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ADDRESSING THE UNMET NEEDS OF PERSONS LIVING WITH PULMONARY HYPERTENSION: A Call to Action

WHY ACTION IS NEEDED FOR PULMONARY HYPERTENSION

Most of us take breathing for granted. People living with pulmonary hypertension do not. They often struggle to breathe and doing any kind of activity can be difficult. Pulmonary hypertension (PH) is the broad, inclusive name for a group of chronic diseases that affect the lungs and the heart. Some forms of PH are rare, progress rapidly and are debilitating and deadly. In PH, the arteries that carry blood from the heart to the lungs narrow for reasons that are not yet entirely understood. The heart struggles to pump blood through the narrowed arteries, resulting in high blood pressure in the lungs and the enlargement of the heart. Eventually, the overworked heart wears out, and heart failure and death can result.

Global estimates suggest that PH affects 20-70 million people worldwide.^{1, 2} It may be caused by several underlying conditions, but often there is no identifiable cause. Symptoms usually do not appear until the disease has progressed, meaning diagnosis and treatment may be delayed. PH does not discriminate, and while it is more common among females it occurs irrespective of age, race, and ethnicity. It can strike our colleagues, our neighbours, our family, and ourselves.³

Unfortunately, generally approved treatments⁴ exist for only around one percent of people diagnosed with PH – those with two rare forms of the disease: Pulmonary arterial hypertension (PAH), Chronic thromboembolic pulmonary hypertension (CTEPH). Even with therapy, most patients with these forms of the disease have a reduced life expectancy, although timely diagnosis and better disease management can significantly improve that timeline.

The struggle to do something as essential as breathing is both frightening and debilitating and has a dramatic impact on people's lives. That is why this call to action is urgently needed:

- People with PH need timely diagnosis in order to receive appropriate treatment as managing the disease in the early stages helps to reduce both the physical damage and the impact on quality of life
- Expert centres are needed within reach of people with PH. These need to have multidisciplinary medical teams who are trained and experienced in the diagnosis and treatment of PH to ensure that the right treatment is provided to the right people
- Researchers must continue to investigate innovative and improved treatments until a cure is found
- People living with PH must be empowered with their voice amplified by patient associations during the creation of health care policy
- People living with PH must have access to the support that patient associations can offer, and these they must have the resources they need to serve people with PH
- The availability of psychosocial support must be assured so that people are supported through very difficult times in managing the impact on their lives.

This paper focuses on Europe, however the information is applicable worldwide. More needs to be done in recognising and treating PH globally, within the EU and other European countries.



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CALL TO ACTION

1. Improve access to expert care

- Establish, properly fund and maintain, and integrate expert centres in local healthcare systems:
- High-volume expert centres, staffed by a multidisciplinary team of physicians who are trained and experienced in pulmonary hypertension (PH) care, should provide the diagnosis and care of PH patients

PHAEUR PE

- Expert centres are necessary to ensure that currently available drugs are prescribed and used appropriately •
- Patients where PAH or CTEPH is suspected should be referred to expert centres without delay
- Regularly review national and EU policies based on real life data to ensure and facilitate the implementation of the cross-border healthcare directive
- Increase access to transplantation by enacting and regularly reviewing organ donor policies and maintaining processes • that enable organ transplantations. All EU countries should develop and maintain comprehensive and humane organ donation policies, which ensure high-prioritised status on the waiting list for eligible PH patients
- Develop and regularly update PH clinical practice guidelines
- Ensure that drugs or combinations of drugs for PH patients are prescribed by expert physicians, and that patient access is not limited by national policies
- Establish, regularly update and maintain national policies which ensure continuous access to care even in special situations

2. Improve awareness and screening

- Initiate PH awareness campaigns for both professionals and public
- Create training programmes on PH for health care professionals
- Create national screening and diagnosis programmes, tailored to PH patient subgroups
- Raise awareness of the potential for curative surgery and angioplasty for chronic thromboembolic pulmonary hypertension (CTEPH) and the need to appropriately evaluate CTEPH patients

3. Encourage clinical research and innovation

Ensure more policy, academic support, funding and incentives for:

- Fundamental, basic science, PH research
- Research that leads to effective treatments for all forms of PH and ultimately a cure for PH
- Capacity of existing centres to support clinical trials and investigational research
- Research to determine non-invasive methods for measuring pulmonary pressure and cardiac output

4. Empower patient associations

- Facilitate real-life information exchange between PH patient associations and policy makers through roundtables, working groups, and other activities to ensure that the patient voice is heard and considered during decision making
- Include patient associations in health care policy debates, early clinical trial design discussions, regulatory activities for medicines, and relevant decision-making processes
- Empower patients to make contributions through a proactive inclusive approach to ensure that people with PH are able to talk about their experiences and treatment, providing the input needed to make decisions fundamental to the lives of people living with PH
- Increase the capability of patient associations to serve patients more effectively, particularly through the provision of accurate, evidence-based, regularly updated information
- Encourage balanced financial support, including government funding, for patient associations so that they can continue to be independent

5. Ensure availability of psychosocial support

- Ensure that PH treatment encompasses treatment for the "whole" patient. National systems of integrated care must be instituted, encompassing all aspects of medical, psychosocial, nutritional, and rehabilitative support for patients and their carers
- Ensure that patient associations have secure, sustainable sources of funding so that the people who best know what it is like to live with PH can support people living with PH, including through telephone help lines
- Afford disabled status to people living with severe forms of PH so that they can access key services, and are enabled to lead a more independent life

ADDRESSING THE UNMET NEEDS OF PEOPLE LIVING WITH PULMONARY HYPERTENSION

Introduction

The term pulmonary hypertension (PH) describes a condition where high blood pressure affects the right heart and the vessels of the lungs. Some forms or "subtypes" of PH are rare and can progress rapidly, as well as being debilitating and deadly.

Other forms are more common and less aggressive, yet still impact people's lives. In PH, the arteries that carry blood from the heart to the lungs narrow for reasons that are not entirely understood. The narrowed arteries force the right side of the heart, which pumps blood to the lungs, to work harder. Eventually, this wears out the heart, symptoms worsen, and heart failure and death can result.5 PH does not discriminate. Although some forms are more common in young adults and in women and it sometimes runs in families, it occurs irrespective of age, race, and ethnicity.

The symptoms of PH, which may include shortness of breath during exercise, fatigue, dizziness and fainting spells, vary from patient to patient, and usually do not occur until the disease has progressed. This delays diagnosis and treatment.

Diagnosis and treatment of PH is complex and belongs in expert hands. Fortunately, most regions in Europe now have established PH centres⁶ and it is important that patients with suspected or confirmed PH are referred to these expert centres.





