ISSN 1933-088X

Advances in Pulmonary Hypertension

Vol 21, No 2; 2022

Official Journal of the Pulmonary Hypertension Association

Disparities in 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.

Advances in
Pulmonary Hypertension
Official Journal of the Pulmonary Hypertension Association

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Allen Press, Inc.

Advances in Pulmonary Hypertension is available online at www.AdvancesinPH.org.

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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*Advances in Pulmonary Hypertensio*n is available at www.AdvancesinPH.org. This site offers enhanced capabilities including a dedicated DOI and cross-referencing potential, as well as other features valuable to practitioners, researchers, and educators. Registration is recommended to access all site features and benefits.

Disparities in Pulmonary Arterial Hypertension Care: Challenges and Solutions

Health disparities have a detrimental effect on the clinical outcomes and quality of care received by minorities in the United States. Compared with the rest of the population, minorities with pulmonary hypertension (PH) are at risk for worse outcomes due to difficulty accessing healthcare, lack of or limited insurance, poor socioeconomic status, and distrust of the healthcare system, among other factors. By disproportionately impacting vulnerable patients, the delay to diagnosis and the barriers to introducing therapies has the potential to worsen health disparities in PH, especially when compounded by the challenges facing patients and families during the COVID-19 pandemic. At present, there is a major unmet need for health policy initiatives to protect minorities, likely due to the lack of studies demonstrating the extent of health disparities. This issue of *Advances in Pulmonary Hypertension* is part of an ongoing effort by the Pulmonary Hypertension Association (PHA) to advocate research avenues and changes in health policy in favor of minorities that could have a profound and lasting impact on improving the quality of healthcare experienced by minority populations afflicted with PH.

In "The Impact of Socioeconomic, Racial, and Ethnic Disparities on Pulmonary Hypertension Diagnosis and Treatment", Talwar and colleagues provide a comprehensive review of available evidence that points at how genetics, sex, age, race and socioeconomic status influence the quality and outcomes directly associated with health care delivery. Most importantly, the authors advocate for the prioritization of research efforts seeking to understand the individual contribution of these factors and the potential long-term benefit for improving clinical outcomes in vulnerable populations of PH patients across the United States.

In the article "What Rare Disease Patient Advocacy Groups Are Doing to Mitigate the Effects of Disparities", Drell and her colleagues from National Organization for Rare Disorders (NORD) share case studies that exemplify the current social and health care challenges faced by patients suffering from rare diseases who belong to minority groups. The important role that non-profit advocacy organizations play in helping patients face discrimination and health care inequalities is discussed and recommendations are made to guide clinicians, health care practitioners and caregivers on how to support those patients who are most vulnerable to experience health inequity due to limited resources and access to medical care.

In the article "Hispanic Ethnicity and Social Determinants of health: Harnessing Data from The Pulmonary Hypertension Association registry" Bernardo and Colleagues discuss the interplay between biologic, socioeconomic and racial factors in PAH with special emphasis on the Hispanic population. The authors also point towards the noticeable underrepresentation of minorities such as Hispanics in most PAH registries and even in randomized clinical trials. The implications of underrepresentation in research are far reaching and may further contribute to disparate care of the minority patients.

Finally, in the round table discussion, Dr. Talwar moderates a lively discussion with healthcare providers and members of the PHA centered around their own experiences managing patients at risk for health disparities, their efforts to advocate for wider PH medication access, and their vision for what changes must be implemented in our health care system to avoid placing PH patients at a disadvantage as a result of socioeconomic status, race/ethnicity and other risk factors associates with disparities. Solutions to address and ultimately eradicate disparities will need to eliminate healthcare bias, increase patient access, and increase diversity and inclusion in healthcare providers.

Addressing health disparities is a challenge that requires the pooling of federal, community, and professional resources to facilitate the development of research projects, interventions, educational materials, and health policy designed to change clinical outcome among vulnerable minority groups. We thank all the authors who provide their time and effort to help prepare this issue of *Advances* and hope that the information herein will serve to spark initiatives to address health inequities and improve health care access for all our PH patients.

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REGULAR ARTICLE

The Impact of Socioeconomic, Racial, and Ethnic Disparities on Pulmonary Hypertension Diagnosis and Treatment

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Health disparities have a major impact in the quality of life and level of clinical care received in minority populations in the United States. Underrepresented patients with pulmonary arterial hypertension (PAH) may be at risk for worse outcomes. Furthermore, advances in biomedical research have provided extensive knowledge on the genetic role in the pathogenesis of PAH but whether these also impact minorities is incompletely understood. Health disparities in patients with PAH create an enormous barrier in health care delivery. Understanding the contributors to health disparity represent a fundamental step towards personalized medicine and further improvement in PAH care.

INTRODUCTION

Health care delivery disparities are an important consideration for any disease process, as they significantly impact quality of life and outcomes for minorities.[1] Health disparities are defined as significant differences in health care that are closely linked to racial ancestry, social, economic, and/or environmental differences.[2] Today, in the United States, nearly 36% of the population belongs to a racial or ethnic minority group, with this figure likely to increase over the coming years.

Pulmonary arterial hypertension (PAH) is a cardiopulmonary process resulting in right heart failure from elevated pulmonary artery pressures that predominantly affects women and has a median survival of 3 years without treatment.[3] PAH is an interesting disease to evaluate through the lens of health care disparity, as it is rather less common than other cardiovascular diseases but still has a high mortality.[4] Still, the extent of how health disparity affects PAH diagnosis and treatment is understudied.

Information currently available at this intersection is largely from historical cohort studies using registries. Such investigations have demonstrated that age, sex, race/ethnicity, country of origin, medical treatments, and socioeconomic status (SES) may be associated with specific types of PAH, response to therapy, and survival. The scope of this article is to summarize health disparities that exist with PAH, and to shed light on possible areas for improvement.

RACE/ETHNICITY AND PAH

Racial differences in the manifestations of various respiratory disorders have been well documented and it has been suggested that it leads to health care delivery disparities.[5] Still, there is a paucity in the literature of studies describing the impact of race on the prevalence and etiology of pulmonary hypertension. The study of race as it relates to pulmonary hypertension is made particularly difficult because pulmonary hypertension registries lack adequate representation of different races/ethnicities. For instance, when compared to the demographics of the general population, the demographics of patients in the registry to evaluate early and long-term PAH disease management (REVEAL) are quite different. African Americans are relatively overrepresented in the registry (with a prevalence of 12.2% versus 10.9% in the general population). Meanwhile, Hispanics are underrepresented (with a prevalence of 8.9% versus 11.5% in the general population).[6]

More recently the Pulmonary Hypertension Association (PHA) registry has been assessing the adherence to guidelines, treatment patterns, quality of life, and outcomes of patients with PAH and chronic thromboembolic pulmonary hy-

Key Words——health disparities, pulmonary arterial hypertension, socioeconomic status, race, sex
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Disclosure: The authors have no conflicts of interest.

pertension who begin their care at pulmonary hypertension centers accredited by the PHA for their track record in the care of patients with PAH; self-reported race/ethnicity, primary language spoken at home, and various individual indicators of SES are also collected in this registry. The data from this registry suggest that health-related quality of life appears to correlate with socioeconomic measures like education status, and also the clinical PAH measures like right atrial pressure and pulmonary vascular resistance.[7]

High pulmonary artery systolic pressure in heart failure patients is known to be a significant risk factor for hospitalization.[8] Interestingly, racial disparities exist within this metric. In 2017, the CARDIA study found an association between Black race and higher echocardiographically recorded pulmonary artery systolic pressure.[9] Additionally, a study by Yang et al.[10] showed that, after controlling for clinicodemographic covariates, African Americans were associated with a 41% greater risk for PH than Caucasians. The authors further noted that African American patients with PAH were typically younger, and had a higher rate of heart failure, more severe pulmonary hemodynamics, and more prevalent cardio-metabolic/renal disease than Caucasians. However, Medrek et al.[11] have reported that, based on their analysis of the REVEAL registry, race/ethnicity is not a significant predictor of mortality in PAH. These contradictory findings merit further investigation.

Connective tissue disorder disease–associated PAH is one subgroup that shows clear differences in presentation between races/ethnicities.[12] Scleroderma-associated PAH (SSc-PAH) is most common connective tissue disorder associated with pulmonary hypertension (with a prevalence of 5%-12%).[13] There is a suggestion that scleroderma-associated PAH patients tend to be less responsive to therapy and have a worse prognosis than patients with other types of PAH.[14] A retrospective study by Moore et al.[15] found that African American scleroderma patients have more severe pulmonary hypertension and more severe cardiac involvement than non–African American patients. It has also been reported that Hispanic patients are more likely to have portopulmonary hypertension.[16]

Recent investigations suggest that there may be significant differences in health care delivery between races. Parikh et al.[17] demonstrated that adjustment for insurance status dampens the association of race with survival for those with PAH. Al-Naamani et al.[16] reported that Hispanics are less likely to be treated with PAH-specific medication regimens. In addition, Valverde et al.[18] analyzed local epidemiological data of PAH in Latin America and found that the percentage of idiopathic PAH patients in Latin America is higher compared to European studies and the REVEAL registry.

The relationship between race/ethnicity and PAH disease presentation needs to be studied further. It has been suggested that Black and Hispanic patients have more severe disease at the time of presentation.[19,20] Though the exact reason for this remains unclear, many factors have been proposed for this observation. For instance, impaired nitric oxide balance in Black population may predispose this population to vasculopathy.[21] Other investigators have suggested structural differences in the pulmonary vasculature between different races. Kawut et al.[22] proposed that right ventricular mass is lower in African Americans than in Whites. Ventetuolo et al.,[23] on evaluation of 463 single-nucleotide polymorphisms in 10 candidate genes in 2761 genotyped participants, found that polymorphisms in the gene CY1P1B1 were associated with the differences in the right ventricular ejection fraction (RVEF) in Black women. The study also found race-specific differences in the relationship between urinary estrogen metabolites and RVEF: though there was no relationship in Black and Chinese American populations, there was a positive correlation between estrogen metabolites and RVEF in White patients.[23]

The response to PAH-directed therapy is also heterogeneous and may, to some extent, be related to race. Data to support this assertion exist for the endothelin pathway. It has been demonstrated that Black patients had increased circulating levels of endothelin-1 compared with white patients.[24] The cytochrome P450 pathways, which are an important factor in at least endothelin receptor blockers, show a significant racial variation and could help explain the differences in response to these medications.[25] These findings underscore the importance of population-based investigations to better understand PAH genotypes in various ethnicities and races.

SES AND PAH

The interplay between SES and population health is clear. To some extent, SES dictates the type of insurance patients have [26] and may therefore be reflective of a patient's ability to follow up with physicians.[27] Still, of all the measured demographics in health care today, SES is often unreported.[28] SES particularly has a measurable and significant effect on cardiovascular health. This is true even more so for disadvantaged individuals who have many biological, behavioral, and psychological risk factors.[29]

Talwar et al.[30] evaluated patients with PAH using their home zip code as a surrogate for SES. There was an inverse correlation between functional class at the time of initial evaluation and household income.[30] One possible explanation for severe disease at initial presentation and delayed diagnosis in lower SES individuals is that these individuals may have significant barriers to access health care. This presents a problem specifically for PAH, which requires referral to a specialist center and a right-heart catheterization for diagnosis.

Similarly, Wu and colleagues[31] showed that lower SES (as measured by educational level, annual household income, occupation, and medical reimbursement rate) was associated with a higher risk of clinical worsening and mortality for patients with idiopathic PAH. These findings were independent of hemodynamics, demographic variable, and medical treatment characterstics.

