

Health Disparities in Patients with Pulmonary Arterial Hypertension: A Blueprint for Action

An Official American Thoracic Society Statement

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Background: Health disparities have a major impact in the quality of life and clinical care received by minorities in the United States. Pulmonary arterial hypertension (PAH) is a rare cardiopulmonary disorder that affects children and adults and that, if untreated, results in premature death. The impact of health disparities in the diagnosis, treatment, and clinical outcome of patients with PAH has not been systematically investigated.

Objectives: The specific goals of this research statement were to conduct a critical review of the literature concerning health disparities in PAH, identify major research gaps and prioritize direction for future research.

Methods: Literature searches from multiple reference databases were performed using medical subject headings and text words for pulmonary hypertension and health disparities. Members of the committee discussed the evidence and provided recommendations for future research.

Results: Few studies were found discussing the impact of health disparities in PAH. Using recent research statements focused on health disparities, the group identified six major study topics that would help address the contribution of health disparities to PAH. Representative studies in each topic were discussed and specific recommendations were made by the group concerning the most urgent questions to address in future research studies.

Conclusions: At present, there are few studies that address health disparities in PAH. Given the potential adverse impact of health disparities, we recommend that research efforts be undertaken to address the topics discussed in the document. Awareness of health disparities will likely improve advocacy efforts, public health policy and the quality of care of vulnerable populations with PAH.

Keywords: pulmonary hypertension; health disparities; health policy; genetics

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Overview

Health disparities exert a disruptive influence on the clinical outcomes and quality of care received by minorities in the United States. Although initiatives addressing health disparities have made significant advances, there are still major gaps that will benefit from ongoing research efforts. “Pulmonary hypertension” (PH) refers to a group of diseases characterized by abnormally elevated pulmonary pressures caused by various chronic conditions (Table 1). Of the various forms of PH, pulmonary arterial hypertension (PAH) stands out as a rare disease that affects predominantly women, with an estimated median survival of 2.8 years without treatment (1). Available clinical guidelines stress the importance of early diagnosis and initiation of therapy to ensure optimal outcomes, reduce

morbidity, and maintain quality of life (2). Compared with the rest of the population, minorities with PAH may be 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. Although few studies have addressed these issues, our review of the available data suggests that patients belonging to minority groups may have worse outcomes compared with other populations. The committee reviewed the available literature on health disparities to formulate the following recommendations:

- There is accumulating evidence that certain minority groups have a genetic predisposition for cardiovascular diseases, but whether this is also the case for minorities with PAH is unknown. Given the prognostic importance of mutations, the group recommends that

the value of performing genetic screening and providing gene counseling, particularly to patients with idiopathic and familial PAH, should be assessed by future research.

- Patient registries have historically lacked adequate representation of racial and ethnic minorities, which limits our capacity to determine whether there are differences in clinical phenotypes and implementation of therapies. The committee recommends that efforts should be made to ensure adequate representation of minorities in clinical registries and to prepare questionnaires that include questions relevant to minorities in accessible languages.
- Socioeconomic status (SES) is defined by a number of variables, including education, occupation, marital status, health insurance coverage, and income. Lower SES has been linked to higher incidence of health disparities in minority populations with cardiovascular diseases (3), making this one of our top priorities to study. In PAH, SES has been associated with worse functional class at presentation, as patients with lower income were likely to present at specialized healthcare centers with more advanced PAH. The committee recommends that SES should be included 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.
- Healthcare practitioners working in local and regional healthcare systems have the opportunity to identify minority populations at risk and to create effective plans for interventions; however, their capacity to do this is determined by identification of and access to educational and community-based resources that will attract patients to seek healthcare. The committee recommends (1) the use of educational resources for both patients and practitioners and (2) a multidisciplinary approach that should incorporate social workers and medical interpreters to ensure trust and respect for both parties.
- It is well established that PAH can result from exposure to certain drugs and toxins, infections, liver disorders, autoimmune disorders, and congenital heart disease (2). In addition, environmental stressors such as

Table 1. Classification of Pulmonary Hypertension

1. Pulmonary arterial hypertension
 - 1.1. Idiopathic PAH
 - 1.2. Heritable PAH
 - 1.2.1. *BMPR2*
 - 1.2.2. *ALK-1, ENG, SMAD9, CAV1, KCNK3*
 - 1.2.3. Unknown
 - 1.3. Drug and toxin induced
 - 1.4. Associated with:
 - 1.4.1. Connective tissue disease
 - 1.4.2. HIV infection
 - 1.4.3. Portal hypertension
 - 1.4.4. Congenital heart diseases
 - 1.4.5. Schistosomiasis
- 1'. Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis
- 1''. Persistent pulmonary hypertension of the newborn
2. Pulmonary hypertension due to left heart disease
 - 2.1. Left ventricular systolic dysfunction
 - 2.2. Left ventricular diastolic dysfunction
 - 2.3. Valvular disease
 - 2.4. Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
3. Pulmonary hypertension due to lung diseases and/or hypoxia
 - 3.1. Chronic obstructive pulmonary disease
 - 3.2. Interstitial lung disease
 - 3.3. Other pulmonary diseases with mixed restrictive and obstructive pattern
 - 3.4. Sleep-disordered breathing
 - 3.5. Alveolar hypoventilation disorders
 - 3.6. Chronic exposure to high altitude
 - 3.7. Developmental lung diseases
4. Chronic thromboembolic pulmonary hypertension
5. Pulmonary hypertension with unclear multifactorial mechanisms
 - 5.1. Hematologic disorders: chronic hemolytic anemia, myeloproliferative disorders, splenectomy
 - 5.2. Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangiomyomatosis
 - 5.3. Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
 - 5.4. Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure, segmental PH

Definition of abbreviations: PAH = pulmonary arterial hypertension; PH = pulmonary hypertension.

pollution, living conditions, and nutrition are known to reduce quality of life and the mental health of patients, and may be directly involved in PAH pathogenesis. The committee recommends that studies be performed to identify specific stressors in relevant geographical areas and associations between stressors and medical compliance, outcomes, and quality of life.

- 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. 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. The committee recommends partnering with professional and advocacy organizations to increase awareness and to increase collaborative efforts to lobby for new laws to protect patients with PAH.

Introduction

According to the 2010 U.S. Census, approximately 36% of the population belongs to a racial or ethnic minority group, and these numbers will likely increase over the next decade. However, compared with the rest of the U.S. population, many minorities experience reduced quality of life as a result of health-related problems, in contrast to the rest of the U.S. population (2). To address this growing problem and prevent the potential catastrophic consequences that this trend will have on the U.S. health economy, government-sponsored efforts have been undertaken to understand the major sources of health disparities and to implement effective policies.

