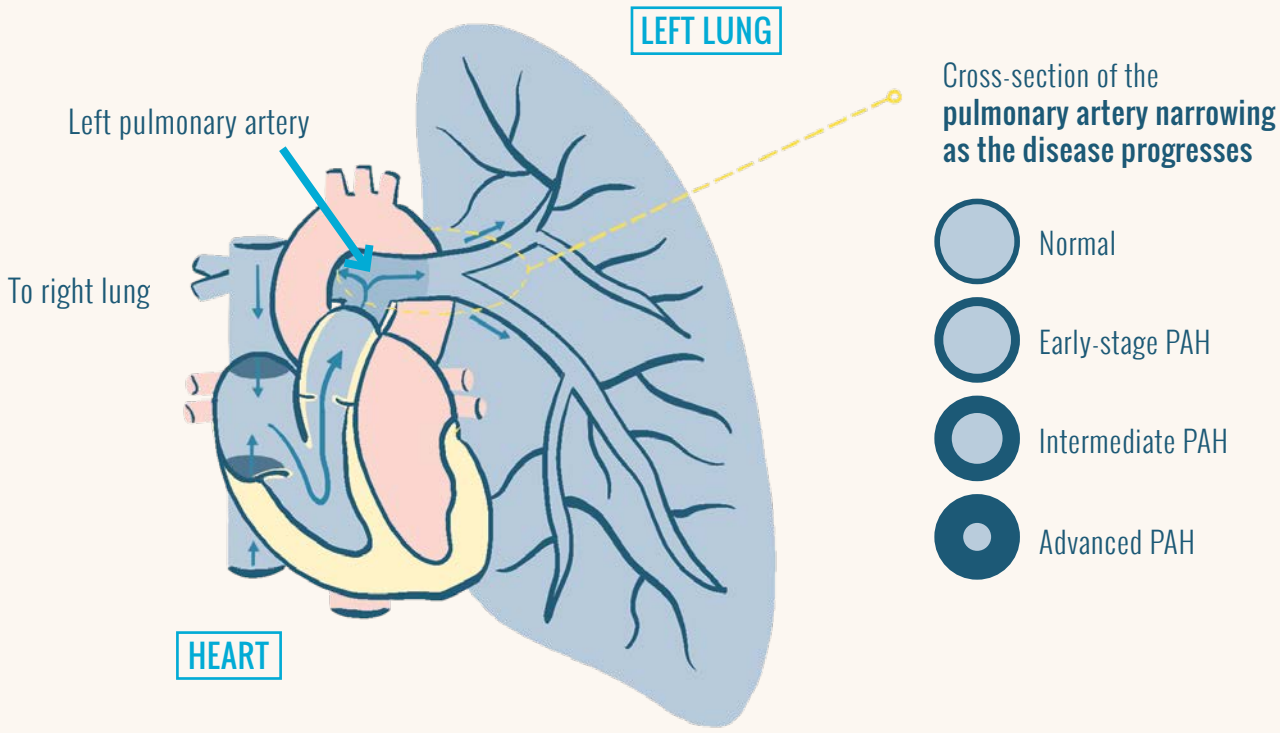
| | | | |
|---|---|---|---|
| – Support targeted awareness campaigns for PH, with PAH positioned as a treatable form of PH where timely diagnosis is vital for improved survival. | – Establish national standards of care for PH expert centres, an accreditation system and a training programme for centres to ensure quality PAH care. | – Invest in the development of national registries that collect data on PAH to enable data-driven decision-making and reduce variations in health outcomes. | – Invest in and integrate psychological support as a key component of care delivery to improve the quality of life for people with PAH. |
| – Ensure the availability and performance of key tests for the diagnosis of PAH in different settings. | – Organise forums for PH centres/ networks and patient associations to encourage exchange of knowledge and best-practice care for PAH. | – Direct funding to PH/ PAH research for the development of innovative treatments, tools and care models. | – Ensure the participation of PH associations in decision-making, especially for research, standards of PAH care and reimbursement of treatment. |
| – Increase awareness among groups at high risk of developing PAH. | | | |

# WHAT IS PULMONARY ARTERIAL HYPERTENSION?

**Pulmonary arterial hypertension is a rare and progressive form of pulmonary hypertension, for which advances in treatment are accelerating.**

**Pulmonary arterial hypertension (PAH) is a progressive disease that leads to heart failure and high rates of death.** It causes narrowing of the blood vessels in the lungs, requiring the heart to work harder, which can lead to acute heart failure and, eventually, death.[2 13] Despite the availability of treatments and advances in clinical guidelines, one in five people with PAH dies within three years of diagnosis.[29 30] While lung transplantation can be successful in extending survival for people with advanced PAH, there are inequities in access to transplants and people with PAH have a high risk of dying while on a waiting list.[28]

**FIGURE 1.** Pulmonary arterial hypertension



**What is the difference between pulmonary hypertension (PH) and PAH?** PH is defined as blood pressure of over 20 mmHg and vascular resistance over 2 WU in the pulmonary artery.[1] It is an underdiagnosed disease that involves both the cardiovascular and respiratory systems, requiring multidisciplinary care. PAH is a specific type of PH that arises when the pulmonary arteries (the vessels carrying blood from the right side of the heart to the lungs) narrow due to an increased number of muscle cells, inflammation and/or blood clots.[2]

**How does PAH lead to right heart failure?** The narrowing of the pulmonary arteries creates resistance, requiring the right side of the heart to work harder.[2] Eventually, structural changes occur in the heart as it compensates for the increased resistance. This can result in heart failure, which is when the heart can no longer pump enough blood to meet the body's needs.

**Who is affected by PAH?** PAH is estimated to affect approximately 4 in 100,000 people.[1 31] It affects people of all ages and is more common among women than men, but men tend to have worse outcomes.[32 33] Recent evidence indicates that the difference in prevalence among women and men declines with age.[1]

**People with PAH live with an invisible disability that affects every aspect of their lives.**
Symptoms can be non-specific at first, such as fatigue and shortness of breath, but can become debilitating as the disease progresses[4] – for example, by hindering a person's ability to walk and significantly affecting their daily life.[3 5 7-9] Even when they are receiving treatment, people with PAH may be unable to go to school or work, maintain social relationships or perform other daily activities such as grocery shopping and household tasks.[6 10 11] However, because the impact of their condition is usually not visible, people with PAH are often misunderstood by those around them and healthcare professionals.[3 6 11 34-36] PAH can also affect a person's mental health – almost half of people with the disease also live with depressive symptoms, and one third live with depression.[12]

**'PAH is invisible, so even close friends and family don't believe you. It's difficult to get recognition for your disability and receive social and psychological support. It's not easy to find a job that is compatible, or to hold your place in society.'**

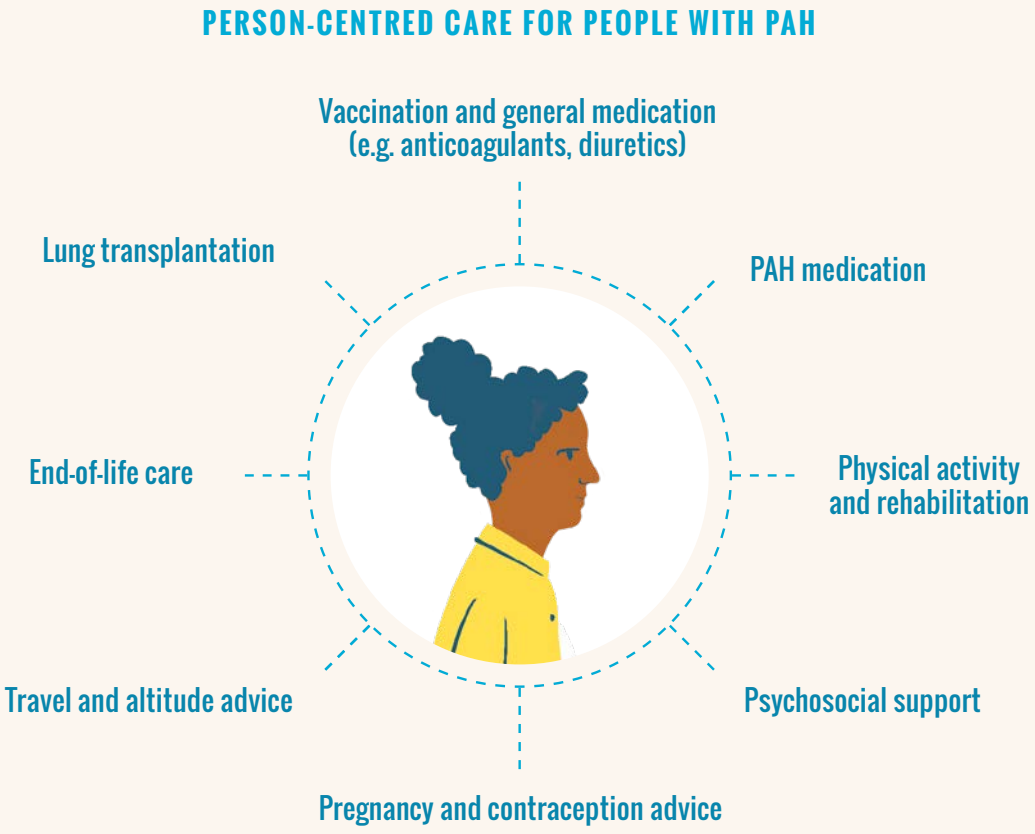
**Mélanie Gallant,** person with lived experience, France