A study by Jin et al.[32] stratified patients with connective tissue disorder–associated PAH based on SES. The study found that connective tissue disorder–associated PAH patients with low SES had a much lower 5-year sur-

vival than patients with middle or high SES (75.7% versus 81.4% versus 87.9%, respectively). These results are consistent with those found by Moore et al.,[15] who reported that the hazard of death for patients with scleroderma decreased by 15.5% for every additional $10,000 of household income (independent of race). Examination of SES in systemic sclerosis suggests that higher wealth and more equitable access to health care services may mitigate increased mortality attributable to specific ethnic groups.[33]

Current guidelines and management algorithms do not factor the effect of SES on the disease process. However, from the emerging data it is evident that SES plays an important role in health-related quality of life and clinical outcomes. It will be worthwhile to pay more attention to SES as a major variable in research studies, as it will help identify vulnerable patients with risk factors that are unique to underrepresented minorities in the United States.[4] This also argues for a push towards greater inclusion of different races/ethnicities in various clinical trials of PAH, as is true for a multitude of other disease states as well.[34] There are many reasons as to why underrepresented minority patients do not participate in trials including lack of access to trials and lack of education about the purpose of clinical trials.[35] Language barriers also often preclude minority patients from participating in trials. However, such issues are easily surmountable and should be resolved so that future trials in clinical medicine provide adequate representation to underrepresented minorities.[36]

SEX, AGE, AND GENETIC CONTRIBUTORS TO HEALTH CARE DISPARITIES IN PAH

Sex disparities in PAH cannot be ignored. Although PAH predominantly affects females (females are 1.8 times more likely to be affected by PAH relative to their male counterparts)[6] they remain underrepresented in clinical research.[37] Sex also has an effect on survival; it is well established that females with PAH have better survival compared to males. Interestingly, the survival benefit for females appears to decline with age[38] and correlates with declines in estradiol levels.[39] The discrepancy in incidence and outcomes in men/women is commonly referred to as the PAH-estrogen paradox.

According to Ginoux et al.,[40] the patient age at time of diagnosis of PAH is increasing. They reported that compared to young patients, elderly patients have a longer time to diagnosis, more comorbidities, worse New York Health Association functional class, and a worse prognosis. When compared with younger patients, very elderly patients have a longer delay in access to a regional referral center for pulmonary hypertension.[40] It is also known that patients 65 years of age or older have the worst prognosis.[41,42]

Personalized medicine, also known as individualized medicine, is a rapidly emerging field in which medical treatments are tailored to an individual's genomic characteristics in order to provide more targeted interventions for patient care.[43] While the pathophysiologic cascade in PAH is not completely understood, there have been many advances in the molecular pathways that contribute to the pathology. To date, it has been established that certain genes contribute to hereditary PAH (particularly bone morphogenic protein receptor type II).[44,45] Other genes that may be involved include endoglin,[46] caveolin-1,[47] potassium channel two pore domain subfamily K member 3,[48] and eukaryotic translation initiation factor 2α kinase 4.[49] PAH susceptibility has been linked to common variants of genes encoding prostacyclin and endothelin-1 pathways,[50,51] calcium signaling,[52] sex hormone metabolism,[53] and the endostatin gene.[54] Most of these pathways have not been studied under paradigms that include minorities and therefore may have inherent selection bias.[55]

CONCLUSION

Disparities certainly exist in health care delivery in the context of PAH. Recent investigations have revealed associations between genetics, sex, age, race, SES, and PAH outcomes. Understanding the contributions of these factors, as well as the broader context of health care delivery, represent a fundamental step towards personalized medicine and further improvement in PAH care.

For future research into PAH, integration of SES into the traditional risk prediction models may allow improved management of individuals with high risks for this disease. Education of physicians and other health care providers facilitating PAH awareness, addressing cross-cultural training, and recognizing the risk factors associated with different races, sexes, etc. is crucial.[4] Lastly, refocusing health care laws that advocate for minorities is important.

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REGULAR ARTICLE

What Rare Disease Patient Advocacy Groups Are Doing to Mitigate the Effects of Disparities

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Compared with chronic diseases affecting larger populations, rare disease (RD) patients experience great inequities in diagnosis, care, and research. Within RDs, health disparities compound these inequities, as marginalized communities experience additional barriers in accessing clinical care and are often underrepresented from participation in research and clinical trials. For almost 40 years, the National Organization for Rare Disorders (NORD), a RD umbrella organization with over 300 nonprofit organizational members, has led efforts to understand and address inequities for the RD community through innovative research, programming, and collaboration with patients, caregivers, practitioners, and external stakeholders. The beginning of the COVID-19 pandemic in 2020 brought to light longstanding disparities and discrimination for marginalized communities as well as pivotal racial justice movements. These events spurred many RD nonprofit organizations' interest in increasing outreach and engagement with minoritized communities within RDs and diversifying their organization internally. Building on the increased interest in diversity, equity, and inclusion (DEI), NORD has focused on collecting case studies from within NORD and its member organizations to capture current efforts to improve DEI within the RD ecosystem. One way clinicians can work to mitigate the effects of disparities is to collaborate with RD patient organizations; this article provides a means by which clinicians and researchers can understand some of the challenges RD nonprofit organizations face in bridging disparities and learn about solutions to supporting marginalized patients within their communities. Clinicians are encouraged to join NORD in our policy efforts advocating to ensure patient access to health care providers practicing in a different state vis-à-vis telehealth.

INTRODUCTION TO NORD

For those active in the pulmonary hypertension (PH) advocacy space, the origin story of the Pulmonary Hypertension Association may be familiar: in the early 1990s, 3 patients and a nurse caregiver met around a kitchen table in Florida with lofty goals of support, education, and cures.[1] What may not be known is that these patients found each other by writing letters to the National Organization for Rare Disorders (NORD). National Organization for Rare Disorders staff not only connected them with one another for this historic first meeting of PH patients but provided support as their fledgling nonprofit grew: "For most of the early and mid-1990's (sic) the organization was a kitchen table operation regularly seeking advice on organizational and management issues from NORD."[2(p2)]

National Organization for Rare Disorders' history is rich with stories of helping patients and caregivers connect and advocate as central, equal partners in research and drug development. Often alone, geographically isolated, misunderstood by their family and friends, and afraid after delayed diagnoses led to advanced disease progression, people living with rare disease (RD) face inequities in access to care, research participation, and lack of treatment options.

It was the lack of treatments in the late 1970s that spurred a call to action leading to the creation of an ad hoc coalition of RD leaders who sought to change the research paradigm during a time when little was being done to study RDs or develop treatments. After successfully advocating for the passage of the Orphan Drug Act of 1983 (which created financial incentives for the development of treatments for RDs), this coalition became the foundation of NORD.[3]

For almost 40 years, NORD has served as the hub of the RD community, leading efforts to drive progress, overcome inequities experienced by patients across all RDs, and advocate for the collective representation of all affected by RDs in the United States. During this COVID-19 pandemic era of heightened international awareness of health disparities, NORD has brought increased attention to engaging historically marginalized groups—such as people of color, low-income Americans, and members of the lesbian, gay, bisexual, transgender, queer or questioning, intersex, asexual, including other sexual identities (LGBTQIA+) community—

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Disclosure: The authors have no relevant personal financial relationships to disclose.

face greater barriers to accessing and receiving health care.[4]

In this piece, we endeavor to answer the following questions:

- What are the general inequities experienced by patients across all RDs? What issues affect all patients with RDs that are not experienced by common, well-known conditions?
- Do certain RDs face greater inequities more so than others? If so, why?
- Within a RD, are there communities that experience barriers to access of diagnosis, care, research, support, information, and treatment?
- What have other RD organizations done to address inequities in their community?
- What programs, services, and resources have NORD—the leading umbrella organization in the United States—undertaken to mitigate the effects of disparities?

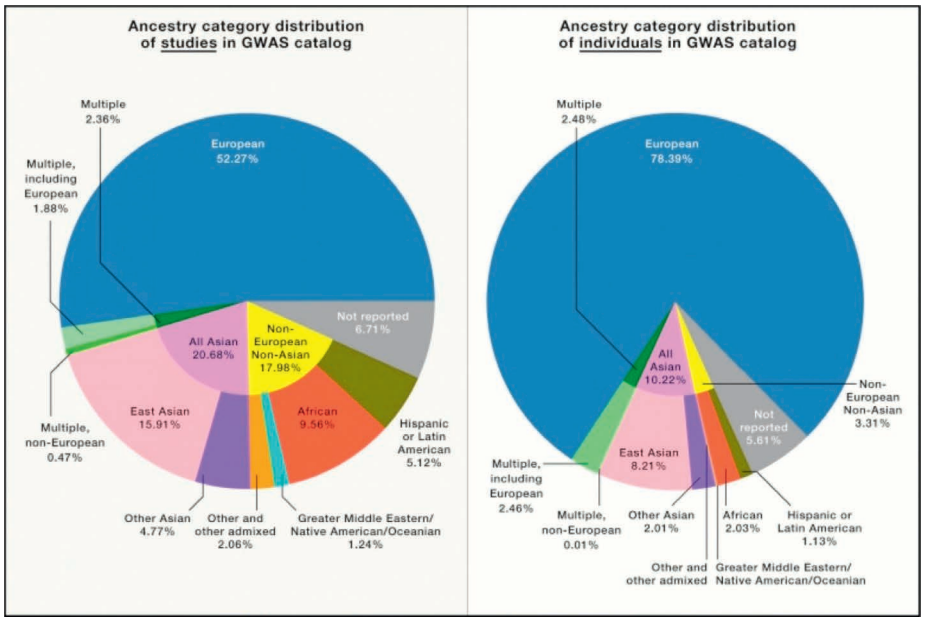

Figure 1: The missing diversity in human genetic studies. Reprinted with permission from Sirugo et al.[11]

DEFINING DISPARITIES

For the purposes of capturing the current landscape of RDs as it relates to health disparities, we define "health disparity" as a systematic, conceivably avoidable health difference according to characteristics associated with marginalization or discrimination, such as race, ethnicity, nationality, skin color, socioeconomic resources, religion, geography, gender, sexual orientation, gender identity, age, disability, illness, political, or other affiliation.[5]

Collectively, RDs are widely recognized as a public health challenge due to significant disparities, including delays and barriers to diagnosis, access to treatment, and quality management of care (eg, access to specialists).[6] It is estimated that approximately 400 million people live with a RD globally, and on average, it can take up to 5 years for people to receive an accurate diagnosis.[7,8] Though more than 7000 RDs have been identified, only 10% of these conditions have US Food and Drug Administration (FDA) approved treatments.[9] These barriers, along with an overall paucity of medical knowledge, research, and literature, leave millions of people living with RDs with inadequate resources to manage their care.