Whereas most efforts have focused on tackling diseases with the highest rates of morbidity and mortality in the U.S. population (e.g., cardiovascular diseases, cancer, chronic obstructive pulmonary disease), less attention has been given to PAH, for which current estimates indicate a prevalence of 15–50 cases per million (4, 5). Of major importance, survival is dependent

on early diagnosis and institution of therapy. To date, little work has been done to determine whether minorities affected with PAH are at higher risk of worse outcomes compared with nonminorities and whether measures can be undertaken to effectively improve access and quality of care for these patients. In a study involving a Veterans Affairs cohort with 340 patients with a documented right ventricular systolic pressure greater than 60 mm Hg by echocardiography, only 17% carried a diagnosis of PAH in their medical record (6). This is of particular concern, as one specific dilemma in the treatment of PAH is that (1) even mild increases in pulmonary artery pressure are associated with increased mortality (7) and (2) delays in diagnosis are associated with worse outcomes (8). A review of the U.S. National Center for Health Statistics database for the years 1994 to 1998 for death attributed to PAH by sex, age, and race over nine geographic regions revealed that African American women with PAH had the highest rates of mortality across all ages (9). Although this has not been confirmed, it raises the possibility that these issues could contribute to the observed health disparities reported and support an urgent need to address how these factors could have a direct effect on the diagnosis and treatment of PAH in minority groups.

Purpose

Given the known effect of health disparities on health-related quality of life for other common disorders, it is likely that minorities suffering from PAH could benefit from a revised approach that incorporates the recommendations of the *NIH Roadmap for Medical Research*, which calls for integrating clinical, basic, and social science research to identify and treat factors directly related to disparities in health outcomes (4). The American Thoracic Society (ATS) is committed to medical education of both healthcare professionals and patients, with the goal of improving global lung health and advocating for health policy that will directly benefit the welfare of patients with lung disorders such as PAH. We believe in initiating efforts to confirm the existence of health disparities in PAH care, and propose that possible research avenues and changes in health policy should be a priority for the ATS and

other professional research societies, as this could have a profound and lasting impact on improving the quality of healthcare experienced by minority populations afflicted with this devastating disease.

Definition of Health Disparities and PAH

Health disparities between population groups are defined as significant differences in health that are closely linked to racial ancestry, social, economic, and/or environmental differences. Health disparities adversely affect groups of people who have experienced greater obstacles to health based on their racial or ethnic group; religion; socioeconomic status; sex; age; occupation; mental health; cognitive, sensory, or physical disability; sexual orientation or sex identity; geographic location; or other characteristics historically linked to discrimination or exclusion (10).

PH is defined as an increase in mean pulmonary arterial pressure equal to or exceeding 25 mm Hg at rest as measured by right heart catheterization. PH is classified into five groups (*see* Table 1) based on cause and hemodynamics criteria. PAH (i.e., World Health Organization [WHO] group 1 PH) is further defined by (1) mean pulmonary arterial pressure equal to or greater than 25 mm Hg, (2) a pulmonary artery wedge pressure not exceeding 15 mm Hg, and (3) pulmonary vascular resistance of at least 3 Wood units in the absence of other causes of PH (WHO groups 2–5) (2).

Methods

Fifteen experts in PAH clinical care and research (basic, translational, and clinical), together with public health and policy researchers with an interest in health disparities, were selected to discuss current strategies to diagnose and treat patients with PAH in the context of a research framework applied to study health disparities in the United States. To meet our goals, the following topics were selected for review:

1. Role of national PAH registries in collecting clinical data for research in health disparities
2. Role of genetics of PAH pertinent to clinical phenotypes in underrepresented minorities

3. Role of environmental stressors in influencing patient attitudes and response to therapy
4. Role of socioeconomic status in identifying at-risk patient populations with PAH
5. Role of medical education in establishing the basis of a mutually respectful and productive relationship between minority patients and healthcare practitioners
6. Partnerships between federal departments and medical societies to develop health policy and advocacy for minorities with PAH

Before the face-to-face meeting at the 2016 ATS International Conference, the chair and vice-chair performed a search of the medical literature to collect available literature on health disparities research in PAH and other relevant medical disorders, and distributed it to the rest of the panel. In March 2016, the committee held the first teleconference to go over the topics to be included in the research statement. Six teams were formed, and the members were assigned to undertake a literature review and provide a preliminary summary to the group in time for the second teleconference. Literature searches were performed in Medline, and results were limited to human studies published in English for all publication years. The group met face to face on May 14, 2016 in San Francisco at the ATS International Conference, where each of the topics was presented as a PowerPoint presentation that summarized (1) background, (2) supporting literature, (3) findings, and (4) preliminary recommendations to be included in the research statement. After the meeting, the group worked on the first draft of the research statement and conducted several teleconferences to discuss necessary changes in the content of the document. Potential conflicts of interest were managed in accordance with the policies and procedures of the American Thoracic Society.

Evidence Syntheses

PAH Registries

Registries and observational cohort studies have significantly contributed to our understanding of PAH. The National Institutes of Health (NIH; Bethesda, MD)-

supported Patient Registry for the Characterization of Primary Pulmonary Hypertension elucidated the clinical characteristics and natural history of 187 U.S. patients with primary pulmonary hypertension (now called *idiopathic PAH*) enrolled from 1981 to 1985 (1, 11). Consequently, a number of cohort studies and registries have studied predictors of outcome and survival of PAH in the modern era. These studies have focused on individual centers, consortia of centers, and entire countries (12–20). Not surprisingly, variations in patient age, sex, race/ethnicity, country of origin, medical treatments, and SES have been linked with types of PAH, response to therapy, and outcomes. Although some of these findings may be inherently explained by genetic and biological differences between patients, some are likely attributable to environmental factors, income and SES, prenatal and environmental exposures, cultural differences, diet, and availability and affordability of medical treatments. Data from registries that study such factors could direct interventions that would be further tested in randomized clinical trials to improve outcomes in high-risk patients.

Small, single-center cohort studies have suggested that race and SES may be associated with survival in PAH. A study of incident patients with PAH in the United States found that patients who were black or Asian had a higher risk of death independent of other covariates, such as cardiac index (16). Wu and colleagues studied a cohort of 262 incident Chinese patients with idiopathic PAH, which 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 (3). These findings were independent of hemodynamics and other demographics and were not explained by differences in medical treatments. Several cohort studies have shown that men with PAH have a higher risk of death than women (21, 22), explained in one study by differences in improvement in right ventricular (RV) function with PAH therapies (23). REVEAL (Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management) was a United States-based, multicenter (55 centers), 5-year observational disease registry. REVEAL

enrolled 3,515 consecutive consenting group 1 patients (2,555 previously diagnosed and 960 newly diagnosed [i.e., within 90 d of enrollment]) between March 2006 and December 2009 (12). Surprisingly, Brown and colleagues found that sex, race/ethnicity, and geographic region were not associated with time to disease recognition in PAH (24). Frantz and colleagues also identified regional heterogeneity in prostanoid use in this cohort; however, this was not explained by race or geography (25). On the other hand, in unpublished work from REVEAL, patients were stratified into ZIP code-based median income, using 2000 U.S. Census data (<\$40,000, ≥\$40,000 and <\$60,000, ≥\$60,000 and <\$80,000, and ≥\$80,000/yr). Black and Hispanic races were reported at a higher frequency in the lower two income categories (15.98 and 10.20%, respectively) compared with the two higher income categories (6.49 and 4.67%, respectively). Clinically, the highest percentage of functional classes 3 and 4 at baseline was noted in the <\$40,000 income group compared with the other income groups. Lower income groups had longer times to disease recognition: mean (±SD) of 19.2 (±45.2), 20.1 (±41.5), 18.5 (±39.8), and 17.0 (±42.1) months for the income groups <\$40,000, ≥\$40,000 and <\$60,000, ≥\$60,000 and <\$80,000, and ≥\$80,000/yr, respectively.