**‘Hope is essential. It’s important for people with PAH to maintain their health and wellbeing as much as possible, as future medical advancements may offer new treatments to improve their condition. I tell doctors never to leave PAH patients without hope.’**

**Pisana Ferrari,**
person with lived experience, Italy

**Scientific advances have opened up opportunities for new treatments that improve survival and halt the progression of PAH**. In the past two decades, increased understanding of the biological processes involved in PAH has facilitated the development of treatments that alleviate symptoms. These treatments have allowed people with PAH to live longer and with a better quality of life *(Figure 1)*.[10 26] However, there remains no cure for PAH.[37 38] New treatments are under development to target other biological pathways, address the underlying disease causes and halt disease progression.[39]

**FIGURE 2.** PAH treatment comprises a range of core elements to improve outcomes and quality of life[1]



# WHY DO DECISION-MAKERS NEED TO ACT NOW?

**'I spent more than ten years trying to understand the cause of my worsening symptoms. Three cardiology-related physicians, two respirologists, several emergency physicians and a GP never considered PH. It was not on their radars as a potential diagnosis.'**

**Beth Slaunwhite,** person with lived experience, Canada

## THE COST OF INACTION


€100 million
every year

**Despite being a rare disease, PAH drives substantial costs for health systems and societies.** The development of treatments for PAH continues to grow,[39] but delays in access lead to costly hospitalisations and additional therapies such as lung transplantation and oxygen therapy.[15-18] In Spain, for example, PAH is estimated to cost the health system €100 million every year.[14]

**Unacceptable delays in access to a PAH diagnosis and life-saving treatment drive suffering and poor outcomes.** From the start of their symptoms, people with PAH can wait two years or more for a diagnosis.[4 19 20] During this time, they typically see three or more healthcare professionals, and two in five people are misdiagnosed, leading to further delays. By the time they receive an accurate diagnosis, the person's symptoms will have worsened to a more severe stage that significantly affects their functioning,[19 21] which is associated with an increased risk of death.[22] Additionally, irreconcilable variations in the recorded prevalence of PAH across different regions around the world suggest that many people with PAH are going undiagnosed.[40-43]

**Delayed access to PAH care is a missed opportunity to both improve health outcomes and reduce healthcare costs.** Studies have shown that earlier diagnosis and treatment of PAH can reduce the risk of disease progression and death.[23-25] Earlier diagnosis of PAH could save up to $4,000 per patient per month in the US.[16]

## INEQUITIES IN ACCESS

**Many people with PAH face geographical and financial barriers to accessing expert care.** The diagnosis of PAH requires right heart catheterisation, which must be conducted by highly specialised healthcare professionals at a PH expert centre.[1] However, PH expert centres are not equally accessible around the world. According to the Pulmonary Hypertension Association (PHA) Europe database of expert centres, Greece has no expert centres, while other countries only have a few.[26 27] Despite a recent increase in the number of PH expert centres in the US, there are still 15 states with no accredited centres.[44] Consequently, some people with PAH have to travel long distances to attend their medical appointments and receive comprehensive care – often without financial support, creating additional barriers to accessing care.[26 44 45] More than 25% of people with PAH in the US live over 40 miles (64km) from their healthcare team.[45] In some countries, people living with PAH often have to travel long distances for care; for example, there are just seven main PH centres across all of Italy for a population of almost 60 million people.[26] The Italian Pulmonary Hypertension Association (Associazione Ipertensione Polmonare Italiana, AIPI) reimburses travel and hotel expenses for people who earn under a threshold income.[26]

**Effective medications for PAH are costly and, with different models of funding and reimbursement for PAH treatments across the globe, there are major inequities in access to life-saving therapies.** The costs of PAH treatments are generally high, although there are significant differences between countries. Clinical guidelines recommend combination therapy for people with PAH at high risk of death;[43] in Canada, the cost of these treatments may reach more than $230,000 per year.[46] Consequently, not all people with PAH have access to these life-saving treatments; for example, some countries in Eastern Europe still do not reimburse treatments for PAH.[26 27] In countries such as the US, treatment adherence is low because people with PAH face financial barriers such as low income or a lack of medical insurance.[44]

**Access to lung transplants remains inequitable.** Although progress has been made with transplant waiting lists, people with PAH still face barriers in access to transplantation due to problems with current organ allocation systems.[28] In the US, for example, people with PAH have the lowest rate of lung transplant and the highest rate of waiting-list mortality compared with people living with other diagnoses.[28]

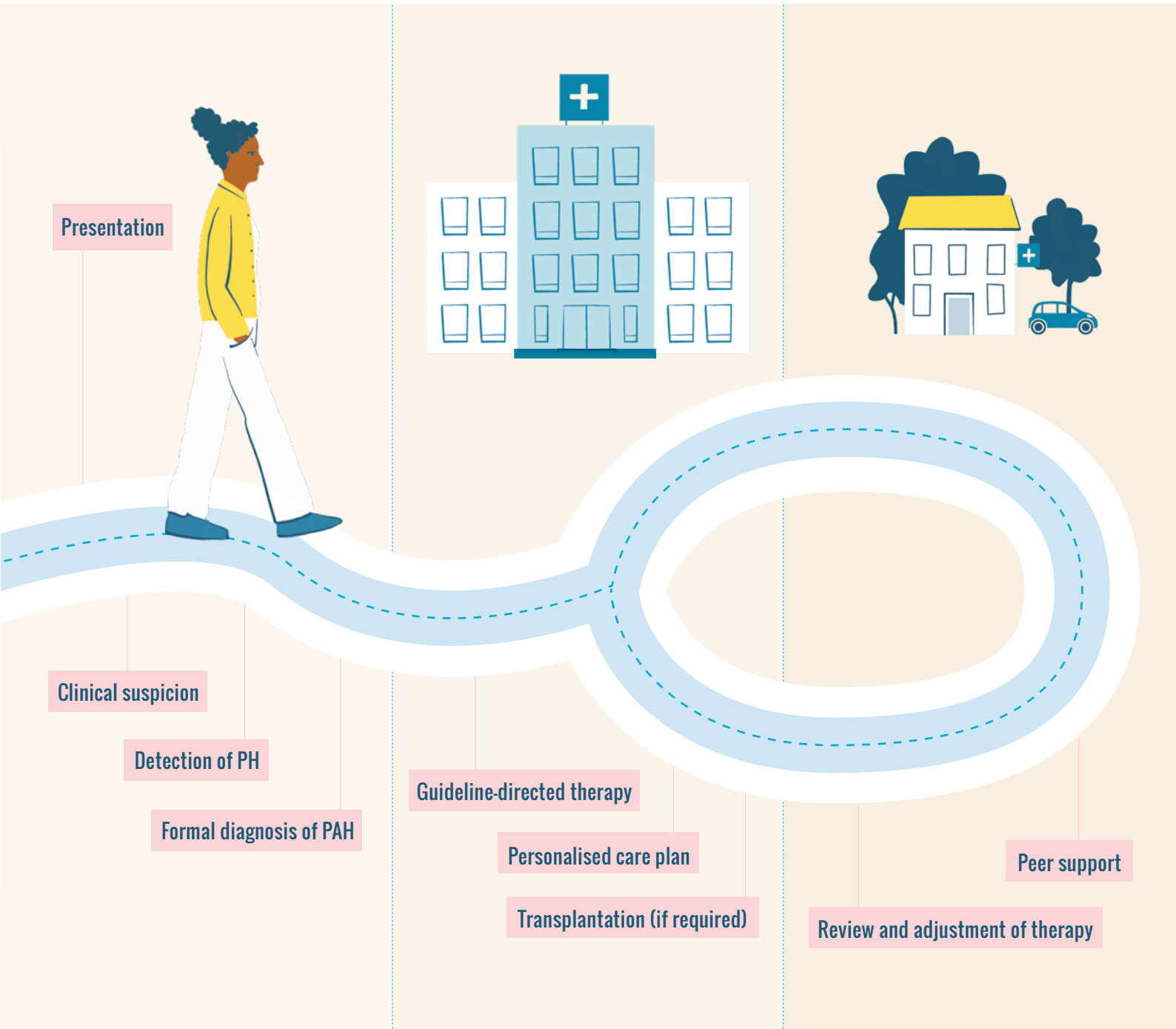
# WHAT IS THE OPTIMAL PAH PATIENT JOURNEY?

