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Societal Impact of PH/ Multi-Faceted PH

Program Description

The mission of *Advances in Pulmonary Hypertension* is to serve as the premiere forum for state-of-the-art information regarding diagnosis, pathophysiology, and treatment of pulmonary hypertension (PH). The 2018 Nice revision of the World Symposium on Pulmonary Hypertension (Simmonneu G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019;53(1). DOI:10.1183/13993003.01913-2018) serves as a guide to categories of PH addressed in *Advances in Pulmonary Hypertension*. While focusing on Group 1 PH (PAH: pulmonary arterial hypertension), the other categories (Group 2, PH due to left heart disease; Group 3, PH due to lung diseases and/or hypoxia; Group 4, PH due to pulmonary artery obstructions; Group 5, PH with unclear and/or multifactorial mechanisms) are also addressed. This mission is achieved by a combination of invited review articles, roundtable discussions with panels consisting of international experts in PH, and original contributions.

Objectives

- Provide up-to-date information regarding diagnosis, pathophysiology, and treatment of PH.
- Serve as a forum for presentation and discussion of important issues in the field, including new paradigms of disease understanding and investigational trial design.

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Advances in Pulmonary Hypertension is directed to cardiologists, pulmonologists, rheumatologists, pediatricians, internists, and other health care professionals involved in the treatment of patients with PH.

Advances in Pulmonary Hypertension: Official Journal of the Pulmonary Hypertension Association is a quarterly publication directed by an editorial board of renowned pulmonary hypertension (PH) experts with oversight by PHA's Scientific Leadership Council. The mission of *Advances in PH* is to assist physicians in their clinical decision-making by informing them of important trends affecting their practice and providing an analysis of the impact of new findings and current information in peer-reviewed publications. Each article is reviewed and approved by members of the Editorial Board.

While most articles are invited by the Editorial Board, the following submissions will be considered for publication:

- Reviews that summarize and synthesize peer-reviewed literature to date on relevant topics
- Letters to the Editor
- Clinical case studies

Submitted manuscripts are reviewed by the Editorial Board and other experts in the field. Acceptance of manuscripts is determined by factors such as quality, relevance, and perceived value to clinical decision-making.

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In this issue of *Advances in Pulmonary Hypertension*, we focus on often overlooked, but important, aspects of pulmonary arterial hypertension (PAH) care: mental health, social determinants of health, diet, physical activity and caregiver support. As healthcare professionals, we tend to focus on well-defined clinical aspects of PH that we can easily understand and treat with PAH therapy such as 6-minute walk distance, right ventricular function, and pulmonary vascular resistance. Moreover, PH affects much more than the right heart and often has a profound impact on an individual's mental health, socioeconomic status, quality of life and physical activity. It can also impact the lives of PH caregivers. In this issue, we focus on aspects of PAH that have a significant impact on our patient's daily lives.

In Mental Health and PH: APRNs and RNs Having a Positive Effect, Lillian Hansen and Jacqueline Brewer discuss the impact of PH on mental health outlining the important role for APRNs and RNs to screen and address conditions such as depression and anxiety. In Wearable Devices in Pulmonary Arterial Hypertension: What are we Trying to Learn, Drs. Daniel Lachant and James White discuss the variety of factors that impact physical activity in PAH and review the use of wearable technologies to monitor physical activity as a therapeutic target and clinical trial endpoint. As guest editors, Dr. Burger and I also explore the role of caregivers in PAH care in a roundtable discussion of caregivers, including parents and partners of PH patients. We gained valuable insight into how PAH affects caregivers and we also learned about ways we can better support PH caregivers. Natalie Taylor and Dr. Gustavo Heresi also discuss how diet and exercise may play a role in improving right ventricular function in PAH. And lastly, Drs. Bernardo, Jose and Elwing review the significance of socioeconomic status and social determinants of health in clinical outcomes of PAH patients and discuss strategies for addressing these issues in patient care. That discussion is a call to action for pulmonary hypertension clinicians to both improve understanding and escalate awareness of social determinants of health to promote improved outcomes for PAH patients.

We all espouse a patient-centered approach that requires attention to areas beyond conventional clinical decision-making. It is our hope that the focus in this issue of *Advances in Pulmonary Hypertension* on understudied and often overlooked aspects of PAH care ignites more interest in these important areas.

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Mental Health and PH: APRNs and RNs Having a Positive Effect

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Pulmonary hypertension is a complex and progressive disease. Patients suffering from pulmonary hypertension may also experience mental health issues. Screening and treatment for mental health issues in the pulmonary hypertension population is imperative but remains a challenge. Advanced practice registered nurses and registered nurses are key to overcoming these challenges.

Patients with pulmonary hypertension (PH) frequently suffer from mental health conditions, including anxiety and depression.[1] Despite the effect on health care use and treatment outcomes, a paucity of data exists on effective screening and treatment implementation strategies in caring for the mental health of PH patients.[2] This publication provides an overview of mental health concerns in patients living with PH, key factors to consider when implementing mental health screening and interventions into PH practice, and a focus on the important role of advanced practice registered nurse (APRN) and registered nurse (RN) in screening for mental health concerns in PH patients.

INTRODUCTION

PH is a chronic, debilitating disease characterized by hemodynamic abnormalities of the pulmonary vasculature and progressive right heart failure. The physical manifestations of the disease include dyspnea, fatigue, exertional intolerance, and syncope. Most patients experience a significant delay from time of symptom onset to diagnosis, up to 18 to 47 months for chronic thromboembolic PH and idiopathic pulmonary arterial hypertension, respectively.[3] Uncertainties during this delay, along with poor outlook related to a permanent and potentially fatal diagnosis, and isolation stemming from physical limitations, can be traumatic.[1,4] Patients may be unable to work, struggle financially, need to undergo frequent invasive procedures, and feel burdened by complicated treatment regimens, all of which worsen quality of life.[1]

Because of this complex nature of living with the disease, patients with PH frequently suffer from mental health disorders, commonly anxiety and depression. Anxiety and depression may be present in up to 50% of patients with PH and 3 to 8 times more common than in the general population.[1] Adjustment disorders are also seen in 38% of PH patients and may precede and evolve into anxiety and depression, stemming from diagnostic delays and the cumulative effect of the mental health issues throughout the disease course.[1,3] Many PH patients have preexisting mental illness, the symptoms of which may be exacerbated by the complexities and stress of chronic disease. In addition, patients with PH experience challenging life events, for example the death of a loved one, chronic substance abuse, and relationship issues, which may intensify anxiety and depressive symptoms.

Anxiety in PH patients has been shown to be significantly correlated with elevated pulmonary vascular resistance and reduced cardiac index.[5] The combination of PH and depression may contribute to worse mortality and need for lung transplant.[6] Despite PH therapy, the presence of anxiety and depression is strongly associated with declining New York Heart Association functional class.[2] Depression symptoms, such as fatigue, change in appetite, disturbed sleep, and concentration difficulty, often overlap with symptoms of PH. Such symptoms may be dismissed or assumed to be part of the PH disease process and not addressed separately by the health care provider.[2,7] Lack of proper training to assess and treat anxiety and depression

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in patients with PH may also contribute to delays in diagnosis or underdiagnosis of these mental health disorders.[2]

EFFECT ON HEALTH CARE USE AND TREATMENT OUTCOMES

Living with a chronic, complex, and typically progressive illness, patients with PH have high use of health care services, including outpatient, inpatient, and procedural needs.[8] In combination with chronic disease, mental health disorders like anxiety and depression further increase the need for health care services exponentially.[9] This increased health care use consequently increases health care costs, up 33% to 169% in patients with anxiety and depression.[9] In PH patients who suffer from anxiety and depression, the presence of such mental health disorders has been shown to correlate specifically with an increased demand for outpatient visits and a nearly 2-fold rise in unscheduled communication events, such as email, phone calls, and other correspondence.[10]

Mental health issues can also affect the overall treatment success in patients living with a chronic disease. For example, depression can promote low adherence to treatment regimens, which portends overall poor disease outcomes.[11] Adherence to treatment is crucial for PH patients because of the progressive nature of the disease, lack of curative therapies, and risk of unrecoverable disease worsening with lapses in therapy. A critical time to screen for depression is when a patient displays signs of nonadherence to treatment.[11] Therefore, screening for mental health issues including anxiety and depression prior to starting treatment or when displaying signs of nonadherence becomes imperative to achieve positive disease outcomes.

SCREENING FOR MENTAL HEALTH CONCERNS IN PH PATIENTS

In the overall medical community, screening for mental health issues, particularly depression, remains shockingly low at only 2.29% with clinic visits.[12] However, diagnosis of anxiety and depression requires frequent screening for symptoms throughout the disease course. For PH patients, such screening ideally should begin at the time of diagnosis for early detection and with discrimination from preexisting mental health conditions.[1,2] When screening patients, it is important to have readily available psychiatric support and crisis management teams to address acute concerns.[10]

Many screening tools exist for anxiety and depression, such as the Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaire (PHQ9), Beck's Depression Inventory (BDI), General Anxiety Disorder (GAD-7), and Beck Anxiety Inventory (BAI).[1,5] However, no standardized screening approach specific to PH patients has been developed. European Society of Cardiology and European Respiratory Society PH guidelines indicate the need for a multidisciplinary approach and adequate diagnostic screening tools for identification of patients requiring referral for psychiatric treatment and psychologic support.[13,14]

APRN AND RN ROLE IN SCREENING

The nursing role has commonly been perceived as one involving compassion, care, and human connection. The close relationship that develops between the nurse and patient is built on trust, which provides a sense of comfort to the patient and allows for open and honest dialogue on topics that may be deemed difficult, such as depression and substance abuse.[15] Both RN and APRN roles in the PH program are positioned to institute trust and openness to uncover issues surrounding mental health.

Screening for anxiety and depression in PH patients performed by RNs and APRNs often occurs casually through conversation. Such informal screening by PH RNs occurs on a regular basis through various means of conversation, including telephone triage, email or portal correspondence, and support group interactions. During clinic visits, APRNs spend a considerable amount of time focused on interpersonal communication, often more than two-thirds of the clinical time, allowing for ample opportunity for informal assessment of mental health.[16] This time and space during a PH clinic visit allow for more open disclosure of personal information such as stressors, feelings, and symptoms. Variables that may not be disclosed otherwise are often discussed with APRNs because of the "better human connection" and the perception that APRNs "translate things a little better, from the medical to the personal".[17] It has been shown that when nurse practitioners screen and manage depression in combination with chronic diseases in general, patient quality of life increases.[12]

TREATMENTS FOR MENTAL HEALTH CONCERNS IN PH PATIENTS

Once diagnosed with anxiety and depression, it is unclear what treatment interventions are best suited for PH patients and if guidelines for mental health treatment in the general population apply.[2] Pharmacotherapy in patients with PH may be underused, as only 8% to 25% of PH patients with diagnosed anxiety or depression are treated with psychopharmacotherapy.[2] PH providers, including APRNs, may consider treating their patients with pharmacotherapy or consider referring to another provider for such treatment. Outside of pharmacotherapy, several studies have investigated interventions for treatment of anxiety and depression in PH patients, with benefit noted from progressive muscle relaxation techniques, slow-paced respiration therapy, and weekly Zen integrative therapy.[5] In addition, participation in cognitive behavioral therapy, cardiopulmonary rehabilitation, and patient support groups have beneficial effects on well-being and fatigue, however there is limited evidence specific to PH patients with regard to mental health.[2,4]

Patient support groups exist worldwide for PH patients and serve to provide specific information and knowledge pertaining to the unique disease processes afflicting PH patients. Support group discussions address the burdens patients experience physically, socially, and psychologically from living with PH. Based on our experience, support from peers suffering from PH can be highly beneficial, as overall quality of life for PH patients can

decline throughout the disease process. Many patients feel overwhelmed and lonely living with a rare condition like PH, thus bonding with others who are also suffering similarly can provide a valuable social connection as well as important information about PH disease management.[2] RNs and APRNs can provide information to patients about local patient support groups and resources from the Pulmonary Hypertension Association.

Exercise plays a valuable role in the care of those suffering from PH. Physical activity can have increased beneficial effect, especially in those who also suffer from mental health issues due to the release of endorphins with exercise.[18] Studies have shown that the positive effects of exercise and physical activity can be analogous to antidepressant therapy.[18] Patients with PH, despite the physical limitations related to the disease, can still engage in some form of exercise or physical activity. The most obvious example would be enrollment in pulmonary rehabilitation, during which patients not only participate in medically supervised exercise, but also engage socially with staff and other patient participants. The exercise and social interaction that occurs during pulmonary rehabilitation can have a positive effect on overall physical and mental health and wellness.[2] APRNs or RNs can suggest or provide referrals for patients to pulmonary rehabilitation programs.

OUR EXPERIENCES WITH IMPLEMENTATION

While existing in other disciplines, such as collaborative care models in primary care and psychosocial care in oncology, the PH discipline lacks a mental health care model that integrates appropriate screening and diagnostic tools with psychosomatic support from medical and psychiatric providers.[1,10,19,20] In our busy PH practices, we have implemented a variety of strategies, highlighted in Table 1, including formal and informal screening in conjunction with on-site and community resources (Table 2), which have varied over the years depending upon staffing availability, provider interest, and team dynamics.