Healthy blood vessel



Blood vessel of a person with PAH

Types of Pulmonary Hypertension

Pulmonary hypertension is the broad classification for a group of debilitating diseases that affect the heart and lungs. There are five subtypes of PH. Some are rare; some occur more frequently. Each subgroup has different underlying causes and must be treated differently. In fact, treatments that work in some forms of PH may be ineffective and even harmful in other forms of PH.^{7, 8, 9, 10, 11}

	Definition	Etiology	Frequency	Treatment
Group 1	Pulmonary Arterial Hypertension	Idiopathic (unknown cause), heritable (genetic) or drug-associated PAH, associated with connective tissue disease, portal hypertension, congenital heart disease, HIV infection	Rare (newly diagnosed in 5-10 patients per million adults)	Several medications available and approved (including oral, intravenous and subcutaneous drugs), often used in combination
Group 2	PH associated with left heart disease	Systolic and/or diastolic dysfunction of the left heart, valvular heart disease	Relatively common, affecting up to 50% of patients with advanced left heart disease	Treatments primarily target the underlying condition, no established treatment. PH, studies are on the way. PH center should be contacted in case of severe PH
H Group	PH associated with to lung disease or hypoxia	Various chronic lung diseases including COPD, interstitial lung disease (ILD), hypoventilation syndromes, high altitude; asthma is usually not associated with PH, but can be a co-morbidity	Relatively common, affecting 10-30% of patients with COPD or ILD	Treatments primarily target the underlying condition, no established treatment. PH studies are on the way. PH center should be contacted in case of severe PH
Group 4	CTEPH (chronic thromboembolic pulmonary hypertension)	Organized clots in the lungs which obstruct pulmonary arteries	Rare (newly diagnosed in 3-6 patients per million adults and in 2-3% of patients who have recovered from acute pulmonary embolism)	Several treatment options including surgery, balloon angioplasty and medication. Therapy should be determined at CTEPH center
Group 5	PH associated with other diseases	Includes sarcoidosis, pulmonary histiocytosis, hematologic disorders, and other conditions	Rare, insufficient data for most of these conditions	Treatments primarily target the underlying condition. Patients with severe PH should be referred to PH centers

Symptoms of Pulmonary Hypertension

Irrespective of the type of pulmonary hypertension, symptoms may vary.

As PH worsens, the patient may find it hard to perform any physical activities, affecting their ability to work or perform even the simplest of tasks. Patients' daily activities are therefore often limited, and they report a substantially reduced quality of life.¹²

"This is a totally invisible illness. Many times, even the family does not believe it, since they see a healthy-looking person, who is gasping for air. Nobody can truly understand the limitations of the patients." • Dora, Hungary

Diagnosis of Pulmonary Hypertension

Once the symptoms raise the suspicion of PH, the first step is usually a cardiac ultrasound examination (echocardiography). Several other diagnostic tools such as a chest X ray and an electrocardiogram (ECG) are often useful as they help in identifying the cause of the symptoms, and in determining the next diagnostic steps.



"My PH diagnosis has taught me that, even though not everything may be possible for me anymore, I can choose my own narrative and find alternatives." • Maleen, Austria

The diagnostic approach¹³ to PH depends a lot on the patient's history and the findings of the initial investigations. If an echocardiography shows signs of severe PH and/or severe right heart dysfunction, immediate referral to a PH centre is strongly advised. The PH centre will perform further investigations to confirm the diagnosis of PH, determine its cause and its severity, all of which are prerequisites to starting the best possible therapy. In countries without a PH centre, patients should be referred to respiratory or cardiology experts. Right heart catheterisation (RHC) is still considered mandatory to make a diagnosis of PH.

Right heart catheterization is an invasive procedure, but safe in experienced hands. It remains the only tool that provides a complete haemodynamic assessment, which is needed to ensure a proper diagnosis and classification of PH in order to make the best possible treatment decisions.

"It was a shock to get my PH diagnosis. Next came a determination to keep alive. This was 17 years ago..." • Hall, Norway

Treatment of Pulmonary Hypertension

While we have well established treatments for PAH (group 1) and CTEPH (group 4), there are no generally accepted and approved treatments for other forms of PH in Europe; however, a new treatment option is approved for PH-ILD patients in the US.

Treatment of PH should focus on the individual. In PAH, structured risk assessment,^{14, 15} has been developed to guide treatment decisions. Risk is determined by several clinical measurements, including a 6-minute walking test, echocardiography and haemodynamics taken during right heart catheterisation. The goal of the therapy is achieving and maintaining a low-risk profile which is associated with good exercise tolerance and normal or near-normal right heart function. In studies, patients with PAH who gain a low risk profile through medical therapy have 5-year survival rates of 90% or higher.^{16, 17}

"When I talk with patients looking for a diagnosis I always tell them the following: If you do not have PH you excellent doctor and you are in good hands." • Leonardo, Italy

The treatment of PAH is often based on a combination of medicines, which are available as tablets, and are usually well tolerated by patients with PH. Other forms of medications (intravenous or subcutaneous pumps to ensure steady dose of medicines) are also available, however some of them put a considerable burden on the quality of life of patients. In many patients with PAH, the use of combination therapies provides much better short term and long-term results than starting with a single therapy.¹⁸ Still, physicians may prefer the latter option in some patients for medical reasons. In patients with advanced disease, it may be necessary to add additional treatments such as prostacyclin therapy. These therapies are more burdensome, but technical improvements such as fully implantable pumps are making them safe and increasingly patient-friendly.¹⁹

For CTEPH, there is now a wide range of therapeutic options including medical treatment, surgery to remove blockages (pulmonary endarterectomy) or catheter-based interventions to re-establish vessel patency.²⁰ The best treatment must be identified individually and ideally, this is done at expert centres where all options are available.

,For me, part-time work means being able to be useful and get involved in society." • Milena, Czechia

These centres are not only capable of providing the best possible care but also have access to the latest developments and participate in clinical studies, which is usually the only way to receive new medications that have not yet been approved and – at the same time – the best way to move the field forward.

Prognosis of Pulmonary Hypertension

All forms of PH are associated with symptoms which can be severe and life threatening. The most common symptom is the limitation in physical activity or exercise. Many forms of PH result in a reduced life expectancy. Yet, there is hope. Two or three decades ago, patients with newly diagnosed PAH were facing an 80-90% risk of living for less than 5 years after receiving their diagnosis, and lung or heart-lung transplantation was sometimes the only treatment available. Today, these numbers have improved substantially.

Unfortunately, there is still no cure for PAH and even today, some affected patients may eventually need a lung transplant or die from their disease. However, novel treatments are currently being developed which for the first time offer the potential to partially or even extensively reverse the pulmonary vascular changes leading to PH. There is still a long way to go, but the treatment options for the many forms of PH are constantly improving and so is the outlook for the affected patients.

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IMPROVE ACCESS TO EXPERT CARE

- - of PH patients
 - used appropriately
- Regularly review national and EU policies based on real life data to ensure and facilitate the implementation of the cross-border healthcare directive
- status on the waiting list for eligible PH patients
- Develop and regularly update PH clinical practice guidelines
- Ensure that drugs or combinations of drugs for PH patients are prescribed by expert physicians, and that patient access is not limited by national policies
- Establish, regularly update and maintain national policies which ensure continuous access to care even in special situations

To reliably diagnose and to effectively treat rare diseases, such as pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH), resources and experience need to be concentrated in dedicated expert centres. However, these centres need to be well positioned within national healthcare systems, so that they deal with the right patients. Clear and realistic pathways, from suspected disease by GPs (general practitioners) to advanced treatment by experts, must be elaborated and implemented. These pathways should reduce the delay in receiving advanced care, without overwhelming expert centres with unnecessary referrals from other services where common causes of PH can be more easily identified.

Establish and Support Networks of Expert Centres

High-volume expert centres, staffed by a multidisciplinary team of physicians who are trained and experienced in PH care, should provide the diagnosis and care of PH patients. High-volume expert centres have repeatedly been shown to bring the best outcomes for patients, greatest patient satisfaction, lowest complication rates, shortest length of hospital stay, and best value for health

• Establish, properly fund and maintain, and integrate expert centres in local healthcare systems:

 High-volume expert centres, staffed by a multidisciplinary team of physicians who are trained and experienced in pulmonary hypertension (PH) care, should provide the diagnosis and care

· Expert centres are necessary to ensure that currently available drugs are prescribed and

• Patients where PAH or CTEPH is suspected should be referred to expert centres without delay

 Increase access to transplantation by enacting and regularly reviewing organ donor policies and maintaining processes that enable organ transplantations. All EU countries should develop and maintain comprehensive and humane organ donation policies, which ensure high-prioritised

care payers. In fact, the European Union Committee of Experts on Rare Diseases (EUCERD) "recognises the European added-value of networks of expertise in the field of rare diseases, and cites the need to improve 'universal access to high quality healthcare for rare diseases, in particular through the development of national/ regional centres of expertise."²¹

The European Organisation for Rare Diseases (EURORDIS) in its Declaration of Common Principles on Centres of Expertise and European Reference Networks for Rare Diseases²² in 2008 and the European Council Recommendation on European Action in the Field of Rare Disease expressed the "utter need for Centres of Expertise and European Reference Networks for Rare Diseases."