PAHQURI (Pulmonary Arterial Hypertension-Quality Enhancement Research Initiative) is a United States-based, multicenter (60 centers), 3-year observational disease registry of 791 patients with PAH. In PAHQURI, employment status (employed vs. unemployed or receiving disability) was identified as a predictor of 3-year mortality ($P < 0.0001$) (26). Further work examined the association between race, marital, and employment status and known prognostic PAH parameters (baseline functional class, BNP levels, and 6-min walking distance) and death. Of note, race and ethnicity were not associated with these outcomes (unpublished data).

MESA (Multi-Ethnic Study of Atherosclerosis) is an NIH-funded prospective cohort study of community-based participants without clinical cardiovascular disease at baseline, oversampled for racial/ethnic minorities (27). A subset of participants had available magnetic resonance imaging assessment of

RV size and function. There were significant differences between black, white, Asian, and Hispanic participants in RV size and function, independent of other confounders (28). Age- and sex-related differences were also seen, with older participants having smaller RV size and men having significantly lower RV ejection fraction than women (29). Genetic variants in genes in sex hormone pathways impacted on RV morphology and function in a sex- and race-specific manner (30), suggesting that possible disparities in outcome between men and women and different races and ethnicities could be attributable to differences in baseline RV morphology and/or function. Traffic-related air pollution and particulate matter also impacted on the RV (31, 32); such environmental exposures may differ across patient populations with pulmonary vascular disease, and could impact outcomes, especially in low-SES populations.

Several active registries may be useful for future studies of disparities in the care and outcomes of patients with PAH. The Pulmonary Hypertension Association (PHA) Registry is assessing adherence to guidelines, treatment patterns, quality of life, and outcomes of patients with PAH and chronic thromboembolic pulmonary hypertension, who begin their care at pulmonary hypertension care centers, accredited by the PHA for their track record in the care of patient with PAH. Self-reported race/ethnicity, primary language spoken at home, and various individual indicators of SES (including residence address) are collected in this registry. Over time, this information will be used to measure adherence to diagnostic and treatment guidelines, assess patient outcomes, improve the quality of care, and facilitate research studies in PAH and chronic thromboembolic pulmonary hypertension. Another ongoing registry is PAHQuERI Ex (PAHQuERI Extension), a United States-based, multicenter (71 centers), 3-year observational disease registry of 799 consecutive consenting group 1 patients with PAH focused on treatment practices and adherence to PAH treatment guidelines. The data collected by these registries will provide much needed insight and help identify vulnerable populations affected by health disparities.

Several features of current and future registries will be critical for studying disparities in generalizable ways. The use of common data elements ensures standardization of data (and collection

methodologies), facilitating the comparison of results across studies and the aggregation of information into meta-analyses. The collection and coding of self-determined race, ethnicity, and other factors, using consistent approaches, is necessary to ensure that data are defined in the same way, use the same standards, and employ the same vocabulary. This allows not only for generalizability to populations but also for sharing and exchange of information across registries.

As heart and lung structure and function may be impacted by events ranging from the prenatal period to old age, registries should span the life cycle (33, 34). The inclusion of children and their parents should be the norm in registries. Studies should target individuals with preclinical disease or at increased risk (e.g., systemic sclerosis) for PAH to identify potential secondary prevention approaches. Validated and standardized translations of data collection instruments and quality of life questionnaires for PAH into Spanish and other languages will be necessary to include minority populations of interest. Finally, data sharing should be the expectation for all new studies to enable collaborations across registries.

In conclusion, data supporting health disparities from PAH cohort studies and registries are sparse. The lack of consistent associations between demographic and SES characteristics and outcomes in PAH may be due to the paucity of studies focused on disparities and the limitations of the existing data. Although PAH registries are a potentially rich source of insights into health disparities, the conclusions drawn are limited by the granularity of the data on the variables of interest and their interaction. For example, race and income, although frequently used as SES indicators, are inextricable from other socioeconomic-related domains, such as education, employment, environmental exposures, diet, physical activity, and stress. Informed by learning from SES research in other disease areas, new PAH registries should examine these factors as a conglomerate of socioeconomic components (captured in a score or composite), rather than as individual, isolated parametrics.

Genetic Contributors to Health Disparities in PAH

There has been an immense expansion of knowledge that has focused on the cellular and molecular basis of PAH

pathophysiology. Among potential risk factors for the development of PAH, genetic contributors have been well documented by traditional genetic approaches. In addition, transcriptomic, epigenomic, metabolomic, and proteomic techniques are increasingly being deployed in the investigation of PAH pathobiology. These studies have clearly established the contribution of specific candidate genes to hereditary (and in some cases idiopathic) PAH such as bone morphogenetic protein receptor type II (*BMPR2*) (35–38), activin A receptor type II-like 1 (*ACVRL1/ALK1*), endoglin (*ENG*) (39), caveolin-1 (*CAVI*) (40), potassium channel two pore domain subfamily K member 3 (*KCNK3*) (41), and eukaryotic translation initiation factor 2 α kinase 4 (*EIF2AK4*) (42). Common variants of genes encoding prostacyclin and endothelin-1 pathways (43, 44), calcium signaling (45), sex hormone metabolism (46), and the endostatin gene (47) have been linked to PAH susceptibility. A genome-wide association study in patients with familial or idiopathic PAH failed to identify single-nucleotide polymorphisms that reached genome-wide association significance (48). However, in two separate cohorts, an association between PAH (with no known *BMPR2* mutations) and two polymorphisms near the gene that encodes cerebellin-2 (*CBLN2*) was reported (48). Exome sequencing has also identified variants associated with PAH susceptibility (47) and vasoreactivity (49, 50). Several published studies have used genome-wide RNA expression profiling platforms to assess pathways potentially associated with PAH and vasoreactivity (50–52). Similarly, studies suggest that abnormalities in the expression of microRNAs and activity are associated with PAH (53).