Table 1. Screening Strategies

Informal
Conversational
• Patient brings up concerns over anxiety or depression during clinic visit and telephone communication • Provider intentionally asks about symptoms of anxiety or depression during clinic assessment • Specialty pharmacy RNs and pharmacists detect issues with medication adherence, which may correlate with mental health issues • Family raises concerns over anxiety or depression with patient during clinic visit
Observational
• Observe symptoms of anxiety or depression and substance abuse during patient interactions • Patient overall appearance and demeanor raises concerns for mental health issues • Specialty pharmacy RNs observe potential mental health issues during home visits related to home setting and family interactions
Formal (Screening Tools)
• New patient questionnaire includes brief anxiety or depression and substance abuse assessment • Medical assistant performs abbreviated GAD-2 and PHQ-2 questionnaires during clinic visit intake • Patient fills out GAD-7 and PHQ-9 at start of each outpatient clinic visit, then provider reviews form and addresses findings with patient • Patients participating in pulmonary rehabilitation undergo depression screening at start of enrollment

Abbreviations: GAD-2, general anxiety disorder 2-item; GAD-7, general anxiety disorder 7; PHQ-2, patient health questionnaire 2; PHQ-9, patient health questionnaire 9; RN, registered nurse.

Table 2. Intervention Resources[a]

Community and Multidisciplinary Resources
• Refer patient to community counseling services for cognitive behavioral therapy • Refer patient to pulmonary rehabilitation program • Refer patient to outpatient palliative care services • Refer patient to integrative medicine or complementary alternative medicine (ie, guided imagery, massage, acupuncture) • Refer patient to local support group or national peer support line through the Pulmonary Hypertension Association
On-Site Dedicated Mental Health Resources
• High score on GAD or PHQ questionnaire prompts involvement of on-site counselor or social worker, if available • Clinic-based counselor engages and enrolls patients in counseling services • Clinic-based social worker provides community resources and crisis management • Direct referral and scheduling with clinic-based psychiatrist for pharmacotherapy treatment or counseling • Ongoing collaborative partnership between psychiatrist and PH provider regarding medication management

Abbreviations: GAD, general anxiety disorder; PH, pulmonary hypertension; PHQ, patient health questionnaire.

[a]While patient support groups and pulmonary rehabilitation provide healthy social interactions, this is not a replacement for psychotherapy or psychiatric support for patients exhibiting significant anxiety and depression.

CHALLENGES TO IMPLEMENTATION

We have faced various challenges when implementing mental health screening and interventions in our PH programs, including those related to the patient, provider, and health care system. When undergoing screening, patients may experience denial of anxiety and depression symptoms, and social barriers may exist with talking about mental health concerns. They may be hesitant to fill

out screening tools honestly or at all. Long-term success of formal screening has been highly dependent upon support staff to follow a consistent workflow of administering the screening tools. Providers often need to dedicate the bulk of the clinic visit to the complex management of medications and review of test results, leaving little time for in-depth discussion of mental health. Some providers don't feel comfortable discussing emotional concerns with patients because of lack of training. In addition, when the clinic lacks on-site support personnel such as social workers or counselors to assist with acute care needs that can arise, providers may forgo screening for mental health issues during the clinic visit.

Once anxiety and depression are identified, additional barriers can exist in obtaining appropriate interventions. Low education level, lack of insight into the importance of managing mental health symptoms, and social stigmas often prevent patients from obtaining counseling or psychiatric care. Patients may fear experiencing new side effects or drug interactions with PH medications when taking psychopharmacotherapy. In addition, they may feel burdened by polypharmacy and hesitant to add additional medications. Because of mental health clinician shortages, patients often have difficulty finding a mental health care provider who is accepting new patients in a timely fashion and is covered by their insurance, as well as easily accessible by convenient transportation. High copays can exist despite insurance coverage, making longer term counseling or psychiatric care less accessible.

OVERCOMING CHALLENGES THROUGH THE APRN AND RN ROLE

The RN and APRN role in implementing mental health care support for PH patients is multifactorial and, in our experience, integral for long-term success. We have found that APRNs and RNs can develop algorithms for screening patients formally during clinic visits, including workflows for support staff and having screening tools readily available in the clinic setting. In addition, APRNs and RNs can work to develop a list of resources to provide patients who are seeking outside support, such as names and contact information of counseling programs and support groups. APRNs are well equipped to serve as liaisons between the PH practice and community mental health services by setting up collaboration with local psychiatry and counseling programs. This allows for an established referral pathway and fast track referrals for more urgent mental health concerns. By providing education to psychiatry and counseling personnel on the complex nature of living with PH including common PH symptoms, complexities of PH therapy regimens, medication side effects, and difficult treatment decisions, APRNs can help mental health care clinicians improve their ability to address PH-related anxiety and depression. RNs can assess if transportation issues exist and if telehealth counseling is an appropriate option for patients. APRNs and RNs can provide informal emotional support during clinic visits while engaged in conversation with patients who might not feel ready for formal counseling services. RNs can work closely with clinic-based social workers who may be available for acute crisis management needs that can arise when screening patients for anxiety and depression. In addition, they can work with practice administration to highlight the need for on-site support and advocate for the availability of such services for large PH patient populations. APRNs often perform the bulk of follow-up care in PH programs, allowing them close recurrent follow-up on previously discussed mental health concerns and opportunities for ongoing screening.

DISCUSSION

Overall, PH is a progressive disease requiring frequent testing and complex treatment regimens. Many PH patients suffer from mental health issues including anxiety and depression. Despite an awareness that mental health issues are prevalent in our PH patients, we are not screening enough to detect these issues that can affect treatment outcomes, quality of life, and long-term prognosis. We need to be more proficient and diligent with screening and rescreening our PH patients early and throughout the disease process. Methods for screening exist, including formal and informal strategies that can be integrated into our PH practices. Interventions for mental health concerns include but are not limited to pharmacotherapy, counseling, exercise, and social support. APRNs and RNs are perfectly positioned to address such concerns through informal and formal means. Many challenges exist with implementing screening and interventions for anxiety and depression, nevertheless APRNs and RNs are key to overcoming them. APRNs and RNs can truly have a positive effect and be integral in the long-term success of our PH populations.

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REGULAR ARTICLE

Wearable Devices in Pulmonary Arterial Hypertension: What Are We Trying to Learn?

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Background: Wearable technologies (accelerometers) are currently being evaluated as an alternative to the 6-minute walk test as an objective measure of functional status in pulmonary arterial hypertension (PAH). Multiple observational studies incorporating accelerometers have shown patients with PAH have low physical activity (PA) time.

Implications for clinicians: Despite widespread use of accelerometers, PA has not been shown to increase after adding vasodilator therapy, which suggests a behavioral component influencing activity. A decrease in PA from baseline may identify clinical worsening and someone at risk for future hospitalization. *Cardiac Effort*, the number of heart beats used during the 6-minute walk test/6-minute walk distance (beats per meter), has less variability than 6-minute walk distance and provides a comparable clinic measurement in the home setting. Cardiac Effort may provide a better remote measurement than changes in total daily activity when evaluating for clinical improvement.

Conclusions: The amount and duration of PA achieved in patients with PAH is likely related to a combination of right ventricular (RV) function, deconditioning, and environmental factors. Strategies to target all aspects are needed to improve PA. Further studies are needed to determine the optimal remote measure and monitoring period.

Pulmonary arterial hypertension (PAH) is a progressive vasculopathy that results in reduced cardiac stroke volume and impairment in gas exchange.[1] As a result, dyspnea on exertion and fatigue are often the first presenting symptoms. As PAH progresses and symptoms worsen, physical activity (PA) decreases, and deconditioning along with skeletal muscle dysfunction also contribute to worsening symptoms.[2,3] The 6-minute walk test (6MWT) is a commonly used test to monitor and objectively assess functional capacity in PAH[4]; 6-minute walk distance (6WMD) has significant prognostic value and is included in the major contemporary risk assessments.[5,6] Changes in 6MWD can also be helpful in detecting clinical improvement.[7] Variability in longer 6MWD can make detecting functional improvement difficult because the day-to-day variation may equal or exceed improvements expected with therapeutic change.[8,9] During the pandemic, telemedicine and concerns about respiratory exposure decreased the number of 6MWTs performed. This accelerated already growing interest in using wearable technology to measure changes in PA as an alternative to 6MWT.

Wearable devices can measure multiple different parameters including PA, sleep, heart rate, oximetry, and respiratory rate.[10] They are being used in disease monitoring and screening as well as in outcomes assessment.[10] Accelerometers (to measure PA) passively collect data and can be attached to different areas of the body. In PAH, wearable devices have been primarily worn on the wrist,[11–14] hip,[13,15,16] chest and thigh,[12,17] and arm.[18] Activity counts are determined by changes in acceleration during a period of time (epoch, typically 60 seconds); proprietary algorithms transform counts into activity classifications.[19] One of the most popular activity count classifications was developed on healthy individuals wearing a hip-based accelerometer walking on a treadmill.[20] The wrist- or hip-worn Actigraph has been the most widely used accelerometer in research with over 20 000 publications[19] and is commonly used in PAH.[12–16,21] Unfortunately, different proprietary algorithms between commercially available devices makes comparing output (step counts and activity time) extremely difficult.[12,22] Calculating vector magnitude ($\sqrt{x^2 + y^2 + z^2}$) and mean amplitude deviation are 2 emerging ways to analyze postprocessed acceleration data.[13,15,17]

Physical inactivity remains a significant problem in the United States, with less than half of adults meeting the Centers for Disease Control and Prevention (CDC) and American College of Sports Medicine (ACSM) activity recommendation (>150 minutes of moderate intensity aerobic activity, 3.0–5.9

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metabolic equivalent (MET), every week and strength training 2 or more days per week). Specifically, above 65 years old, PA levels decrease, with 61% of adults not meeting the CDC-ACSM recommendation and classified as physically inactive.[23] Light PA is classified as activities between 1.5 and 3 METs[24]; sedentary behavior is defined as <1.5 METs,[25] ie, sitting and watching television. It is possible to achieve the CDC-ACSM PA recommendation and spend a significant amount of time in sedentary behavior. Many accelerometers use METs as criteria for activity classification. It is worth highlighting that a 6MWD of 320 m (2 miles/h) would be classified as light activity even though, for some PAH patients, this exertion is at their physiologic limit. In that instance, they would never cross the threshold to moderate PA with an accelerometer because a walking speed of 3 miles/h (~480 m 6MWD) would be needed to generate enough activity counts. Since the 6MWD is the most physically demanding activity most patients do, baseline 6MWD may provide a rough estimate of what someone will do with home monitoring. External factors, such as anxiety and depression, likely influence PA level in a chronic disease state.[26]

Accelerometers have been used in PAH for over a decade. The initial reporting used an arm-based biaxial accelerometer and showed PAH patients had decreased daily steps and activity time compared with a control cohort.[18] A second report then found PAH patients had very high sedentary time measured by a hip-based accelerometer.[15] Since then, multiple observational studies have shown that PAH patients have low PA time measured by multiple different types of accelerometers worn on different areas of the body (Table 1). It also appears that scleroderma PAH patients also have less PA time than idiopathic PAH.[18,3] In contrast, 1 Spanish cohort of PAH patients had a high percentage (61%) of patients meeting the >150 minutes of moderate PA time.[21] Many patients with PAH are deconditioned at time of diagnosis from months of progressive symptoms; anecdotally, our patients report that ignorance about how to start an exercise program safely leads to further deconditioning and persistent, often disabling, symptoms of dyspnea or fatigue even once they have begun effective therapy.

There have been few reports on the reproducibility of activity measurements in stable compensated patients with PAH.[16,27,28] Matura et al[16] used a hip accelerometer and found no difference in activity parameters when comparing two 1-week intervals within a 4-week period. Using a wrist accelerometer, Hemnes et al[11] suggested a Hawthorne effect as patients increased their activity during the initial monitoring period. They show how activity dropped over time, perhaps because they forgot about the device. To account for that, those authors excluded the first week of monitoring and used the second week to assess for changes. They found no change in activity after 12 weeks of monitoring in the control group. In the Effect of Selexipag on Daily Life PA of Patients with PAH (TRACE) study, using a wrist accelerometer, researchers found no change in a 14-day average (each monitoring period) after 24 weeks of placebo control.[14]

Accelerometers can be worn on multiple locations on the body. Wrist-based devices are the most used in research[10] and likely provide higher compliance and patient acceptance. Truncal monitoring (hip, chest, or thigh) logically produces information with less noise introduced by isolated forearm movements. We found that, in patients with PAH, there is significant discrepancy in PA time and daily steps measured when simultaneously wearing a chest or thigh and a wrist accelerometer. Surprisingly, we found wrist-based measurements correlated strongly with PAH variables of interest, which suggests that patients may use their arms to accomplish activities of daily living.[12] Further studies are needed on the best location for monitoring in PAH, balancing patient acceptance and meaningful data.

Accelerometer reported measurements (activity time, intensity, and daily steps) are associated with PAH variables of interest, specifically criteria included in risk scores. Not surprisingly, authors of multiple studies have shown a strong correlation between baseline 6MWD and PA (Table 1). Daily steps also have a very high correlation with 6MWD,[11,14] while steps and PA time also associate with functional class. It would seem reasonable that PA might be related to right ventricular (RV) function. The data are mixed on NT-pro BNP and RV function correlating with activity parameters (Table 1).

Authors of 2 reports assessed activity in patients with PAH during the COVID pandemic.[12,30] The first used a pedometer to measure steps. They classified activity as low or moderate to high using 5000 steps as a cutoff. Interestingly, patients segregated almost equally into the 2 classifications; there was no difference in NT-pro BNP between groups, and the low activity group had an impressively high 6MWD of 503 m.[30] In our cohort, we also found low PA time and daily steps; NT-pro-BNP was correlated (r = –0.50) with total PA time but even stronger with patient-reported inactivity time (r = 0.76).[12] While it seems clear that physiologic capacity (RV function) influences PA, behavioral factors also influence PA.