These calls and the cross-border healthcare directive²³ have ultimately led to the concept of European Reference Networks (ERNs) established in 2017.

The European Reference Network for respiratory diseases (ERN-Lung) is an example of international collaboration of most experienced EU centres caring for patients with advanced forms of PH. However, ERN-LUNG does not cover all European countries and not all EU countries are represented; it is growing dynamically. In order to become a full member numerous criteria to be met and national healthcare authorities' involvement is needed. Some of the countries are represented by affiliated partners and patient associations making the directory of reference PH centres incomplete and in some cases the access for patients difficult.

The way that PH patients are managed varies substantially across regions and countries. For instance, in France and the UK, centralised structures with selected expert centres are authorised to prescribe drugs for PAH, while other physicians are not allowed to do so. In other countries, such as Germany, expert centres and non-specialised health care facilities and practitioners both diagnose and treat PH patients. The optimal solution for a healthcare system should take into account the demography and dimensions of the country, as well as the existing infrastructure.

In larger countries PH centres should form a collaborative network to share expertise. Leading expert centres with high volume of patients should offer comprehensive PH diagnosis and a full portfolio of advanced treatment options. Leading centres should be supported by satellite expert centres, which could continue medical treatment, adjusted according to locally performed risk assessments. This structure would reduce the need for patients and their families to travel long distances, although leading centres could still be called upon when necessary.

Each EU country should be directly linked to and nominate at least one national PH-expert centre to the ERN-LUNG-Pulmonary Hypertension Core Network. Membership of this network offers the opportunity to consult and refer, exchange expertise and strengthen state of the art and standard practices. ERN-LUNG-PH is particularly active in establishing guidance to form optimal patient pathways, from suspicion, to diagnosis and therapy.

In a disease such as pulmonary hypertension, which includes rare diseases subtypes, expert centres should:

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health, other regulatory authority or health care payers) testing

pathway and identifying which patients to fast track where PAH or CTEPH is suspected

- Prescribe disease-targeted drug therapies for PH for the entire duration of treatment
- Provide written patient information and have formal links with patient associations Adhere to specific standards of care and guidelines (as detailed below)
- Undertake a clinical research programme including entry of patients into randomised controlled trials
- Participate in the development of a network of PH centres within their country
- Reference Networks)
- Undertake clinical audits which report outcomes and are comparable with other expert centres in the same country and preferably in other European countries
- Provide a minimum of one to two years' training in PH for colleagues, junior doctors, and nurses within the expert centre
- appropriate patient referrals to expert centres
- Perform thoracic surgery and organ transplants
- Actively participate in international exchanges of research and other clinically relevant data.

The size of an expert centre should depend on the population and demographics of the country in which it is located. Each country, however, should have at least two adult and one paediatric centre. In general, a recommendation on the minimum number of patients seen and new patients diagnosed by an adult centre should be followed. A recommendation should be in place for paediatric centres as well.

Define and Facilitate Patients' Pathways Within Healthcare Systems

Establishing PH expert centres and their networks will see success only when they are correctly positioned within national healthcare systems.²⁴ This requires a comprehensive system controlling the flow of patients who need a PH diagnosis and treatment decisions. The system should enhance access to PH expert centres for patients with suspected PAH and CTEPH, but direct other forms of PH to standard cardio-respiratory care. This should avoid overburdening expert centres, increasing waiting times and delaying treatment for patients who really need it.

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- Be accountable to the organisation that designates their expert centre status (e.g., department of
 - Diagnose patients with a medical team including expert staff in echocardiography, imaging, cardiac catheterisation laboratory, lung function laboratory and cardio-pulmonary exercise
 - Be active in providing consultations, including using digital health platforms to provide advice to patients, general practitioners (GPs) and other health professionals on the optimal diagnostic
 - Manage patients with a team of physicians who are trained and experienced in the treating PH. The team should include respiratory physicians, cardiologists (including adult congenital heart disease specialists), rheumatologists, haematologists and experts in clinical genetics, critical care, anaesthetics, family planning, palliative care, mental health and rehabilitative medicine. This team should have close links to other clinical services including pulmonary endarterectomy surgery (PEA), balloon pulmonary angioplasty (BPA) and lung/heart-lung transplantation teams

Apply for some form of presence within International PH Centre Networks (e.g. European

• Undertake an educational programme for health care professionals to raise awareness about

To reach clinically relevant goals there is an urgent need to:

- Describe standarised patient pathways with different entry points and optional fast tracks to expert centres, whenever justified
- Develop and regularly update evidence-based information for patients describing symptoms of pulmonary hypertension and how to obtain a diagnosis. This should be available in local languages and distributed widely in collaboration with national and European patients' organisations
- Develop and regularly update information for GPs on symptoms and signs suggestive of pulmonary hypertension based on current clinical practice guidelines and facilitated by availability of PH expert information points
- Provide dedicated information points issuing advice to patients and GPs with the aim of controlling the flow of patients to cardiological or pulmonological centres and advising fast track referral to PH expert centres
- Create high-quality tele-consultation platforms for health care professionals to allow direct comprehensive multidisciplinary consultations of clinical cases with PH expert centres. These platforms should allow national PH expert centres to consult with highly specialised PH expert centres in other countries
- Support user friendly access to reimbursed cross border on-site consultations and treatment in top international PH expert centres whenever necessary.

These actions agree with and complement proposals from leading scientific societies.

The ERN-LUNG has developed a comprehensive Patients' Pathway for suspected rare lung diseases, including PH. This pathway includes an information point providing advice to patients and GPs (EXABO – Expert Advisory Board). EXABO^{25, 26} is aimed to direct patients to either regular health service providers or to ERN-Lung centres for further diagnosis and care.

ERN-LUNG: Patient Pathway via Core Networks for specific diagnosing and Cross Border Care

Patient with unclear respiratory disease referred by tertiary centre (e.g. local, regional, national referral/Supporting Part ner referral) sent to presumed specific ERN -LUNG Core Network



* As soon as satisfying solution identified, pathway will be left and patient referred either to a dedicated HCP-CN Member or to a non-ERN clinical centre at a national level

Patient Pathway for specific diagnosis and Cross Border Care. According to ERN-LUNG.

ERN-LUNG'S CPMS, a multimedia consultation platform, shares anonymous clinical and high-quality imaging studies with European experts. It has been designed for cross-border consultations between ERN centres, which ensures that not the patients are travelling, but the knowledge. While CPMS has its challenges, providing a less resource intensive or better funded mechanism is needed. This needs to take into consideration the reimbursement of the costs incurred with consultation to achieve life saving decision-making, and to avoid the need for cross border patient referral, with all of its related logistic and financial problems.

Special situations affecting access to care

Remote consultations and tele-medication will be important in the future, as highlighted during the COVID-19 pandemic. Adequate infrastructure and funding need to be in place to better serve the patients and ensure the continuity of the healthcare services during even challenging times.

Cross-border collaboration, disaster mitigation plans and playbooks are needed to address challenges resulting from armed conflicts. Access to healthcare services is to be guaranteed which takes into account the needs of the continuous medication required by PH patients.