In spite of these significant advances, little is known regarding the role of genetic contributors to PAH susceptibility in minority populations, as all of the above-referenced studies used cohorts of European descent. These observations are consistent with a position report detailing a major lack of diversity in biomedical research study subjects and the significant barrier that the lack of diversity imposes to the full understanding of factors that lead to disease or health (54). There are, however, examples of studies evaluating the role of race and ethnicity in the genetic susceptibility to other lung disorders. For example, racially specific variants have been

associated with acute respiratory distress syndrome susceptibility in African American patients (55). Variants in human *MYLK* (encoding myosin light chain kinase, a key regulator of cytoskeletal dynamics and vascular permeability) were associated with increased susceptibility to acute respiratory distress syndrome and sepsis in subjects of African descent, with these single-nucleotide polymorphisms being extremely rare in non-African populations (56, 57). Racial- or ethnic-specific variants are also associated with asthma and chronic obstructive pulmonary disease susceptibility and with asthma severity both in African Americans (58–63) and Latinos (62, 64–66). Candidate gene and genome-wide association studies have not only confirmed associations between “European descent” risk variants in African Americans and Latinos but have also uncovered novel variants specific to racial and ethnic populations (58, 59, 67, 68), with rare and low-frequency variants linked to asthma susceptibility in African Americans and Latinos (69). Another important consideration is the overall contribution of ancestry to disease risk stratification and susceptibility. For example, African ancestry increases asthma susceptibility (61, 70), whereas Native American ancestry is associated with a lower risk of asthma and a greater bronchodilator response to β -agonist treatment (71–73). This is particularly evident in Latinos who have descended from Native American, European, and African populations. Asthma prevalence, morbidity, and mortality are highest in Puerto Ricans (with the highest proportion of African descent), intermediate in Dominicans and Cubans, and lowest in Mexicans and Central Americans (with the lowest proportion of African descent DNA) (74).

The integration of molecular, genomic, and clinical medicine in the postgenome era provides the promise of novel information on genetic variation and pathophysiologic cascades in PAH. The current challenge is to rapidly translate these discoveries into viable biomarkers that identify susceptible populations and facilitate the development of targeted therapies for patients with PAH. This challenge will not be fully met in an environment lacking studies evaluating the role of genetics, race, ethnicity, and magnitude of PAH susceptibility/severity in minorities. The technology to meet this challenge is now readily available; however,

given the limited nature of PAH, future studies will require a global approach involving multiple investigators and multiple, highly diverse patient cohorts. Efforts such as the National Biological Sample and Data Repository for Pulmonary Arterial Hypertension (also known as the PAH Biobank), the Pulmonary Vascular Disease Phenomics Program (PVDOMICS) in the United States, and BRIDGE-PAH in the United Kingdom represent platforms from which future studies could be launched.

Socioeconomic Status

SES is defined as an individual’s social and economic standing, and is a measure of an individual or family’s social or economic position or rank in a social group (75). It is generally a composite of several measures including income, education, occupation (including employment status), location of residence, and housing (including home amenities), and may also include participation in social organizations (75–77). Of all the measured demographics in healthcare today, SES may be the least reported but the most influential in a patient’s access to healthcare and clinical outcomes (Figure 1) (78). The United States, which uses a combination of private and government-sponsored health

insurance, is in contrast to other countries, which provide nationalized health coverage or none at all. However, despite efforts by many national governments to provide all members of society with equal access to healthcare, SES still has a profound effect on life expectancy and is still independently a risk factor for death, as higher income is associated with greater longevity (79).

Traditional SES measures include occupation, education, and income (Table 2) (80). Each of these measures captures a distinct aspect of SES, and may be correlated with other measures. Examples include occupation, employment status, education, and direct measures of family income (80). Obtaining traditional measures of SES may not always be feasible because of missed recordings, personal nature of questions, discrepancies in reporting, and instructional review board constraints. In addition, it may be difficult to assess income because of inaccurate patient reporting, employment status changes, or unforeseen circumstances. Also, as SES in epidemiological studies is often retrospective, relying on traditional measures of SES may lead to a bevy of missing data (80). Braveman and colleagues noted that there is an inherent problem in measuring SES, which could affect research

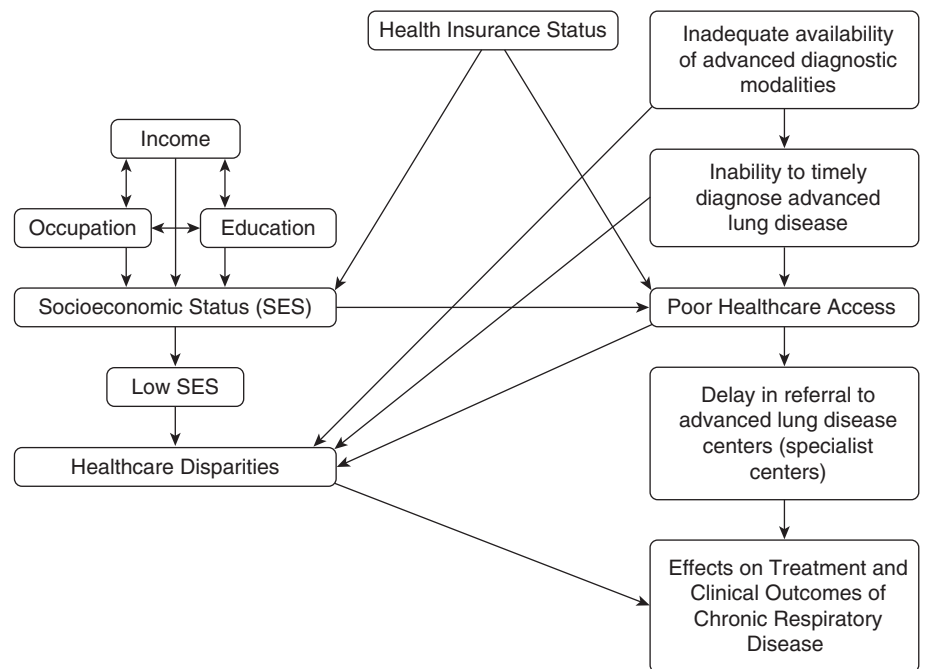


Figure 1. Proposed relationship between socioeconomic status and healthcare access in the setting of pulmonary arterial hypertension. Adapted by permission from Reference 131.

Table 2. Traditional Measures of Socioeconomic Status

-
- Occupation
 - Employment status (e.g., employed/unemployed/retired)
 - Specific occupational group
 - Aggregate occupation groups
 - Blue-collar/white-collar workers
 - Education
 - Years of education (aggregate)
 - Highest educational level completed (i.e., high school, college, etc.)
 - Credentials earned (e.g., high-school diploma, bachelor's degree, graduate degrees)
 - Income
 - Individual annual income
 - Annual household income (aggregate)
 - Family income
-

findings and conclusions with implications for practice and policy (81). For such reasons, surrogates for the measurement of SES, such as *contextual measurements*, have been formulated. Contextual measures of SES focus on ecological and geographic variables and may involve a combination of both and are more feasible to obtain. Contextual approaches to SES examine the social and economic conditions that affect all individuals who share a particular social environment. Examples of contextual measures of SES may be at the neighborhood level and include ZIP codes, census tracts, census block groups, or census blocks (80).