There are few longitudinal observational studies in which authors evaluate PA and daily steps in patients with PAH. Marvin-Peek et al[29] used a wrist accelerometer and found daily steps were negatively correlated with clinical worsening. Interestingly, they found 6MWD was not associated with clinical worsening; higher daily steps and longer 6MWD were associated with maintenance of functional class. Sehgal et al[28] found in their cohort that a decline in activity occurred over 4 weeks preceding hospital admission. Both studies suggest there may be an opportunity to intervene and prevent hospitalization if providers recognize a decline in activity. The Pulmonary Hypertension Association Registry (PHAR) is now incorporating physical activity in PAH (ACTiPH) as an ancillary study.[31] One goal of the study is to evaluate home activity monitoring on adult and pediatric participants in PHAR with accelerometers every 6 months to determine whether PA is associated with health care utilization and/or outcomes in PH.

Accelerometers are also being used to assess for clinical improvement in PAH.[11,13,14,32] Unlike 6MWD, a mean-

Table 1. Studies Incorporating Activity Monitoring in PAH

Reference	No. patients	Age (y)	SPD or PA time (min/%)	6MWD (m)	FC (II/III)	NT-pro BNP	Activity correlation		
							RV	QOL	6MWD
Mainguy et al[18]	25 total		Step: 5041 (3357) 3234 (2437)			NA	No	NA	Yes
	Idiopathic: 15	47 (15)		401 (89)	11/4				
	CTD: 10	58 (10)		349 (129)	5/5				
Pugh et al[15]	20 total Idiopathic: 7 CTD: 7	54 (14)	Sedentary: 92% Light: 6.8% Moderate: 1.1% >3 METs: 7.5 min	NA	10/7	NA	No	NA	Yes
Matura et al[16]	15 total Idiopathic: 5 CTD: 4	51 (16)	Sedentary: 611, 84% Light: 73, 10% Moderate: 18, 2%	413 (66)	12/3	216 (65, 531)	NA	Yes	Yes
Cascino et al[27]	35 total	61 (12)	Steps: 4391 (2442)	460 (107)	NA	NA	NA	Yes	Yes
Sehgal et al[28]	30 enrolled with 23 having usable data.	50 (13)	Steps: 5847 (3321)	401 (102)	14/11	268 (85, 754)	No	Yes	Yes
Minhas et al[13] (Phantom)	55 total Idiopathic: 27 CTD: 13	61 (10)	Steps: 3860 (2830) Sedentary: 610 (508–680) Light: 165 (131–190) Moderate: 8 (2–13) VM: 355 600 (158 400)	424 (113)	35/16	NA	Yes	Yes	Yes
Minhas et al[13] (Penn)	60 total Idiopathic: 30 CTD: 18	50 (18)	Steps: 7960 (2710) Sedentary: 333 (255–396) Light: 236 (207–260) Moderate: 16 (12–29) VM: 1 860 000 (613 800)	403 (129)	28/27	NA	No	No	Yes
Lachant et al[12]	22 total		Steps: 3254 (5781)				No	No	Yes
	Treatment naïve idiopathic 4/CTD 2	61 (13)		395 (229, 429)	3/3	1827 (112, 3852)			
	Treatment intensification idiopathic 3/CTD 2	53 (17)		377 (152, 498)	1/5	2029 (50, 3845)			
	Stable idiopathic 6/CTD1	53 (15)		381 (352, 459)	10/0	214 (137, 360)			
Gonzalez-Saiz et al[21]	75 total Idiopathic: 31 CTD: 13	48 (14)	Sedentary: 600 (125) Light: 137 (61) Moderate: 30 (21)	NA	15/22	510 (904)	No	NA	NA
Marvin-Peek et al[29]	41 total	47 (40–57)	Steps: 4656 (3649–6256)	427 (360, 480)	26/15	NA	No	NA	No

Abbreviations: 6MWD, 6-minute walk distance; CTD, connective tissue disease; FC, functional class; MET, metabolic equivalent; NA, not applicable; PA, physical activity; PAH, pulmonary arterial hypertension; QOL, quality of life; RV, right ventricular; SPD, steps per day; VM, vector magnitude count.

ingful change in PA or steps is not yet known in PAH. Authors are using different devices and location, making comparisons difficult. They also have different criteria for acceptable wear time. The largest clinical trial to date that incorporated activity as an endpoint in PAH is the TRACE study.[14] After 24 weeks of placebo-controlled selexipag, authors found no significant change in nonsedentary (light) PA, moderate to vigorous PA, or steps per day (Table 2). They also found no change in 6MWD, NT-pro BNP, or PAH–Symptoms and Impact scores. In contrast, Hemnes et al[11] evaluated the effect of a behavioral intervention on increasing activity. After 12 weeks, they found the intervention group increased steps more than the control group (Table 2). Interestingly, there was no difference in 6WMD. This suggests there may be a strong behavioral aspect to activity in PAH; pharmacologic interventions alone may not be enough to increase PA even if capacity for PA is increased. Dr. Evan Brittain[33] is now evaluating whether incorporating customized text messages of encouragement based on daily activity improves health-related quality of life in PAH in the study MObile Health InterVEntion in PAH (MOVE PAH). In this single-centered study, instead of just monitoring activity, they are using Fitbit Application Program Interface to create encouraging text messages that will be sent 3 times/day based on the current daily activity metrics. One hundred stable patients with PAH will be randomized to receive the text intervention or not for 24 weeks. Interestingly, the outcomes being assessed are

Table 2. Clinical Trials Incorporating Activity Monitoring in PAH

Author	No. Patients	Age (y)	Steps/day or PA time, min (%)		6MWD (m)	FC (II/III)	NT-pro BNP/BNP	Activity correlation		
			Baseline	Change				RV	QOL[a]	6MWD
Howard et al[14]	Selexipag: 53 Idiopathic: 40 CTD: 8	49 (15)	Sedentary Koster: 394 (101)	1.1 (–16, 18)	453 (130)	33/20	207 (36, 9811)	NA	NA	Yes
			Freedson: 666 (102)	–13.3 (–33, 6)						
			MVPA: 118.5 (58)	0.3 (–9.1, 9.6)						
			11.5% (5.5)	0.3 (–0.7, 1.2)						
			Steps: 3729 (2327)	0.3 (–317, 316)						
	Placebo: 55 Idiopathic: 42 CTD: 10	50 (14)	Sedentary Koster: 397 (122)	–17 (–33, 0.04)	450 (99)	41/14	162 (16, 3871)			
			Freedson: 651 (115)	–27 (–46, –8)						
			MVPA: 115 (67)	–2.0 (–11, 7)						
			11% (6)	0.3 (–0.6, 1.2)						
			Steps: 3238 (2038)	–202 (–512, 109)						
Hemnes et al[11]	Intervention: 20 Idiopathic: 13 CTD: 3	47 (41–54)	Steps: 4611 (3322, 8619)	1409 (–32, 2220)	431 (396, 456)	15/2	28 (10, 54)	NA	NA	NA
			Total activity: 227 (128–325)	10 (–36, –58)						
			Moderate: 4.3 (1.8, 13.3)	1.6 (–5.1, 16.1)						
	Control: 22 Idiopathic: 18 CTD: 4	47 (36–58)	Steps: 4709 (3795, 6135)	–149 (–1010, 735)	442 (362, 494)	12/3	53 (16, 90)			
			Total activity: 216 (184, 254)	–16 (–44, 29)						
			Moderate: 3.4 (0.3, 10.9)	–0.6 (–4.5, 1.4)						

Abbreviations: 6MWD, 6-minute walk distance; CTD, connective tissue disease; FC, functional class; MVPA, moderate vigorous physical activity; NA, not applicable; PA, physical activity; QOL, quality of life; RV, right ventricular function.

[a]Both studies collected QOL data but did not compare it to activity.

changes in Short Form Survey (SF-36), emPHasis-10, change in a supervised home-based 6MWD and Borg Dyspnea Score, resting heart rate, and time to clinical worsening. This strategy of incorporating real-time monitoring with text messaging may prove to be a better strategy to improve mobility in PAH.

We are clearly in our infancy in studying accelerometers to measure PA in PAH. Commonly used algorithms were primarily developed on a young healthy population,[20] and the thresholds used to classify activity may be inappropriate to use in a group of PAH patients. The step count feature may not be accurate in patients with altered gaits (eg, scleroderma) or patients who require a walker or oxygen. There are still many unknowns about the best device or location and the wear duration (per day and days per period). Some agreement and conformity will be required, or it will be very hard to compare results from different studies. We are also still determining which features of PA are most stable, most sensitive to a (favorable) therapeutic change, and most predictive of a clinical event. Wrist-based devices likely have a higher compliance rate than truncal devices but will report more isolated forearm movement in the measurements. It remains unclear whether this is good or bad.

In the past, the 6MWT was performed routinely with clinic or research visits. During the pandemic, investigators studied a home 6MWT on an outside 30 m walking space with a team member monitoring it remotely.[34] While an important proof of principle, this approach is probably not scalable. We have previously reported on a strategy to heart rate monitoring continuously during the 6MWT and measure *cardiac effort* (CE),[17,35,36] which is the (number of heart beats used during the 6MWT)/6MWD (beats/m). Cardiac effort is more reproducible than 6MWD, tracks with clinical improvement, and correlates with RV function.[35,36] We have also found that a chest-based electrocardiogram heart rate monitor is more accurate and has less data loss than wrist-based devices that incorporate photoplethysmography.[17,35] Using a combination of chest accelerometry and electrocardiogram heart rate monitoring, we had patients perform unsupervised 6MWTs in the home setting on a variable-length course of their choosing.[17] The median walking length was 40 feet. We found that 6MWD was lower in the

home setting (than clinic), but after adjusting for heart rate, CE was reasonably similar to that measured in the clinic. Cardiac effort allows for a measurement that can be repeated frequently at home and compared with values from clinic. This could help with drug titration and identify clinical worsening. Given the behavioral factors, which seem to affect PA measures, a standardized test like CE may home in on physiologic limitations or improvements related to RV function with less burden (no requirement to wear a device all the time).

Finally, the data illustrating the behavioral component for reduced PA in PAH patients suggest an opportunity for meaningful intervention. Novel strategies, such as the electronic encouragement studied by Hemnes et al,[11] are likely useful to help improve PA in patients. We as providers can also be sources of encouragement: the PHA sponsored a set of professionally produced exercise videos (5 Videos To Safely Start a Home Exercise Routine) to help promote PA, aerobic conditioning, and strength in patients with PAH who were unable to attend pulmonary rehabilitation.[37] Perhaps wearable devices could be used to design remote rehabilitation programs to push patients toward safe limits and allow them to track their progress toward more PA (and perhaps better quality of life).

In summary, PA is low in our patients, and the available evidence suggests that this is at least in part due to physiologic limitations (RV function). We have much to learn about how to study PA, and there is clearly a behavioral component to reduced PA which will confound attempts to use PA as a measure of clinical improvement in therapeutic studies. Standardized home exercise testing (with CE as the measure) may be closer to the heart of the matter in terms of studying physiologic limits and the risk for clinical worsening, but wearable devices could help us disseminate and measure exercise interventions which could be of real value to our patients.

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PULMONARY HYPERTENSION ROUNDTABLE

The Role of Caregivers in Pulmonary Hypertension Care

This spring, Dr Hilary DuBrock, Mayo Clinic, Rochester, and Dr Charles D. Burger, Mayo Clinic, Jacksonville, Florida, gathered to discuss the role of caregivers in pulmonary hypertension care with Michele Freeman, Eric Olayos, Jenna Olitsky, Dr Scott Olitsky, and LaKeshia Orr.

Dr Hilary DuBrock: Welcome, everyone, to our roundtable discussion with caregivers for patients with pulmonary hypertension. Dr Burger and I are serving as guest editors for an issue of *Advances in Pulmonary Hypertension* focused on the societal and multifaceted aspects of pulmonary hypertension beyond diagnosis and treatment: topics such as mental health, diet, and exercise, and caregivers. Caregivers may be spouses, partners, parents, or friends, and they play an important part in the care of PH patients, but yet we often don't talk about them or their role as an integral member of the care team.

We know a lot about how PH affects our patients, but we actually know very little about how the disease affects caregivers. Our roundtable today is a discussion with PH caregivers to gain insight into their experience and to perhaps provide some advice and suggestions for how we as PH clinicians can better support our patients and their caregivers. Dr Charles Burger and I will be facilitating the discussion. I am Hillary DuBrock, a pulmonologist and pulmonary hypertension specialist at Mayo Clinic in Rochester and Director of the Mayo PH Fellowship program.

Dr Burger is a pulmonary hypertension specialist and Professor of Pulmonary and Critical Care Medicine at Mayo Clinic in Florida and also served as the past Editor-in-Chief for *Advances in Pulmonary Hypertension*. We have several patients and caregivers with us today for this discussion. First of all, thank you so much for taking the time to participate in this roundtable discussion.

We really appreciate your time and also are very grateful to you for all that you do to help care for your loved one with pulmonary hypertension. I thought we could just start with brief introductions. So let's go around the virtual room here so each of you could tell us a little bit about yourself and your role as a caregiver. Michele, would you like to start?

Michele Freeman: Oh, okay. Obviously, I'm a caregiver. My husband has had pulmonary arterial hypertension for 10 years. I'm also a support group leader for pulmonary hypertension, and I do the caregiver facilitator call once a month. Like many other caregivers, I work full time, so just add that in.

Eric Olayos: My name is Eric Olayos, and I've been caregiver for Pam, who's my wife and she's been diagnosed with PAH since 2012. I've been a caregiver since day one. This past summer, she was in Mayo Clinic, Jacksonville, for 60 straight days in ICU. She went into kidney failure. We're dealing with that on top of the PH. It's a long—as Dr Burger has probably known us for quite a while—this is a very tough position. It really is.

Dr DuBrock: Yes, it can be really hard when you're managing PAH and also dealing with complications and the impact of PH on other organs as well. It can certainly be very challenging.

Eric: That's my full-time job. I'm retired.

Dr DuBrock: That sounds like a lot.

Eric: It is.