Latest evidence from consensus-based clinical guidelines and quality indicators illustrates what should happen at every stage of the PAH patient journey, from the moment a person starts experiencing symptoms to the long-term reality of living with the condition.[1 47]

## DIAGNOSIS

## PERSONALISED TREATMENT

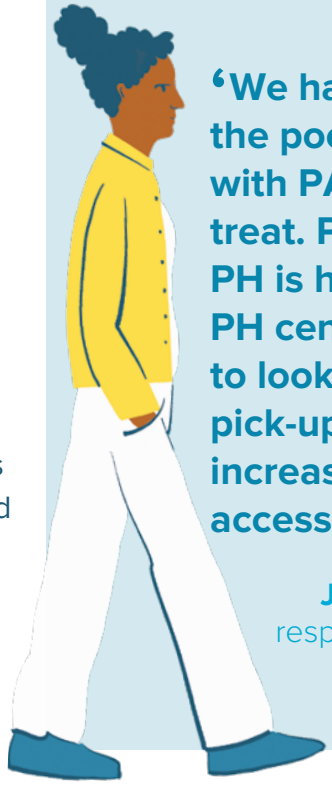
## SUPPORTING PEOPLE TO LIVE WELL WITH PAH



## DIAGNOSIS

**I. Presentation**. A person experiences shortness of breath and fatigue that limit their physical activity.[19 48] Although the symptoms are vague, they seek medical help.

**II. Clinical suspicion**. The person receives medical support for the first time, most likely in primary care.[1 4] The primary care physician listens to the person's experiences, takes their medical history and performs a thorough physical examination.[43] The physician suspects a cardiac or respiratory condition and conducts appropriate tests (e.g. electrocardiogram, blood tests, chest X-ray).[49] These may come back negative or without abnormalities.[20] However, the physician is aware that some diseases can be difficult to identify, especially if they are rare, and makes a referral to a specialist, namely a cardiologist or pulmonologist.



**'We have to widen the pool of people with PAH that we treat. Prevalence of PH is high around a PH centre. We need to look at improving pick-up rates and increasing equity in access to diagnosis.'**

**Jay Suntharalingam,**
respiratory physician, UK

**III. Detection of PH**. The specialist conducts non-invasive lung/cardiac and other tests to understand the underlying cause of the symptoms.[1] They order an echocardiogram with appropriate parameters to determine the probability of PH. If the probability is high, the specialist makes a fast-track referral to a PH expert centre.[47] The echocardiogram may be complemented with a computed tomography (CT) scan to confirm the results.

**Alternative path: screening those at high risk of PAH.** The specialist taking care of a person at high risk of PAH (for instance, a first-degree relative of someone with hereditary PAH, or a person with portal hypertension or systemic sclerosis) is aware of the need for screening. If tests indicate a probability of PAH, they make a referral to a PH expert centre.[2 50]

**IV. Formal diagnosis of PAH**. At the PH expert centre, a multidisciplinary team adheres to high-quality standards of care according to the latest clinical guidelines (see *Organisation of pulmonary hypertension diagnosis and care*).[47] They conduct right heart catheterisation to confirm a diagnosis of PAH, along with other tests to assess how well the person's lungs work, potential risks, the level of physical activity they can perform, and their quality of life (*Box 1*).[1] People with PAH can see their condition deteriorate in a short period of time,[1] so the time frame between experiencing the first symptoms and the formal diagnosis should be as short as possible.

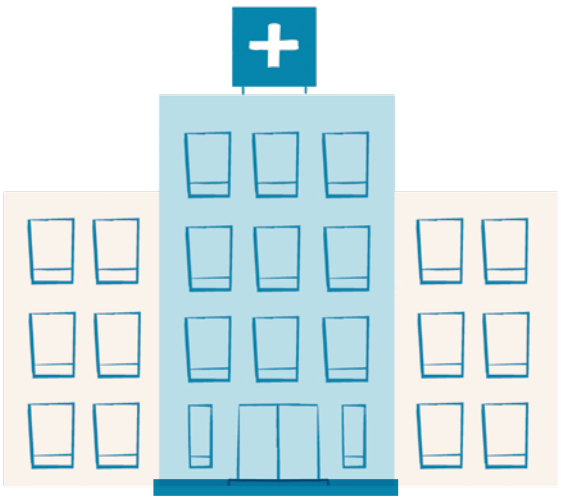
**Box 1.** PAH diagnosis and risk assessment

**Right heart catheterisation** is the gold-standard test for a definitive diagnosis of PAH.[1] It is an invasive procedure in which a catheter is inserted into the pulmonary artery to directly measure blood pressure. Other tests attempt to differentiate the cause of PH, and to determine whether the person has PAH or PH associated with a different condition (i.e. lung or heart disease). These include tests for pulmonary function, a ventilation/perfusion scan to exclude chronic thromboembolic pulmonary hypertension (CTEPH), screening for connective tissue diseases, a CT scan of the lungs, drug screening, HIV testing and exercise tests.[47]

Risk assessment will help classify the person with PAH as low, intermediate or high risk, which relates to the calculated likelihood of one-year mortality.[1 51] A thorough risk assessment at the time of diagnosis should also include their level of functioning, physical tolerance (with a six-minute walk test) and quality of life.[47] Healthcare professionals should monitor the person with PAH, evaluating the effectiveness of their treatment at least every six months and tracking changes in biomarkers, physical functioning and quality of life using validated risk-assessment tools.[52] If low risk is not achieved, healthcare professionals should promptly liaise with an expert multidisciplinary team to take measures that mitigate disease progression and, if needed, escalate treatment to reduce the person's risk.

## PERSONALISED TREATMENT

**V. Guideline-directed therapy**.
The multidisciplinary team follows the latest clinical guidelines for PAH and provides the most suitable treatment while also reviewing the patient's risk status and making adjustments when necessary. While there is no cure for PAH, the team can provide treatment that allows the person with PAH to live longer and with a better quality of life, with the possibility of switching to or adding newer treatments as they become available.[10 26]



**VI. Personalised care plan**. The multidisciplinary team conducts an in-depth analysis and develops a personalised care plan, taking into account factors that could affect the patient's response to treatment, as well as the patient's own perspective and experience.[47 53-55]
The team may also make a referral to genetic testing and counselling services, along with pulmonary rehabilitation.[1 47]

**VII. Transplantation (if required)**. If the person with PAH is on maximal medical therapy but the treatment does not have an adequate effect and their risk of death remains intermediate or high, healthcare professionals will promptly assess their suitability for a lung transplantation referral.[1] If the individual is eligible for transplant, they are put on a waiting list.[26] Early referral for transplant is recommended so that the person with PAH can be educated about the process and benefits of transplant. If they do require a transplant and successfully receive one, they will no longer have PAH. Studies show that transplant extends survival and improves health-related quality of life.[56 57] However, the person will become immunosuppressed so will still need medical follow-up and treatment.[1 26]

## SUPPORTING PEOPLE TO LIVE WELL WITH PAH

**VIII. Review and adjustment of therapy**. If a patient's treatment becomes ineffective or has a limited ability to control symptoms and side effects (such as pain, infections and limited life functioning), healthcare professionals will offer a different treatment, if possible.[58] If a new treatment becomes available, that may also be offered.[59]

**VIX. Peer support**. Expert centres work with patient organisations and make referrals so that the person with PAH can access support from others living with the condition.[27] Patient support groups can help people with PAH feel understood and receive advice on how to continue living a meaningful life with their condition.[26 27 60] They can also facilitate access to psychological and social support that helps them manage their mental health, relationships, pregnancy, finances, education, employment and other aspects of life.[60]

# WHAT ARE THE KEY CHALLENGES ACROSS THE PAH PATIENT JOURNEY?

## DIAGNOSIS

### I. Presentation

CHALLENGE: The person may initially ignore the vague symptoms of PAH, such as breathlessness and fatigue.[48] They may delay seeking help, while their symptoms get worse.