PAH and SES. Despite the development of numerous therapies over the past 20 years, the delay to diagnosis has not decreased over the past three decades (1, 82). Although its role has not been as exhaustively explored in PAH, SES is associated with more severe disease at presentation (83). A study by Talwar and colleagues (83) showed that as median income decreased, the WHO functional class at presentation of both patients with PH and patients with PAH increased. This association between median income groups and WHO functional class at initial evaluation was statistically significant. One possible reason for the delayed diagnosis and more severe disease at presentation for lower SES individuals may be reduced access to advanced diagnostic procedures such as right heart catheterization (84).

SES not only plays a role in the diagnosis and treatment of the disease, it also has a profound effect on the clinical outcome of these patients. In a study by Wu and colleagues, it was found that lower SES was strongly associated with a higher risk of

death in PAH. Patients who were considered to have lower SES had a higher unadjusted mortality rate, with 3-year survival estimates of 50.1, 70.8, and 86.0% in increasing tertiles of SES (3). After adjustment for age, sex, clinical features (WHO group), hemodynamics, and type of PAH therapy, the hazard ratios for death were 2.98 (95% confidence interval, 1.51–5.89) in the lowest tertile of SES and 1.80 (95% confidence interval, 0.89–3.63) in the middle tertile of SES compared with the upper tertile (*P* for trend, 0.006). What this study highlights is that despite disease severity, hemodynamics, or treatment type, patients with lower SES have a higher risk of all-cause mortality in PAH.

SES: measurement and unequal treatment subsections. Determining how key determinants of health are measured and presented as medical and insurance data has been of interest to the National Research Council of the National Academies. In their report entitled *Eliminating Health Disparities: Measurement and Data Needs*, the National Research Council highlighted the importance of these data in understanding health disparities, generally accepted measures of these determinants, and the collection of these data by the Department of Health and Human Services (HHS), state-based agencies, and private-sector organizations (85). The HHS collects key determinant data in medical data primarily through surveys or administrative data systems. Surveys such as the National Health Interview Survey also serve as a sampling frame for the Medical Expenditure Panel Survey and the National Survey of Family Growth, which allow for data linkage. Each of these surveys collects the following categories of race: White,

Black, Asian, American Indian or Alaska Native, or Native Hawaiian or Other Pacific Islander. Respondents may also indicate multiple categories of race or Hispanic ethnicity. Some surveys, such as the National Health Interview Survey and the National Immunization Survey, allow respondents to choose an Asian or Latino nationality. With respect to SES, all three of the aforementioned surveys collect data on employment status, occupation, sources and amounts of income, and education levels. The Medical Expenditure Panel Survey also collects data on wealth by asking about the estimated value of assets and debts. Collection of language use and acculturation data in these surveys is typically limited to items such as place of birth, country of origin, and language spoken at home or language of interview.

Provider-based surveys are conducted among hospitals, physicians' offices, and clinics. Data records are prepared in conjunction with the service provided. HHS surveys include the National Ambulatory Medical Care Survey, National Hospital Discharge Survey, Healthcare Cost and Utilization Project, and the National Home and Hospice Care Survey. In these surveys, race and ethnicity data may be collected by staff from the record or sometimes by asking the patient about their race and ethnicity. Missing data are common in provider-based surveys as well. The prevalence of missing race and ethnicity data can range between 20–40% and 30–87%, respectively, depending on the survey.

The collection of SES data in provider-based surveys is limited at best. The reason for collecting such data is to ensure payment for the service provided. This may include information that pertains to the individual or the government program in which the individual is enrolled. In addition, provider-based surveys rarely collect data on acculturation and language use. The only survey that does, the National Survey of Substance Abuse Treatment Services, collects data on the language offered in treatment services. For rare diseases, such as PAH, one of the challenges of a national survey is sample size. Typically, national surveys do not employ a case-control study design, therefore making it difficult to assess PAH. A cost-effective solution to this would be to include a supplemental survey of individuals with PAH in national surveys. Medicare data has provided

researchers an opportunity to study health disparities for decades. The primary source of racial/ethnic data linked to Medicare records is the Medicare Enrollment Database (EDB). Race/ethnicity in the EDB is obtained from the Social Security Administration (SSA). However, racial/ethnic data are not available for all Medicare enrollees, and racial/ethnic categories have changed over time. For registrants after 1989, no racial/ethnic data were collected because race/ethnicity on birth certificates was deemed unnecessary by the SSA. However, if an individual has applied for a new social security number or changed his or her name, using an SS-5 form, then racial/ethnic data would have been collected. Until 1980, categories of race/ethnicity included White, Black, Other, and Unknown for those not reported. Since 1980, race/ethnicity has been categorized into White, Non-Hispanic; Black, Non-Hispanic; Hispanic; North American Indian or Alaska Native; and Asian, Asian American, or Pacific Islander. However, data by these categories were collected only for individuals who filled out an SS-5 form. In 1994, racial/ethnic data from SS-5 forms were integrated into records to correct and fill in missing information. This integration reclassified 30% of individuals to a new race/ethnicity. Updates were repeated in 1997, 2000, 2001, and further planned annually. In 1997, a postcard survey was mailed to enrollees with Latino surnames and with "Other" or "Missing" race codes. Forty-three percent of postcard recipients responded to the survey. In addition, race was also obtained from beneficiary-level information from 32 states for Medicaid enrollees as well as from the End-Stage Renal Disease Medical Evidence Report. However, high levels of misclassification of race/ethnicity have been reported when compared with the Medicare Current Beneficiary Survey, a household survey of HHS. Interestingly, the lowest levels of misclassification occurred among white or black individuals.

Data on SES are not collected by Medicare, but socioeconomic status can be estimated by merging SSA earnings data with EDB data. However, there are certain problems with this estimation. First, this applies only to jobs that are covered by Social Security. Therefore, data may not be obtained for some immigrant populations with undocumented earnings. Second, it is

not a reliable measure of lifetime income for individuals who did not work their entire lifetime in the United States. Third, it does not capture wealth, which may be significant compared with earnings. This is particularly relevant for spouses who worked very little but who have substantial wealth from their working spouses, and/or for divorced spouses who worked little while married. Last, for individuals who meet the maximum earnings for Social Security, actual earnings are not reported. Neither acculturation nor language data are collected by these data sources. Other resources such as the Medicare Current Beneficiary Survey and the Medicare Satisfaction Survey of the Consumer Assessment of Health Plans Survey (CAHPS-MSS) ask about race/ethnicity and socioeconomic status. CAHPS-MSS also collects data on acculturation and language use. Both sources rely on administrative data, which reduces the problem of misclassification dramatically. Other public insurance data sources, such as the Indian Health Service, collect demographic data but do not assess socioeconomic status or language use. State-based collection of medical and insurance data includes the Vital Statistics Birth and Death Records, Hospital Discharge Abstracts, and Medicaid and the State Children's Health Insurance Program. In the Vital Statistics Birth and Death Records, the reporting of race/ethnicity, education level, and country of origin or parents are standardized. However, death certificates do not contain country of origin or language use. Race/ethnicity categories for Asians are improved beyond traditional categories mentioned above to include separate Asian categories, separate Pacific Islander categories, and a "Specify" line for tribe. Hispanic ethnicity was recommended to be added as additional data. With respect to misclassification, white individuals are misclassified the least and nonwhite individuals were misclassified significantly more often. The worst rates of misclassification were among American Indian and Alaska Native populations, Asians and Pacific Islanders, which were often misclassified as White. Hospital Discharge Abstracts are mandated by 37 states, 27 of which include nonstandardized methods of collecting race/ethnicity. Data in the Healthcare Cost and Utilization Project, the national-level data set for hospital discharge data, vary by state level.