Jenna Olitsky: I'm Jenna Olitsky. I'm the patient. I've had pulmonary arterial hypertension for 5 years. This is my father, Scott Olitsky, who is my caregiver for—I work full time. He's retired, so he helps a lot with all this.

Dr Scott Olitsky: I'm Scott Olitsky, as Jenna mentioned. I'm retired from clinical practice, a pediatric ophthalmologist. I work on a volunteer basis for Cure HHT, which is the international foundation for hereditary hemorrhagic telangiectasia, which runs in our family, which Jenna has. As you all know, a small percentage of patients with HHT developed PAH.

Dr DuBrock: Thank you both for being here.

LaKeshia Orr: Hi, everyone. I am not a caregiver. I'm actually a patient. I was diagnosed with PAH in 2017. It was already advanced. I was already at function class IV, so I'm not quite sure how long I had been living with PAH. Now I'm happy to report I am at function class I, and I'm doing better on all accounts and living life.

It feels like a second chance at life, and I'm just really thriving and really happy to be an inspiration and to share my story wherever possible. I am the Loma Linda University Hospital pulmonary hypertension support group leader and have been for a few years now. Then just last year in June, I had the opportunity to speak at conference in Georgia. I was on a panel about self-care for PH patients.

Dr DuBrock: Thank you for being here. Do you have specific people in your life who help to support you as caregivers?

LaKeshia: It's a community of friends and family members. It's very interesting to me that so many of my friends know my med schedule. They're like, "Hey, it's 9:00. Did you take your meds?" I'm like, "I'm about to. They're right here."

Dr DuBrock: That's great. It takes a village. You all talked a little bit about who

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you care for in terms of your loved one with pulmonary hypertension. Could each of you tell us a little bit about your roles and responsibilities as caregivers? Do your roles relate to medication administration or just navigating the health care system or communicating with health care providers or insurance companies, just a little bit about what you do in your role as a caregiver?

Michele: I guess I could start with what's going on. My husband was like almost every PH patient I know, was misdiagnosed for many years. Then a year after he was diagnosed, he also developed a brain tumor. At first, the doctors weren't going to operate on because they didn't think he was going to live, and they finally did. A lot of dealing with PH in the beginning was really fighting the system, "No, no, he's not just old." Finding the right doctors, it's almost like dating. You're going to go through a few that just don't work for you, and then getting the health care team put together is the next important step.

Actually, he's doing pretty okay now with meds going from being really, really sick in the beginning. Now it's more supporting him—such as I've got a family calendar with all the doctor's appointments. Is everybody where they need to be? He does have a timer for his meds, but even that he doesn't always do them on time. Like the other day he says, "Oh, I couldn't figure out why I felt so bad all day. I didn't take any meds." I get that a lot. Then the other thing is even helping them emotionally. I think a lot of people don't realize that, with caregivers, our life also changes completely.

We have to change everything and be willing to be part of this. That took a little bit of adjustment, too. I think everybody kind of goes, "Why me?" It was just the black cloud overhead kind of thing. Again, the one thing that keeps me going is the hope. We go to conference—and I am sorry I missed your presentation LaKeisha. You would've been a great presentation, but keeping aware of things, learning what's going on, really keeping me abreast of what's going on in the field I think is really helpful.

It does consume your life and completely change it, such as when we traveled in June to Atlanta for conference. It's like taking a baby. Do we have the oxygen condenser? Do you have everything that is necessary? Did you bring your meds? Seriously, he doesn't remember all those things, and you've really got to make sure everything's there. It's a lot of equipment, but we did it. It worked. It was fun. It took a lot of planning.

Dr DuBrock: Thank you. It's a big responsibility and a lot to remember. Travel and things like that are certainly not as easy as they were before, I imagine. Does anyone else want to discuss their role and what responsibilities and experiences they have had as a caregiver?

Eric: Oh, I'll go next. When Pam was first diagnosed, like I said, it was back in 2012. She had been struggling for about 3 years. Doctors like your normal everyday doctor would say, "Oh, maybe it's pneumonia, or maybe it's bronchitis, or maybe it's asthma, or maybe it's all just in your mind." It really wasn't. She was lucky enough to hook up with a pulmonologist in Chicago. He recommended—he did all kind of tests, and he realized that the condition that she was in was way beyond what his expertise could do. He said, "I'm going to send you down to Dr Mardi Gomberg down at the University of Chicago Hospital." That's where she was diagnosed.

Immediately, she basically started Pam on Veletri—not Veletri, what was the one before that? Flolan. She was on Flolan for about a year and a half or 2 years until I finally retired and we moved from the Chicago area down to Florida and down—now we were on the West Coast of Florida, and we came over to the Mayo Clinic where we got ahold of Dr Burger. We've been with Dr Burger. Now since he's trying to transition away from Pam, and now we're working with Dr Moss. I will say that, as far as the technology goes, we're 20 minutes away from Mayo, so we rely on a lot of what Mayo has to offer us to keep up with Pam's care.

She goes to kidney dialysis on Tuesdays, Thursdays, Saturdays, which really restricts us as far as really going anywhere or doing anything. We had gone on about 35 cruises in about the last maybe 15 to 20 years. We've had to forego that now because you can't get dialysis on a cruise ship—you can, but it's very, very, very expensive, and Medicare, and what I have is Tricare, they don't cover it. Everything that we do now is literally for Pam. I used to ride my Harley 7 days a week. I haven't started it up in 3 months. I used to go bowling and play softball. That's out of the question now because I can't really take Pam with us because she can't sit out in the hot sun very long.

We've really had to restrict as far as stuff that I do. I cook. I clean. I vacuum. I do the laundry. I cut the grass. I plant the flowers. I literally make the bed. I literally, literally do everything because she also has extreme osteoarthritis of the right hip, so she can't walk. She can barely stand. She's basically wheelchair bound all the time. It's been extremely difficult and tiring from the time I get up in the morning until the time I lay her in bed. It's literally working to keep her going and keep everything functioning in the house.

Dr DuBrock: That sounds like a lot.

Dr Charles Burger: Eric has always accompanied his wife to the appointments. I have personally and I know my staff have valued that immeasurably. I just want to give props to you guys who have jumped into this caregiver role. We couldn't do what we do without you. Really admire your dedication to the folks that are in your lives that have pulmonary hypertension and to you, LaKishia, who has pulmonary hypertension and your dedication to taking good care of yourself.

Eric: I want to add one more thing. One lucky thing in my favor is that I'm a retired Navy hospital corpsman, and I also have degrees as a medical technologist running hospital labs. That's luckily in my favor. That's the only other thing I'll put into it.

Dr Olitsky: I guess I can go next. Jenna's story is probably in some ways similar about diagnosis. Fortunately,

at the time of her diagnosis, we were already plugged into a HHT Center of Excellence institution that happened to be run—the director was also a PH specialist. We were fortunate that, once diagnosis was made, treatment started pretty quickly. That was 5 years ago. In terms of my role, I think, somewhat similar to what has already been said, I manage a lot of special medicine specialty pharmacy issues, getting the meds shipped, watching out for the prior authorizations when they're due, making sure everything comes in on time.

Jenna doesn't need any help dealing with her medicines, but I take on a lot of that role because I do have some of that time, and Jenna works full time. Along the line of what Eric was saying, I don't know how other people can do this. Sometimes I feel fortunate, maybe a little atypical as a caregiver, being a physician, that I know this system a little bit, although it's shocking to me how difficult it can be. Many times, Jenna or my wife has heard me hang up the phone and say, "I do not know how somebody without a medical background could take care of their loved one."

Getting told that Remodulin is not coming on time or that it was denied when insurance changes and just knowing that that's not going to happen, but all the work that it takes, I'm sure as with the rest of you I've been on the phone with insurance companies for hours and hours a day, and I don't know how somebody else who's working full time could do that. My wife, Jenna's mother, also helps quite a bit with some of the things, some of the chores that [are] probably not in her best interest to be doing when we can. Like someone said, I do a lot of research in what's up and coming. I go with Jenna to her appointments to talk to her doctors about options with her care.

Again, I think that's something that I find very important to do. Sometimes Jenna gets a little frustrated with those conversations perhaps at times. Again, I don't know how other caregivers can do that sometimes. I feel very fortunate that I have the time and the knowledge to be able to do that for her. Before the pandemic, I know Jenna traveled internationally a lot. Hopefully, we'll get back to that. I look up and see where centers are to give her the information when she's traveling overseas. It takes a lot of time, as you all know. I know I'm preaching to the choir here.

Michele: I want to jump in on that, too, because I'm a licensed counselor, and I work with people with other chronic illnesses. I know the system, and I found that, sometimes, it's like beating your head against the wall. I thought about that, too: what do people do when they don't know it? At least I'm familiar with what's going on. It is difficult, and you've got to really be aggressive. I used to be nice and nonconfrontational, and now I don't care anymore. You learn to be pushy. You learned to go, "No, this isn't right," and you do what you have to do it to keep your loved one alive.

Dr Olitsky: The squeaky wheel gets the grease sometimes, and it's not the person's fault on the other end. Many of them don't understand what these medications are, that certain medications can never be stopped. Some of it's educating the people at the specialty pharmacies.

Dr DuBrock: Thank you. It sounds like being a caregiver and navigating the health care system is really challenging both before and after diagnosis. After diagnosis, roles relate to disease management and dealing with insurance companies and medications, but also before diagnosis, you as caregivers play an important role as patient advocates to help find the right specialists and determine the diagnosis. That's something I think I hadn't really appreciated is that the role of a caregiver really starts even before pulmonary hypertension is diagnosed.

Michele: The other thing they didn't bring up as many of us travel, it's 3.5 hours one way to the specialists in Portland because, here, there's no local specialist or ones that I would go to or recommend because I know all of them. Many of us will need to travel distances to get the help we need.

Eric: As a matter of fact, we actually moved to Jacksonville from the West Coast of Florida in November just so that we could be only 20 minutes away from Mayo because, otherwise, was a 3.5-hour drive. I understand exactly what you're saying, Michele. I know exactly.

Dr Burger: I have a follow up to some of the things that you guys have said. What have you found to be the value of networking, if at all?

Michele: Without a question, that's why the support groups are so great because people will support and help one another. We tell other members, "Oh, this is what I do," or, "I was having trouble with TYVASO side effects. What do you do to mitigate the side effects?" Also, for doctor recommendations, we're a great network. We just had someone new to the area, and everybody goes, "Don't go there; go here." That really does help.

A patient with pulmonary hypertension can't make it just with the caregiver. There's got to be other people involved with it, too, and other ones that you can ask about. How do you talk to the insurance companies? What do you do? What do you push through? There's always somebody that went, "Oh, yes, I had this problem. This is what I did." It's very, very important to be successful.

LaKeshia: I definitely want to chime in here and say that, whether you have a patient or the caregiver, our relationship with pulmonary hypertension can feel very lonely because of the stats. It's random. It's rare. I think the last time I read a stat, it said that, out of every 1 million people, 15 people have pulmonary arterial hypertension. You're just not interacting with people in your normal life if not for these support groups and these small communities. It's very important that we stay tapped in and connected to one another because, sometimes, it's a relief to know that there's someone else you can reach out to who knows what you're dealing with and can just relate. It's very important, and I love to be in and facilitate spaces like this.

Dr Olitsky: I think one of the things that comes up with networking is es-

pecially on social media. It can be good and bad. I see a lot of people asking for medical advice which may not always be the best thing. What is helpful is talking to other patients about experiences. How do they handle a side effect? What can you expect when you try a new medicine? That's been very helpful to network with people for those reasons.

Michele: The other thing I found with any kind of chronic illness and pulmonary hypertension, especially in the beginning or even looking at the two of you patients here in this group, you do not have oxygen on. You don't look sick. There's also difficulties with family members and friends not realizing how serious PH is. I've heard that even though you may have your placard so that you can park in handicaps and the observing public is frowning, the nosy people asking you why you're doing this. I think that makes it harder when you're very much aware of the fact that you don't obviously look like there's something wrong with you, and yet there is something very, very wrong.

Jenna: I will say I experience this in a lot of traveling, especially on planes. You preboard and get many questions, why a preboard if you look so young? You don't look obviously like you need it. I will say that I think I can handle it. It's always nice to have someone else who understands as well if you needed them to explain or if I need someone to help carry my bag. That's why they're preboarding with me and have them also understand that.

Eric: We traveled once from O'Hare Airport in Chicago, where we used to live. We had to have—it was like for a week's vacation on Saint Croix. We had to have like one carry-on for just her Flolan, and we had to have another bag for a CPAP machine because the docs were thinking, at that time, she was having that particular problem. There was one other bag I think for some odd reason or another.

We're there with three carry-on bags, and we walked up to the person that was actually checking our tickets to get onto the airplane. She looked at Pam, and we all had medical tags on all three bags. That woman looked at Pam and said, "Do you really need three bags for medicine?" Like we were trying to make them feel—honest to God. There was another person in security that wanted to take her—she had three pumps because we were going out of the country.

The guy wanted to put it through the x-ray machine, and we said, "No, can't do that." He looked at her, and he grabbed the two extra pumps, and he literally was about a foot and a half away from putting it in the machine. I almost had to grab him by the shoulder, which I'm sure if I would have done that, then they would have had 30 different guys with guns pointing at my head. It's incredible how they don't believe that you're sick. I agree with you, Michelle. It's very difficult. It really is.

LaKeshia: I just wish there was more education, especially in the people who work in the airports, the TSA, around this disease process or what the medicine may look like. When I first was cleared to fly, I went away for a month, and I had all of my little Veletri cartridges packed in my carry-on bag. I went through security, and they had to swab each one of them individually. All these things, and just like I'm just reminding myself to stay in gratitude because I'm happy that I'm waiting to fly. I'm happy that I'm breathing. Like just be patient. They don't know. This is an opportunity to educate. Sometimes I don't feel like educating people. Sometimes I just want to get on about my day.