Increase availability of Lung and heart and Lung transplants for endstage Pulmonary Hypertension

Heart-lung transplantation and bilateral lung transplantation are last resort measures in PH and PAH. Transplanted organs provide a long-term survival benefit for patients with advanced PH, improving blood flow, the ability to exercise, alleviated shortness of breath, and improving long-term survival. Current guidelines recommend assessing patients regularly whether they are at low, intermediate, or high risk of death. In patients who do not meet low risk criteria with optimised medical therapy, evaluation for lung transplantation should be considered. It is less clear when eligible patients should be actively listed for transplant, however, high-risk patients have a better chance of survival with transplantation than without.²⁷



PH patients awaiting transplantation often experience rapid disease progression and are therefore in more critical need of donor organs than are patients with other diseases. Unfortunately, this urgent need is not adequately reflected in the different organ allocation systems across Europe. These organ allocations should be adapted and patients with severe PH who are at high risk despite optimal treatment should be prioritized on the transplant waiting lists.²⁸

Transplants should be performed only in high-volume specialized expert centres. These centres should allow for the possibility of trans-border referrals and using expertise that transcends geographic borders.

Transplants are, however, associated with major shortcomings, including the need for lifelong immune-suppression (to reduce the likelihood of rejection of a transplanted organ), and the risk of infection.

From a distance, I can say that my long journey in the world of pulmonary hypertension was full of ups and downs. When I realized that I was on the waiting list for a lung transplant, I gathered all my inner strength because I knew that this was the only way to climb my personal Everest. I became the winner in the hardest battle, to save my own life." • Natalia, Bulgaria

Common political will, improved legal and institutional frameworks, appropriate funding and benchmarking can contribute to better transplantation programs and ultimately to more organs.²⁹

Standards of Care and Clinical Guidelines³⁰

Whatever the health care system, physicians should focus on obtaining the best outcomes for their patients. Among the Council of the European Union Recommendations on action in the field of rare diseases, one important goal is to "gather expertise at the national level and support the pooling of that expertise with European counterparts" to encourage "sharing of best practices on diagnostic tools and medical care" and improve standards of care for patients with rare diseases.³¹

The European Society of Cardiology and the European Respiratory Society, have published evidencebased guidelines³² for PH care and regularly review and update it as necessary: the next edition is expected in August 2022. These should serve as a guide and model for national standards of care. Any

A document describing standards of care for pulmonary hypertension centres should consider inclusion of standards about PATIENT-CENTRED CARE REFERRAL DIAGNOSIS AND ASSESSMENT CARE AND TREATMENT PATIENT MONITORING, REVIEW, AND FOLLOW-UP SHARED CARE PSYCHOSOCIAL SUPPORT AND PALLIATIVE CARE COMMUNICATION WITH HEALTH CARE PROFESSIONALS OUTSIDE THE EXPERT CENTRE EDUCATION AND TRAINING OF EXPERT CENTRE STAFF RESEARCH AND DEVELOPMENT TRANSITION OF PATIENTS FROM PAEDIATRIC TO ADULT SERVICES THORACIC SURGERY AND TRANSPLANT

differences at a national level from internationally endorsed guidelines, which may be justified by country specific limitations, should be minimised. Universal standards should be reached in the shortest possible time. At the same time lay summaries of the guidelines should be developed and made available to the patients to contribute to the better understanding of their condition.

Treatment Access

In a rapidly advancing disease area such as PH, healthcare professionals should have sufficient flexibility to provide the right combination of drugs and other treatments in the right sequence for their patients. National policies that limit the availability of treatments, or that impose "fail first" restrictions where the cheapest drug is provided first, do not support the evolving standard of PH care. Equally, they do not focus on the holistic care of patients, may lead to poor outcomes for patients, and hinder treatment options which might be a result of shared decisions of the patients and treating physicians.

Moreover, many orphan drugs and treatments for rare diseases are still not reimbursed nationally for unacceptably long periods of time after being approved for use. As should be the case with all treatments for life-threatening conditions, where access can save lives, PH treatments should be reimbursed after approval. The healthcare system should ensure that all recommended treatments for PH patients prescribed by expert PH physicians are not limited by local or national payers' policies prioritising their own interests over those of patients with severe forms of PH.

have access and that is why I use all my energy to equalize these rights. I'll be happy when the medicine is available to all." • Vera, Bosnia and Herzegovina





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IMPROVE AWARENESS AND SCREENING

- Initiate PH awareness campaigns for both professionals and public
- Create training programmes on PH for health care professionals
- Create national screening and diagnosis programmes, tailored to PH patient subgroups
- Raise awareness of the potential for curative surgery and angioplasty for chronic thromboembolic pulmonary hypertension (CTEPH) and the need to appropriately evaluate CTEPH patients.

Screening and diagnosis

There are no approved therapies for most forms of PH. While there are several established treatment options for PAH, a rare disease, unfortunately PAH treatments may be harmful in other forms of the disease. For these reasons, systematic screening programmes³³ for at-risk groups are essential to diagnose patients as quickly as possible, before disease progression, to substantially improve patient prognosis.

disease and it may contribute to earlier diagnosis." • Tanja, Finland

Given that PH symptoms are often non-specific (i.e. symptoms do not necessarily point to a PH diagnosis), a large-scale public screening campaign would be unaffordable and ethically questionable: patients would need to undergo invasive diagnostic procedures and incur the risk of false-positive diagnoses. Therefore, screening programmes should be initiated only to ensure timely diagnosis of PH in high-risk patient associations. All these at-risk patients should undergo a physical examination at regular intervals, incorporating ultrasound, to look for the early signals of PH.

The following patient subsets should be specifically targeted for screening:

- People who have shortness of breath for no apparent reason
- Family members of patients with heritable PAH (with BMPR2 or other mutations)³⁴
- form of PAH
- 200 people living with HIV also has PAH)
- five percent.38
- screen for the development of PH post-repair.⁴¹

Chronic thromboembolic pulmonary hypertension (CTEPH)⁴² deserves particular attention because it is the only form of PH that can be cured without needing transplantation. CTEPH has been observed in 0.1 to 3 percent of patients who have survived pulmonary embolism (PE)⁴³. Persisting clots impede blood flow, which in turn leads to right ventricular failure, causing death. If the clots are removed, a normal blood flow can be restored.

Organised clots can be removed with pulmonary endarterectomy (PEA). For patients not eligible for PEA balloon pulmonary angioplasty (BPA) has emerged as a therapeutic option. In addition, medical therapy has been approved for patients with inoperable CTEPH. The role of a multi-disciplinary team for the optimal management of patients cannot be overemphasised. Lastly, clinical screening algorithms may help in recognising CTEPH in patients with PE using their medical history.

disease." • Nina, Slovenia



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Patients with connective tissue disease (CTD): Some diseases, such as systemic sclerosis³⁵, lupus erythematosus, and, to a lesser extent, rheumatoid arthritis, dermatomyositis, and Sjögren's syndrome, bring an increased risk for PH. PAH associated with CTD is the second most prevalent

Patients with HIV/AIDS³⁶: The prevalence of PAH in HIV patients is about 0.5 percent (i.e., one in

Patients with portal hypertension³⁷ (an increase in pressure in the vein that carries blood from the digestive organs to the liver): PAH is a well-established complication in patients with established liver disease (occurring in one to two percent of such patients). In patients with severe liver disease, such as those scheduled for liver transplantation, the incidence of PAH rises to approximately

Patients with congenital heart disease³⁹: Systemic-to-pulmonary shunts (congenital heart defects) are among the most frequent congenital heart diseases, and an estimated five to 10 percent of this large patient group have PAH.⁴⁰ Clinical research in this population, even in the most severe forms of PAH, shows that available drug therapies are effective. Although surgical repair of congenital heart defects within the first year of life prevents progressive PAH in the vast majority of patients, repair in later infancy or early childhood does not preclude the development of progressive PAH later in life. All patients who have surgery should be followed long-term to

Awareness

Improved awareness about PH is essential among primary health care professionals to ensure correct and appropriate diagnosis. Only when general practitioners (GPs) are adequately educated about PH will they know how to recognise disease symptoms and to refer patients for expert care at an expert centre.