This often leaves race/ethnicity data incomplete and inconsistently formatted.

With the limited data that we have regarding PAH, it is imperative that further research be conducted to determine the effect of SES on these patient populations. There seems to be a profound effect of SES on disease severity and clinical outcomes in PAH. It is plausible that lower SES patients also suffer from lack of healthcare supportive services. In general, it is believed that these patients will benefit from support group prescription (86), but other interventions may be required to address the challenges posed by PAH.

Environmental Stressors and Pulmonary Vascular Disease

There is a paucity of data examining the impact of the physical and social environment on pulmonary vascular disease. Exploring the contributions of environmental stressors has the potential to be a useful endeavor for improving our understanding of the mechanisms underlying this disease, and for highlighting some strategies to prevent or slow the progression of disease.

Air pollution. Outdoor and, to a lesser extent, indoor air pollution has been shown to increase risk of morbidity and mortality associated with cardiopulmonary diseases such as myocardial infarction, stroke, arrhythmia, heart failure, chronic obstructive pulmonary disease, and asthma (87). This relationship may be even more pronounced in developing nations that lack environmental protection plans; findings from the Health Effects Institute (Boston, MA) demonstrate that ambient particulate matter and household air pollution are now the fourth and fifth leading causes of death in East Asia (88). However, much less is known about the relationship between ambient pollution and pulmonary vascular disease (89, 90). There is a strong rationale for a link between specific types of air pollution, such as particulate matter, and vascular disease (91). Prior epidemiologic and basic studies have demonstrated hypercoagulability in response to particulate matter exposure, evidenced by increased plasma levels of factor VIII, von Willebrand factor, and fibrinogen (92, 93). Air pollution may also influence RV structure and function, independent from underlying cardiovascular disease. As shown by Leary and colleagues, using cardiac magnetic resonance imaging from a

large cohort of patients in MESA Air (Multi-Ethnic Study of Atherosclerosis and Air Pollution), exposure to nitrogen dioxide was associated with increased RV mass and larger RV end-diastolic volume (32). However, whether exposure to air pollution in general or to specific components influences the risk of development of PAH or is a disease modifier remains to be demonstrated.

Diet/nutrition. A wealth of data indicates that types of diet are associated with either protective or damaging effects on cardiovascular health. The mechanism of the effect of diet on cardiovascular function is not completely understood, but is thought to be mediated through oxidative stress and resultant endothelial dysfunction. Comparably fewer data exist regarding the association between diet and pulmonary vascular disease and, unfortunately, these data are conflicting. Nutrient deficiencies have been associated with PAH and are implicated in the pathogenesis of pulmonary vascular remodeling. Specifically, iron deficiency has been implicated in the pathogenesis of pulmonary vascular remodeling (94, 95). Clinical associations between iron deficiency, even in patients without overt anemia, and severity of PAH have been reported (96, 97). A clinical trial of supplemental iron in idiopathic PAH is currently ongoing (98).

Medical Education: Educating Providers, Raising Awareness, and Addressing Implicit Bias

Racial and ethnic minority patients tend to receive a lower quality of healthcare than white patients (99). The sources of these disparities are complex and multifactorial, and involve the patients, health systems, and healthcare providers (99). When sociocultural differences between patient and provider are not appreciated in the medical encounter, the result is patient dissatisfaction, poor adherence, poorer health outcomes, and racial/ethnic disparities in care (100–105). There is a paucity of data specifically looking at health disparities in minority populations of patients with PAH, but one can assume the negative effects are similar to those of other chronic diseases such as cardiovascular disease and cancer.

Physician bias toward certain racial or ethnic groups is a real problem and has been described. In a study by Schulman and colleagues, physicians who were asked to

recommend treatment for hypothetical patients of varying races and sexes were found to recommend cardiac catheterization significantly less often for black females than for any other group of patients with the same symptoms, after controlling for the physician's assessment of probability of coronary arterial disease, age of patient, level of coronary risk, type of chest pain, and exercise test results (106). In another study examining the association between pediatricians' attitudes toward race and prescribing medications, there was the presence of a pro-white bias, as participants implicitly associated African American patients with nonadherence despite absent explicit biases. In addition, postsurgical narcotic medications were prescribed less frequently for African American children with pain, again associated with a pro-white bias (107). These implicit (or "unconscious") biases of physicians are pervasive throughout society, and therefore not unexpected among physicians.

There are many potential reasons why healthcare providers in settings with large number of minority patients may not be aware of PAH. Providers may miss the diagnosis because of the presence of more common diseases such as obesity, asthma, diabetes, heart failure (both with reduced or preserved ejection fraction), and drug or tobacco use (6). There are also challenges associated with obtaining accurate histories because of language and/or cultural barriers. Last, providers may have more difficulty getting studies (echo, right heart catheterization) approved and/or scheduled (6). Furthermore, minority patients with PAH are frequently seen in emergency departments where they use healthcare resources, but are not referred for specialist care (108, 109). Solution strategies include developing educational strategies aimed at specifically targeting healthcare providers in these settings, and emphasizing the role of early diagnosis and early referral. Strategies should also include educating healthcare providers about unique triggers of PAH in their patient populations, such as environmental exposures, substance abuse, and comorbidities and associated conditions. Furthermore, education should focus on emphasizing the frequent occurrence of PAH/PH in left heart disease, chronic lung disease, sleep-disordered breathing, cirrhosis, drug abuse, and HIV infection. Strategies that allow for timely referral of patients with suspected PAH/PH

to a specialist should be identified and emphasized. Last, strategies should be developed to make insurance companies aware that advanced treatment methods, although expensive upfront, will pay off in the long term in the form of reduced admissions, emergency department visits, and overall healthcare use. For example, several PAH medications have been shown in studies to reduce hospitalizations and use of expensive healthcare resources (110–112). The Pulmonary Hypertension Association's Early Diagnosis Campaign is addressing many of these issues for the general population; this existing framework could be modified to specifically address the needs and challenges of providers and emergency room physicians in areas with large numbers of minority patients.