Eric: Yes, for sure.

Jenna: Can I tell you how many times I have to explain my Remodulin pump is not a diabetic pump that can't be disconnected to go through body scanner. Then I have to go through a metal detector instead which then gets you flagged, and then you have to go through the whole system. If they recognize it as a diabetic insulin pump, why can't they just recognize it as a different medical device? It might look the same, but it has a different function.

Dr DuBrock: We talked about some of the challenges of caregiving. What aspects of being a caregiver do you find most rewarding?

Michele: I think when they start improving. Like I said, my husband was so sick in the beginning, but he has improved with the right combination of medications. The last time he was in a study, they thought that he was on the actual drug. It turned out he was on the placebo. There is improvement, which is nice that you can see, even though we're told in the beginning you keep going downhill till you die. There can be plateaus or even getting a little bit better. We're seeing some differences in prognosis which was way different than 10 years ago. I think that's what Eric said.

It is difficult to imagine improvements in the beginning. Ten years ago, they were saying with treatment that you died in 5 to 7 years and without treatment 2 to 3 years. That was the way it was. It's nice to see that there's people living longer and pretty good lives. That's what I find the joy of it when you see the person you're taking care of is doing better.

Eric: Pam is now pretty much confined to a wheelchair because of her bad hip. One of the really nice things is that people open doors for us, being a little bit curious. The other thing is that, whenever we go to Mayo Clinic for her various different appointments, the docs are always very, very encouraging. They always tell her that it's not that she's going to get better because she's real serious with her PH, but she's doing a good job of maintaining. That's probably one of the things that Dr Burger and Dr Moss have always instilled in Pam is that her numbers look good, and they've not had to increase her Veletri. Things are maintaining, which is pretty good.

Dr Olitsky: I would say, as we all know, patients with PH have good days and bad days, and the good days make you feel really good for what you can do to bring those along, being able to do things that might not be possible without our help sometimes. Also, as I mentioned, we love to travel internationally as a family. We hope to get back to that,

being able to do some trips. That might mean that we go together just because we feel it's safer be able to do that again. Those are what make the time that you put in worthwhile.

Dr DuBrock: How prepared did you feel to become a caregiver? It sounds like it's a major part of your daily life now, and how prepared did you feel in the beginning to take on this role?

Michele: I don't know. I think I was pretty lost, and that was also before I started working with chronic illness. That's when I realized there was a need for it in my work, and I switched it. Yes, you don't know what to expect. You really are in the unknown. Because like they said, don't go online. Of course, we did, and we all do it. You don't know what to expect. There's good information and misinformation out there. It was hard. I think joining Pulmonary Hypertension Association made a huge difference because then I had a source and found other places and other drug companies that had some really good information. In the beginning, you don't even know what it is. I never heard of it.

Eric: When Pam was first diagnosed, again, luckily, I was a hospital corpsman for 20 years. I had a good background as far as what medical care I'd be able to do for her. Now as she's gotten because of her hip, I've taken over literally a lot more than I started out with. Being a corpsman and, again, a medical technology degree, I was able to do things with her Flolan and her Veletri. I make her meds every night. That didn't scare me in the least because, luckily, I had that background.

There I've been to some conferences where I talk with some of the guys that care for their ill wives, and these guys they throw their hands up, and they say, "I have no clue what I'm doing." It's just rote memory at this point. I wonder, if I didn't have that medical background, would I have been able to do things like that? Some woman said that, when her husband—after 2 years, he divorced her. Pam was the one that was talking to this woman.

She asked the husband the reason why he's asking for a divorce. He says, "When you first was diagnosed, they said that you may have had 2 years to live. It's been 2 years. I'm out here." We're sitting here going, "Oh, my God, this is the kind of stuff that we hear every day." Being a caregiver didn't faze me, but what has shocked me is the overwhelming amount of work literally that I do from the time I wake up in the morning. Just before I got on this conference call, I had to fold a load of laundry. It just never ends. It just goes and goes and goes.

Dr Olitsky: I don't know how things are now, but when I was in medical school, pulmonary hypertension was probably a paragraph in a pathology textbook. We do have another family member with HHT and pulmonary hypertension. We had some idea when Jenna was diagnosed what this would entail. Better or worse, I was a couple of months away from my retirement. As we all said, I don't know that this would be possible if I was still working to be able to do this as needed when the time comes.

Michele: I'll add to that. Luckily, our son had to get a place to live in and moved back home just temporarily just before my husband got sick. That's the only reason why I've been able to work. I told him, now he can't leave. He's in his 30s. Because it's nice when we have to go, "Oh, got to go to the hospital. Bye. Take care of the dogs." It's like what you were talking about. It's not just me. It's not just me. Otherwise, it'd be really hard. I wouldn't be able to work. I'm able to work because there's other family members here.

LaKeshia: When I was diagnosed, I was actually living on my own, and my pulmonologist, right away, he knew it was going to get worse before it got better. He said that I should not be living alone, and so I moved back in with my parents. Again, the onset of all of this was sudden, but then it was also very severe. Within getting diagnosed, I got discharged from the hospital on oxygen.

We had to make sure there was an oxygen concentrator at my house before I could leave. I got done [with] the pump like a month and a half later. I want to give kudos to CVS Specialty Pharmacy and the resources that they provide because I had a nurse come visit me in the hospital and teach us how to mix the Veletri and the home visits. I think they were weekly for me at first.

They were very, very helpful to helping me and my family of caregivers adjust and adapt, and having someone that we could call or text or really reach out to with questions was a huge help. The reality of it was, again, it was very sudden. My parents were still working, and they were helping out when they could. My dad was mixing my medicine, but they got tired. I don't know if it was just because of life or because of all of their responsibility.

I actually had to become a little bit more independent, and then I started mixing my medicine myself. It sucks, I have to say it, but it's a reality. Sometimes it can get tiring, and I only felt comfortable saying that after you shared that the husband said he was out after 2 years because I remember someone coming into my hospital—I mean, room, at bedside and saying, "Hey, you have something called pulmonary arterial hypertension." I was like, "Okay."

Eric: A lot of people think that it's high blood pressure.

Michele: Exactly.

LaKeshia: As they walked out, and then I pull my cell phone and I said, "What is pulmonary arterial hypertension?" I pulled up an article that said 27 to 44% of people made it 5 years, and I'm still here, and I'm doing better. I think that's something to celebrate, and I'm very happy to be here and to be able to share. Yes, it was tough, and it was a big adjustment for all parties involved.

Dr Burger: You're to be congratulated on your success story. It's very admirable.

LaKeshia: Yes. Thank you, doctor.

Dr DuBrock: Are there other educational resources or supports for patients or caregivers that you think would be

helpful at the time of diagnosis? You mentioned PH support groups and networking have been helpful. Are there other resources that were helpful or you think could have been helpful at the time?

LaKeshia: I think everything that they're doing over at PHA is phenomenal. I wish I would've been introduced to [the] wealth of knowledge and help and personnel there sooner. I don't think I found out about PHA until much later.

Michele: I think one thing that's a little different, but everybody's hinted upon it, it would've been a lot nicer if the doctors here even understood what it was. Even after my husband was diagnosed, he had to go to the ER, they still were still saying, "Oh, it's cardiovascular. You need nuclear medicine imaging." I'm saying, "No, it's not. You are missing something." They ignored at the ER the diagnosis or did not understanding what it is the PH diagnosis. I found that to be a problem. The other misconception with medical professionals is that pulmonary hypertension is high blood pressure.

My husband didn't have high blood pressure at all when he was diagnosed. He didn't have swelling legs, which made it really hard, too, to get the diagnosis. It would've been nice if the medical world was a little more open to it or listen to the symptoms that were given, but because I do not have a medical degree, they discounted what I was telling them. I'm already lost. I don't know what it is, and then when you come across medical people that have no idea what it is either, that made it very hard.

Eric: Luckily, Pam and I were always near centers that had those people that were experts in that field. We relied on those folks from the beginning, University of Chicago Hospital and also Mayo Clinic. We've been very fortunate, and I will be the first person to admit that we rely on—Dr Burger knows Tanya, and she does a lot of work for Pam as far as making sure that the different companies are up to date with the insurance forms and Medicare numbers and on and on and on, although I probably, and Pam does, too—we probably could have done it on our own, but it would've been much, much, much harder. We relied on the Mayo Clinic and University of Chicago Hospital folks, their expertise, in order to get all that stuff done. So, Doc, thank you.

Dr Olitsky: I think we consider ourselves very fortunate to be plugged into some of the people that we've had contacts with actually long before Jenna's diagnosis. I think that's a little unusual that we have those connections, but I would say that, where certain drugs, certainly subcutaneous Remodulin and some of the challenges, having somebody that you can speak to about when that gets started, there's so many challenges, I'm sure, with many of these medicines.

The subcutaneous route of providing Remodulin has some unique challenges to it, I'm sure. We had clinical care coordinators who helped with that, but I'm not sure everybody has that. Probably having somebody to speak to a mentor or somebody that can help you in the beginning would probably be very helpful for many people. I know people have reached out to Jenna when they get started, so I know she's helped some people, and probably there are a lot of people who could use that help in the beginning.

Jenna: I was going to say the peer-to-peer, like LaKeshia was talking about, someone who knows exactly what you're going through. I know I've talked to people on Sub-Q Remodulin before who say, "This location I put it in, it's not really working. What have you used that has worked for you?" It's not something that a clinician can tell you because you're the one who are is doing it, not even the caretaker either. It's you trialed-and-error this that has worked for you, and you can pass that on, and hopefully, they pass it on.

Dr Olitsky: Something as simple as a position, I can tell you, I wouldn't have thought about this. Something as simple as what's the best adhesive to put on so you can take a shower, so you don't have to pull your site when it gets wet and go through that week again. Something just that simple is really the quality of life, the improvement is enormous.

Jenna: Also, someone to, like you say, commiserate with going through site changes, it's someone else who's directly understanding how you feel. Caretakers see how you are looking or see the difference of how you're feeling. Someone else won't understand not feeling like getting out of bed today, how's your site going, or just having that peer-to-peer relationship of having someone who directly understands.

Michele: On the same word of that, I was just thinking, with my husband, having someone that understands how tiring it is to have to take meds every 4 hours really, really becomes really tiring, and I can understand it. Like you said, it's nice to have someone else go, "Yes, I was there with you." I understand, and this is what I've done for it.

Dr Olitsky: I know, in my previous clinical work, there were certain patients with certain diagnoses. I had patients who I asked, "Would you be willing to speak to a family the next time they're diagnosed?" I think, if that's made available to patients, it can be immensely helpful.

Jenna: I won't speak for LaKeshia, but I know, if anyone were to ask another PAH patient if they wanted to speak to them about their journey or what has worked for them or what they've found, there's little tricks we learned to do throughout the day, like getting ready for a trip or how to tell even your friends what meds you're taking or, if you're with them, how they can also understand, which was difficult in the beginning, too, just having that mentorship between someone else who's not just diagnosing you and you have been through it.

LaKeshia: No, Jenna, you can totally speak for me. Yes, I agree. I am that person now, and I'm very open, and I allow people to connect me to newly diagnosed patients, and I'm always willing to talk. I remember, in the beginning, something as simple as not knowing

that I had a choice in my dressing cover, I was just using the same thing that I always use until I saw someone else with a different dressing, and I was like, "Ooh, I want that one." I just—it's a matter of asking and requesting it on the refill call. Those little tips and tricks are so helpful, and that's why it's really important that we connect with one another. I think caregivers with caregivers and patients with patients will all just benefit holistically.

Michele: It does help. The other thing that wasn't brought up that also dawned on me is that the patients and, of course, caregivers would be aware of it. There's a punitive aspect with our world. What'd you do wrong? What did you do to get it? You did something. To me, it doesn't matter if you did something. Let's say you took FenPhen or something like that. It doesn't matter anymore, but there is this that attitude, "Oh, you made your bed; lie in it. You did something wrong." I found, in general, because everybody's so stressed, there's not a lot of support for people that fall into disability with a chronic illness category.

LaKeshia: Especially an invisible one.

Michele: Especially an invisible one, exactly. You're very much aware of that even though you're going, "I'm okay." You also know you're being judged in many, many ways by people.

LaKeshia: Yes. I used to use the little motorized scooter cart things in the stores, and I would just always feel like people think I'm playing on the thing. Like, no, it's really difficult for me to walk around the store. I don't want to have to say that, and you're right, Michele.

Jenna: Even as you talked about with handicap placards, they're not easy to get, and I had to ask how to get it for PAH. I asked around because it didn't really fall into a certain category. My walk test is good enough that it doesn't fall into that specificness, but you do get dirty looks when you pull in there with it. I have to explain it's helpful to me. I don't need to walk across a completely empty parking lot to get to a store when you can just be right there.

Dr Burger: One question that I found intriguing that we haven't talked all that much is, what is—what are the best ways to leverage technology, both from the standpoint of being connected as a community but also in your relationship with your providers, good, bad, and the ugly?

Michele: One of the things that COVID brought was telehealth, which was nice, and hopefully, Medicare doesn't screw that up. I hear rumbles about that. That made it good. Then also, I've heard of some companies trying to develop things, and it's not on the market yet that you could even do blood work or something from your house that goes automatically to them.

More communication with each other, a little bit easier communication, maybe that's what I'm getting at. I think technology is going to be really important with it. One of the things that has helped with people in rural areas and other things that you don't have to necessarily go in to get test results. You can see it online. I found technology is going to really help a lot.

Eric: I have to agree.

Dr Olitsky: I completely agree about telehealth, something in my practice we had fought to get for, and then COVID hit, and now it's okay. I think maybe the next step is for many people who have to travel hours to see a physician, maybe being able to be seen offsite by a physician extender who's on a telehealth call with a provider at the same time.

Michele: Oh, that's a good idea.