"I wish that PH was well known to everyone. This would bring greater public understanding to patients, who are often condemned to be simply out of shape or even lazy. • Tadeja, Slovenia

Awareness campaigns have been launched in various countries by patient associations and pharmaceutical companies. One of these, World PH Day, has grown to become a global initiative with more than 80 associations participating worldwide.

,With and without PH, I always have beautiful dreams about the future, that's what we call hope. However, when I start thinking about the essence, my dreams became clear as day; to have an understanding and basis." • Danijela, Serbia

Awareness campaigns are also needed for patients at risk for forms of PH so that they can be made aware of the condition and provided with information that lets them know where to find educational material and sources of support, including PH patient associations. As is the case with all rare disorders, these campaigns should be targeted at locations where they are most effective – for PH this is in cardiology, pulmonology, infectious disease, hepatology, and internal medicine clinics, sports and workplaces and for sports medicine physicians and nurses.

Awareness campaigns among the general public are also very important as these improve acceptance and understanding of PH and encourage people with common symptoms to seek a diagnosis.



ENCOURAGE CLINICAL RESEARCH AND INNOVATION

- Ensure more policy, academic support, funding and incentives for:
 - Fundamental, basic science, PH research

 - Capacity of existing centres to support clinical trials and investigational research
 - output.

To develop new treatments for PH, more translational research is needed. Translational research moves from theoretical studies to practical application, beginning with basic research in the laboratory and ultimately progressing to clinical research at the patient's bedside. Translational research has proven to be a powerful process that drives clinical research. Encouraging translational research in PH will not only strengthen the research infrastructure, but also potentially accelerate the discovery of new, safe, and effective treatments for all forms of PH.

While funding for basic research and clinical trials has increased understanding of PH and resulted in a number of approved drugs, compelling research questions remain, covering:

- with which particular drug.
- for clinical deterioration.
- been used. Future clinical trials must use more complex, clinically relevant endpoints.
- EmPHasis-10, PAH-SYMPACT), which are monitored and assessed during the clinical trials.
- of this HTA is necessary. Similar assessments should also be developed in other fields of PH.

• Research that leads to effective treatments for all forms of PH and ultimately a cure for PH Research to determine non-invasive methods for measuring pulmonary pressure and cardiac

 Clinical trials in PH subtypes other than PAH: While PAH has been the subject of a substantial number of investigations, clinical studies in other PH subgroups are less frequent. PH associated with left heart disease is, for example, the most common form of PH, yet no specific treatment is available. For patients with PH associated with lung disease the first positive prospective randomised controlled trial with a PAH drug was published in 2021. However, further studies need to follow, in order to understand which patients within this group should be treated and

Treatment outcome goals: Research is needed to clarify outcomes (tailored to severity of disease, age, and other factors), such as covering enhanced quality of life, improved functional capacity, and greater independence. In addition, evidence-based clinical risk stratification should be used in clinical practice with the goal of having as many patients as possible achieve a low-risk state

Clinically relevant endpoints for clinical trials: The majority of PH studies employ the six-minute walk test as a measure of the ability to exercise. However, its validity as an endpoint is compromised as age and orthopedic conditions may interfere with the ability to walk for six minutes. In recent clinical trials new, more clinically relevant endpoints, such as the time to clinical worsening, have

Quality of life: Quality of life is a pivotal concern for all patients. Consequently, guality of life data should be available for all approved drug treatments. Health-related quality of life⁴⁴ (HRQoL) data should be collected based on PH specific quality of life questionnaires (eg. CAMPHOR,

PH health technology assessment (HTA): At present, only one HTA is available for PAH treatment, which assesses the "clinical and cost-effectiveness of epoprostenol, iloprost, bosentan, sitaxentan and sildenafil for pulmonary arterial hypertension within their licensed indications."⁴⁵ Because new drugs are now available for PAH, and given the increasing use of combination therapy, an update

- Non-invasive diagnostic tests: Currently, the only definitive way to diagnose PAH is through right heart catheterisation (RHC). This is a costly and highly stressful procedure for the patient – particularly for infants and children – that carries risks if performed by inexperienced clinicians. Research must focus on the refinement of non-invasive diagnostic measures. For the time being, RHC is the gold standard for diagnosing PH and assessing response to therapy. In an experienced centre, the benefit-to-risk profile strongly favors performing an initial RHC for diagnosis and eventually subsequent RHCs to assess disease severity and patient response to treatment.
- Real life data: While results from approximately 30 randomised controlled clinical trials have been published on various PAH drugs and their combinations, data on patient management in clinical conditions is still limited. Observational data are needed and clear rules for primary and secondary use of health data. In line with the vision concept⁴⁶ of European Health Data Space (EHDS), better (cross-border) data exchange and access to such data is needed. Information from the management of PH patients in expert centres yields useful data, and as the number of expert centres increases, more data will be available. Equally registries will provide data from following individual PH patients over several years.
- Al and machine learning: Artificial intelligence (AI) and machine learning are to be used to transform clinical decision support systems by creating streamlined diagnostical processes and new treatment options. Large volume, structured and quality data, validated algorithms and the understanding of clinicians are needed to better capitalise on the possibilities of AI, especially in image recognition.⁴⁷
- More paediatric studies: The prevalence of pulmonary hypertension in children is not known, but it does occur. This is most commonly because of premature birth, prolonged mechanical ventilation, certain types of heart disease, diaphragmatic hernia, or family history. Paediatric patients often have comorbidities⁴⁸ (i.e. other diseases or disorders) that make the cause of PH difficult to determine. More studies are needed to understand the causes of paediatric PH and to identify optimal diagnostic tests and treatments. There are far fewer paediatric PH centres than there are adult centres. Because of the frequent need for anesthesia during right heart catheterisation (necessary for an accurate PH diagnosis), children with suspected PH should only receive care at paediatric PH centres of expertise with dedicated paediatric cardiologists and paediatric anesthesiologists.

Finally, given the lack of currently available treatments for most forms of PH, patients who qualify for clinical trials should not find their participation barred by policies that do not allow reimbursement for clinical trials and "experimental" treatment. Rather, insurance companies and reimbursement agencies must understand that these studies are often the only treatment option available for many patients, and therefore facilitate their enrolment in appropriate trials.

EMPOWER PATIENT ASSOCIATIONS

- Facilitate real-life information exchange between PH patient associations and policy makers through roundtables, working groups, and other activities to ensure that the patient voice is heard and considered during decision making
- Include patient associations in health care policy debates, early clinical trial design discussions, regulatory activities for medicines, and relevant decision-making processes
- Empower patients to make contributions through a proactive inclusive approach to ensure that people with PH are able to talk about their experiences and treatment, providing the input needed to make decisions fundamental to the lives of people living with PH
- Increase the capability of patient associations to serve patients more effectively, particularly through the provision of accurate, evidence-based, regularly updated information
- Encourage balanced financial support, including government funding, for patient associations so that they can continue to be independent.

As part of providing holistic care in the often bewildering maze that follows a PH diagnosis and throughout the whole patient journey, healthcare professionals need to refer patients to and collaborate with patient associations. Patient associations provide a wealth of experience and knowledge-based counsel, advice and direction. They offer peer-to-peer support and are an important contact point to discuss concerns and needs. Patient associations also build health literacy and enhance skills to cope with financial and psychological challenges, contributing to the main components of patient empowerment,^{49, 50} and advocate for policy change, and ultimately resulting in a better quality of life for patients.⁵¹

A study from 2021 revealed that participation in PH patient support groups meaningfully improved the health-related quality outcomes of those patients. Being part of a patient association helps improve understanding of the condition and associated medical procedures, contributes to adherence to medication, and to confidence in carrying out self-care.⁵² The two main reasons given for people living with PH to join patient associations are to learn more about the disease and to meet other people with the same condition. People with PAH who feel well-informed also find it easier to cope with their disease⁵³. PAH patient stories and shared experiences can help people to manage their own disease, offering support in finding solutions to their own individual challenges.⁵⁴ Patient associations play an important role in providing advice and make an invaluable contribution in representing people living with PH,⁵⁵ their carers and their interests. Through active involvement and advocacy, patient associations help ensure that national rare disease plans, guidelines and policies are implemented.⁵⁶ Many of the unmet needs of people living with PH can be addressed with the involvement of the patient community, particularly for the rare disease types.