### II. Suspicion

CHALLENGE: The primary care physician may attempt to address common conditions that lead to breathlessness, perhaps by treating asthma or mental health conditions.[20] If the physician does not know the underlying cause, the person may become anxious and frustrated as their symptoms persist and worsen.[1 20]

### III. Detection

CHALLENGE: The person may visit a specialist who:

– does not order appropriate diagnostic tests, decreasing the probability of a correct diagnosis[61]

– does not ensure that the echocardiogram includes the appropriate parameters for a correct interpretation[4 62 63]

– misdiagnoses a more common condition, such as chronic obstructive pulmonary disease or heart failure, terminating the diagnostic effort without arriving at a diagnosis of PAH.[4 20]

If the person's condition continues to deteriorate, they may be referred to different specialists, potentially leading to unnecessary referrals and duplicated tests.[4 19 20] In the meantime, their symptoms may continue to worsen and increasingly affect their daily functioning.[64]

### IV. Formal diagnosis of PAH

CHALLENGE: The person with suspected PH may be in a country where no PH expert centre is suitable for them (for example, a centre with expertise in children). If there is a centre available, it is possible that:[26 65]

– it is far away, hindering the person's ability to attend medical appointments without financial support
– there is a long waiting list to receive expert care
– it does not meet standards of care according to the latest guidelines.

The person may not have a diagnosis of PAH confirmed appropriately, and consequently may be unable to access appropriate care and treatment.

## PERSONALISED TREATMENT

### V. Guideline-directed therapy

CHALLENGE: Healthcare professionals may be unable to provide the treatments recommended in clinical guidelines because they are not available in their country, or because the person with PAH cannot afford to pay for them.[26 27] If their financial and personal circumstances allow, the person with PAH might travel to another country to receive the appropriate treatment.[27] Even in countries with better access, the person may not receive appropriate treatment due to a lack of adherence to clinical guidelines for provision and escalation of therapies.

**'In Bulgaria, people with PAH do not have access to intravenous therapy. So if you need it, you must travel abroad. I received my intravenous therapy from Greece for two years before my double lung transplantation.'**

**Natalia Maeva,** person with lived experience, Bulgaria

CHALLENGE: If the person with PAH does have access to treatment, they might have to cope with a burdensome delivery method that affects their daily life. These could include carrying an infusion pump that may have side effects such as pain and infections[58 66] or an oxygen tank that reduces their mobility.[27 67] This may limit their ability to travel, work and socialise.[6] They may also experience numerous side effects that can become intolerable,[68 69] resulting in a low quality of life and the discontinuation of their treatment.[69 70]

### VI. Personalised care plan

CHALLENGE: Potential differences in response to treatment have been found in relation to sex, ethnicity, age and symptom severity, but little is known about how specific PAH treatments affect different population subgroups.[53 54] Limited understanding of how to develop a tailored treatment plan results in a lack of personalised care, potentially leading to ineffective treatment and additional healthcare costs.[15 17]

### VII. Transplantation

CHALLENGE: When a healthcare professional considers a referral for lung transplantation, the person with PAH may already be deteriorating rapidly and the optimal window for a referral might have been missed.[57] Early referral is necessary because when referrals are late there may not be enough time to carry out appropriate assessments. Additionally, some transplant allocation systems use a priority score, such as in the US, with parameters that are unfavourable for people with PAH: they may be on the waiting list behind people with other conditions despite being at a higher risk of death.[56 71] People from countries with limited access to transplantation may struggle to be accepted for a lung transplant in another country.[27]

**'Over nearly 40 years, I've gone through denial, isolation, anger, depression and, finally, acceptance. The diagnosis forced lifestyle changes, like giving up motherhood, work and moving closer to better care. These changes brought frustration and fear, but I've always had strong support from family and friends. My carers have supported me emotionally, financially and practically, helping with treatment decisions and understanding the disease.'**

**Barbara Bujar**, person with lived experience, Poland

**'The priority score for lung allocation in some countries does not reflect clinical parameters that affect patients with PAH since it is the only indication for lung transplantation that does not involve the lung parenchymal tissue. As such, people with PAH face inequities in access, having the lowest rate of transplantation and the highest waiting-list mortality.'**

**Nicholas Kolaitis**, pulmonologist, US

## SUPPORTING PEOPLE TO LIVE WELL WITH PAH

### VIII. Review and adjustment of therapy

CHALLENGE: People with PAH have voiced the need to increase their involvement in decisions about their care. Treatment decisions can be complex, involving the escalation of different therapies according to risk, and evolving the prognosis and medical response over different stages of the disease. In addition to core therapy, long-term general measures and supportive therapies should be initiated in support of the person's wider health. These may include therapies such as oxygen therapy, diuretics, arrhythmia and protective cardiovascular medications as well as non-cardiac surgery and cancer care.[45 72] People with PAH also require support and advice with lifestyle changes, family planning and pregnancy, psychosocial support and planning life events or travel. A person-centred, collaborative approach to care – alongside optimal palliative care – leads to greater patient involvement and empowerment in managing PAH.[55]

> **'As we see advances in diagnosis, care and treatment, we are going to have more and more people growing up with PAH. We have to figure out how we're going to help them live full lives with a chronic illness.'**
>
> **Jamie Myrah,** patient advocate, Canada

### VIX. Peer support

CHALLENGE: The person with PAH may not have access to a patient support group and may feel misunderstood by the people around them, creating feelings of isolation.[27] Without access to appropriate help, a person with PAH may not have the tools or support to address the impact of their condition on their life. They may experience a deterioration of their mental health and struggle to establish or maintain relationships. If the person with PAH cannot easily go to school or work because of their condition, it may be difficult for them to find or keep a job and they may struggle financially.[8]

# WHAT ARE THE KEY OPPORTUNITIES TO ACT ON PAH?

## OPPORTUNITY 1

### Increase awareness of PH and implementation of its diagnostic tests to reduce the time to a PAH diagnosis.

Experts have suggested that misdiagnoses and delays are due to a lack of awareness of PH among healthcare professionals, who often do not consider the condition a potential cause of unexplained breathlessness.[4 20] Ensuring the appropriate diagnostic tests could increase the probability of a correct diagnosis of PH; even small improvements in the diagnostic work-up could result in a significant increase in accurate diagnoses.[61]

### PRIORITY ACTIONS

- **Support targeted PH awareness campaigns, with PAH positioned as a treatable form of PH where timely diagnosis is vital for improved survival.** It is crucial that PAH is linked with existing campaigns to increase awareness of PH more widely, such as World PH Day and PH Awareness Month, among others. Awareness resources may emphasise the importance of an early diagnosis to ensure the timely delivery of treatment that can improve outcomes. Resources may include targeted messages prompting healthcare professionals to identify vague symptoms such as unexplained breathlessness for the correct diagnosis of PH.

- **Ensure the availability and performance of key tests for the diagnosis of PAH in different settings.** Various tests are needed to diagnose PAH, some of which require specialist expertise in PH. Decision-makers must ensure that key diagnostic tests are reimbursed in the appropriate setting and that clear guidance is available for healthcare professionals (see *Organisation of pulmonary hypertension diagnosis and care*).

- **Increase awareness among groups at high risk of developing PAH.** There is an increased risk of PAH among people with conditions such HIV, connective tissue disease, methamphetamine-use disorders and liver disease. Increased awareness of this heightened risk is needed among front-line providers caring for people with these conditions and relatives of people with inheritable forms of PAH.

## OPPORTUNITY 2

### Establish networks of accredited PH expert centres to ensure access to best-practice care.

There are clinical consensus documents for PAH that establish guidelines for best-practice care and quality indicators.[147] However, many PH centres do not meet these standards of care.[65] Strong networks of PH centres that uphold international standards have the potential to improve care, reducing inequities in access to best-practice care across regions and improving outcomes for people with PAH.

### PRIORITY ACTIONS

- **Establish national standards of care for PH expert centres, an accreditation system and a training programme to ensure quality PAH care.** While there are established networks of PH expert centres in Canada and Europe (the PH subgroup of the European Reference Network on rare respiratory diseases, ERN-LUNG), as well as multiple identified care centres in the US (PHA-accredited Pulmonary Hypertension Care Centers), there are significant differences in the quality of care delivered across PH centres (see case study on page 27).[65] The PH clinical and patient communities must work together with decision-makers to establish standards of care and referral pathways that are achievable given the resources available, assessing PH centres and accrediting those that meet the set criteria. This could be accompanied by a training programme that equips healthcare professionals with the knowledge and skills they need to provide high-quality care for PAH.

- **Organise forums for PH centres/networks and patient associations to encourage exchange of knowledge and best-practice care for PAH.** Coordinated communication among the PAH community, both within and between countries, is essential to allow for the exchange of the latest clinical knowledge and person-centred approaches (see case study on page 26). Peer learning can also provide insights into new initiatives, inspiring the implementation of innovative programmes (such as AI-driven detection of PAH) and care models across regions.