This challenging health care landscape is further magnified for people belonging to marginalized communities living with rare conditions. Eighty percent of RDs are genetic in origin, and genome-wide association studies (GWAS) play a crucial part in identifying them.[10] A 2018 analysis of GWAS revealed that, of the individuals included in studies, 78% were European, while only 10% were Asian, 2% were African, and 1% were Hispanic. All other ethnicities represented <1% of GWAS (Figure 1).[11] The implications of the lack of diversity in genomic studies can have rippling effects on communities of color seeking accurate diagnoses as well as effective treatments for their RD. This can be seen in genetic carrier screening for RDs like cystic fibrosis (CF), where a 25-mutation carrier screening panel considered to be panethnic detected close to 90% of CF carriers in white and/or Ashkenazi Jewish populations. The same panel detected only 72% of carriers in Hispanic Americans, 64% of carriers in African Americans, and 49% of carriers in Asian Americans.[12]

Disparities are not only evident in the lack of accurate diagnostic tools for diverse populations in RD but also in funding for research. While CF affects less than half the number of people as sickle cell disease (SCD) does, CF has received more than 3.5 times the amount of funding from the National Institutes of Health (NIH) and 440 times the funding from national foundations (Figure 2). Industry was also more likely to fund CF versus SCD trials (mean ± SD trials, 15.6 ± 5.3 versus 6.8 ± 1.8; $P = .001$). This difference in funding is thought to possibly correlate with a decrease in research output as well as delayed drug development for SCD. From 2008 to 2018, CF had 4 new FDA drug approvals, while SCD had 1; there were 11 novel FDA drug indications for CF, and only 2 for SCD.[13]

Recent studies in RDs have examined how the impact of social determinants of health—which include economic stability, education access and quality, health care access and quality, neighborhood and built environment, and social and community context—can impact people in different marginalized groups, including race, gender, geographic region, and socioeconomic status (SES).[14] Using US data for multiple causes of death between 1999 and 2016, authors of a 2019 study analyzed all sarcoidosis-related deaths. The highest number of sarcoidosis-related multiple-cause-of-death

Table 2. Disease-Specific NIH Funding and Combined Foundation Expenditures

Funding or expenditure	Year											
	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Mean (SD)	*P* value
NIH funding (in millions), $												
SCD	80	63	73	65	65	70	75	75	92	105	76.3 (13.2)	.05
CF	90	86	86	79	86	78	77	80	89	91	84.2 (5.3)	
Per person affected												
SCD	889	700	811	722	722	778	833	833	1022	1167	812 (147)	<.001
CF	3000	2867	2867	2633	2867	2600	2567	2667	2967	3033	2807 (175)	
CF:SCD ratio of NIH funding per person	3.38	4.1	3.53	3.65	3.97	3.34	3.08	3.2	2.9	2.6	3.37 (0.46)	NA
Foundation expenditures (in millions), $												
SCD	10.3	9.83	9.27	8.42	7.38	7.73	8.03	9.13	11.2	10	9.14 (1.23)	<.001
CF	199	175	109	175	148	163	171	313	487	367	231 (119)	
Per person affected												
SCD	115	109	103	94	82	86	89	101	124	112	102 (13.7)	<.001
CF	6634	5823	3644	5816	4928	5443	5715	10 428	16 227	12 240	7690 (3974)	
CF:SCD ratio of foundation expenditures per person	58	53	35	62	60	63	64	103	131	109	75 (30)	NA

Abbreviations: CF, cystic fibrosis; NA, not applicable; NIH, National Institutes of Health; SCD, sickle cell disease.

Figure 2: Comparison of US federal and foundation funding of research for sickle cell disease and cystic fibrosis and factors associated with research productivity. Reprinted with permission from Farooq et al.[13]

mortality rates were found in non-Hispanic Black people and those identifying as female.[15] Similarly, it is well established that geographic location, one's zip code—even from block to block—can affect not only a person's quality of life but also their lifespan.[16] In an effort to document sarcoidosis patient-reported challenges in receiving care based on low- and high-income zip codes, authors of a study revealed that patients in both income brackets shared similar concerns in their health care management but noted that people residing in the low-income zip code communities more often reported concerns about racially biased discrimination in care as well as income bias.[17]

For certain populations, like the Amish community, geographic and technological barriers can play a role in access to health care. Culturally, many in the community choose not to use technology such as cellular phones, computers, or the Internet. Due to the founder effect, the Amish community is also disproportionately affected by certain RDs, including pyruvate kinase deficiency (PKD).[18] In September of 2019, NORD hosted an externally led Patient Focused Drug Development (EL-PFDD) meeting, sharing the experiences of patients and caregivers impacted by PKD directly with FDA regulators. While living only 300 miles away from the site of the meeting, the PKD community was unable to participate in person because they travel by horse-drawn carriages and are unable to participate in telephone and Web polling because they choose not to use the technology. To ensure their equitable access to participate in the EL-PFDD and share their voices and experiences with stakeholders, NORD staff collaborated with a leading clinician in central Pennsylvania who hosted a Patient Day so that NORD could "bring the meeting to them," explaining the reason why their perspectives are important to FDA and what they hoped to gain from collecting paper survey responses in person.[19]

Efforts like NORD's are essential to help identify gaps and barriers for marginalized communities as well as build relationships within the communities to address these gaps. Rare disease advocacy groups play a critical role in connecting people affected by RDs with up-to-date research, resources, and support services, all of which can improve their access to quality health care, treatments, and potential cures.

CASE STUDIES FROM NORD MEMBER ORGANIZATIONS

Since 2017, Angioma Alliance (AA), a patient advocacy and research organization serving those with cerebral cavernous malformation (CCM), has dedicated 25% of its annual budget to diversity, equity, and inclusion (DEI) efforts. Most recently, the organization launched an initiative to address diagnostic and treatment disparities for Black CCM (B-CCM) patients.

The Need

It is well documented that there is a disproportionate number of CCM cases in Hispanic Americans of Mexican descent. However, published studies on CCM prevalence rates in African Americans have been severely lacking, and there is a significant disparity in B-CCM patient engagement. Authors of studies suggest there should be

The Problem: Largest CCM Patient Databases in the US

Institution/Project	Total US Adult Registrants	Total Black Registrants	% Black Registrants
Angioma Alliance	914	16	1.75%
U of Chicago	512	45	8.8%
BVMC	537	2	0.4%
Mayo Clinic	282	5	1.8%
Total	**2245**	**68**	**3.0%**

Figure 3: Cerebral cavernous malformation (CCM) patient databases.

17000 Black Americans diagnosed with CCM,[20] yet in 2020, there were only 68 patients who identified as Black in the 4 major US clinical databases (Figure 3).

In 2021, AA launched Breaking Barriers for Black Health Empowerment to understand B-CCM patient experiences and develop culturally appropriate interventions to improve self-advocacy, care, and research engagement.

Angioma Alliance patient registry data pointed to clinical differences between B-CCM patients and the larger registrant cohort. Black CCM patients reported greater disability, with an average Modified Rankin Scale score of 2 in comparison with an average score of 1.3 in all other registrants. Fifty percent of Black registrants reported spinal cord lesions. Spinal cord lesions are an uncommon finding in the greater patient cohort (<15%), and hemorrhage in these lesions leads to acute, often severe, symptoms. Less dramatic CCM symptoms—mild functional neurological deficits, headache, and partial complex seizure—may not lead to diagnosis in Black patients possibly because patients may not receive appropriate referrals.[21]

The Breaking Barriers program also conducted a preliminary qualitative study of B-CCM patients using semistructured interviews which were transcribed and coded. Contrary to expectations, this cohort did not report delayed diagnosis or limited access to quality acute care. Instead, B-CCM patients universally reported a lack of aftercare referrals. This resulted in little patient education or health monitoring and nonexistent mental health or case management services. While underdiagnosis may play a role in reduced patient engagement, lack of aftercare services may have an equivalent or greater impact.

Program

The Breaking Barriers initiative has launched a 4-pronged approach to the challenge of health disparities among B-CCM patients (Figure 4). First, the program is facilitating the development of a cohesive community between known B-CCM patients through virtual connections and medical education events. Membership in a private Facebook group and Zoom support groups provide patients with access to invited CCM expert guest speakers and up-to-date disease information.

Second, the program supports aftercare through a "second look" program in which B-CCM patients are offered the opportunity to meet one-on-one with AA staff for needs assessment

Breaking Barriers Initiatives

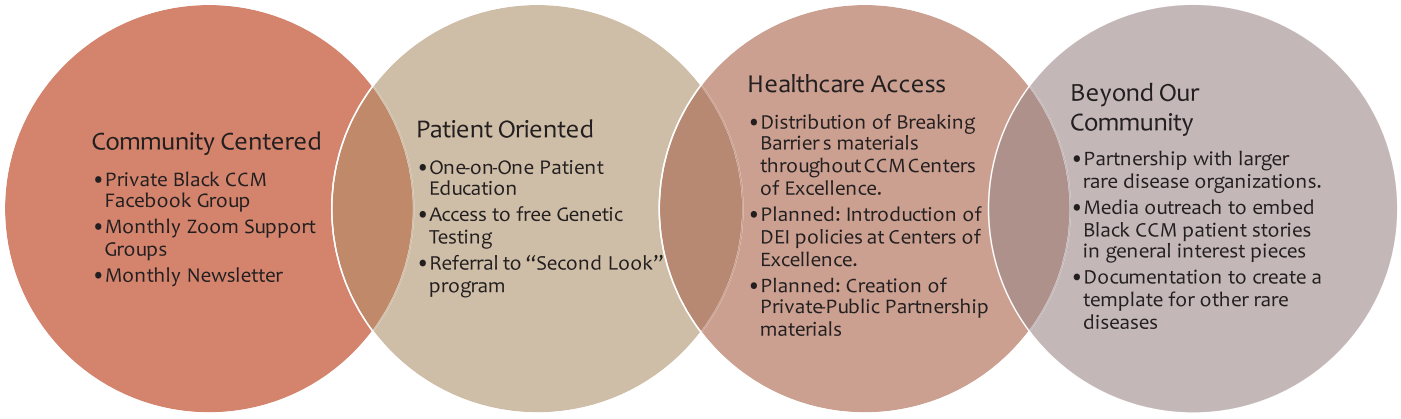

Figure 4: Breaking Barriers initiative.

and referrals to CCM experts; specific AA staff have decades of experience in the community, are trained in patient engagement/sensitivity, serve as case managers, and do not provide medical guidance; one staff member is a licensed clinical psychologist and another has a master's in public health. A third staff member was hired who is a registered nurse and is a certified case manager. Angioma Alliance also provides free genetic testing for patients where appropriate (meeting phenotype criteria) and individual patient education to bolster health self-advocacy.

Third, the program addresses disparities within clinical research and care. The CCM Health Index, an industry-sponsored patient-reported outcomes measure (PROM), required multiple rounds of recruitment through the varying phases of its development. In the initial cross sectional study phase, 323 participants were recruited, 13% of whom identified as members of racial or ethnic minorities. Subsequently, for the longitudinal study phase of development, the organization successfully advocated for patient compensation. Additionally, targeted outreach and communication strategies, like doubling email messaging to Black and Latinx patients living with CCM, were implemented to improve reach and engagement with marginalized and underrepresented patients. Angioma Alliance recruited 616 patients for the longitudinal study phase, and, as a result of these efforts, 29% of this cohort identified as members of minority groups. Angioma Alliance is now adding DEI requirements to CCM Center of Excellence criteria and is developing continuing medical education materials to assist with diagnosis and care in community hospital settings.

Challenges and Learnings

While the first year of Breaking Barriers was successful, the program faced several challenges. In response to the initiative announcement, a major donor withdrew their support. Foundation support mitigated the loss and offset the budgetary impact.

The initiative struggled with patient engagement. The B-CCM registry increased by 250% in the first year of the program (Figure 5); unfortunately, the absolute number remained small. The engagement challenge was particularly evident with male patients. As an example, semistructured interviews were conducted with 11 women, but only 2 men were willing to participate.

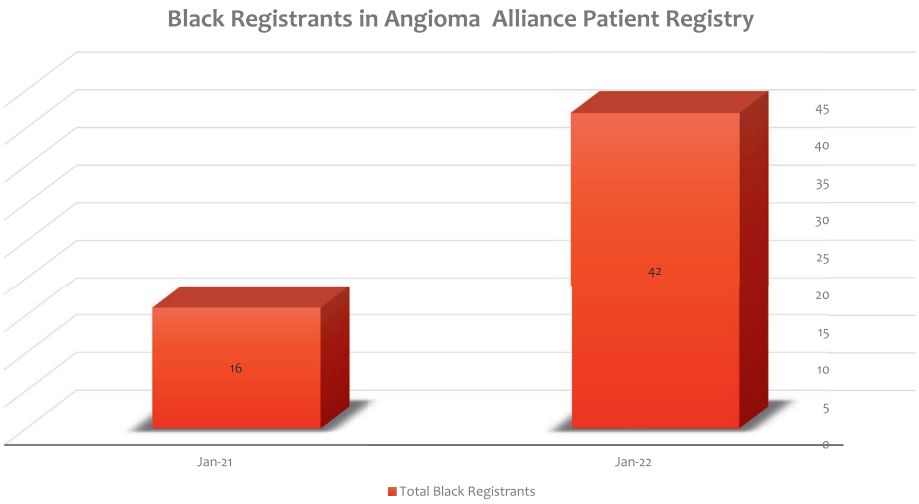

Figure 5: Growth in Black patients in the Angioma Alliance registry.