People living with PH have participated in the creation and review of medical guidance (ERS statement, ESC/ERS guidelines), in steering committees for clinical trials, in scientific meetings at the European Medicines Agency⁵⁷, advocacy events in the European Parliament and have contributed to many discussions with pharmaceutical companies to better meet patients' expectations. Despite this active role more work is needed to advance to a patient centred approach. The establishment of HTA (health technology assessment) panels, guideline working groups, clinical trial boards and committees, regulatory advisory committees, and other advisory bodies should start with including patient representatives. Policy and decision makers at all levels should actively seek and involve patient associations to incorporate the perspectives of people living with PH in matters which impact their lives.

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For patient associations to be as effective and efficient as possible, these key conditions need to be met:

- Close collaboration and awareness of the health care community and other stakeholders, so that patients can be informed of the opportunities available and have a higher likelihood of taking advantage of those opportunities
- Political and social environments that respect, consider and understand the value of the not-forprofit organisations' counsel
- Balanced and sustainable funding, including tax deductibility of contributions to not-for-profit organisations, subsidies, and incentives to ensure the long-term viability of the organisations
- Broad-based support for patient associations in political spheres and within civil society.

Thanks to the hard work, efforts and dedication, patient associations became well-respected partners, but, *there is still a lot of work ahead of us."* • **Gergely, Hungary**

Beside patient associations' contribution to the health-related quality of life improvement of patients, they also make changes in the public and political domain by their advocacy role and by representing the collective identity of their members.⁵⁸ Involving people living with PH and patient associations in the establishment of PH-related health services should be fundamental to all health systems.



ENSURE THE AVAILABILITY OF PSYCHOSOCIAL SUPPORT

- Ensure that PH treatment encompasses treatment for the "whole" patient. National systems of integrated care must be instituted, encompassing all aspects of medical, psychosocial, nutritional, and rehabilitative support for patients and their carers
- Ensure that patient associations have secure, sustainable sources of funding so that the people who best know what it is like to live with PH can support people living with PH, including through telephone help lines
- services, and are enabled to lead a more independent life

Many patients feel isolated, frustrated and alone after a PH diagnosis.⁵⁹ This can directly lead to debilitating mental health issues such as depression and suicidal thoughts, so support is needed to help people with PH cope with the impact on their lives.⁶⁰ PH treatment should address the whole patient, meaning the full range of patient needs. This includes support during complex treatment management challenges, disruptions in professional lives and addressing the limitations on the activities of daily living including social and recreational activities.

physical care

Provision of information, and guidance

All categories of psychosocial support are critical in supporting people with PH and their carers. Multidisciplinary health care teams should include social workers and psychological counselors and work closely together with patient associations to address the often unmet needs of patients.⁶¹

Psychosocial assessment should be a routine component of medical treatment. Psychosocial screening tools are needed to identify patients and families at risk for emotional and mental distress. Studies show that such tools are relatively quick to develop and deploy, and that patients are willing to participate in such evaluations.⁶²

"I had a big problem getting a car purchase allowance (from national social insurance). However I managed to obtain the parking permit without any problems." • Anna, Slovakia

Even with state-of-the-art treatment, the failure to address the psychological and social issues associated with PH can lead to serious consequences. These include a lack of adherence to treatment, depression, complications in accessing or obtaining reimbursement for treatments, and delayed treatment response. Psychosocial problems can be exacerbated by several issues such as insufficient skills and information to help someone living with PH cope with their illness, anxiety, depression, and the impact of their illness on their family, social and professional lives, including school.

• Afford disabled status to people living with severe forms of PH so that they can access key



Based on Taylor SE. Social support: A Review. In: Friedman MS, editor. The handbook of Health Psychology, Oxford University Press; New York, NY: pp. 189-214.

People living with PH, their family members and carers also need up-to-date and reliable information about all aspects of the disease. An international survey found that very little information on the emotional impact of PAH was provided to people with PH, and what was provided verbally was forgotten due to the shock of the diagnosis.⁶³ The lack of information combined with feelings of insecurity or isolation can lead to a perception of inadequate care.⁶⁴

PH patient associations and health care professionals must work collaboratively to produce comprehensive and standardised PH information packages. These should include easily understandable medical information, details about the patient journey and guidance about psychosocial effects, financial issues, and other aspects of living with the disease. PH patient associations need secure ongoing funding so that they can produce new and update existing informational materials and websites.

workplace, from their friends, many of them suffer alone, they are afraid of breaking up, getting a divorce. Those looking for a partner often face it that there are not many people who can accept an incurable disease. Our *meetings, by being there for them.*" • Eszter, Hungary

PH is often invisible due to the restrictions of movement and the lack of visual signs of the disease. People living with PH often have significant limitations in their ability to move, function and exercise and should be understood to have a serious disability with disabled status granted.⁶⁵ This status would allow PH patients to have access to special parking, reduced transit fares, leave from work, and other services which help reduce reliance on government agencies and other institutional services.

Programs to strengthen the PH community and raise awareness of the disease among the medical community and general public, are an essential source of support for patients, their families, carers, and the physicians and medical staff who treat them. Equally, activities and events sponsored by patient associations must be encouraged and supported.

It is very important to find a positive perspective and a healthy balance to deal with all the negative impacts of

SUMMARY

Pulmonary hypertension can be a life-threatening condition that, depending on type and severity, will impact the ability to perform routine daily life activities. PH may accompany other diseases or may be a disease on its own. Some forms of PH are very rare while others are guite common. Although there are effective treatments for only some subtypes of PH, innovative research offers the potential for new and improved treatments for all subtypes – and hopefully, one day, a cure.

Pulmonary hypertension can affect any of us. The struggle to do something as automatic and essential to life as breathing is both frightening and disheartening. People who live with PH are often challenged on a regular basis by this simple activity, which most of us take for granted and do not even think about.

It is critical for people living with PH to be appropriately diagnosed and treated in a timely manner, for treatments to be prescribed only for those patients who will benefit from those treatments, and for innovative research to continue to investigate new and improved treatments until a cure is found. To achieve this, we call for:

- significant experience in PH.
- results in new therapies for all PH subtypes and ultimately a cure.

Breathing is not an activity that people living with PH take for granted. Let us not hold our breath but move forward now.

person!" • Agnieszka, Poland



1. To establish, properly fund and maintain, and integrate expert centres to local healthcare systems for the diagnosis, treatment, and management of PH in all countries to ensure that those at risk of and living with PH are properly diagnosed, and appropriately treated by clinicians with

2. To ensure more policy, academic support, funding and incentives for innovative research which

ABOUT PHA EUROPE

PHA Europe is a patient association that works to enhance awareness of pulmonary hypertension across Europe, promote optimal standards of care for people living with the disease, ensure the availability of approved treatments, and encourage research for new medicines and therapies. To accomplish its mission, PHA Europe helps its 34 affiliated national patient associations located throughout Europe to collaborate effectively with healthcare professionals, specialised clinics, governmental and regulatory agencies, and industry, so that all work together productively toward mutual goals.