There is also evidence that sociocultural differences between patient and provider influence communication and clinical decision making (113). Evidence suggests that provider-patient communication is directly linked to patient satisfaction, adherence, and subsequently, health outcomes (102). The gaps that are present in physician understanding of health disparities include lack of time, difficulty with a language barrier, no formal training in health disparities education, and personal biases that can affect judgment in the decision-making process. Sociocultural factors are critical to the medical encounter, yet cross-cultural curricula have been incorporated into undergraduate, graduate, and continued health professions education only to a limited degree (114). A meta-analysis conducted by the Agency for Healthcare Research and Quality, consisting of a systemic review of 91 articles that measured the impact of cultural competence training on the quality of care provided to minority patients, found that this training yielded improvement in provider knowledge, attitudes, and skills in this area, as well as improvements in patient satisfaction (115). Cross-cultural training of healthcare providers also provides a medium for educating providers on how to interact with minorities (114, 116, 117). In particular, technology-based learning (e-learning) is a powerful and effective tool for cross-cultural education at all levels (115). It allows for extensive training of a large group of learners in a short amount of time to achieve a uniform set of skills (115). In the current healthcare environment of limited time and financial

resources, e-learning provides an excellent mechanism for extensive, high-quality cross-cultural education for medical students, residents, and practicing clinicians (115). However, there have been challenges to cross-cultural curricula, with resistance to curricula that are viewed as “soft” or lacking an evidence base (116). To enhance and improve the medical education curriculum, it is critical and necessary to expose medical students to free clinics, underserved populations, and health disparities in a community (118). One example of how this can be performed was provided by a study that evaluated whether quality improvement interventions improve care and outcomes for minority patients suffering from depression (119). This study randomized 46 primary care practices to usual care or a quality improvement program. Providers in the intervention group were exposed to trained local experts who educated clinicians and taught workshops on depression treatment models. Participating clinicians also received written manuals, and access to monthly lectures and meetings (119). In addition, intervention group providers were exposed to trained local psychotherapists who provided cognitive behavioral therapy, and trained local nurses to serve as depression specialists to educate, assess, and monitor patients. Last, the intervention group also included a workshop where participants received materials (written and video) to educate patients (119). All materials were in English and Spanish, and Latino and African American providers were featured in the educational videos. Providers received information regarding cultural beliefs and ways of overcoming barriers (119). A secondary aim of this study was to ensure inclusion of minorities. The results demonstrated that patients in the intervention group were more likely than control subjects to receive counseling or use antidepressants (50.9 vs. 39.7%; $P < 0.001$) and less likely than control subjects to meet criteria for depression (39.9 vs. 49.9%; $P = 0.001$) (119). Thus, health disparities education could improve provider-patient communication and help eliminate the pervasive racial disparities seen in medical care today (120).

Patient Education

The population groups within which disparities exist are multidimensional. Perhaps the most historically studied and

legislatively focused, however, have been population groups defined by race and ethnicity. In 2002, the Institute of Medicine issued a report, *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*, which concluded that racial and ethnic minorities tend to receive a lower quality of healthcare than nonminorities (121). This report set out to assess the extent of racial and ethnic differences in healthcare, and to evaluate the potential role of bias, discrimination, and stereotyping at the level of the patient-provider interaction as well as at the institutional and health system levels.

The role of the interaction between the healthcare provider and patient has been described as a crucial source of healthcare disparity. As we start from the perspective of the patient, it has been described that minority patients are more likely to follow medical advice if the treating physician is also from a minority background (104). In the study by Cooper-Patrick and colleagues (104), when adjusted for patient age, sex, education, marital status, health status, and length of visit, patients rated their recent primary care visit as more participatory with race-concordant physicians than with race-discordant physicians. In turn, patient satisfaction was highly associated with participatory decision making. In a Kaiser Northern California study, identified predictors for patient-physician race concordance included patients' ability to choose their physician, limited English proficiency, and availability of minority physicians, particularly for African American and Hispanic groups (122). This suggests that, if available, patients tend to choose their physician based on similar race and language proficiency. Reasons for patients to trust and seek out a physician of a similar race or ethnicity include concerns regarding communication and decreasing the language barrier, as well as the increased likelihood of empathic treatment and joint decision making if a patient's physician shares the same background (123).

In addition to the patient-physician interaction, health and healthcare disparities stem from more global and systemic barriers to providing care. In a study by Morrison and colleagues, in a random selection of 30% of New York City pharmacies, only 25% of nonwhite neighborhood pharmacies supplied a sufficient amount of opioids to treat severe pain, compared with 72% of white

neighborhood pharmacies (124). Moreover, the use of professional interpreters is associated with improved patient understanding of disease and appears to raise quality of clinical care for non-English-speaking patients toward the level of care for patients without language barriers (125, 126). At present, there are policy and governmental forces in place to legislate for improvement in more equal access to care and services such as language services. As an example, in 2010, HHS established the HHS Disparities Action Plan to reduce racial and ethnic health disparities. This called for increased funding for availability of influenza vaccinations to uninsured populations, increased numbers of grants available for more data collection on the health of vulnerable populations, and the provision of blueprints and standards for healthcare organizations to implement culturally and linguistically appropriate services (127).

Patient education can be achieved through the provision of educational material in languages other than English, ideally free of charge. Patients are often hesitant to report symptoms, and a paternalistic approach to medicine may still be prevailing. To alleviate this, the PHA existing toolkit for self-advocacy should be refined to better serve these patients, thus enabling patients to ask better disease-specific questions through better understanding of their disease process. Community outreach can raise awareness through health fairs that not only educate about the disease, but also target subspecialists (pulmonologists/cardiologists). However, to do so, there must be a concerted effort and support from local governments and major professional societies alike (101, 128).

Health Policy

In 2000, the Minority Health and Health Disparities Research and Education Act of 2000, the first major legislation focused on reduction of disparities, created the National Institute on Minority Health and Health Disparities (NIMHD) within the NIH. The vision of the NIMHD is “an America in which all populations will have an equal opportunity to live long, healthy, and productive lives.” To accomplish this, the NIMHD raises national awareness about the prevalence and impact of health disparities and disseminates effective individual-, community-, and population-level interventions to reduce and encourage elimination of health disparities (129). The work of the NIMHD to improve inclusion of

health disparity concerns in research includes a strategic plan that focuses on three key elements to be considered at all NIH centers: (1) conduct and support intensive research on the factors underlying health disparities; (2) expand and enhance research capacity to create a culturally sensitive and culturally competent workforce; and (3) engage in aggressive, proactive community outreach, information dissemination, and public health education.