Finally, a Breaking Barriers support group discussion led to an unexpected finding. At least 5% of familial CCM cases include vascular skin lesions—deep blue nodules, punctate capillary malformations, and hyperkeratotic capillary venous malformations.[22] Support group patients requested assistance with lesion identification. An expert in CCM cutaneous lesions scoured the literature but could find no examples of these lesions on Black skin. This initiated a project to collect images within the Breaking Barriers patient cohort for a potential future publication.

Angioma Alliance's Black Health Empowerment (Breaking Barriers) program is moving beyond the B-CCM community. Breaking Barriers hired a media relations firm to identify opportunities to feature B-CCM patients in larger mainstream media stories.

Although this program may have lost a major donor, the merit of the initiative attracted support from other funders, including a multiyear grant from the Chan Zuckerberg Initiative Rare as One program, a grant program for which only 50 of the 1200 RD nonprofit organizations were selected for funding in its first 3 years of grant cycles. National Organization for Rare Disorders supports the AA and shares their work as a model to the 1200 organizations they serve.

NATIONAL ORGANIZATION FOR RARE DISORDERS' WORK IN MITIGATING THE EFFECTS OF HEALTH DISPARITIES

Supporting RD Nonprofit Capacity

Previous case studies exemplify the more advanced RD nonprofit organizations in our network. The AA has a team of 9 full-time employees (FTEs), and Sarcoidosis Research Foundation has a team of 11 FTEs.[23] However, in NORD's 2018 survey of our member organizations, 81% of our members have fewer than 5 FTEs, and the majority are managed with no FTEs (Figure 6); 1 in 5 operate with a budget of less than $25000 and nearly half with less than $200000.[24] Essentially, our survey demonstrates many RD organizations are underresourced and do not have the means to implement DEI principles within their work, despite their tremendous interest.

In addition, the leadership, staff, and board of directors of RD nonprofits do not always represent the diversity of their communities; across all nonprofits, board members are 78% white, while about 61% of Americans are white.[25] Rare disease nonprofit leadership likely reflects these trends in America: homogenously white and of a mid to upper

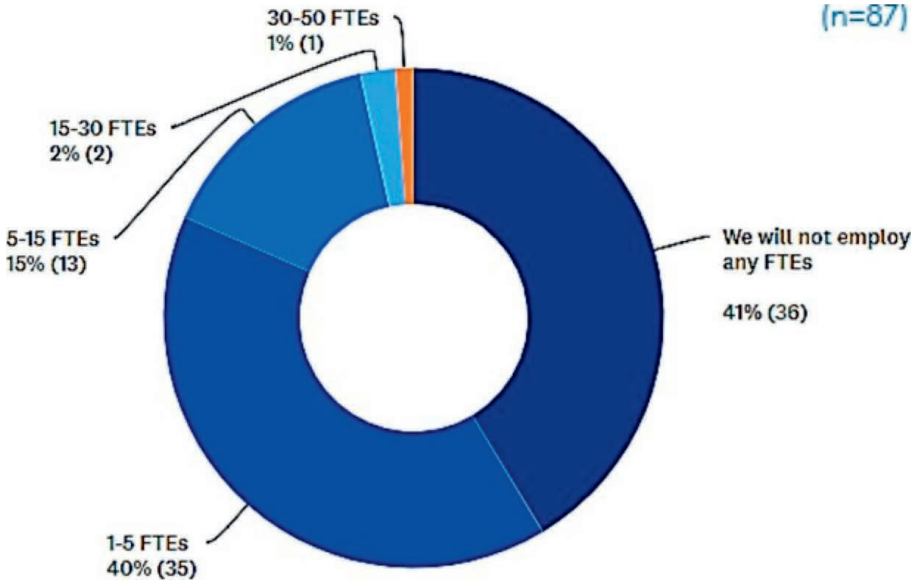

Figure 6: National Organization for Rare Disorders 2018 survey of full-time employees (FTEs).

level of SES. As a result, their outreach may fail to reach or even recognize marginalized communities impacted by their RD, and subsequently. patient engagement with their organization may not reflect the full diversity of the disease state.

National Organization for Rare Disorders is the oldest RD umbrella nonprofit in the United States—a leader in the RD patient advocacy ecosystem with a rich history of helping to establish many of its member organizations, providing best practices, education, and training. Given these close ties, NORD is well positioned as a trusted convener and seen as exemplary in assisting patient organizations to examine their activities and adopt more inclusive practices. In the fall of 2021, NORD developed a 3-part webinar series and 3-part toolkit providing leaders and staff of RD patient organizations a deeper understanding of how health disparities in marginalized populations affect the RD community as well as suggesting strategies to authentically connect with people of color, those who face language and/or literacy barriers, and those in remote or underserved areas who may lack access to online resources and the medical expertise necessary to manage their care. More than 1000 leaders of hundreds of nonprofit organizations registered and participated in the webinar series, which focused on (1) foundational knowledge of concepts around DEI and its intersectionality with RDs, (2) inclusion practices and their role in RD advocacy, and (3) the importance of diversifying nonprofit leadership and strategies to increase representation on nonprofit board of directors.

Supporting Treatment Access for Low-Income RD Patients

Commencing in 1987, NORD's patient assistance program is one of the first in the nation, providing financial support for helping low-income patients obtain lifesaving or life-sustaining medication they could not otherwise afford. These programs provide eligible individuals with financial assistance for health insurance premiums, copay costs for medical consultations, medications, diagnostic tests, and supportive therapies. Additionally, they may provide financial support for travel for clinical trials and/or consultations with disease specialists.

In 2021, NORD awarded $40698802 in patient assistance, helping 9419 patients with 265 RDs across the United States and 5 US territories. Of these patients, 959 were assisted with medical expenses not covered by health insurance and 7636 assisted with health insurance premiums and/or copay expenses. We offer travel and lodging assistance for 11 clinical trials.

When we set up a program, we look at the disease state and demographic makeup of its population—is there a higher risk or propensity for specific age, race, ethnic, or religious groups? When we identify a population being disproportionately older, we consider possible technology barriers and design resources to make enrollment in our program accessible to this community. Similarly, when we identify a population as having a higher proportion of Spanish speakers, we will develop materials in Spanish. We have several members of our team who are fluent in Spanish, as this language is the most widely spoken in the United States outside of English.[26] We want our programs to be accessible to all ethnicities in the United States, so we use Language Line, a telephone service that offers on-demand live translation of various languages into English. Thus, even if a caller is unable to speak English but fluent in say, Mandarin or Portuguese, we can just access Language Line for immediate translation.

We promote our patient assistance programs working with our members and the 1200 RD nonprofits in our network. In the future, we hope to use our new Centers of Excellence to develop new outreach programs to marginalized communities. To date, our centers are in 21 states and the District of Columbia, including largely rural areas in Alabama, Nebraska, and Oklahoma, to name a few.[27]

Our Patient Assistance Program not only supports patients directly, but our program model and learnings from our work are passed onto our member organizations when they approach us for assistance in setting up their own programs.

National Organization for Rare Disorders' Legislative Action for Bridging Disparities

Since our inception and for nearly 40 years, NORD has been the leader in advocating at the federal and state level for health policy designed to improve the lives of RD patients by increasing access to the following:

- Affordable, comprehensive health care coverage;
- New and innovative therapies to treat RDs; and
- Diagnostic tools that will enable early and accurate diagnosis.

In recent history, we have worked to support paid family and medical leave, as well as telehealth.

This includes our work in supporting the Affordable Care Act's essential health benefits and affordability provisions, advocating for Medicaid expansion at the state level, supporting patient protections to enable timely prescription drug access, and opposing Medicaid eligibility restrictions. Since 2017 alone, we have drafted and asserted our position vis-à-vis 812 policy statements, congressional and state legislature testimonies, and cosigned letters on RD health care access and research.[28]

Working within various coalitions with large and small nonprofits, we have spearheaded the RD response to policy by bringing hundreds of organizations together to elevate and integrate the RD community's needs into broader patient advocacy efforts within our health care system. At the state level, our Project RDAC is working to establish robust Rare Disease Advisory Councils (RDAC) in all 50 states to analyze the needs of the community and make recommendations to state legislatures on how to improve public policy related to rare diseases.[29]

One of the most pressing issues the RD community currently faces is ensuring that telehealth is appropriately and permanently integrated into our health care system to effectively meet the needs of RD patients and their caregivers. Expanded access to telehealth throughout the pandemic has been particularly beneficial to the estimated 25–30 million Americans living with RDs, reducing their risk of exposure to COVID-19 and helping them better manage their complex health conditions from the safety of home.

Before the COVID-19 pandemic started, we surveyed our RD community and asked about their access to providers. We found that 39% of RD patients travel more than 60 miles for their medical appointments. Therefore, it is no surprise that RD patients have had such a positive reception to expanded telehealth access because of the pandemic. One of NORD's COVID-19 surveys found that, of the 88% of patients who were offered a telehealth appointment, 92% of those who accepted the appointment said it was a positive experience, and 70% would like the option for telehealth for future medical appointments.[30]

Rare disease patients tend to require regular contact with their health care team because their diseases tend to be complex, requiring ongoing monitoring, testing, evaluation, and treatment management.[9] With RD specialists commonly operating out of academic medical centers and children's hospitals—the majority of which are in urban areas—geographically disparate people experience significant barriers to care including transportation and childcare costs and taking time off work or school.[31] We have heard in countless FDA patient-focused drug development meetings of stories where parents of a RD child had to uproot their entire lives, moving cross-country, staying in hotels, and changing jobs to access care.[32] Therefore, access to specialist care is too often limited to those of higher SES who have medical literacy, physician advocates, occupational flexibility, and other privileges.

For the past 2 years, in response to the clear call from RD patients and families in our community surveys, NORD and advocates in our Rare Action Network have worked together and in partnership with other patient groups to advocate to ensure telehealth is available to meet the needs of RD patients and their caregivers.

National Organization for Rare Disorders believes that effectively integrating telehealth into our health care system will lead to better outcomes for RD patients by reducing barriers care, shortening the time it takes to get an accurate diagnosis, and increasing access to providers with RD expertise. In support of these goals, we developed principles[33] to help guide our telehealth policy efforts. To date, many states and private insurance companies have already integrated aspects of telehealth into their plans and programs, yet there is more work to be done.

Both the federal government and states have the power to regulate aspects of telehealth, including telehealth licensure requirements, reimbursement rates, and eligible services. In January of 2022, NORD joined hundreds of organizations in advocating for a pathway to comprehensive telehealth access, considering the eventual end of the federal COVID-19 public health emergency declaration—a circumstance that enabled telehealth expansion at the outset of the pandemic.[34]

National Organization for Rare Disorders also joined a letter to congressional leaders with over 400 organizations supporting permanent telehealth Medicare reforms, as well as collaborating with the ALS Association, the Alliance for Connected Care, and 235 other patient organizations to call on governors to protect patient access to telehealth. From 2020 to 2022, we have advocated through 30 letters, statements, and testimonies for telehealth access and expansion.[2]

There are still barriers to care involving telehealth: low-income, elderly, and rural Americans can lack access to broadband services—whether because the technology infrastructure does not exist in their community, they cannot afford it, or they lack technology literacy to use it in their homes.[35] Therefore, NORD has advocated for the coverage and reimbursement of audio-only telehealth services because it can help bridge this digital divide. National Organization for Rare Disorders mobilized our advocates and the larger RD community to successfully advocate for the inclusion of several telehealth provisions in the omnibus appropriations package passed signed into law in March 2022. These provisions will prevent patients, particularly Medicare beneficiaries, from experiencing a sudden drop in telehealth coverage while we continue to advocate for more comprehensive legislation at the state and federal level. The bill would collect data on how telehealth is improving access to necessary care, even when it is across state lines, which is particularly important for our policy

efforts around ensuring patient access to health care providers practicing in a different state.