Its regular interactions with patients and patient advocates uniquely position PHA Europe to understand the high unmet needs of people living with PH. Accordingly, PHA Europe decided to revisit its position paper 'Call to action' from 2012 and to convene a pulmonary hypertension roundtable to provide a forum for the sharing of PH knowledge and expectations across diverse stakeholders and geographic boundaries.

The 34 roundtable members are drawn from across the globe – from Asia-Pacific, Canada, Europe, Latin America, and the US. The membership reflects a wide range of clinical, patient, research, regulatory and industry interests, and includes numerous key opinion leaders at the forefront of PH care and treatment (see page 27 for a list of members).

The multidisciplinary nature of the roundtable helps members translate their unique understandings of patient, professional, and policy maker perspectives on PH treatment and care into direct action. Among the aims of the roundtable were a) to equip health policy makers with the information they need to make decisions that reflect the best interests of PH patients, and b) to ensure a scientific basis for informed treatment decision-making.

Due to the COVID pandemic face-to-face meetings were replaced by online meetings and extensive drafting work on the 'Call to action' position paper. Some of the parts were almost completely rewritten in light of the new developments. The revision covered various key topics such as the need for all PH patients to have access to optimal screening and diagnosis, appropriate treatment, patient empowerment and psychosocial support, and integrated care through centres of expertise.

The messages in this document are universal and transcend geographic boundaries because PH patients around the globe share similar concerns and face the same challenges relative to diagnosis, treatment, and care. Our call to action identifies areas of most urgent need and recommends effective ways to address those needs. Implementation of these strategies will afford PH patients access to high quality services, treatment, and support, whilst ensuring the most efficient and effective use of limited health system resources.

It should be noted that our recommendations do not necessarily imply the need for a significant increase in funding for treatment and care as much as a reallocation of existing resources. Currently funding is often inefficiently allocated, largely due to delays in diagnosis, misdiagnosis, and delayed, inappropriate, and fragmented treatment. Our call to action suggests appropriate methods to address these critical shortcomings so that existing resources are effectively and efficiently allocated for improved patient outcomes.

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REFERENCES

- 1. Hoeper MM, Humbert M, Souza R, et al. A global view of pulmonary hypertension. The Lancet Respiratory Medicine 2016;4:306-22.
- identification of the most accurate estimates from a systematic literature review. Pulm Circ 2021;11:2045894020977300. doi: 10.1177/2045894020977300
- DOI: 10.1016/S2213-2600(18)30268-6
- 2017;14:603-614. doi: 10.1038/nrcardio.2017.84
- Failure. Circulation 2020;141:678-693. doi: 10.1161/CIRCULATIONAHA.116.022362 [doi]
- 6. The list of ERN-Lung reference centres is available at https://ern-lung.eu/reference-centers-2/
- Galie N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task 7 Lung Transplantation (ISHLT). Eur Respir J 2015;46:903-75.
- 8. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J 2019;53.
- 9. 2019;53:10.1183/13993003.13901897-13992018. Print 13992019 Jan. doi: 1801897 [pii]
- 10. Nathan SD, Barbera JA, Gaine SP, et al. Pulmonary hypertension in chronic lung disease and hypoxia. The European respiratory journal 2019;53:10.1183/13993003.13901914-13992018. Print 13992019 Jan. doi: 1801914 [pii]
- 11. Kim NH, Delcroix M, Jais X, et al. Chronic thromboembolic pulmonary hypertension. The European respiratory journal 2019;53:10.1183/13993003.13901915-13992018. Print 13992019 Jan. doi: 1801915 [pii]
- 12. International Patient and Carer Survey on the impact of PH 2012: https://www.phaeurope.org/wp-content/uploads/PAH_Survey_FINAL.pdf
- doi: https://doi.org/10.1183/13993003.02311-2021
- 15. Kylhammar D, Kjellström B, Hjalmarsson C, et al. A comprehensive risk stratification at early follow-up determines prognosis in pulmonary arterial hypertension. European heart journal 2018;39:4175-4181. doi: 10.1093/eurheartj/ehx257
- 16. Hoeper MM, Kramer T, Pan Z, et al. Mortality in pulmonary arterial hypertension: prediction by the 2015 European pulmonary hypertension guidelines risk stratification model. Eur Respir J 2017;50.
- Respir | 2017;50.
- Journal 2019;53.
- hypertension. J Heart Lung Transplant 2018;37:1235-44.
- 20. Kim NH, Delcroix M, Jais X, et al. Chronic thromboembolic pulmonary hypertension. Eur Respir J 2019;53.
- 21. European Union Committee of Experts on Rare Diseases (EUCERD), "EUCERD Report: Preliminary analysis of the outcomes and experiences pdf, accessed 8 November 2011.
- 22. Document available at http://www.eurordis.org/publication/centres-expertise-european-reference- networks-rare-diseases.
- healthcare
- org/publication/eurordis-recommendations-integration-european-reference-networks-erns-national-health-systems
- Rare Respiratory Diseases. Stud Health Technol Inform. 2018;247:236-40.
- Rare Respiratory Diseases. Stud Health Technol Inform. 2020;270:986-90.
- 27. Olsson KM, Richter MJ, Kamp JC, et al. Refined risk stratification in pulmonary arterial hypertension and timing of lung transplantation. Eur Respir J 2022. doi: 10.1183/13993003.03087-2021
- NAL 14.01.2020 Joint-Statement-of-the-Thematic-Network-on-Organ-Donation-and-Transplantation.pdf
- 30. Text for the Standards of Care section has been provided by Dr. J. Simon R. Gibbs, Clinical Senior Lecturer in Cardiology, National Heart and of Cardiology.
- 31. Council Recommendation of 8 June 2009 on an action in the field of rare diseases, Official Journal of the European Union, 3 July 2009 C151/7 [EN], available at http://eur-lex.europa.eu/LexUriServ/ LexUriServ.do?uri=CELEX:32009H0703(02):EN:NOT.
- 32. Galie N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task

Leber L, Beaudet A, Muller A. Epidemiology of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension:

29

3. Rich S, Haworth S, Hassoun PM, Yacoub M: June 2018, Pulmonary hypertension: the unaddressed global health burden, Lancet Respiratory,

4. Lau EMT, Giannoulatou E, Celermajer DS, Humbert M. Epidemiology and treatment of pulmonary arterial hypertension. Nat Rev Cardiol

Rosenkranz S, Howard LS, Gomberg-Maitland M, Hoeper MM. Systemic Consequences of Pulmonary Hypertension and Right-Sided Heart

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

Vachiery JL, Tedford RJ, Rosenkranz S, et al. Pulmonary hypertension due to left heart disease. The European respiratory journal

13. Frost A, Badesch D, Gibbs S, et al. Diagnosis of pulmonary hypertension. The European respiratory journal 2019;53:10.1183/13993003.01904 14. Hoeper MP, C; Olsson, KM. COMPERA 2.0: a refined 4-strata risk assessment model for pulmonary arterial hypertension. Eur Respir J 2021.

17. Boucly A, Weatherald J, Savale L, et al. Risk assessment, prognosis and guideline implementation in pulmonary arterial hypertension. Eur

18. Galiè N, Channick RN, Frantz RP, et al. Risk stratification and medical therapy of pulmonary arterial hypertension. European Respiratory

19. Richter MJ, Harutyunova S, Bollmann T, et al. Long-term safety and outcome of intravenous treprostinil via an implanted pump in pulmonary

of pilot European Reference Networks for rare diseases," May 2011, http://www.eucerd.eu/EUCERD/upload/file/Reports/ERNAnalysis2011.

23. Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border

24. EURORDIS Recommendations on the Integration of European Reference Networks (ERNs) into National Health Systems https://www.eurordis.