## OPPORTUNITY 3

### Increase PAH research to address inequitable access to effective treatment.

Despite experts citing inequitable access to treatment as one of the biggest challenges for people with PAH,[26 27 43 60] there is little research or data collected on these inequities. Besides building evidence about inequities, there is a need to invest in basic science, translational, clinical and real-world research to allow the ongoing improvement of PAH treatment and care.

### PRIORITY ACTIONS

- **Invest in the development of national registries that collect data on PAH to enable data-driven decision-making and reduce variations in health outcomes.** National registries are a key instrument for advocates and decision-makers to investigate inequalities in PAH care. The data collected could serve as a benchmark across regions and countries, indicating areas where further investment and innovation are required to ensure that all people with PAH have access to best-practice care and improved outcomes. One example is the US-based PHA registry, a non-funded registry of patients new to PHA-accredited Pulmonary Hypertension Care Centers.[73] Although this registry is non-funded and investigators enrol patients on a volunteer basis, it has already led to numerous publications that have changed clinical practice (see case study on page 27).[74]

- **Direct funding to PH/PAH research for the development of innovative treatments, tools and care models.** Decision-makers must provide the research funding needed to gain a better understanding of which treatments are suitable for people with PAH and can reduce healthcare costs.[15 17] There are also promising tools that would benefit from funding, such as the use of AI to facilitate the early detection of PAH[4 62 63] and implantable pulmonary artery recorders for the ongoing risk assessment.[75] Some countries, including the UK, have invested in new care models, such as breathlessness clinics, that could fast-track the detection of PH.[4]

## OPPORTUNITY 4

### Improve decision-making and health-system design to prioritise the needs of people with PAH and their quality of life.

People with PAH and other patient advocates see quality of life – including mental health and the ability to carry out daily activities such as going to school or work – as a key issue that must be addressed by healthcare professionals, researchers and decision-makers.[6 26 27 60] It is essential to involve people with PAH in the decision-making process to ensure that the health system caters to their needs.

### PRIORITY ACTIONS

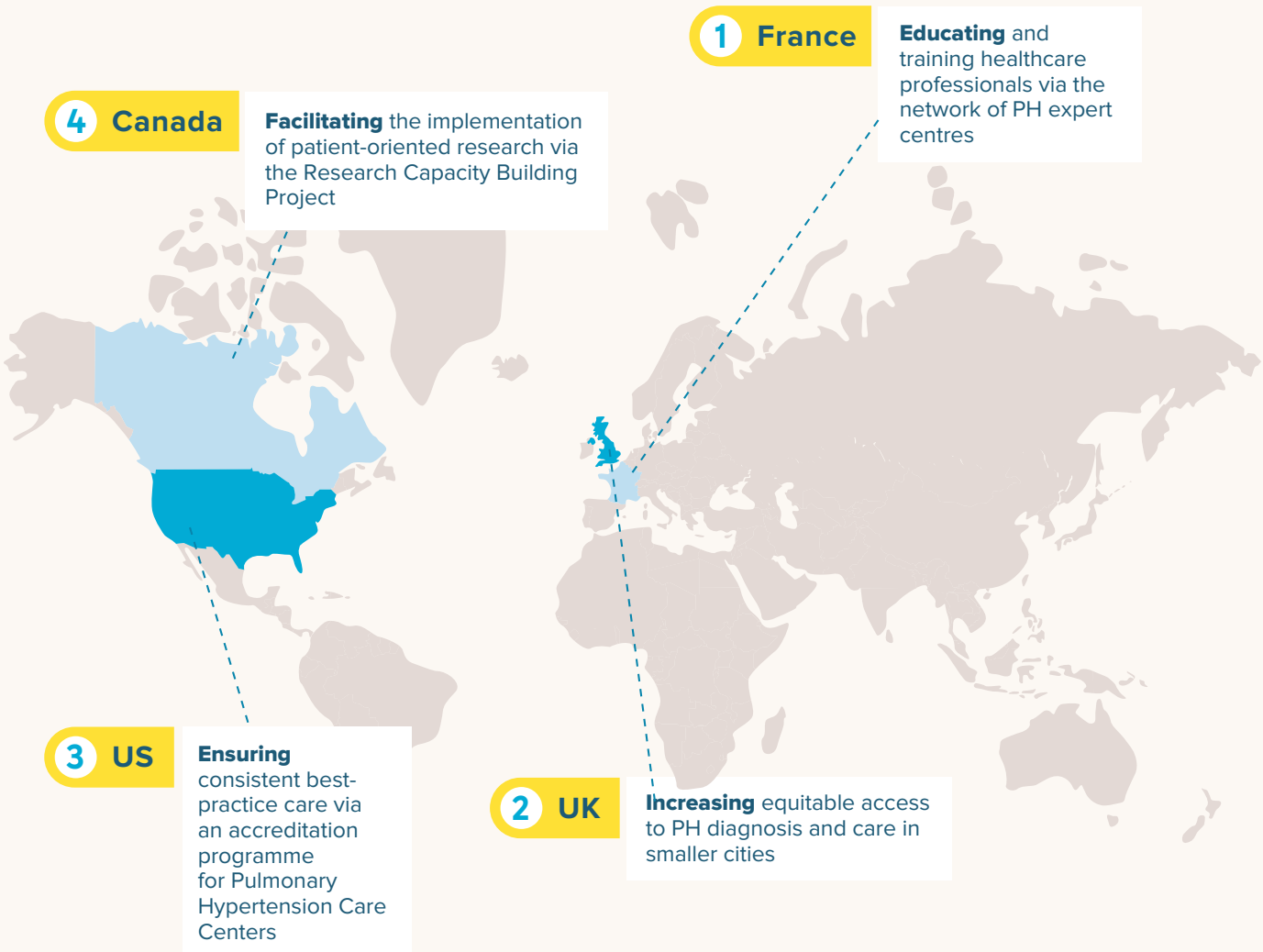
- **Invest in and integrate psychological support as a key component of care delivery to improve the quality of life of people with PAH.** It is common for people with PAH to have problems with their mental health;[12] experts have highlighted how challenging it is for a person to receive a diagnosis for a disease with no cure and, in some cases, few available treatments.[27] But the condition's impact on mental health is rarely acknowledged by healthcare professionals.[76 77] Decision-makers must provide funding to further address this topic and ensure that people with PAH have access to psychosocial support.

- **Ensure the participation of PH associations in decision-making, especially in research, quality standards of PAH care and treatment reimbursement.** While clinical research increasingly includes quality-of-life measures related to health, there has been little research on the improvements that people with PAH most want to see – such as the ability to accomplish daily activities related to leisure, relationships and work.[6 78] As called for in rare diseases more widely, patient perspectives and priorities must be reflected in research and clinical practice, and considered alongside other expert input into regulatory and reimbursement decisions. More opportunities for people with PAH to feed into decision-making are needed, such as through formalised patient input into clinical guidelines and national standards for PAH care, or personal testimonies on the disease's impact on daily life. For example, in Spain, the national PH association arranged a meeting with the minister of health to discuss the development of a national strategy for PH as well as the importance of early diagnosis, expert care and access to treatment for people with PH.[79]


24

# WHERE IS PROGRESS BEING ACHIEVED?

The case studies have been selected in collaboration with the Steering Committee to highlight some of the PH programmes that have achieved progress in the implementation of best-practice care for people with PAH.



## 1 CASE STUDY 1. Educating and training healthcare professionals via the network of PH expert centres in **France**

**Background:** The Department of Respiratory, Pulmonary and Intensive Care Medicine has been a leading reference centre for expert PH care in France since 2005.[80] In 2007 and 2008, the centre led the development of a network of 23 regional PH care centres.[80]

**Impact:**
The network focuses on improving healthcare practitioners' awareness of PH diagnostic and care pathways, facilitating research and training, and unifying stakeholders with shared clinical data and common guidelines.[80] It has developed targeted initiatives, including:[81]

- a national protocol for diagnosis and care to support the delivery of an education programme for all healthcare professionals involved in PH treatment
- PAH and Education, a programme rolled out within the network that aims to provide education on optimal integrated care for people with PAH. It includes a multidisciplinary team of a doctor, two nurses, a pharmacist, a dietitian, a physiotherapist and a genetics consultant.