CONCLUSION

As an umbrella for hundreds of RD nonprofits, NORD is well situated to observe and learn DEI best practices from these communities, share organizing strategies, and develop new resources synthesizing these learnings to distribute across the entire spectrum of RD organizations. Our overarching goal continues to be to help patient advocacy organizations understand concepts relating to various social determinants of health as well as ways they can help address inequities through diversifying board leadership; reevaluating the design and marketing of their Websites, campaigns, and activities; and encouraging more diverse research participation.

Long-term, this type of programming helps to build strong and culturally competent leaders across the RD community that can continue to mentor and support others—ultimately leading to greater representation for all individuals living with or caring for someone with a RD.

National Organization for Rare Disorders will continue its commitment to understanding barriers to health care in the RD community and lead efforts to spur change by conducting scientific and policy research and studies as well as convening practitioners, leaders from NIH, FDA, patient advocacy organizations, patients, and caregivers in discussions and collaborations to improve access to care for all communities within the RD advocacy space.

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REGULAR ARTICLE

Hispanic Ethnicity and Social Determinants of Health: Harnessing Data from The Pulmonary Hypertension Association Registry

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Pulmonary arterial hypertension (PAH) is a chronic, progressive, and debilitating disease associated with increased cardiopulmonary morbidity and mortality. Current knowledge is derived from registries and landmark clinical trials, although concern exists that minorities are underrepresented in these datasets, and it remains unknown if there are intrinsic differences in minorities and disadvantaged groups. The Pulmonary Hypertension Association Registry offers a unique opportunity for the understanding of the unique social background of minorities in the United States because it routinely collects information related to socioeconomic factors such as annual income and health care insurance. Furthermore, representation of Hispanic patients may be slightly higher than in other US-based registries.

In this review, we discuss the interplay between biologic, socioeconomic, and racial or ethnic factors in PAH, with special emphasis on the Hispanic population. We describe the unique socioeconomic profile of Hispanic individuals and propose next steps to improve representation and fight inequality for Hispanic patients with PAH.

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a progressive pulmonary vascular disorder, characterized by progressive remodeling and narrowing of the pulmonary arterial tree,[1] resulting in increased right ventricular (RV) wall stress, abnormal RV mechanics, and if left untreated, right heart failure and death.[2,3] Despite significant progress in the understanding of the disease biology, delays in disease recognition and diagnosis are common, and most patients present at advanced stages. As such, emphasis should be on prompt recognition of the disease and associated factors that could be associated with higher risk of disease progression.[4]

Factors associated with progression of disease include age, severity of symptoms, PAH subtype, exercise capacity, metrics of RV function, hemodynamics, and biomarkers such as natriuretic peptides.[5–7] Current clinical models of PAH progression are derived from large randomized clinical trials (RTCs) and registries; however, concern exists that minorities and Black, Indigenous, and people of color (BIPOC) are underrepresented in these registries and RCTs.[8–10]

PULMONARY HYPERTENSION IN MINORITIES

Noticeable underrepresentation of minorities such as Hispanics in most PAH RCTs and registries exists (Figures 1A and 1B). This is an area of concern because most prognostic models in PAH are derived from these datasets, and patients of diverse backgrounds get treated from data that may not represent the same diversity. Accurate racial and ethnic representation is important to determine the generalizability of treatment approaches and outcomes in PAH.[10]

For instance, in the landmark SERAPHIN trial, only 14.7% of participants were of Hispanic ethnicity compared with 54.5% of White participants[11] (Figure 1A). Moreover, in the REVEAL registry (Registry to Evaluate Early and Long-term PAH Disease Management), the proportion of Hispanics was 8.9%, while the expected proportion of Hispanics should have been close to 11.5%, based on US census estimates (Figure 1B). Similarly, the proportion of Asian or Pacific Islander participants was 3.3% in comparison with an expected proportion of 6.1%.[9]

As such, the American Thoracic Society statement on health disparities in patients with PAH emphasized that PAH registries should be organized to reliably capture information related to race or ethnicity and socioeconomic factors and that socioeconomic factors should be addressed since they may allow identification of patients at the greatest risk for treatment noncompliance.[8]

Then the need to further describe the interplay between the biologic,

Key Words—ethnicity, Hispanics, PHAR, pulmonary arterial hypertension, social determinants of health
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Disclosure: The authors have no conflict of interest to declare.

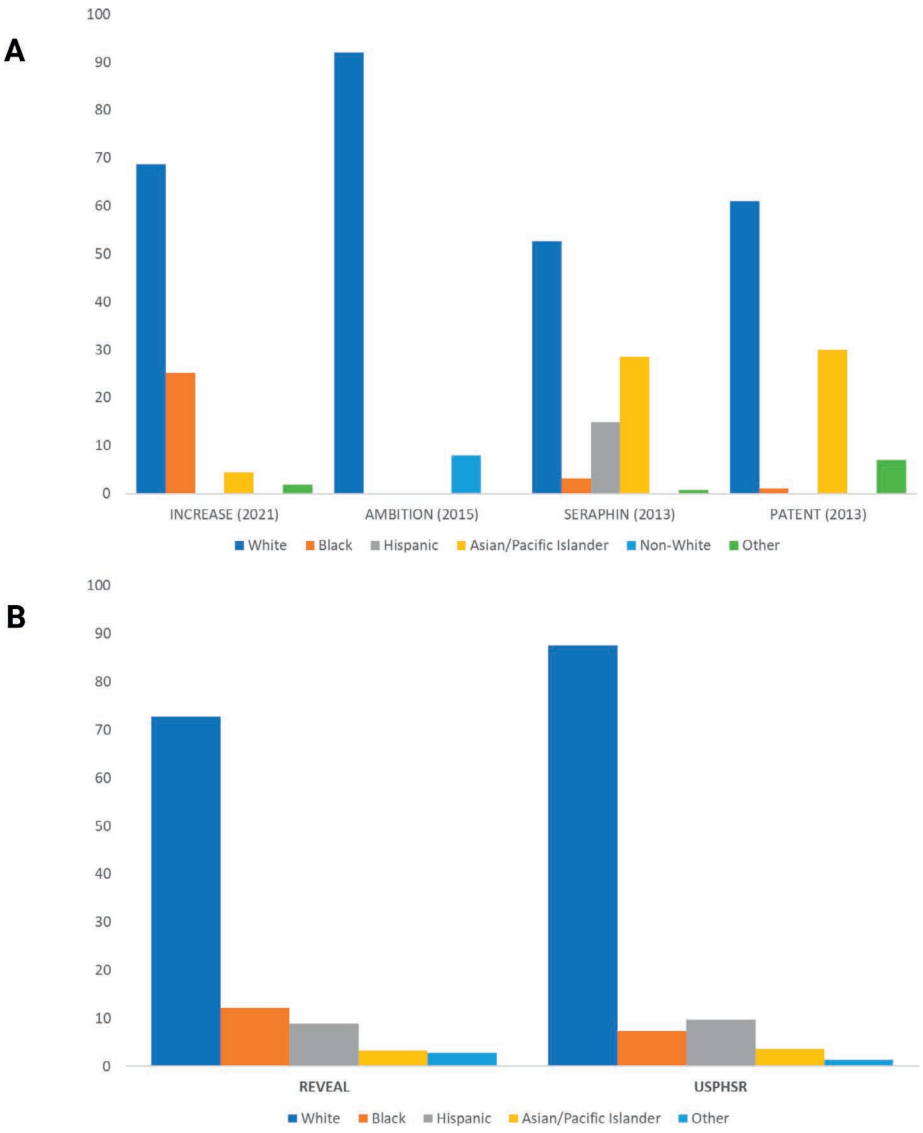

Figure 1: Representation of minorities and BIPOC in PAH clinical trials and registries. (**A**) Data in PAH clinical trials and (**B**) data in US-based registries. BIPOC = Black, Indigenous, and people of color; PAH = pulmonary arterial hypertension; REVEAL = Registry to Evaluate Early and Long-term PAH Disease Management; USPHSR = United States Pulmonary Hypertension Scientific Registry.

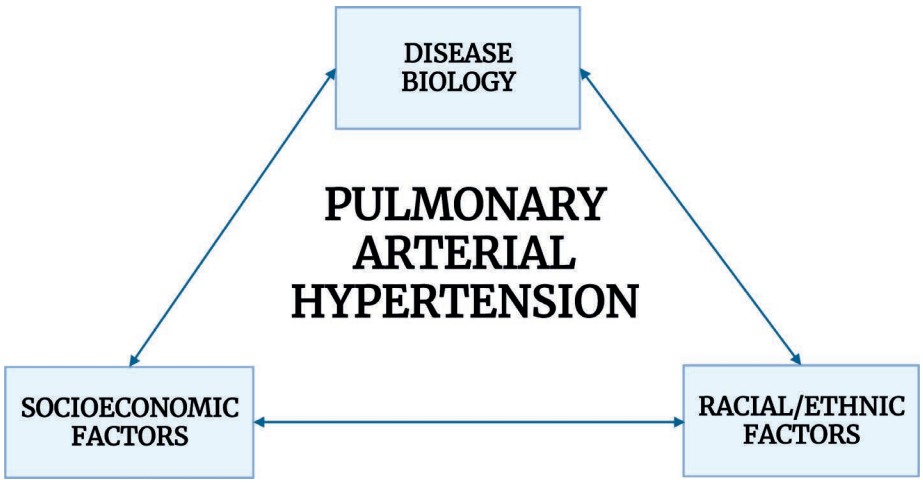

Figure 2: Interplay between biologic, socioeconomic, and racial/ethnic factors in PAH. PAH = pulmonary arterial hypertension.

socioeconomic, and racial or ethnic factors of the disease becomes evident (Figure 2).

PULMONARY HYPERTENSION AND SOCIOECONOMIC FACTORS

Socioeconomic status (SES) refers to an individual's social and economic standing and is a measure of social or economic position or ranking in a social group.[12] SES is a composite of several measures including income, education, occupation, residence, and housing, among others.[8] Unfortunately, socioeconomic factors are not routinely collected in most PAH registries, such as REVEAL.

Authors of a few studies have addressed the significance of SES in PAH. Wu et al[13] found that SES was an independent factor associated with impaired clinical outcomes in a cohort of patients with PAH in China. SES was measured as a composite metric of education, annual income, occupation, and medical reimbursement rate. Individuals in the lowest tertile of SES had increased hazard ratios for all-cause mortality, after adjusting for age, sex, World Health Organization (WHO) functional class, pulmonary vascular resistance, and PAH treatment. Talwar et al[14] found that patients with the lowest annual income had higher WHO functional class on initial presentation in a large US medical system database. Median annual income was estimated based on zip codes of study participants. On the other hand, authors of a relatively recent study from Scotland did not find an association between social deprivation and either severity of disease (WHO functional class) or all-cause mortality.[15] In this study, the investigators used geographical data zones to infer SES.

Social determinants of health (SDOH) refer to conditions in which individuals are born, grow, live, work, and age[16] and are implicated in health inequalities and poor conditions of daily life, which disproportionately affect certain groups such as minorities and BIPOC.[17,18] We will discuss SDOH in PAH in more detail later in this review.