Dr Olitsky: There are certain technologies now, being able to listen to somebody's heart, that wasn't available 10 years ago, things that might cut down on some of those trips for some patients.

Eric: I was going to say that, since we're so close to Mayo Clinic, what really fascinates my wife is that, no matter what discipline she goes in for an appointment, every doctor has read her profile. The latest information that she has had from her previous appointment is now [in there], and everybody is so up to date on every single thing that's going on with her. That's just incredible for us. Dr Burger, you know what I'm talking about there.

Michele: I like that many of the medical facilities in Oregon have electronic records that talk to each other. You can actually see several different ones at once—I do think that's a really good thing. I also like the idea of having the ability to read the test results as soon as they are completed. I hated it when, in the past, medical professionals would just say everything is fine, and you don't know what they mean. What is fine in relation to what? What do you mean? We're not stupid. I want to see the results along with past trends. I can actually see what the doctors get. Maybe they don't like it, but I think that helps us to be successful with this disease. The more education you have, the better you can handle this.

Dr Burger: Actually, we do like it. It can be difficult at times when results are released before we have a chance to discuss with you because we understand that that can generate anxiety on your part until you have a chance to have that conversation. I think, all in all, you are better informed, having access to the results of your test results. After all, it's your data. We're supportive of that, although there are some challenges from time to time.

Dr DuBrock: We only have a few minutes left, so let's go around the room and see if anyone has any closing comments that they would like to add or any advice for clinicians and health care professionals about how we can better support PH patients and caregivers.

Eric: As far as my aspect goes, I like this idea of having a roundtable dealing with caregivers. I don't think enough emphasis is given to the caregiver. Obviously, it's the patient that we're all trying to make better. I get that. There's a lot of times when the caregivers really don't

have anyone to turn to, and I think that anything that comes up dealing with caregivers is a good idea.

Michelle: Yes. The thing I would add is I wish, here, the pulmonologists here would support our support groups. I'd make up a flier. I send it each month on what's on the meeting topic and speaker will be and I get nothing. In fact, that's why our group is still online because we have two members here left after COVID, so our group reaches out to all of Oregon, but it would be nice to have more locals attend.

Dr Olitsky: I think, as someone who's really worn three hats at times, a patient, a physician, and a caregiver, I can't say enough about the physicians we've interacted with. They treat our family extremely well. They're very tolerant of my involvement, I'll say, some maybe more than others. I think our experience is they understand how important caregivers are in this incredibly complex disease.

Jenna: I was going to say the respect of both the patient and caregiver has been very helpful and very understanding. I can't appreciate it enough because I know, if I didn't relay the information sometimes, I know that that's what he's here also for. If it's just me, it wouldn't be relayed as correctly. The fact that they can interact with both [of] us is very helpful.

LaKeshia: I have been so blessed and lucky to be connected to Dr Paresh Giri since early on in my diagnosis. He's been my only pulmonologist. He recently moved practice, and I'm moving, too, because I'm afraid to have to get a new provider. I'm so afraid of having a relationship with someone who doesn't listen to me or who doesn't take my concern seriously. I hear those stories, and it lets me know how lucky I am to have the relationship that do with my pulmonologist, and I just value it. Yes, that's just the last thing I wanted to say. It's the relationships that we have with the providers are so important.

Jenna: I just moved providers, so I understand. I didn't want to let go.

LaKeshia: I cannot let go.

Jenna: I just did. I'm very comfortable. I'm very happy. I understand it took almost, what, two to three?

Dr Olitsky: Yes, for almost 3 years, we were driving halfway across the country to avoid flight.

Jenna: From California to St. Louis.

Dr Olitsky: It was time, but we're fortunate that, although we were nervous, we know we're in great hands still.

LaKeshia: The referral process has been ridiculous. I had an appointment in March, and they said they were going to give me the referral to go see my provider at the new place. Here I am in April, I was supposed to see him April 17th, but the referral still wasn't processed. I was like, "What is going on?" I'm a patient. I just want to trust in the process and in the system that things will get done. It really got to the point where I was just like, "Can I go and pick it up myself? Would they give it to me in hand?" They're like, "They'll give you a copy of the referral." I went to place one, got the referral in hand, took it to place two, gave it to them. Now it's being processed, but I don't want to have to intervene like that.

Michelle: With technology, that shouldn't happen. I've heard complaints with—from doctors, "Why do I have to go through this rigmarole every time with insurance companies?" Difficulties with things such as trying to find the code that is required or even what is covered, it can and should be much easier.

Dr DuBrock: Any last comments, Dr Burger?

Dr Burger: I would just like to express my appreciation to all of you. I've found this conversation very illustrative, and I would agree 100% we need to have more of these discussions and be able to share information like this, connect patients, connect caregivers, connect the entire community around the common goal obviously of ultimately, hopefully, maybe curing pulmonary hypertension, certainly making people's lives better that deal with this extraordinary challenge. Kudos to Eric because I tracked him down at the last minute to connect through, and he was willing to jump in. Thanks to all of you.

Dr DuBrock: Yes, thank you all so much for participating today. It was really helpful and educational for me to hear about how the caregiver plays a role, not just in caring for their loved one but also navigating the health care system, providing emotional support, and also educating the community about pulmonary hypertension. Thank you for participating today and for all that you do.

REGULAR ARTICLE

Diet and Exercise Intervention in Pulmonary Hypertension

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Current pharmacologic treatments for pulmonary arterial hypertension lead to vasodilation of the pulmonary arteries, increasing cardiac output and reducing pulmonary vascular resistance in patients with pulmonary arterial hypertension. Right ventricular failure is a leading cause of death in patients with pulmonary arterial hypertension, but there remain no promising leads in the treatment of right ventricular failure. Current research demonstrates that metabolic abnormalities, particularly regarding insulin resistance and glucose intolerance, may be pathologic in the development of right ventricular failure in patients with pulmonary arterial hypertension. In this review, we will address the potential role diet and exercise may play in improving right ventricular failure in patients with pulmonary arterial hypertension.

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a progressive pulmonary vascular disease marked by remodeling of the precapillary vasculature, leading to increases in afterload of the right ventricle (RV). This often progresses independently of hemodynamic changes and despite treatment to RV failure, a leading cause of death in patients with PAH.[1]

Current pharmacologic treatments for PAH include prostacyclins, phosphodiesterase inhibitors, endothelin receptor antagonists, and soluble guanylyl cyclase inhibitors.[2] These medications lead to vasodilation by targeting well-known mediators of vascular smooth muscle contraction. Through a delicate balance of medical therapy, providers aim to slow the progression of disease and cardiac remodeling in patients with PAH. While research is ongoing to find alternate pathways to treat PAH, there remain no promising leads in the treatment of RV failure.[3]

Historically, PAH was most noted in young women. In recent years, an epidemiologic shift has been observed: more often, PAH is diagnosed in older men and women with a high prevalence of comorbid obesity and diabetes.[3,4]

Glucose intolerance is a hallmark of diabetes but has also been frequently noted in PAH patients[5,6] and has been noted to be pathogenic in several PAH animal models.[7-9] Additionally, markers of insulin resistance and glucose intolerance are indicators of worse prognosis in PAH,[10] and current evidence suggests that diet and exercise interventions may play a valuable role in treating RV dysfunction in PAH.

METABOLIC ABNORMALITIES

It is clear is that patients with PAH experience metabolic changes that include increases in glucose intolerance/insulin resistance.[3,11] We have shown that patients with idiopathic PAH show glucose intolerance with decreased insulin secretion after an oral glucose challenge,[5] a response consistent with that of patients with type 2 diabetes mellitus and suggesting β-cell dysfunction. A subsequent study using the hyperglycemic clamp however did not show decreased insulin secretion but increased hepatic insulin clearance, explaining the low circulating levels of insulin.[12] This study did not show skeletal muscle insulin resistance, but substantial abnormalities in lipid metabolism.[12] Studies conducted by the Vanderbilt group yielded similar results.[12-15] Using oral glucose tolerance test and metabolomic data, Hemnes et al showed reduced glucose uptake in patients with PAH, without enhanced insulin secretion.[15] This, along with elevated plasma nonesterified fatty acid content, reduced high-density lipoprotein cholesterol,[16] and increases in lipid deposition in skeletal and cardiac muscle, implies that the insulin resistance in PAH patients is mediated by a dysregulation of lipid metabolism.[15] Notably, low plasma HDL-C is a strong predictor of poor outcomes in patients with PAH.[16,17] Experiments performed in murine models with induced PAH indicate that this dysfunction is pathogenic, leading to progressive decline of RV function.[8,9]

There is evidence that insulin resistance can affect the RV, even without a diagnosis of PAH[18,19] and that these changes negatively impact patient outcomes in those with concomitant PAH and diabetes.[3] In the failing PAH RV, nutrient intake is increased, but glucose and fatty acid oxidation are decreased.[20] Through the use of fluorodeoxyglucose-positron emission tomography, it is possible to visualize changes in metabolism in the RV, specifically increased glucose uptake, which is associated with poor RV function.[20,21] Importantly, some improvement in the RV has been found with the administration of drugs that ameliorate insulin resistance, such as metformin.[7] In a

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phase II trial, metformin has been shown to be safe in patients with PAH,[22] and ongoing trials continue to explore potential effects of pharmacologic modulation of glucose metabolism in PAH patients.[23]

EXERCISE

Pulmonary rehabilitation is increasingly ordered for individuals with obstructive and restrictive lung diseases and is a recommended facet of PH treatment.[24] Beginning in 2015, European Society of Cardiology/European Respiratory Society (ESC/ERS) Guidelines included a Class IIb recommendation of exercise in patients with pulmonary hypertension.[25] These recommendations stem from a set of studies that describe the benefits of supervised exercise in patients with pulmonary hypertension.[26] The landmark Mereles trial was the first randomized controlled trial (RCT) on exercise in patients with PAH, and investigators demonstrated significant improvements in exercise capacity, quality of life, and cardiopulmonary fitness.[27] Following Mereles, other trials with varied exercise protocols continued to support these findings,[28] demonstrating sufficient evidence to support the ESC exercise recommendations.

Since the 2015 recommendations, further trials were completed to define safety and efficacy of exercise in PAH,[29] to determine effective exercise protocols,[30] and to identify mechanisms by which exercise exerts these effects[31] (Table). Most recently, the ExPAH study[31] explored the effects of exercise on cardiac magnetic resonance imaging, in which the investigators noted improvement in stroke volume, reflecting improvement in RV function. The authors noted difficulty with recruitment, with only 16 participants agreeing to take place over 4 years. This led to trial underpowering; however, their results were supportive of those from Ehlken et al, who was the first group to report changes in hemodynamics in response to exercise training.[29] While the hemodynamic changes from the ExPAH[31] did not meet significance, there was a trend to improved pulmonary artery wedge pressure. Ehlken et al also found meaningful improvements in the hemodynamics of patients after 15 weeks of training.[29]

The WHOLEi + 12 trial[30] investigated the potential role of resistance training in PAH rehabilitation. For this study, the primary endpoints included changes in upper and lower body power, which are markers of skeletal muscle function. PAH is marked by peripheral muscle weakness[32-34] and increases in resting energy expenditure,[5] which is believed to contribute to the exercise limitations of these patients. For 8 weeks, participants underwent exercise training, including aerobic, resistance training, and inspiratory muscle training, leading to interaction effects for lower and upper body power in the exercise group. Expectedly, there was an increase in Vo_2max and maximal inspiratory muscle strength in the training group, though increases in 6-minute walk distance did not reach significance. Finally, the largest exercise RCT in PAH to date was published with 116 participants having completed a 15-week training regimen, demonstrating high feasibility and safety of exercise training, along with continuing demonstration of improvements in exercise capacity.[32]

Exercise training is demonstrably effective at improving quality of life and exercise capacity in PAH patients.[30,32] There have also been noted improvements in hemodynamics.[29,31] Taken together, this evidence encouraged the ESC/ERS to give a Class I recommendation for supervised exercise training in patients with PAH.[25]

DIET

Currently, there are no recommendations or advice regarding diet for practitioners who care for patients with PAH.[25] While there is clear clinical benefit to maintaining fluid balance with diuretics and a low-salt diet, there are no RCTs exploring this. The absence of these trials forces us to extrapolate potential benefits from other conditions that present similar metabolic abnormalities, such as diabetes, left-sided heart failure, and even cancer.[11,36] In each of these conditions, there is improvement to be seen with dietary modifications, despite the dearth of RCTs available.[37]

The Mediterranean diet has been shown to improve the signs and symptoms of diabetes,[38] showing reductions in HbA1c, more than control diets and improvements in lipid profiles, including total cholesterol, triglyceride, and HDL-C.[39] A diet characterized by lower red meat intake, higher fish and unsaturated dietary fat intake, and moderate alcohol intake, individuals who adhere to a Mediterranean diet show demonstrable improvement in glucose handling in those with type 2 diabetes and in healthy controls.[38] Given the metabolic similarities among patients with PAH and diabetes, it is reasonable to conclude that there may be some benefit to dietary intervention as an adjunct to traditional PAH medications. Several observational studies have been performed that demonstrate reductions in cardiovascular risk, heart failure, and stroke in cohorts that adhered to a Mediterranean diet.[40-43] Though these studies are limited by their observational nature, these results may still be an indicator of potential benefit.

An alternative to the Mediterranean diet is the Diet Against Systemic Hypertension (DASH). Again, few RCTs exist in this realm, and those that have been performed are of small sample size.[11] However, in left heart failure, these studies show promising improvements in endothelial function,[44] improved handling of long-chain fatty acids and L-carnitine,[45] and improvements in diastolic function and ventricular-arterial coupling.[46] Despite the absence of studies available to determine ideal dietary interventions in PAH, potentially useful interventions may be extrapolated from studies involving similar conditions.