## 2 CASE STUDY 2. Increasing equitable access to PH diagnosis and care in smaller cities in the **UK**

**Background:** The UK has a centralised approach to delivering PH care, with a network of seven expert centres ensuring a high standard in PH treatment, care and research.[82] A number of local 'shared care' services have been developed to facilitate access to PH expert care for people who live far away from the expert centres.[42 82] For example, since 2005, the Royal United Hospital in Bath – which is around two hours by train from the nearest expert centre – has offered a shared care service that delivers multidisciplinary care (including cardiology, respiratory, rheumatology and radiology departments) locally, with oversight from the expert centre, Royal Free London.[82]

**Impact:**
The PH shared care service in Bath has expanded steadily and addressed inequities in access to a PH diagnosis, managing around 150 referrals per year.[42 82] Since the service was established, the recorded prevalence of PH has grown from 5 to 63 cases per 1 million people in Bath's catchment area, suggesting that a large number of people would have remained undiagnosed and not received appropriate treatment without this service.[82]

## 3 CASE STUDY 3. Ensuring consistent best-practice care via an accreditation programme for Pulmonary Hypertension Care Centers in the US

**Background:** In 2014, PHA US and a group of 28 global leaders in PH care and research (the Scientific Leadership Council) developed the PHA-accredited Pulmonary Hypertension Care Centers programme.[83] The centres can also enrol patients in the PHA registry to collect data and measure health outcomes.[74]

**Impact:**
The accreditation programme has created a network of 67 PH expert centres equipped to deliver high-quality PH care nationwide.[74 83 84] Depending on a centre's resources, two types of accreditation are available: Regional Clinical Programs and Centers of Comprehensive Care, the latter with the capacity to provide more advanced care.[73] Enrolling patients in the PHA registry helps healthcare professionals gain a better understanding of best practice in care and treatment, and improve long-term outcomes.[74]

## 4 CASE STUDY 4. Facilitating the implementation of patient-oriented research via the Research Capacity Building Project in Canada

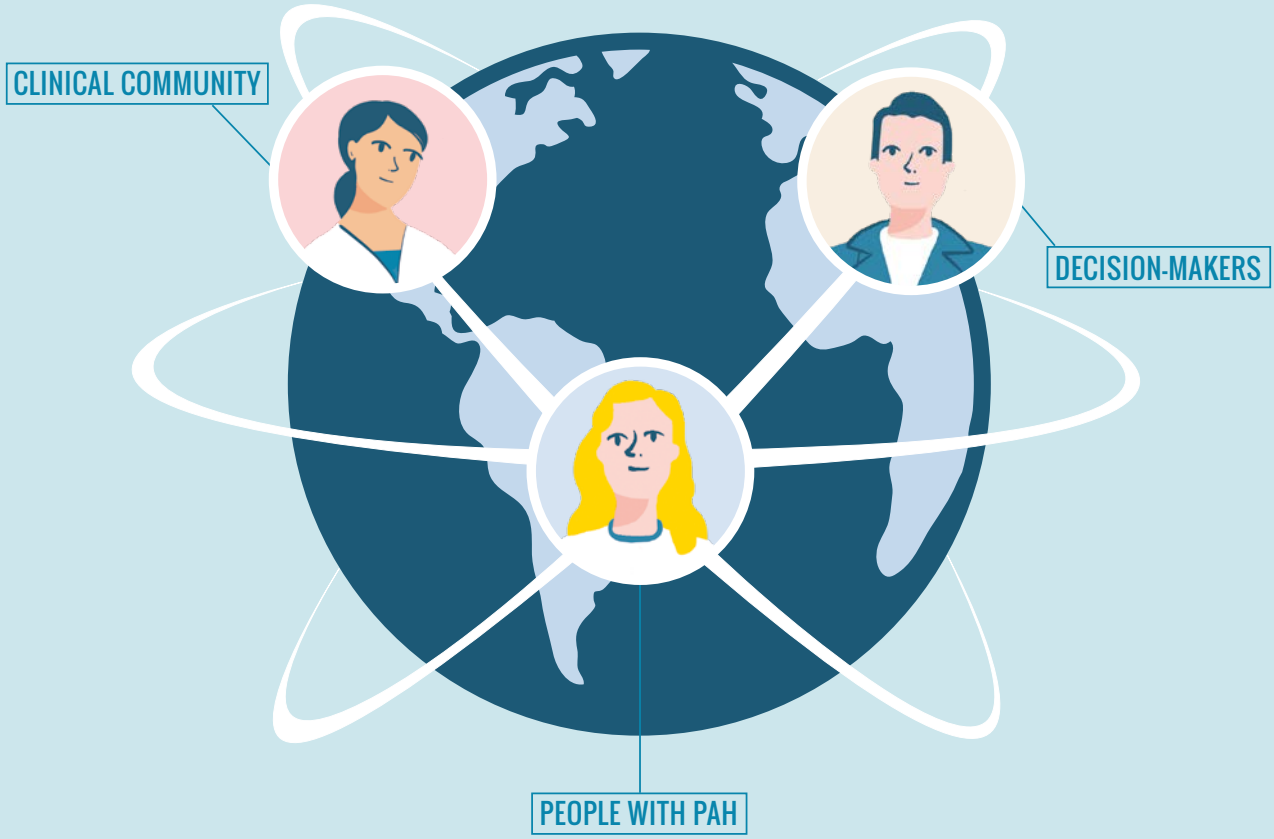
**Background:** In 2022, PHA Canada launched the Research Capacity Building Project, an initiative to develop a common framework for researchers, clinicians and patient partners to implement patient-oriented research.[85] It takes a collaborative approach, where people with PAH, their carers and families are proactive partners of healthcare providers and decision-makers in setting priorities and participating throughout the research process.[85 86] In 2024, for example, PHA Canada developed a survey to consult people with PAH on their unmet needs; the results will be used to provide input into Canada/Quebec's health technology agencies.[87]

**Impact:**
The project has focused on implementing three main areas of work:[86]

- **The PH Clinical Trials Network** aims to improve information sharing, coordination and collaboration across research centres, overcoming the problems of decentralised clinical trials.
- **The Canadian PH registry** was expanded to increase patient participation and include biological samples (including human tissue and blood specimens) that could be collected during right heart catheterisation to maximise data on PH and improve research capacity.
- **Patient education and training** provide learning opportunities for people with PH and their carers to improve communication and advocacy skills, to help them collaborate with scientists and clinical researchers.

# A WAY FORWARD

We thank colleagues working on patient advocacy, clinical practice and research to improve the lives of people with PAH around the world. There have been excellent contributions from PH associations and the clinical community, but we also need support and investment from decision-makers to continue moving forward. We hope this document provides clarity on the most compelling messages for a policymaking audience and the actions that the PAH community needs the most.