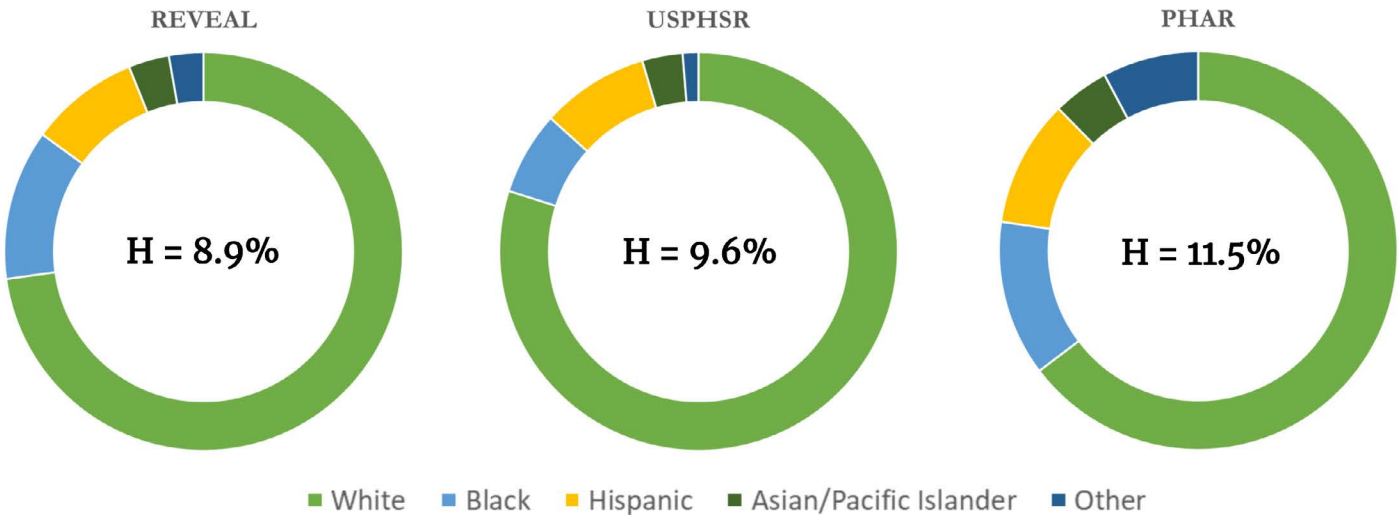

Figure 3: Representation of Hispanic patients in PAH registries. H = Hispanic patients; PAH = pulmonary arterial hypertension; PHAR = Pulmonary Hypertension Association Registry; REVEAL = Registry to Evaluate Early and Long-term PAH Disease Management; USPHSR = United States Pulmonary Hypertension Scientific Registry.

PULMONARY HYPERTENSION AND RACE OR ETHNICITY

Race is defined as "major living subspecies of man differentiated by genetic and physical characteristics," while ethnicity involves factors such as cultural heritage and sociocultural background.[9] Ethnicity is a concept closely related to SDOH: It refers both to the social factors promoting or undermining the health of individuals and the social processes underlying an unequal distribution of these factors, leading to differences in access to health care services and ultimately health care disparities.[19,20] We prefer to use the term ethnicity in lieu of race to encompass both genetic and cultural attributes.[21]

Racial or ethnic factors have been an area of interest in PAH, and most studies have been performed with Black and Hispanic patients.[9,22,23] Regarding Black patients with PAH, a higher frequency of connective tissue disease (i.e., scleroderma)[9] as well as a different response pattern to endothelin-receptor antagonists has been reported.[24] No convincing evidence of differences in survival have been found.[25] We will focus most of our discussion on the Hispanic population.

In general terms, Hispanic patients with PAH tend to be younger and have a higher frequency of congenital heart disease and portopulmonary hypertension.[8,9] Authors of studies evaluating clinical outcomes in Hispanic patients with PAH have shown differing results. Karnes et al[26] used data from the PAH Biobank and found that Hispanic patients with idiopathic or hereditary PAH may have slightly better survival than non-Hispanic Whites, after adjusting for age, sex, pulmonary vascular resistance, and use of prostacyclin analogues (heart rate [HR] = 0.46, 95% confidence interval [CI] = 0.21–0.99). These findings were not replicated on a study by Medrek et al[25] using the REVEAL dataset, where no association between Hispanic ethnicity and survival was found, after adjusting for age and PAH etiology (HR = 0.97, 95% CI = 0.76–1.24).

It is important to note that neither the PAH Biobank nor REVEAL routinely collect socioeconomic metrics: The authors of these studies could not account for differences in SES or SDOH. As others have previously emphasized, studying the association between race or ethnicity and health care outcomes without assessing the impact of socioeconomic factors offers an incomplete picture of the problem.[27–29]

THE PULMONARY HYPERTENSION ASSOCIATION REGISTRY

An important mechanism of health inequality in PAH is the lack of inclusivity in registries and RCTs.[10] Not only is there underrepresentation of minorities and BIPOC in most datasets, but most US registries do not routinely collect socioeconomic metrics, except for the Pulmonary Hypertension Association Registry (PHAR). PHAR is a multicenter US-based registry of patients treated at different pulmonary hypertension care centers. PHAR prospectively collects data from adults and children with PAH and chronic thromboembolic pulmonary hypertension.[30,31]

PHAR is a particularly unique dataset because metrics of SDOH such as income, education level, occupation, and health insurance are routinely collected. Furthermore, the representation of Hispanics in PHAR is slightly higher than REVEAL and other registries (Figure 3). As such, PHAR allows for the assessment of significance of SDOH in PAH, as previously reported.[32]

SDOH IN HISPANICS: DATA FROM PHAR

As mentioned above, authors of prior studies on clinical outcomes in Hispanic individuals with PAH had shown differing results and had not been able to assess the significance of socioeconomic metrics. Using data from PHAR, we recently performed a comprehensive characterization of Hispanic patients with PAH not only in terms of demographic and clinical factors but their social and economic profiles.[33] Hispanic patients were younger, had higher frequency of congenital heart disease, had higher pulmonary pressures and pulmonary vascular resistance, but had no major

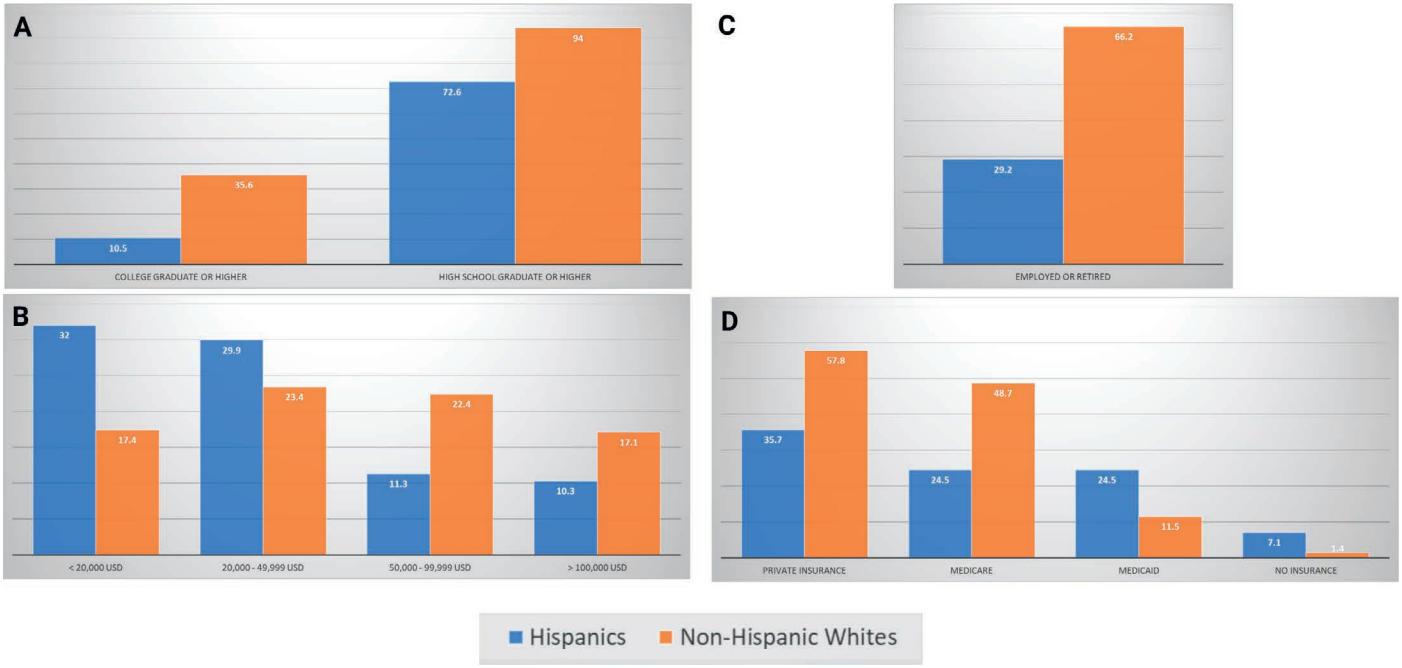

Figure 4: Social determinants of health in Hispanic and non-Hispanic White patients with PAH. Comparison of (**A**) education level, (**B**) total annual income, (**C**) occupation, and (**D**) health care insurance. Adapted from Bernardo et al.[33] PAH = pulmonary arterial hypertension.

differences in WHO functional class, exercise capacity, natriuretic peptides, or PAH therapy.

Hispanic patients had a disadvantageous socioeconomic profile as compared with non-Hispanic Whites. Hispanics had lower education level, had lower annual income, were less likely to be employed or retired, and were less likely to have access to Medicare or commercial insurance (Figures 4A–4D). For instance, up to a third of Hispanics were living with an annual income lower than $20000 per year as compared with 17.4% of non-Hispanic Whites. Only 29.2% of Hispanics were either employed or retired compared with 66.2% of non-Hispanic Whites.

No differences existed in transplant-free survival between Hispanics and non-Hispanic Whites, after adjusting for age, SDOH, and other covariates (hazard ratio = 0.76, 95% CI = 0.35–1.62; P = 0.474). However, while no differences in survival were found, Hispanic patients had a higher number of emergency room visits, with an incidence of 3.1 visits per person-years as compared with 2.1 in non-Hispanic Whites (incidence rate ratio = 1.452, 95% CI = 1.326–1.590). The total number of hospitalizations and the number of cumulative days in the hospital were also higher among Hispanics.

Despite having a similar severity of illness at baseline, a higher frequency of emergency visits and hospitalizations suggests that disease control was less optimal in Hispanics, which could be related to a disadvantageous SDOH profile. Lower-income patients face several challenges regarding PAH care, such as inability to afford the cost of medications or medical testing.[10,33]

IMPROVING REPRESENTATION OF MINORITIES WITH PAH

As described through this review, an important mechanism of health inequality and disparities in care in PAH is the lack of inclusivity in national registries and clinical trials.[10] Patient registries have historically lacked adequate representation of minorities and BIPOC, limiting our capacity to determine differences in clinical phenotypes and implementation of therapies.[8] We agree with the statement from the American Thoracic Society,[8] and 2 important messages are that (i) PAH registries must be organized to reliably capture information concerning race/ethnicity and SES of patients, and (ii) SES should be included in the risk stratification to help identify patients with PAH who may be at greatest risk for noncompliance.

We agree with Goel et al[10] on their proposal of future next steps against inequality in PAH, such as optimizing access to PAH centers (where RCTs are being conducted), identifying and addressing inherent biases in providers and patients regarding health literacy, financial burden, or nonadherence patterns, and eliminating language barriers for access to RCTs. The fights against inequality will require joint effort among providers, hospitals, health insurers, industry, patients' associations, and professional societies such as the Pulmonary Hypertension Association and government. It is time for action.

CONCLUSIONS

Noticeable underrepresentation of minorities such as Hispanics in most PAH registries and RCTs exists. While clinical outcomes in PAH may not be due to race per se, noticeable differences exist in the access to specialized care for minority and BIPOC patients. Lower-income patients face several challenges regarding PAH care, and it is pivotal to assess the significance of socioeconomic metrics and SDOH in patients with PAH. Finally, we believe that PAH registries must be organized to reliably capture

information concerning race/ethnicity and SES of patients, and PHAR is an important step forward in this goal.

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Disparities in PH

This spring, Dr Arunabh Talwar, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Northwell Health; Dr Vinicio de Jesus Perez, Stanford University; Dr Patricia George, National Jewish Health; Juliana Liu, Stanford Health Care; and Dr Elizabeth Joseloff, Vice President, Quality Care & Research, Pulmonary Hypertension Association (PHA), gathered to discuss real world experiences in dealing with health disparities and what the PHA can do to address them.