CONCLUSIONS

There is a demonstrated need for greater investigation into the role of diet and exercise as adjunct therapy in the treatment of PAH. While benefits of therapeutic intervention have been seen in quality of life and time to clinical worsening, no treatment has been developed to directly improve RV function in patients with PAH.

Table. Randomized-Controlled Exercise Trials in Pulmonary Arterial Hypertension. Completed Clinical Trials for Vasodilator Therapy in CTEPH

Year	Study	Patient population	(N)	Intervention	Primary endpoint	Main finding
2006	Mereles et al[27]	Pulmonary Arterial Hypertension or CTEPH	21	3-week inpatient, 12-week outpatient, low-dose cycle ergometer and walking training	6MWD and patient reported quality-of-life outcomes	• 111m increase in 6MWD • Improvements in QOL, WHO FC. • No change in pulmonary artery pressures
2016	Ehlken et al[29]	Pulmonary Arterial Hypertension or CTEPH	87	3-week inpatient, 12-week outpatient 1.5 hours/day, 7 days/week rehabilitation	Change in peak Vo_2/kg	• Significant improvement in peak Vo_2/kg in the training group • Improvements in CI at rest and during exercise, mean pulmonary arterial pressure, PVR, 6MWD, QOL
2016	WHOLEi + 12[30]	Pulmonary Arterial Hypertension	60	8-week inpatient exercise, including aerobic, resistance, and inspiratory muscle training 3, 5, or 6 times per week.	Peak muscle power during bench/leg press	• Significant improvements in leg/bench press • Training-induced improvement in 5 repetition sit-to-stand test, maximal inspiratory pressure, peak oxygen uptake
2021	Grunig et al[32]	Pulmonary Arterial Hypertension or CTEPH	116	25-day inpatient rehabilitation following the Heidelberg exercise training program	Change in 6MWD	• Significant improvements in 6MWD, WHO FC, peak oxygen consumption
2022	ExPAH[31]	Pulmonary Arterial Hypertension	16	12-week outpatient exercise, either home walking 30 minutes/day, 5 days/week, or a multidisciplinary rehabilitation program.	Changes in right ventricular ejection fraction and stroke volume.	• Inadequately powered • Trends toward improvements in hemodynamic function, QOL, and muscular strength

Abbreviations: 6MWD indicates six-minute walk distance; CI indicates cardiac index; CTEPH indicates chronic thromboembolic pulmonary hypertension; PVR indicates pulmonary vascular resistance; QOL indicates quality-of-life questionnaires; WHO FC indicates World Health Organization Functional Class.

Insulin resistance related to lipotoxicity is likely pathological in the progression of RV failure, indicating a potentially novel pathway for treating PAH. Diet and exercise interventions have proven beneficial in treating similar metabolic abnormalities in conditions such as left heart failure and diabetes and can potentially be harnessed as an adjunct treatment for RV failure secondary to PAH.

Further research is clearly needed to determine the potential benefits of combined diet and exercise interventions in the treatment of PAH. At the Cleveland Clinic, we recently concluded the first interventional diet and exercise trial in PAH patients, called the Pulmonary Arterial Hypertension Improvement with Nutrition and Exercise.[47] The purpose of this study is to evaluate changes in RV function in patients with PAH in response to adoption of a Mediterranean diet and an exercise program, with results forthcoming. More work is needed to define diet and exercise interventions that may prove protective of RV function in patients with PAH to improve quality of life, mortality, and exercise capacity.

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REGULAR ARTICLE

Socioeconomic and Social Determinants of Health: Effects on Pulmonary Arterial Hypertension Care

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There is increasing awareness on the significance of socioeconomic status, social determinants of health, and the role of ethnicity and race in clinical outcomes of patients with pulmonary arterial hypertension. However, to date, underrepresentation of minorities in pulmonary hypertension clinical trials and registries remains. In the present review, we summarize the current knowledge on race, ethnicity, traditional and novel socioeconomics and social determinants of health, and its association with clinical outcomes in patients with pulmonary arterial hypertension. We present case examples on the interplay of these factors for specific disease phenotypes and discuss strategies for addressing these variables at the patient care level.

INTRODUCTION

Pulmonary arterial hypertension (PAH) is associated with impaired quality of life and increased cardiovascular morbidity and mortality as well as increased economic burden. Significant progress has been made in the understanding of PAH, and different prognostic models have been developed to better guide its management.[1,2] However, our current approach of disease management relies on data obtained from large registries and clinical trials where there is significant underrepresentation of minorities.[3] Recent years have brought renewed attention to racial and gender disparities in health, highlighted by recent sociopolitical violence as well as the COVID-19 pandemic.[4]

In the present review, we discuss the significance of race or ethnicity and social determinants of health (SDOH) in PAH. We describe 2 case examples displaying the interplay of negative SDOH, and we discuss the steps needed to improve representation of minorities and to overcome the barriers that SDOH imposes on the care of patients with PAH.

DEFINITIONS

Socioeconomic status (SES) refers to an individual's social and economic standing, reflecting his or her social or economic rank within a given social group.[5] SDOH refer to conditions in which individuals are born, grow, live, work, and age[6] and are implicated in health inequalities which disproportionately affect certain groups such as minorities. Health care disparities refer to differences in health care access closely linked with social, economic, and/or environmental disadvantage.[7]

RACE, ETHNICITY, AND SDOH IN PULMONARY HYPERTENSION

Race or Ethnicity

Most studies on the association between race or ethnicity and outcomes in PAH relate to Hispanic and Black patients. In general, Hispanic PAH patients are younger and have a higher frequency of congenital heart disease and portopulmonary hypertension (PoPH) than non-Hispanic Whites.[8] Reasons behind this association include lack of access to proper medical care in early childhood when congenital heart defects could be detected and corrected[8] in addition to a higher frequency of untreated hepatitis B infection[9] increasing risk of PoPH.

Race and ethnicity have been shown to have effects on outcomes in PAH patients. It has been described that healthy Hispanic patients without PAH have a higher right ventricular (RV) mass than non-Hispanic Whites, which has led to the hypothesis that Hispanic patients could have an inherent biologic advantage regarding RV adaptation.[10] Karnes et al[11] used data from the National Biological Sample and Data Repository for PAH (PAH Biobank) to assess differences in outcomes based on race or ethnicity. In their analysis, Hispanic patients had better survival than both non-Hispanic White and Black patients, even after adjusting for age, sex, hemodynamics, and PAH treatment (heart rate [HR] = 0.46, 95% confidence interval [CI] = 0.21–0.99). The authors focused mainly on idio-

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pathic and heritable PAH rather than other subtypes of PAH, limiting the generalizability of these findings. The authors did not account for differences in social, economic, or environmental determinants of health. Medrek et al[12] assessed the effect of race on PAH outcomes using data from the REVEAL registry, and no association was found on the multivariate analysis (which adjusted for age and PAH subtype). In their analysis, they could not account for differences in SES, as this information was not collected in the REVEAL registry. Bernardo et al[13] used data from the Pulmonary Hypertension Association Registry (PHAR) to describe the profile of Hispanic patients with PAH. Of note, PHAR routinely collects information on SDOH,[14] and surveys are available in Spanish. Hispanic patients had suboptimal health care insurance, lower annual income, lower education level, and were more likely to be unemployed as compared with non-Hispanic White patients.[13] While the unadjusted analysis showed better survival in Hispanic individuals, this association was no longer present after adjustment for age, sex, PAH subtype, and SDOH metrics (annual income, health insurance, and education level). Finally, in a recent study in a Hispanic-enriched cohort, authors showed that commonly used risk stratification tools, such as COMPERA and REVEAL 2.0, performed well as risk predictive tools, both with acceptable mortality discrimination.[15]

Racial variations on etiology of PAH as well as medication responses in non-Hispanic Blacks have also been reported. Black patients with PAH have a higher frequency of connective tissue disease such as scleroderma than White patients[8] and may have a different response pattern to endothelin-receptor antagonists (ERAs).[16] A pooled analysis of randomized clinical trials of ERAs in PAH showed differences in the response pattern of Black patients with placebo-adjusted change in 6-minute walk distance that decreased by 3.5 m, which was in contrast to an increase by 41.5 m in White participants, and this persisted in the adjusted models.[16] It was hypothesized that treatment-response differences could be related to higher endothelin-1 (ET-1) levels in Black patients not sufficiently inhibited by the dose of the ERAs used in the trials.[16,17]

Regarding survival, Parikh et al[18] found that Black patients had increased mortality as compared with Whites (HR = 2.06, 95% CI = 1.18–3.44), but when adding insurance status to the survival model, there were no differences in mortality, suggesting that outcome differences were mostly related to lack of access to care.

Less is known about other minorities with PAH such as Asian patients,[19] Native Americans,[20,21] and Native Hawaiian and other Pacific Islanders. There is limited knowledge about PAH in low- and middle-income countries, which constitutes a significant gap in knowledge.

SOCIOECONOMICS

While effective therapies exist for PAH, economic barriers to proper treatment still exist. The average treatment cost per patient is estimated at $80 000 dollars per year.[22] Deductibles and copayments can lead to substantial out-of-pocket costs, despite active health insurance.[23]

SES has been shown to be an independent predictor for survival in PAH. Wu et al[24] stratified patients with PAH from China in SES tertiles, finding that patients in the lower socioeconomic tertile had increased mortality. Talwar et al[25] used data from a large hospital system in New York and found that patients with lower annual income had higher disease severity on presentation. In a study from Scotland, authors used a geographic index (Scottish Index of Multiple Deprivation) to estimate social deprivation in patients with pulmonary hypertension (PH)[26]; however, unlike the 2 prior studies, no association with mortality or disease severity was found.

RURALITY, HEALTH CARE DESERTS, AND ACCESS TO TECHNOLOGY

Due to the need for specialized care, most patients with PAH receive their treatment at large metropolitan referral centers and frequently must drive long distances for continuity of their care. As such, patients from disadvantaged economic backgrounds could face barriers such as lack of transportation, which leads to missed clinic appointments, inadequate pharmacy access, and delays in medical care.[23,27] Macias et al[28] performed a claims data-based analysis of adults with PH. Mortality risk was significantly higher among those living in small urban counties (HR = 1.48, 95% CI = 1.14–1.92) and rural counties (HR = 2.01, 95% CI = 1.13–3.57), even after adjusting for age, sex, neighborhood poverty rate, race or ethnicity, and disease burden. Efforts to improve access to health care in nonmetropolitan communities include the use of telemedicine. However, successful use of telemedicine relies on having access to proper technology, familiarity with it, and having stable Internet connectivity, which is frequently lacking in rural locations.[29] Lack of access to technology or Internet are considered novel SDOH.[30]

Despite increased numbers of PAH providers in the United States, several states do not have a Pulmonary Hypertension Association (PHA)-certified PH Comprehensive Care Center (PHCCC). Figure 1 displays areas within the United States without an easily accessible PHA-accredited program for PAH care; however, some of these states may have centers with expertise in PAH that are not accredited.

VETERANS

Veterans are considered a vulnerable population, and there is increasing interest in understanding the profile of veterans with PAH. Gillmeyer et al[23] performed a retrospective cohort study of all adult veterans diagnosed with PAH, studying the association between race or ethnicity and SES (including metrics of housing insecurity). This population was predominantly male with only 4% Hispanics. Housing insecurity was found in 3.9%. Patients with lower household income and those without non-VA health insurance experienced significant delays in treatment initiation.

OTHER AT-RISK GROUPS

Other vulnerable populations in PAH include immigrants, prisoners, refugees, and patients with disabilities and mental health disease. There is a lack of information regarding the frequency of this

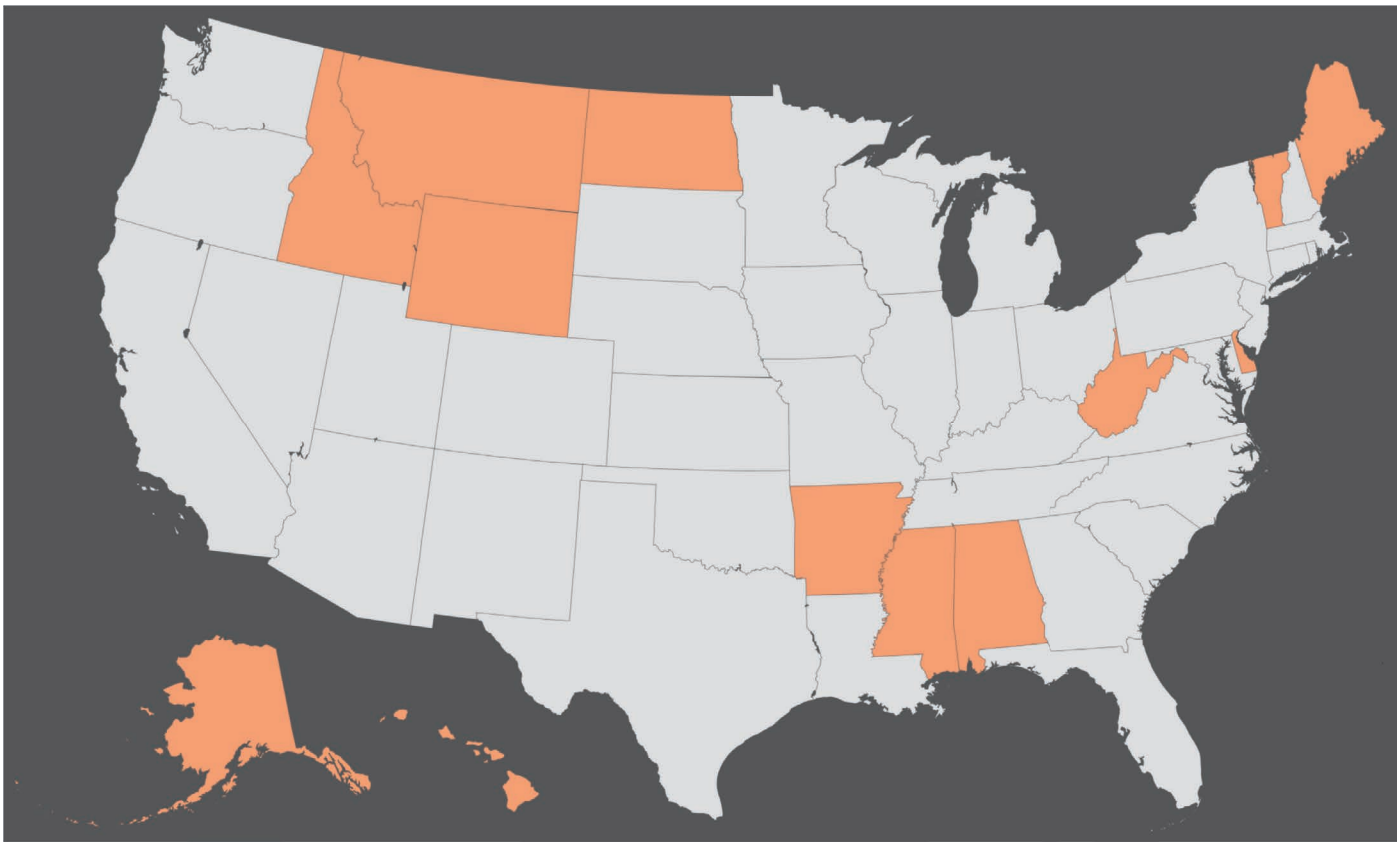

Figure 1: PAH care deserts. Highlighted are the states within the United States without a PHA-accredited center (either Accredited Center of Comprehensive Care or Accredited Regional Clinical Program). Source: phaassociation.org. PAH, pulmonary arterial hypertension; PHA, Pulmonary Hypertension Association.