# REFERENCES


1. Humbert M, Kovacs G, Hoeper MM, *et al.* 2022. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: Developed by the 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 the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG). *Eur Heart J* 43(38): 3618-731
2. Cullivan S, Higgins M, Gaine S. 2022. Diagnosis and management of pulmonary arterial hypertension. *Breathe (Sheff)* 18(4): 220168
3. PHA Europe. Zdenka, Croatia. Available from: https://www.phaeurope.org/get-involved/awareness-campaigns/phae-leaders-stories/zdenka-croatia/ [Accessed 12/03/24]
4. Small M, Perchenet L, Bennett A, *et al.* 2024. The diagnostic journey of pulmonary arterial hypertension patients: results from a multinational real-world survey. *Ther Adv Respir Dis* 18: 17534666231218886
5. Pulmonary Hypertension Association of Canada. Living with Hope: My PAH Journey and the Power of Perseverance. Available from: https://phacanada.ca/Community/Your-Stories/Archive/Living-with-Hope-My-PAH-Journey-and-the-Power-of-P [Accessed 12/03/24]
6. Auriemma CL, Minhas J, Blue R, *et al.* 2023. "It's that invisible illness": Patient and clinician perspectives on outcomes in pulmonary arterial hypertension treatment. *Pulm Circ* 13(2): e12236
7. Sarzyńska K, Świątoniowska-Lonc N, Dudek K, *et al.* 2021. Quality of life of patients with pulmonary arterial hypertension: a meta-analysis. *Eur Rev Med Pharmacol Sci* 25(15): 4983-98
8. Fuge J, Park DH, von Lengerke T, *et al.* 2021. Impact of Pulmonary Arterial Hypertension on Employment, Work Productivity, and Quality of Life - Results of a Cross-Sectional Multi-Center Study. *Front Psychiatry* 12: 781532
9. Halimi L, Suehs CM, Marin G, *et al.* 2021. Health-related quality of life and disease progression in pulmonary arterial hypertension patients: a 3-year study. *ERJ Open Res* 7(3):
10. PHA Europe. Gerald Fischer, PH Austria. Available from: https://www.phaeurope.org/get-involved/awareness-campaigns/phae-leaders-stories/gerald-fischer-ph-austria/ [Accessed 12/03/24]
11. Charbonneau D. 2023. Ottawa school teacher living with rare Pulmonary Arterial Hypertension for more than a decade. Available from: https://ottawa.ctvnews.ca/ottawa-school-teacher-living-with-rare-pulmonary-arterial-hypertension-for-more-than-a-decade-1.6658571 [Accessed 12/03/24]
12. Takita Y, Takeda Y, Fujisawa D, *et al.* 2021. Depression, anxiety and psychological distress in patients with pulmonary hypertension: a mixed-methods study. *BMJ Open Respir Res* 8(1): e000876
13. Naranjo M, Mercurio V, Hassan H, *et al.* 2022. Causes and outcomes of ICU hospitalisations in patients with pulmonary arterial hypertension. *ERJ Open Res*: 10.1183/23120541.00002-2022
14. Zozaya N, Abdalla F, Casado Moreno I, *et al.* 2022. The economic burden of pulmonary arterial hypertension in Spain. *BMC Pulm Med* 22(1): 105
15. Runheim H, Kjellström B, Beaudet A, *et al.* 2023. Societal costs associated with pulmonary arterial hypertension: A study utilizing linked national registries. *Pulm Circ* 13(1): e12190
16. DuBrock HM, Germack HD, Gauthier-Loiselle M, *et al.* 2023. Economic Burden of Delayed Diagnosis in Patients with Pulmonary Arterial Hypertension (PAH). *Pharmacoecon Open*: 10.1007/s41669-023-00453-8
17. Tsang Y, Panjabi S, Funtanilla V, *et al.* 2023. Economic burden of illness among patients with pulmonary arterial hypertension (PAH) associated with connective tissue disorders (CTD). *Pulm Circ* 13(2): e12218
18. McConnell J, Bilir SP, Xu Y, *et al.* 2023. Hospitalization-related costs associated with oral agents targeting the prostacyclin pathway for pulmonary arterial hypertension. *J Med Econ* 26(1): 1349-55
19. Bylica J, Waligóra M, Owsianka I, *et al.* 2020. Time from symptom onset to final diagnosis of pulmonary arterial hypertension in Polish patients. *Kardiol Pol* 78(7-8): 750-52
20. Armstrong I, Rochnia N, Harries C, *et al.* 2012. The trajectory to diagnosis with pulmonary arterial hypertension: a qualitative study. *BMJ Open* 2(2): e000806
21. Strange G, Gabbay E, Kermeen F, *et al.* 2013. Time from symptoms to definitive diagnosis of idiopathic pulmonary arterial hypertension: The delay study. *Pulm Circ* 3(1): 89-94
22. Humbert M, Sitbon O, Chaouat A, *et al.* 2010. Survival in patients with idiopathic, familial, and anorexigen-associated pulmonary arterial hypertension in the modern management era. *Circulation* 122(2): 156-63
23. Gaine S, Sitbon O, Channick RN, *et al.* 2021. Relationship Between Time From Diagnosis and Morbidity/Mortality in Pulmonary Arterial Hypertension: Results From the Phase III GRIPHON Study. *Chest* 160(1): 277-86
24. Hachulla E, Launay D, Yaici A, *et al.* 2010. Pulmonary arterial hypertension associated with systemic sclerosis in patients with functional class II dyspnoea: mild symptoms but severe outcome. *Rheumatology (Oxford)* 49(5): 940-944
25. Papa S, Scoccia G, Serino G, *et al.* 2023. Impact of Parenteral Prostanoids in Pulmonary Arterial Hypertension: The Relevance of Timing. *J Clin Med* 12(21): 6840
26. Ferrari P. 2024. Interview with Karolay Lorenty at The Health Policy Partnership [video call]. 12/01/24
27. Maeva N. 2024. Interview with Karolay Lorenty at The Health Policy Partnership [video call]. 18/01/24
28. Kolaitis NA, Chen H, Calabrese DR, *et al.* 2023. The Lung Allocation Score Remains Inequitable for Patients with Pulmonary Arterial Hypertension, Even after the 2015 Revision. *Am J Respir Crit Care Med* 207(3): 300-11
29. Chang KY, Duval S, Badesch DB, *et al.* 2022. Mortality in Pulmonary Arterial Hypertension in the Modern Era: Early Insights From the Pulmonary Hypertension Association Registry. *J Am Heart Assoc* 11(9): e024969

30. Zelt JGE, Sugarman J, Weatherald J, *et al.* 2022. Mortality trends in pulmonary arterial hypertension in Canada: a temporal analysis of survival per ESC/ERS guideline era. *Eur Respir J* 59(6): 2101552
31. Emmons-Bell S, Johnson C, Boon-Dooley A, *et al.* 2022. Prevalence, incidence, and survival of pulmonary arterial hypertension: A systematic review for the global burden of disease 2020 study. *Pulm Circ* 12(1): e12020
32. Lahm T, Tuder RM, Petrache I. 2014. Progress in solving the sex hormone paradox in pulmonary hypertension. *Am J Physiol Lung Cell Mol Physiol* 307(1): L7-26
33. Osman MS, Michelakis ED. 2018. Immunity Comes to Play in the "Sex Paradox" of Pulmonary Arterial Hypertension. *Circ Res*: 10.1161/CIRCRESAHA.118.313075
34. PHA Europe. Danijela Pešić, PH Serbia. Available from: https://www.phaeurope.org/get-involved/awareness-campaigns/phae-leaders-stories/danijela-pesic-ph-serbia/ [Accessed 12/03/24]
35. PHA Europe. Irene, ANHP Spain. Available from: https://www.phaeurope.org/get-involved/awareness-campaigns/phae-leaders-stories/irene-anph-spain/ [Accessed 12/03/24]
36. Lawrence S. 2017. Why Pulmonary Hypertension Isn't an Invisible Illness to Me [online]. Pulmonary Hypertension News. Available from: https://pulmonaryhypertensionnews.com/columns/why-pulmonary-hypertension-isnt-an-invisible-disease-to-me/ [Accessed 12/03/24]
37. Nabeh OA, Saud AI, Amin B, *et al.* 2024. A Systematic Review of Novel Therapies of Pulmonary Arterial Hypertension. *Am J Cardiovasc Drugs* 24(1): 39-54
38. Pitre T, Su J, Cui S, *et al.* 2022. Medications for the treatment of pulmonary arterial hypertension: a systematic review and network meta-analysis. *Eur Respir Rev*: 10.1183/16000617.0036-2022
39. Condon DF, Agarwal S, Chakraborty A, *et al.* 2022. Novel Mechanisms Targeted by Drug Trials in Pulmonary Arterial Hypertension. *Chest* 161(4): 1060-72
40. Peacock AJ, Murphy NF, McMurray JJ, *et al.* 2007. An epidemiological study of pulmonary arterial hypertension. *Eur Respir J* 30(1): 104-109
41. Humbert M, Sitbon O, Chaouat A, *et al.* 2006. Pulmonary arterial hypertension in France: results from a national registry. *Am J Respir Crit Care Med* 173(9): 1023-1030
42. Suntharalingam J. 2024. Interview with Karolay Lorenty at The Health Policy Partnership [video call]. 25/01/24
43. Humbert M. 2024. Interview with Karolay Lorenty at The Health Policy Partnership [video call]. 24/01/24
44. Cantres-Fonseca O, Kennedy JLW. 2022. Where's the Easy Button? The Many Barriers to Care for Patients With Pulmonary Arterial Hypertension. *J Am Heart Assoc*: 10.1161/jaha.122.027967
45. Anderson N, Schablik J, Classi P, *et al.* 2023. *Understanding Differences in Geographic Access to Care Among Patients Treated for Pulmonary Arterial Hypertension in the United States.* New York: American Thoracic Society
46. Canadian Agency for Drugs and Technologies in Health. 2015. *Macitentan (Opsumit): For long-term treatment of PAH [Internet].* Ottawa: CADTH
47. Aktaa S, Gale CP, Brida M, *et al.* 2023. European Society of Cardiology quality indicators for the care and outcomes of adults with pulmonary arterial hypertension. Developed in collaboration with the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 25(4): 469-477
48. Ivarsson B, Johansson A, Kjellström B. 2021. The Odyssey from Symptom to Diagnosis of Pulmonary Hypertension from the Patients and Spouses Perspective. *J Prim Care Community Health* 12: 21501327211029241
49. Lua S, Church C. 2022. Pulmonary hypertension in the primary care setting. *Prescriber* 33(11-12): 11-18
50. Saygin D, Domsic RT. 2019. Pulmonary Arterial Hypertension In Systemic Sclerosis: Challenges In Diagnosis, Screening And Treatment. *Open Access Rheumatol* 11: 323-333
51. Benza RL, Kanwar MK, Raina A, *et al.* 2021. Development and Validation of an Abridged Version of the REVEAL 2.0 Risk Score Calculator, REVEAL Lite 2, for Use in Patients With Pulmonary Arterial Hypertension. *Chest* 159(1): 337-346
52. 52. Wu SH, Wu YJ. 2022. Regular Risk Assessment in Pulmonary Arterial Hypertension - A Whistleblower for Hidden Disease Progression. *Acta Cardiol Sin* 38(2): 113-123
53. Miller E, Sampson CU, Desai AA, *et al.* 2023. Differential drug response in pulmonary arterial hypertension: The potential for precision medicine. *Pulm Circ:* 10.1002/pul2.12304
54. Zhu HR, Kuang HY, Li Q, *et al.* 2022. Effects of oral targeted treatments in pulmonary arterial hypertension: A systematic review and meta-analysis. *Front Cardiovasc Med* 9: 915470
55. McGoon MD, Ferrari P, Armstrong I, *et al.* 2019. The importance of patient perspectives in pulmonary hypertension. *Eur Respir J* 53(1): 1801919
56. Kolaitis NA. 2023. Lung Transplantation for Pulmonary Arterial Hypertension. *Chest* 164(4): 992-1006
57. Leard LE, Holm AM, Valapour M, *et al.* 2021. Consensus document for the selection of lung transplant candidates: An update from the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant* 40(11): 1349-1379
58. Steringer-Mascherbauer R, Lummersdorfer M, Függer R, *et al.* 2020. Long-term experience with implantable infusion pumps for intravenous treprostinil in pulmonary arterial hypertension-procedural safety and system-related complications. *Pulm Circ* 10(4): 2045894020970830
59. Gallant-Dewavrin M. 2024. Interview with Ismail Sattaoui and Kirsten Budig at The Health Policy Partnership [video call]. 09/02/24
60. Myrah J. 2024. Interview with Karolay Lorenty at The Health Policy Partnership [video call]. 16/01/24
61. de Belen E, McConnell JW, Elwing JM, *et al.* 2023. Gaps in the Care of Pulmonary Hypertension: A Cross-Sectional Patient Simulation Study Among Practicing Cardiologists and Pulmonologists. *J Am Heart Assoc* 12(2): e026413