Dr Talwar: We are here because we are on a crossroad journey with PHA, trying to see how we can help further with the management of our patients. In the last 5 years or so, the issues of diversity and access to health care have come to our attention, and this has become even more important after COVID-19 epidemic. If one was to look at health disparity and access to health care, I would think of it in terms of 5 subsections.

The first is problem identification and then problem analysis. Based on these two subsections, most organizations will then develop an action plan. We'll call that stage plan development. The most difficult part of this process is the next stage, plan implementation. Then comes the time for the organizations to do an impact assessment. If I was to put this process back from the prism of PHA, and particularly focusing on pulmonary arterial hypertension (PAH) and a bigger broad spectrum of cardiovascular diseases, I think we are still at a stage of problem identification. That's why it's more important for us to explore the issues associated with diversity and access to health care. Only by recognizing the problems first can the organizations like PHA come up with an action plan. The purpose of this meeting is to get everybody's thoughts on this, as to where PHA should be moving in terms of providing information and guidance to the health care providers about issues of diversity, socioeconomics, and health care delivery. We also need to examine what we can learn from other patient advocacy organizations about these issues to help provide optimum care to the patients. I'd like to ask Vinicio as to what do you think we have learned from the PHA registry (PHAR)?

Dr de Jesus Perez: Our most recent study published in the *Annals of ATS* this past month used PHAR data to look at clinical characteristics of Hispanics compared to non-Hispanic whites. Interestingly, we found that Hispanics appeared to have an advantage over non-Hispanic whites in terms of morbidity and mortality. While [it] would be very easy to conclude that the benefit seen in Hispanics could be attributed to the level of care and resources available to these patients, we found that the socioeconomic status and health insurance coverage was lower compared to non-Hispanic whites. While we can't fully explain the discrepancies between socioeconomic status and clinical characteristics, these findings emphasize the existence of disparities based on race and ethnicity that likely has an impact on health care outcomes and quality of life for these patients. How other contributors of health disparities such as mental health, addiction, education, and geographic location influence PH clinical outcomes in Hispanics and other race/ethnic groups remains to be fully studied.

Dr Talwar: Vinicio, do you think the PHAR captured enough Hispanic population data to come to this generalization, or you do think this population is still underrepresented in that registry?

Dr de Jesus Perez: While the PHAR has helped us start to answer some of the burning questions surrounding health disparities in PH, we still need to carry out more studies in larger and more diverse populations. That's something that Patty just pointed out in her recent paper on *CHEST*. In that paper, her group documented that there is a significant underrepresentation of racial-ethnic groups in not only registries but also clinical trials. This observation emphasizes a major gap in our clinical data that could be adversely impacting how reliable the data from registries and clinical trials represents our patient population.

Dr George: It's interesting because, when we speak about race in medicine, that it is a social construct rather than a genetic construct, some will argue we shouldn't even mention race in trials and may argue that we should be race-blind in terms of enrolling people into clinical trials and perhaps even registries. My concern here is that, if we are in fact blind to race or other social identifiers, we may blind ourselves to biases in trial and registry enrollment, which will unfairly bias our impressions of prevalence of PH among different racial and ethnic groups.

In our field, there are numerous major clinical trials where race was not reported. I think that reporting this is important to make sure that there is equitable access to these pivotal clinical trials and therapies, and of course, lack of diversity in our trials and registries may also affect the generalizability of the results, a significant issue when we don't see the trials and registries reflect the actual prevalence of the disease.

Dr Talwar: Patricia, let me ask you. Race is at some level considered as a sociopolitical construct. Social scientists have argued that it may not be well reflective of genetics. Still, it has been proven in other chronic diseases that race, health literacy, socioeconomic status do play a significant role in terms of access to health care. The point of it is that, in other cardiovascular diseases like hypertension, there is some men-

tion of race-based treatment protocols. Should PHA be looking into a little bit more detail? What should we be doing in terms of making sure that the clinical trials that are done have adequate representation of the minorities?

Dr George: I would definitely argue against race-based treatment paradigms, as there are no data to support this, and race is a social construct. I do think that accounting for race and other social determinants of health in our enrollment would help us make sure that we [reach] a representative population of people that suffer from this disease.

What can PHA do? I think it starts with a multiplatform strategy that would have to be required to improve enrollment into clinical trials. This first comes from improving access to care for socially disadvantaged groups, so that people get to the PH specialist. To do this, we need to continue to work to improve educational practices aimed at frontline health care providers, who first see these patients early in their disease. We also need to make sure we as health care workers continuously address our own inherent biases and make early and accurate diagnoses and establish treatment plans in an equitable manner. Are there differences in how we treat patients even when they get the right diagnosis? Are people making biased subconscious determinations and prescribing less than standard of care to certain patient populations? If so, why and how can we correct it? In this space, PHA could collaborate with other patient advocacy organizations to provide workshops on implicit bias training in health care workers.

In addition to educating health care providers about PH and inherent bias, we need to also reach out into communities to bring disease awareness about PH and that, with PH and other diseases, it is important to get to the doctor to seek help for symptoms such as shortness of breath with exertion, fatigue, and unexplained symptoms. One way PHA might get involved would be to partner with local medical centers or practices and reach out to disadvantaged communities, with events such as local community health fairs to provide cardiovascular and pulmonary health screening.

Speaking more from a socioeconomic angle, in addition to education of physicians and communities, we need to also make sure that socioeconomically disadvantaged people have the ability to get to the doctor. Do they have health care insurance and access? Does the system allow them to take a day off from work? Does the person have transportation to get to the doctor in a timely manner? We need to also make sure the system allows people to get to a doctor. PHA has an excellent track record in lobbying our representatives in government, so I think contributing our voice to these issues and supporting universal health care and access to health care would be powerful.

Once we have the proper diagnosis and treatment plans, a huge issue is paying for those medications. Especially this last year, I think a lot of us and a lot of our patients struggled with the new patient assistance programs, and there was a lot of stress around getting copays covered. Imagine a person who is socially disadvantaged without somebody truly advocating for them and not in a PH specialist's practice, where people are fully versed on prior authorization and the assistance programs, how will they be able to afford the PH medications? PHA could help by analyzing this issue and by advocating for the simplification of medication prior authorizations and copay assistance programs.

Juliana: From the perspective of access to therapy, when I started in PH almost 20 years ago, it was actually "easier" to get PH drugs. First, there weren't that many options, and the insurance companies weren't really dictating treatments. PH was construed as a rare disease with rare treatment options. Now there are significant barriers such as step therapy requirements or formulary restrictions that are different for every insurance plan. That is not only difficult for people with adequate insurance to navigate, let alone people with Medicaid type of insurance, etc.

As an example, in the state of California, where we are, as of this year, they launched a new Medicaid central insurance clearing house system in which only sildenafil is on the covered drug list. Everything else needs to escalate to an appeal type of process. So for all PH patients on Medi-Cal, they had to redo all prior medications authorizations, resulting in severe therapy disruption.

There was a lot of excitement when generics came to play, that the cost of therapy will go down, but what we found is the opposite for PH treatments. Generics don't necessarily drive the cost down. In fact, it makes it even more difficult for patients to access therapy because previously available grant programs or therapy access programs have been shut down because manufacturers cannot give copay assistance cards, etc., for patients who are on government-based insurance, for example.

The most frustrating aspect of this is that the rules of medication access are not necessarily based on scientific nor standards of treatment. It's not necessarily based on things that are best for the patient or what the clinician recommends for the patient. It's really driven either by policy or financial factors. If there's anything that the PHA can do to help us, it is to collectively speak to lawmakers and other stakeholders to change that. The prohibitive cost of therapeutics is a national discourse going on that certainly touches on PH patients as well. If there's a way in which we can move the needle on that, it would be helpful for our patients. It really is a shame that, for our patients, securing access to therapy is a full-time job every year as insurance formulary rules change and they need to struggle to access foundation funds to pay for life-sustaining therapy.

When the PH care centers (PHCC) initiative came onboard, we talked about, won't it be great if there are certain accredited centers in which, perhaps if you are a patient who gets seen there, then there's an assumption that the treatment is adequate, and therefore, the insurance can move quickly. In fact, that's how it operates in other counties. This is not necessarily because we want to exclude patients out, by no means, but it's simply a balance to control the cost of therapeutics but, at the same time, give adequate care without needless bureaucratic redundancies. What we have

right now is not doing either. What the pandemic has taught the general public, if anything, is how fragmented the US health care system is, and because there are no consistent rules, and every jurisdiction and insurance has its own standards, the prescriber has to navigate through the extremely complicated and inefficient administrative hurdles just to get a patient started or maintained on therapy.

One successful initiative that the PHA was able to advocate for was the centralization of one REMS program for ambrisentan. When generic ambrisentan came online, they set up 2 REMS programs for the drugs. That meant that. depending on your pharmacy and which generic product you were receiving, you had to enroll in one REMS program versus another. That also meant, if your pharmacy stocked another type of ambrisentan, you had to enroll in the other REMS program. As you can imagine, this caused needless delay in therapy. Through the advocacy work of the PHA, Dr Sager and myself, we spoke to the REMS program; we were able to convince the drug manufacturers to disband one of the programs and merge into one entity.

Something that the PHA can do and has successfully done is to partner with us as clinicians to provide a collective voice on behalf of the patients.

Dr Talwar: From listening to both Patricia and Juliana, PHA does try to make its voice heard both at the local and federal policy level. We need to argue for proper access to care for minorities, for ethnic minorities, or people who have low socioeconomic status, which correlates at some level with health insurance as well. PHA obviously needs to focus more on health education, both for the patients as well as for the providers.

Let me ask Elizabeth and Vinicio, what about PHAR? What have they taught us? Where are we moving with this? Secondly, what can we learn from other organizations, like Cystic Fibrosis (CF) Foundation, Pulmonary Fibrosis Foundation, and other patient advocacy organizations, that we can take from them and probably incorporate into PHA's efforts?

Dr de Jesus Perez: The PHAR is certainly a very unique and powerful resource that was designed to capture race, ethnicity, socioeconomic status, and other information missing from previous registries. I would love to hear from Elizabeth since she worked with the CF Foundation and can certainly provide a very important perspective of this.

Dr Joseloff: Sure. I'm happy to talk. The PHAR is now reaching a substantial enrollment number. We're approaching 2000 patients enrolled. We have 11 publications now. The science is coming out that will support data behind these types of studies. There's more information to come in that regard.

If you look at other more mature registries, there are a number of publications and papers that can be used to support these types of studies that can be used to support basic knowledge, patient education, understanding in the community, and also to support advocacy. That's where PHA is heading. We want to be able to leverage with the care centers and the registry to be able to help so that there aren't these disparities and challenges that continue for the PH patient populations.

With our advocacy work at PHA, this is on our radar too, with making sure that we keep everyone in mind and advocate for all patients with PH.

Dr Talwar: I'm hearing that maybe PHA needs to collaborate more with other such organizations to learn from them and share their experience to see where we are. Listen, all these diseases at one time were considered rare. I'm so impressed with CF Foundation, the way they advocate for their patients, how they support their centers, and even help collect data. I think that's amazing and maybe something that we can learn from them as well.

Dr Joseloff: PHA is partnering with the CF Foundation and organizations on advocacy work. Many disease foundations and associations [are] working together as partners for advocacy. That's already ongoing.

Dr George: That's so key because, while we are in one rare disease space, by partnering with other organizations, we bring greater numbers to these important core issues. There is definitely power in numbers, and I'm glad PHA is doing this.

Dr Talwar: One of the things that always has intrigued me as a PHA member is that PHA focuses more on the PHA physicians per se, but the problem starts with the primary care physicians. There is a big gap in timely referral from primary care physicians to the specialist centers. At times patients who don't speak English, either because they are minorities or they have other socioeconomic problems, cannot get to their primary care physicians, or often they cannot explain their symptoms. I feel there is a delay by the time the patient is referred to a proper PH center for care.

What should PHA be doing, Vinicio, so that we can target this particular problem? Is there something that we can come up with in terms of guidelines, or what we have done up until now? Has there been any introspection?