demographic and prevalence of mental health disorders and the distinct barriers to proper care these patients face. Patients with language barriers could face difficulties with understanding their disease process and treatment options. Patients with disabilities or mental health disorders may face limitations of care related to underestimation of their ability to manage advanced therapies such as parenteral prostacyclins and is yet another area with significant gaps in knowledge.

Patients with substance abuse and addiction are a particularly vulnerable population and will be described later (see Populations at Risk). The significance of SES, SDOH, and medical literacy on trust in the medical care system, medication adherence, and treatment compliance is an area in need of further investigation.

REPRODUCTIVE HEALTH CARE

Unequal access to reproductive health care across the United States affects women of reproductive age. Female patients with PAH are counseled against pregnancy based on international consensus guidelines,[31,32] and pregnant patients with PAH are often counseled to pursue termination. With the recent Supreme Court decision to overturn Roe v. Wade, pregnant patients with PH face several challenges affecting their care including the possibility of having to relocate to a different state to pursue termination with its associated logistic costs. This is a significant challenge to all women but may be more pronounced in women of minority communities and lower SES.[33]

SPECIAL POPULATIONS AT RISK

Although SDOH are important outcome modifiers across the spectrum of PH, disease-specific considerations may uniquely elevate the significance, effect, and implications of SDOH in certain subtypes of PAH. Two specific populations, PoPH and methamphetamine-associated PAH (meth-PAH), present a particular challenge of intersecting social and biological factors that may influence patient outcomes in a compounded fashion (Figure 2).

PoPH is a type of PAH that uniquely occurs in patients with portal hypertensive liver disease.[34,35] Patients with PoPH demonstrate worse treatment responses than those with idiopathic PAH (IPAH) despite comparable hemodynamic disease severity at time of diagnosis, and PoPH patients have among the worst survival outcomes of any PAH subtype, with a 5-year mortality in excess of 60%.[34–36] In a recent analysis of PHAR, PoPH patients were less likely to be college graduates and more likely to have annual incomes below the poverty level and to be on Medicare or Medicaid insurance than IPAH patients.[37] Additionally, PoPH patients were prescribed fewer PAH therapies and were less likely to be treated with combination therapy than IPAH patients at time of registry enrollment, despite similar or worse

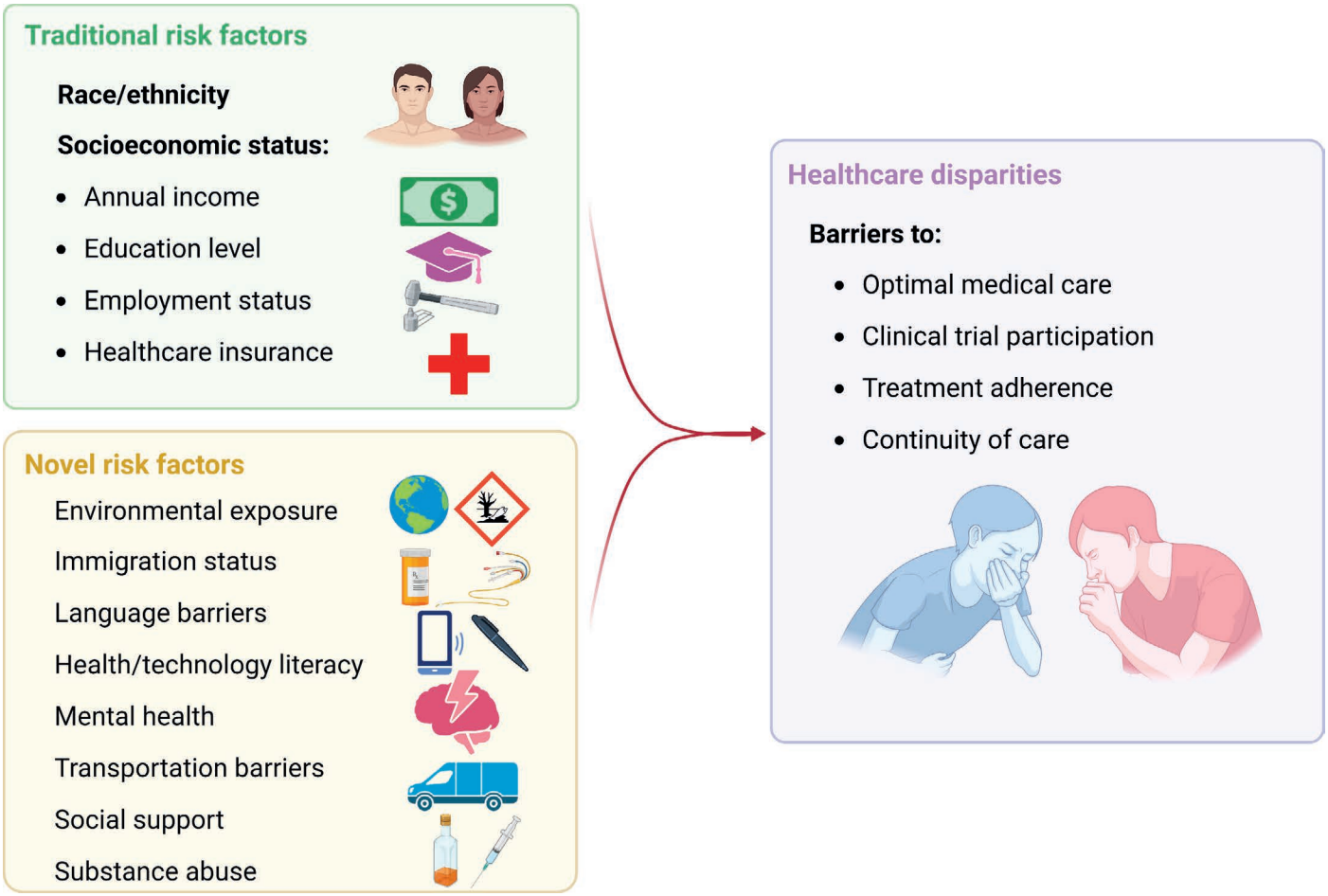

Figure 2: Interplay between biologic, socioeconomic, and racial or ethnic factors in PAH. Traditional and novel risk factors contribute to health care disparities in PAH. These factors usually coexist and exponentially affect outcome care in these patients. Created with BioRender.com. PAH, pulmonary arterial hypertension.

PAH disease severity. When examining health care usage, PoPH patients were significantly more likely to seek care at an emergency department than IPAH patients even after adjustment for age and measures of disease severity.[37] PoPH patients may be particularly vulnerable to the influence of SDOH by both their underlying PAH and their comorbid portal hypertensive liver disease.[38,39] Social deprivation, financial instability, and education level have been linked to both mortality and lower rates of liver transplantation in patients with cirrhosis.[40,41] Disentangling the links between pulmonary vascular disease, portal hypertensive disease, SDOH, and clinical outcomes has the potential to favorably affect outcomes in this high-risk population.

Meth-PAH is defined as PAH associated with significant exposure to amphetamines, predominantly methamphetamine, and is associated with more severe disease, poorer treatment responses, and lower survival than IPAH.[42,43] Meth-PAH patients tend to have suboptimal insurance coverage, lack of education, lower annual income, increased employment instability, and are less likely to receive parenteral prostacyclins than IPAH patients.[42,44] Meth-PAH patients also suffer from worse mental health quality of life scores, and coexisting mental health challenges not only place these individuals at risk for specific SDOH disparities but additionally play a pernicious role in dictating clinical care and patient outcomes.[45] A concerted effort to understand the unique mental health challenges faced by meth-PAH patients and how these difficulties may aggravate existing SDOH disparities and precipitate morbidity, mortality, and care disparities will be necessary to address and ameliorate the effect of these factors on patient outcomes.

ASSESSMENT TOOLS FOR SDOH

Despite increasing awareness of the effects of SES, SDOH, and health care disparities on clinical outcomes, these issues remain an area of patient care not routinely assessed nor acted upon in routine daily medical practice. In 2019, Fraze et al[46] completed a cross-sectional study of US hospitals and physician practices and found that most health care organizations and providers were not assessing for social effects on care, with only 24% of hospitals and 16% of physicians reporting screening for all 5 of the traditional SDOH. In a focused assessment of PAH care centers, Nadipelli et al[47] conducted semistructured interviews of 17 providers and 1 patient advocate and found a high level of awareness of the importance and effects of SDOH on PAH patient outcomes, but the interviewees voiced challenges

regarding routine screening for these factors. There was no consensus on optimal screening strategies, but there was agreement on the importance of this assessment.

There are multiple screening tools for SDOH which are geared for simplicity and can be completed quickly by patients of varying education levels and are available in multiple languages. A few of the available tools are as follows: The Centers for Medicare & Medicaid Services Accountable Health Communities Health-Related Social Needs Screening Tool (AHC-HRSN) survey consists of 10 brief core and 4 supplemental questions.[48,49] The American Academy of Family Physicians has developed an assessment tool through The EveryONE Project that is available in both English and Spanish and includes 11 focused questions that can be completed by patients independently or with assistance of nonclinical staff.[50] Additionally, the Montefiore Social Needs Assessment is an available tool which is a simplified 1-page assessment with 10 binary questions that can be implemented in daily patient care.[51] Further studies are needed to understand which screening tools are most applicable for the PAH population.

INTERVENTIONS FOR AT-RISK PATIENT POPULATIONS

Tackling the often difficult and challenging risk factors for poor outcomes related to SDOH, SES, and health care disparities is a far greater task than identification alone. Action plans need to be in place, and support systems must exist to act on the social, economic, and resource issues that are uncovered by screening. Because of the complexity of this task, the National Association of Community Health Centers, the Association of Asian Pacific Community Health Organizations, and the Oregon Primary Care Association collaborated to create a patient-centered assessment tool which is available in 30 languages, integrated in electronic medical records, and has a companion implementation and action toolkit known as PRAPARE (Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences) which provides a guide to address negative SDOH.[52] Addressing these unique patient needs requires trained and experienced staff. Nadipelli et al[47] reported that PAH providers surveyed stress the importance of social work support in PAH centers to adequately address patient needs. However, this resource is not routinely available in many PAH centers, resulting in the PAH center coordinators and providers taking on the shared responsibility of addressing barriers to care.

IMPROVING ACCESS AND UNDERSTANDING OF PAH SUBGROUPS IN CLINICAL TRIALS AND REGISTRIES

Currently, PAH clinical trials lack diversity and are not representative of the total patient population, thus limiting the understanding of the spectrum of PAH patients and impeding the development of optimal treatment strategies for all patients. Min et al[53] performed a pooled cohort analysis using harmonized datasets from phase 3 clinical trials and found that PAH research participants from 18 trials (1998–2013) were 78% female and 85% non-Hispanic Whites. Additionally, 97% of Asians and 74% of Hispanics in the sample were recruited from Asia and Latin America, respectively. Registry data also significantly underrepresent many PAH subpopulations. There was a predominance of White patients in REVEAL (72.8%), US National Institutes of Health registry (85.4%), as well as in the Surveillance of Pulmonary Hypertension in America Registry (81.5%). Black, Hispanic, and Asian or Pacific Islander patients enrolled at lower numbers than expected based on census data at that time.[3] Increasing awareness of the lack of diversity of enrollment in clinical trials and registries should prompt reevaluation of our screening and recruitment strategies with goals to shift to increasing opportunities for all patients cared for in PAH centers.

CONCLUSIONS

In health care, patients from every walk of life with varied backgrounds, experiences, and cultures seek medical care. Patients come to health care with expectations of equal opportunity for best outcomes. There are multiple barriers that patients can experience in achieving that goal. SES, race, ethnicity, education level, health care literacy, language, and communication barriers can affect successful treatment and quality of experience.

Change needs to occur at the patient care level and must start with identification of modifiable issues through standardized screening with tools to address factors that are negatively affecting patient care and successful treatment. A deep understanding of how to identify, discuss, and address SDOH is imperative to improve the likelihood of positive outcomes for all patients cared for in PAH centers.

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