62. Weatherald J, Humbert M. 2020. The 'great wait' for diagnosis in pulmonary arterial hypertension. *Respirology* 25(8): 790-792
63. Kiely DG, Lawrie A, Humbert M. 2019. Screening strategies for pulmonary arterial hypertension. *Eur Heart J Suppl* 21(Suppl K): k9-k20
64. Slaunwhite B. 2024. Interview with Karolay Lorenty at The Health Policy Partnership [video call]. 12/03/24
65. Doyle-Cox C, Nicholson G, Stewart T, *et al.* 2019. Current organization of specialist pulmonary hypertension clinics: results of an international survey. *Pulm Circ* 9(2): 2045894019855611
66. Segura-Ibarra V, Wu S, Hassan N, *et al.* 2018. Nanotherapeutics for Treatment of Pulmonary Arterial Hypertension. *Front Physiol* 9: 890
67. Kolaitis N. 2024. Interview with Kirsten Budig at The Health Policy Partnership [video call]. 06/02/24
68. Kikuchi H, Goda A, Takeuchi K, et al. 2023. Transition from Intravenous Epoprostenol to Treprostinil Due to Intolerable Side Effects in Patients With Pulmonary Arterial Hypertension. *Am J Cardiol* 206: 31-34
69. Narechania S, Torbic H, Tonelli AR. 2020. Treatment Discontinuation or Interruption in Pulmonary Arterial Hypertension. *J Cardiovasc Pharmacol Ther* 25(2): 131-41
70. Qadus S, Naser AY, Ofori-Asenso R, *et al.* 2023. Adherence and Discontinuation of Disease-Specific Therapies for Pulmonary Arterial Hypertension: A Systematic Review and Meta-Analysis. *Am J Cardiovasc Drugs:* 19-33
71. Hu X, Ding N, Songchen W, *et al.* 2023. Lung Transplantation for Pulmonary Arterial Hypertension: Optimized Referral and Listing Based on an Evolving Disease Concept. *J Cardiovasc Dev Dis* 10(8): 350
72. Escribano-Subias MP. 2024. Interview with Karolay Lorenty at The Health Policy Partnership [video call]. 25/01/24
73. Pulmonary Hypertension Association. 2019. PHA's PH Care Centers (PHCC) Program Accredits Five New Centers. Available from: https://phassociation.org/phas-ph-care-centers-phcc-program-accredits-five-new-centers/ [Accessed 16/05/24]
74. Pulmonary Hypertension Association. Pulmonary Hypertension Care Centers. Available from: https://phassociation.org/PHCareCenters/ [Accessed 01/05/24]
75. Andersen M, Diederichsen SZ, Svendsen JH, *et al.* 2023. Continuous long-term heart rate variability and risk assessment in pulmonary hypertension. *Open Heart:* 10.1136/openhrt-2023-002302
76. Delcroix M, Howard L. 2015. Pulmonary arterial hypertension: the burden of disease and impact on quality of life. *Eur Respir Rev* 24(138): 621-629
77. Bussotti M, Sommaruga M. 2018. Anxiety and depression in patients with pulmonary hypertension: impact and management challenges. *Vasc Health Risk Manag* 14: 349-360
78. Aguirre-Camacho A. 2021. Understanding the perspective of patients with pulmonary arterial hypertension: looking beyond health-related quality of life. *Ther Adv Rare Dis* 2: 2633004020986166
79. Fundación Contra la Hipertensión Pulmonar. 2024. Encuentro clave entre la Ministra de Sanidad y la Fundación contra la Hipertensión Pulmonar para avanzar en la mejora del tratamiento y apoyo a pacientes [online]. Noticias Fundación contra la Hipertensión Pulmonar. Available from: https://www.fchp.es/noticias-hipertensionpulmonar/encuentro-clave-entre-la-ministra-de-sanidad-y-la-fundacion-contra-la-hipertension-pulmonar-para-avanzar-en-la-mejora-del-tratamiento-y-apoyo-a-pacientes.html [Accessed 15/10/24]
80. Assistance Publique Hôpitaux de Paris. [Pulmonary Hypertension Reference Centre] Centre de référence de l'hypertension pulmonaire. Available from: https://maladiesrares-paris-saclay.aphp.fr/maj-centre-hypertension-pulmonaire/ [Accessed 01/05/24]
81. Assistance Publique Hôpitaux de Paris. [Pulmonary Arterial Hypertension Reference Centre] Centre de référence de l'hypertension artérielle pulmonaire. Available from: https://maladiesrares-paris-saclay.aphp.fr/les-centres-de-reference/centre-de-reference-de-lhypertension-arterielle-pulmonaire/ [Accessed 01/05/24]
82. Suntharalingam J, Ross RM, Easaw J, *et al.* 2016. Who should be referred to a specialist pulmonary -hypertension centre - a referrer's guide. *Clin Med* (Lond) 16(2): 135-41
83. Pulmonary Hypertension Association. PHA Scientific Leadership Council. Available from: https://phassociation.org/scientific-leadership-council/ [Accessed 01/05/24]
84. Chakinala MM, Farber HW. 2020. Pulmonary Arterial Hypertension and Specialty Care Centers: We Had a Feeling; Now We Have Data. *Chest* 158(1): 28-30
85. Pulmonary Hypertension Association of Canada. Patient-Oriented Research. Available from: https://phacanada.ca/Research/Patient-Oriented-Research [Accessed 01/05/24]
86. Kelly P. 2022. *Patients as Partners: Investing in a New Era of Patient-Oriented Research.* Vancouver, Canada: PHA Canada
87. PHA Canada. PAH Patient Evidence Submission Survey: sotatercept. Available from: https://phacanada.ca/Research/non-clinical-research-studies/PAH-Patient-Evidence-Submission-Survey-sotatercep [Accessed 01/05/24]



Lorenty K, Harding E, Sattaoui I. 2024. *Meeting the needs of people with pulmonary arterial hypertension (PAH): policy toolkit.* London: The Health Policy Partnership

*This report was drafted by The Health Policy Partnership, who held editorial control under the guidance of the Steering Committee. The content is based on desk research and interviews with experts in the field of pulmonary arterial hypertension. The development of this report was initiated and funded by Merck Sharp & Dohme LLC. Experts provided their time for free.*

The Health Policy Partnership