Dr de Jesus Perez: I cannot speak for PHA, of course, but what I can say is that this is an important problem, and it goes beyond the health disparities aspect. As we all know, many patients, including patients who do not necessarily fall in the bracket of being underserved, get lost in the system for a long time before the diagnosis is suspected. You reported a couple of years that, when these patients finally reach you, they are in a much worse functional class. [I] think, when it comes specifically to addressing health disparities, there are several avenues.

I think insurance plays a key role in financial support, access to centers as well as resources to connect the patient with the practitioner through interpreter services, through matching with providers who are from the same race, ethnicity, religious background, sexual preference, any of these factors because they do play a key role in how patients see us and the trust that they put on us.

With regards to what PHA can do, reaching out and educating the medical community is a major step. Maybe

working with professional societies like the American Medical Association and American Family Medicine could help add PH as part of the educational curriculum for general practitioners and specialists. Also, promoting the implicit bias training for professionals, which can certainly go a long way in mitigating some of these initial additives that we bring with us into a patient encounter can help mitigate mistrust and improve communication between patients and providers.

Dr Joseloff: I would say this is definitely an area of development. Incorporating diversity, inclusion, and equity is definitely an area of focus for PHA. We want to keep diversity, equity, and inclusion in the forefront of all aspects of what we do. That's one of the areas for the care centers that we're focusing on this year, to target outreach to new PH care centers in geographical areas that maybe have gaps in access to PHCCs. That will help us make sure that PH patients get seen by expert health care providers and get the right treatments as early as possible.

Dr Talwar: That brings me to a different issue altogether, which I think is tied to long-term access to care. There are PH centers all across the country. I also look at so many pulmonary training programs. Not every pulmonary training program has the kind of capacity to train fellows in PH. I feel that the PHA physicians, with the backing of the PHA, should make a push to argue for further training in PH for all trainees in pulmonary fellowship. If extensive PH management experience is not available in a particular training program, some facilitation should be made so that trainees can rotate through a program where this kind of experience is available. Vinicio, what do you think?

Dr de Jesus Perez: If I may point out, besides physicians, there's of course nurse practitioners (NPs) and other health professionals who are essential in managing this patient population. I would love to hear from Juliana, who has been working in this field for more than 20 years, what her thoughts are regarding educating nurses, caregivers, and physician assistants (PAs). What do you think? Do you think this is a legitimate goal that we should prioritize?

Juliana: Thank you, Vinicio. In terms of training the nonphysician provider, I think the challenge is that there are so many different pathways into becoming either a PA or a NP. Usually, their training is very diverse, not necessarily as standardized as medical training. Any specialization comes from where you end up working.

That being said, I think PAs, NPs are more attuned to dealing with some of these general health issues that affect health care that may not be so pathobiologically focused. Their training includes ways to see the whole patient and bring in issues pertaining to socioeconomic status, cultural background, etc. Not to say physicians aren't, but there's a strong emphasis at least in the nursing tradition to look at that.

It's impossible to train all these nonphysician providers about PH, but if we can develop a really great digitally accessible curriculum that can be promulgated to these PA or NP societies, for example, can be a great start. Really, they are the frontlines to see and identify the high-risk patient and then refer them to a tertiary center.

They're not going to supplant the role of the PH center, but we really need more hands and feet out there in the community. That might be a good avenue to spread the knowledge, to help us really widen the catchment of these high-risk patients.

Regarding nurses, I often tell people, once they're diagnosed, actually, the nurse's job just starts. It's, how do we ensure that the patients continue on their therapy and do well? I have patients who've been on epoprostenol almost 20 years, and they're doing really well. Why? Because, honestly, the nurse was there to call the patient and make sure every line infection doesn't evolve into sepsis. There needs to be more focus in the PHA in supporting the nonphysician provider and also to bridge the gap between those patients who have difficulty accessing tertiary care centers.

We really need to think of our model of care, not just physician-patient but really to broaden the scope of care through not just nurses but even trained community health educators to help patients understand their disease. They can help improve health literacy, even understand things like insurance access or how to take basic health steps to improve one's overall health or food choices. Much of the guidance around food and things are very mainstream American cultural focus. How do you incorporate dietary recommendations that are ethnically mindful that incorporate traditions from other cultures?

Patients who might not come from the majority culture, sometimes they will just defer to the physician and not ask questions. Even having culturally diverse and meaningful patient education tools builds trust because it signifies to the patient that we hear them and want to try to help.

In California, there is a significant Asian population. We have never had any PH material in different Asian languages. I know that the PHA has a memorandum of understanding with a lot of the international PH groups. We don't have to recreate the wheel. There's a lot of culturally appropriate material that was actually generated overseas that we can incorporate. Leveraging the vast network is something that the PHA can definitely tap into and in turn result in more culturally relevant and pertinent materials.

Dr Talwar: Yes. I would call it as transdisciplinary training and education, which incorporate nurses, PAs, NPs, and physicians. We need to make an effort that enough teaching about PH is provided during training period as well. We need to make sure that PH as a differential diagnosis exists in the mind of health care providers when patients present with all kinds of symptoms.

Patients don't read textbooks, so they present with all kinds of different complaints. If this disease is not on our radar, we are unlikely to think of it, even as our sixth, seventh, or eighth differential diagnosis. That's where I think perhaps things start falling through the cracks.

I think, Juliana, you were right in pointing out, initial screening place right now is done in primary care practices much more by NPs and PAs. We have to think of that territory as well. I have to take them along with us as we move in terms of treatment and other management issues. Hopefully that will then result in early diagnosis and improved outcomes down the line.

Dr George: First off, I'm loving hearing what all you have to say. These are really important points that you bring up. If I were to utilize an organization like PHA in trying to educate people who are on the front line, that's what we're talking about; they don't have to treat PH, but they have to send them to the experts. You have to at least have it on a differential. I would think about, again, partnering with other advocacy organizations in rare diseases.

It's one thing to go out there and educate the world about PH, but in a busy primary care practice, it's hard. Our traditional venues have been in pulmonary medicine and in cardiology. Will it be seen by the frontline physicians? What if you'd have at American College of Physicians national meeting or joint sessions with the American Academy of Family Physicians, for example. There could be a rare disease panel, a "zebra panel," if you will, or an unexplained dyspnea panel, "When shortness of breath is not asthma or COPD," but you actually get representation from different rare diseases to flesh out that differential.

Dr Joseloff: PHA is hosting annually an Associated Diseases Summit. We bring 10 or so organizations of associated diseases together, and we talk about common issues and how we can work together. This is [a] relevant topic to bring to the summit for discussion. I will share this with my colleagues at PHA.

PHA has exhibit booths at other organizations' conferences for awareness and outreach. We'll be having at the PHA 2022 Conference in June a [Pulmonary Vascular Research Institute] and PHA joint session on beyond group 1 PH. This is an example of when we're working together with other organizations.

Dr George: That is super. It would also be amazing to generate a summary article from the Associated Disease Summit and consider getting it cross-published into multiple journals and different specialties.

Dr Joseloff: That's a great idea. Thank you.

Dr George: One other barrier to care I also wanted to mention before our time is up is challenges with telehealth and access to care, highlighted by the COVID-19 pandemic. We work with people from across state lines, and one might think that telehealth is a great option. However, I cannot conduct a telehealth visit with someone across state lines. I can see them in Colorado, where I'm licensed, but I cannot see them if they are sitting in their home in Wyoming or another state. Additionally, there are a lot of issues with telehealth and access to care. Many people even in large cities do not have broadband. They may not have a device that can connect.

PHA could help greatly by advocating with the government for the ability to treat people across state lines, especially when there are no PH specialists in a state or region. Additionally, advocating for expansion of universal broadband, an infrastructure issue, would help us reach more of our patients as well.

Dr Talwar: These are important issues and something very granular. Patients who come from a poor socioeconomic background, they may not have the capability of doing video. They may be able to do telephone. It's very simple. I have seen it in my practice time and again. It's very much correlated with health literacy, socioeconomic status, and to their ethnicity.

In the remaining few minutes, I just want to get everybody's opinion on some other issues. There is some data maybe that—if you look at the subsets of PAH, maybe the collagen vascular disease is more common in the African American, maybe portopulmonary is more common in the Hispanic population. How should that be addressed or put together so that a little bit more resources are put there so that patients with that kind of ethnic minority are able to get equal access to care, Patricia?

Dr George: I have a quick question regarding these statements. Whenever I see this racial prevalence of a subtype of PAH, my larger concern is, are we underdiagnosing the denominator (PAH) in certain patient populations? For example, are we making a connective tissue disease (CTD) diagnosis and then doing appropriate screening (which is excellent), yet missing the diagnosis in the non-CTD PAH subtypes?

Dr Talwar: Absolutely.

Dr George: It may be that only when some people have scleroderma or portal hypertension is PH considered. I think that is more likely than some sort of biologic reason. So maybe that changes how we discuss this issue.

Dr Talwar: It's an access-to-care issue at a much broader level. That's what I believe. That's why I said before that we should educate our providers, including the bigger territory of primary care providers who are the first gateway for these patients. Let's go through one by one and say, what's the most important thing on your mind that we should be doing for next 1 to 4 years in terms of bridging the gap of access to care? Vinicio, let's start with you.

Dr de Jesus Perez: Education. I think we have to be very aggressive about reaching out and educating. I think we know the problem is there. I'm sure that, from the perspective of the primary care providers, there's no problem. They're not aware of it. Again, there's the implicit bias aspect that is playing a major role. I think we just really need to reach out and be aggressive about making sure that the community's educated.

I like Patty's idea that maybe we should start interacting with medical societies so that we can be part of those discussions, give presentations, etc.

Dr Talwar: Juliana?

Juliana: I would say also we could focus on empowering the current providers

and reaching out to different groups' needs. Along with educating providers, we need to create culturally meaningful educational materials, for example, not just in Spanish, but other major languages.

Even in our support group structure, I know that PHA does an excellent job in having demographic-specific groups like the young generation support group. Maybe there is a way to further develop language-based support groups. I think that would be huge. That would be really great to support the patients that are already diagnosed.

Dr Talwar: Patricia?

Dr George: I think those are excellent points. I echo what Vinicio is saying in expanding education, but I think it goes beyond education. I think there's this system problem in US health care that disadvantages people being diagnosed appropriately when they have rare diseases. The problem begins with having 20 minutes to see a new patient and 10 minutes for a follow-up visit. If a health care provider is trying to manage diabetes, hypertension, and social issues like the patient just lost their job (and insurance) and cannot get a ride to clinic, how are they supposed to remember and even think and have time for the doorknob moment when they're leaving the room; then the patient says, "You know what? By the way, when I go up the stairs, I'm a little more short of breath." It is easy to see how someone might have to say, "Okay, here is an inhaler, and I'll see you in 6 months."

It may not always be that health care workers are ill-informed or ill-educated; they are having to take on bigger issues. If I were an advocacy organization like PHA, I'd partner with others and actually discuss this health care system issue as being one of the contributors to delayed diagnosis and delayed therapies in rare diseases.

Dr Talwar: Elizabeth?

Dr Joseloff: These are fabulous ideas and definitely information that will help PHA as we start to grow and expand to make sure that we are addressing these disparities and eliminating the barriers down the road. PHA now has a very extensive accredited care center program network. Continuing to reach out to other PH care centers, we can work towards all PH patients are getting the appropriate care, the highest standard of PH care in the near future.

Dr Talwar: I echo everything that you all have said. I think reducing disparities in a rare disease process like PAH requires a multilevel and a multicollaborative approach. Mind you, PHA has a very important role to play. PHA is a bridge between the patient, health care providers, both PA, NPs, nurses, and physicians. We need to be able to identify the barriers to access to health care, both at individual and community level. We need to lobby for it so that we can provide it with more resources, and if need be, financial efforts so that everybody and anybody in this country who has PH is able to get optimum care without consideration for gender, sex, race, socioeconomic status. Thank you.

Advances in
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