25. Walther D, Steinmann O, Schaefer J, Wagner TOF, Storf H. Conception of an Expert Advisory Board for the European Reference Network for

26. Walther D, Steinmann O, Wagner TOF, Storf H. Implementation of EXABO - An Expert Advisory Board for the European Reference Network for

28. Savale L, Le Pavec J, Mercier O, et al. Impact of High-Priority Allocation on Lung and Heart-Lung Transplantation for Pulmonary Hyper-tension. The Annals of Thoracic Surgery 2017;104:404-411. doi: S0003-4975(17)30296-5 [pii]

29. Joint statement – A Shared Vision for Improving Organ Donation and Transplantation in the EU https://ekha.eu/wp-content/uploads/FI-

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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). The European respiratory journal 2015;46:903-975. doi: 10.1183/13993003.01032-2015 [doi]

- 33. Kiely DG, Lawrie A, Humbert M. Screening strategies for pulmonary arterial hypertension. European heart journal supplements : journal of the European Society of Cardiology 2019;21:K9-K20. doi: 10.1093/eurheartj/suz204 [doi]
- Montani D, Girerd B, Jaïs X, Laveneziana P, Lau EMT, Bouchachi A, Hascoët S, Günther S, Godinas L, Parent F, Guignabert C, Beurnier A, Chemla D, Hervé P, Eyries M, Soubrier F, Simonneau G, Sitbon O, Savale L, Humbert M. Screening for pulmonary arterial hypertension in adults carrying a BMPR2 mutation. Eur Respir J. 2021 Jul 22;58(1):2004229. doi: 10.1183/13993003.04229-2020. PMID: 33380512; PMCID: PMC8295506.
- 35. Weatherald J, Montani D, Jevnikar M, et al. Screening for pulmonary arterial hypertension in systemic sclerosis. European respiratory review : an official journal of the European Respiratory Society 2019;28:10.1183/16000617.16000023-16002019. Print 16002019 Sep 16000630. doi: 190023 [pii]
- 36. Duncan MS, Alcorn CW, Freiberg MS, et al. Association between HIV and incident pulmonary hypertension in US Veterans: a retrospective cohort study. Lancet Healthy Longev. 2021 Jul;2(7):e417-e425.
- 37. Savale L, Guimas M, Ebstein N, et al. Portopulmonary hypertension in the current era of pulmonary hypertension management. J Hepatol 2020;73:130-139. doi: 10.1016/j.jhep.2020.02.021
- 38. Krowka MJ, Fallon MB, Kawut SM, et al. International Liver Transplant Society Practice Guidelines: Diagnosis and Management of Hepatopulmonary Syndrome and Portopulmonary Hypertension. Transplantation. 2016 Jul; 100(7):1440-52.
- 39. Baumgartner H, De Backer J, Babu-Narayan SV, et al. 2020 ESC Guidelines for the management of adult congenital heart disease. European heart journal 2021;42:563-645. doi: 10.1093/eurheartj/ehaa554 [doi]
- 40. Brida M, Gatzoulis MA. Pulmonary arterial hypertension in adult congenital heart disease. Heart. 2018 Oct;104(19):1568-1574.
- 41. Manes A, Palazzini M, Leci E, et al. Current era survival of patients with pulmonary arterial hypertension associated with congenital heart disease: a comparison between clinical subgroups. European heart journal 2014;35:716-724. doi: 10.1093/eurheartj/eht072 [doi]
- 42. Delcroix M, Torbicki A, Gopalan D, Sitbon O, Klok FA, Lang I, et al. ERS Statement on Chronic Thromboembolic Pulmonary Hypertension. Eur Respir J. 2020.
- 43. Pepke-Zaba J, Delcroix M, Lang I, Mayer E, Jansa P, Ambroz D, et al., Chronic Thromboembolic Pulmonary Hypertension (CTEPH): Results from an International Prospective Registry, Circulation 2011; 124(18): 1973-81.
- 44. Delcroix M, Howard L. Pulmonary arterial hypertension: the burden of disease and impact on quality of life. European respiratory review : an official journal of the European Respiratory Society 2015;24:621-629. doi: 10.1183/16000617.0063-2015 [doi]
- 45. Chen YF, Jowett S, Barton P, Malottki K, Hyde C, Gibbs JS, Pepke-Zaba J, Fry-Smith A, Robert J, Moore D, Clinical and cost-effectiveness of epoprostenol, iloprost, bosentan, sitaxentan and sildenafil for pulmonary arterial hypertension within their licensed indications: a systematic review and economic evaluation, Health Technol Assess, 2009; 13(49): 1-320.
- 46. European Lung Health Group Policy brief: Improving lung health through the future of European Health Data Space https://breathevision. eu/images/ELHG_Policy_Brief_-European_Health_Data_Space_2022.pdf
- 47. Artificial Intelligence/Machine Learning in Respiratory Medicine and Potential Role in Asthma and COPD Diagnosis, Kaplan A et al, The Journal of Allergy and Clinical Immunology: In Practice, Volume 9, Issue 6, 2021, Doi.10.1016/j.jaip.2021.02.014.
- 48. Pulmonary Hypertension in Children Part 1: Causes and Symptoms Am J Respir Crit Care Med Vol. 204, P17-P18, 2021
- 49. A process through which people gain greater control over decisions and actions affecting their health [Health promotion glossary. Geneva: World Health Organization; 1998]
- 50. Angelmar R, Bermann BP. Patient empowerment and efficient health outcomes. Financing sustainable healthcare in Europe. 2007:139–162. [accessed 26 February 2009.
- 51. Consensus paper on making health literacy a priority in EU policy, 2016, https://www.eu-patient.eu/globalassets/policy/healthliteracy/ health-literacy-consensus-paper_2016.pdf
- 52. Giri P.C et al Participation in pulmonary hypertension support group improves patient-reported health quality outcomes: a patient and caregiver survey, May 2021, https://doi.org/10.1177/20458940211013258
- 53. Ivarsson B et al. Perceptions of received information, social support, and coping in patients with pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension. Clin Med Insights Circ Respir Pulm Med 2014; 8: 21–28
- 54. Graarup J et al. Patient engagement and self-management in pulmonary arterial hypertension European Respiratory Review 2016 25: 399-407 https://err.ersjournals.com/content/25/142/399
- 55. 55 McGoon MD, Ferrari P, Armstrong I, et al. The importance of patient perspectives in pulmonary hypertension. The European respiratory journal 2019;53:10.1183/13993003.13901919-13992018. Print 13992019 Jan. doi: 1801919 [pii]
- 56. Dharssi, S., Wong-Rieger, D., Harold, M. et al. Review of 11 national policies for rare diseases in the context of key patient needs. Orphanet J Rare Dis 12, 63 (2017). https://doi.org/10.1186/s13023-017-0618-0
- 57. https://www.ema.europa.eu/en/partners-networks/patients-consumers/key-documents#annual-reports-section
- 58. ERS White Book; The role of patient organisations 2013, updated regularly
- 59. Olsson KM, Meltendorf T, Fuge J, et al. Prevalence of Mental Disorders and Impact on Quality of Life in Patients With Pulmonary Arterial Hypertension. Front Psychiatry 2021;31. doi:
- 60. International Patient and Carer Survey on the impact of PH 2012: https://www.phaeurope.org/wp-content/uploads/PAH_Survey_FINAL.pdf
- 61. ERN guidance 2020 https://ern-lung.eu/wp-content/uploads/2020/10/PH-MCC.pdf
- 62. Adler NE, Page AEK (Eds), Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs, Institute of Medicine of the National Academies, 2007: 166.
- 63. PAH patient survey: https://www.phaeurope.org/wp-content/uploads/PAH_Survey_FINAL.pdf
- 64. Rare Disease UK, Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy, http://www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf. 2011.
- 65. Oudiz RJ, Disability in Pulmonary Hypertension, Advances in Pulmonary Hypertension 2021





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