In 2011, in collaboration with the NIMHD, the Department of Health and Human Services developed the HHS Action Plan to Reduce Racial and Ethnic Health Disparities. The HHS Disparities Action Plan sets out a series of priorities, strategies, actions, and goals to achieve its vision of “a nation free of disparities in health and health care.” Within the department, the Office of Minority Health is charged with advancing the goals of the HHS Disparities Action Plan:

- Transform healthcare
- Strengthen the nation’s health and human services infrastructure and workforce
- Advance the health, safety, and well-being of the American people
- Advance scientific knowledge and innovation
- Increase the efficiency, transparency, and accountability of HHS programs

An executive summary of progress to date has highlighted the achievements thus far, to include support of Medicaid expansion under the Affordable Care Act (ACA); support of the CMS program, Care to Coverage; and expanded efforts to inform both patients and healthcare providers of coverage opportunities and identify specific covered programs of benefit to the enrollees. The action plan has also supported efforts at increasing transparency such that data can be accessed to track changes in these health system characteristics over time and to identify areas that require improvement through the Health System Measurement Project. Important provisions in the ACA target health disparities beyond coverage opportunities for uninsured. These efforts mirror those outlined in the HHS Disparities Action Plan above. Importantly, under the ACA, the rates of uninsured have fallen the most in African American and Hispanic populations. African Americans are much more likely than white persons to fall into the coverage gap in the states that have not expanded Medicaid under the ACA.

Regional, state, and local efforts at limiting health disparities are key in decreasing health disparities through local efforts using regional and community-focused interventions. These local interventions can be broad, addressing a region or state; or focused, addressing health disparities in a single neighborhood. Grants previously funded through the Community Transformation Grants program with the Centers for Disease Control and Prevention, Division of Community Health, along with currently funded grants titled Racial and Ethnic Approaches to Community Health (REACH) grants, have provided states, local health departments, universities, and nonprofit groups funds to support local efforts to address health disparities. Community-based foundations also contribute resources to developing initiatives aimed at reducing disparities.

The PHA was created in 1991 by patients with a need to connect with other members of the patient community. In 25 years, the organization has grown to more than 16,000 members nationally, with an annual budget of more than 12 million dollars, and a research portfolio of over 17 million dollars. Traditionally, the PHA has focused its advocacy efforts primarily on legislative and grassroots activities. This has played out both through the efforts described above and those in support of the Pulmonary Hypertension Research and Diagnosis Act, which the organization has worked to pass at the federal level. The PHA’s overall advocacy efforts have focused on impacting patient outcomes, supporting work to find a cure and identify new treatments, and also working to remove barriers, while the grassroots have focused primarily on the PAH bill.

Throughout the organization’s history, members of the PHA’s medical and patient communities have lobbied members of Congress for their support of the PH bill, and in favor of other legislation put forth by coalitions of organizations in support of specific issues impacting patient care. To date, efforts supporting the most PAH-specific of the PHA’s legislative priorities, passage of the Pulmonary Hypertension Research and Diagnosis Act, have resulted in increased awareness among legislators of PAH and the needs of the PAH community, but have yet to result in the passage of the target legislation. Those opposed state that they are averse to disease-specific legislation. Further, in a

climate of continued cutbacks in NIH funding—NIH funding has either been cut or unable to outpace inflation in all but two of the past 14 years—getting the bill passed has proven difficult, even though the legislation itself is budget neutral (130). Despite this resistance, the PHA remains committed to address minority-specific challenges through *PH Care for All*, an initiative that aims to identify and improve on gaps in early diagnosis and treatment for minorities living with PH. The goals of *PH Care for All* are as follows.

Expand legislative advocacy effort to include state and local leaders. Many of the decisions most impacting the target population of *PH Care for All* are actually made at the state and local levels, rather than at the federal level. This is an advantage, as it is typically easier to impact state and local legislators via grassroots efforts, as they are less removed from their constituents than their federal counterparts. *PH Care for All* could be most impactful at this level by advocating for policies related to logistical issues in turn related to diagnostic and treatment access, such as business hours of health clinics and services, availability of interpreter services at health clinics, transportation subsidies for low-income patients, and so on. In addition, Medicare/Medicaid coverage and issues related to third-party payers are more rightly addressed at this level.

Traditionally, the PHA’s state and local advocacy efforts have been largely one-off and conducted by members of the PHA community with varying degrees of success. Organized expansion in this direction would likely call for the development of a core group of trained advocates; the PHA has some infrastructure to support this, in the form of more than 200 volunteers passionate about advocacy. In addition, the PHA has forged a successful relationship with Women in Government, an organization supporting female state legislators. Engagement with this organization and others like it, including the National Conference of State Legislatures, could potentially lead to an increased impact at this level while maximizing the resources available to the PHA. Also, administrative advocacy will afford the PHA the opportunity to influence the rules and regulations that shape a law as it is implemented. For this reason, in addition to seeking amendment to laws that are disadvantageous to the

target population, attention should be given to new legislation intended to positively impact minorities.

Recommendations

1. PAH registries must be organized to reliably capture information concerning race/ethnicity and SES of patients.
2. Genetic screening of large populations should include patients with PAH belonging to minority groups and address the existence of unique genetic determinants.
3. SES should be included in the risk stratification to help identify patients with PAH who may be at greatest risk for noncompliance.
4. Hospitals, health insurers, and providers should be educated on the importance of data on key determinants of health and encouraged to increase their efforts to collect data such as SES as well as race/ethnicity.
5. Partnership with public health divisions, community-based health centers, and existing heart failure outreach programs should be encouraged to collect relevant data concerning adverse environmental exposures and clinical outcomes on vulnerable PAH populations.
6. A cross-cultural curriculum should be mandatory and implemented early in medical training. The PHA and other patient-centered organizations, with the help of specialists in the field, should develop more educational resources for patients and providers in minority communities.
7. Cross-cultural competence needs to be framed as a skill set—similar to a review of systems, or checklist—that can help providers manage challenging cross-cultural cases. It must be seen as (a) practical, actionable, and time efficient, (b) should be taught in a case-based fashion that creates clinical challenges, (c) must be linked to evidence-based guidelines and the peer-reviewed literature, and (d) must leave students with a concrete set of tools and skills.
8. Formal training courses should be developed that address health disparities and cross-cultural competency through online training/modules for accreditation. An ideal educational program would target both providers and patients, and would need to be tailored for PAH-specific needs.
9. Increase awareness among physicians regarding the impact of implicit or unconscious bias toward particular population groups in the setting of PAH.
10. Increase the amount of racial and ethnic minority physicians in the healthcare provider workforce to promote race- and language-

concordant patient–physician interactions.

11. Legislate governmental standards regarding access to cultural- and language-appropriate services across all healthcare organizations.

Conclusions

PAH is a rare but devastating disease that, if untreated, is associated with reduced quality of life and poor outcomes. Minorities in the United States are likely at high risk of poor outcomes due to lack of proper access to healthcare and limited resources to assist them in living with the disease. The limited number of research studies to date has slowed our progress in understanding the impact of health disparities and the development of effective strategies to overcome these barriers to proper healthcare. Our proposed research recommendations represent the first effort to address these issues and improve the quality of care of this vulnerable population. Despite being limited to WHO group 1 patients in the United States, this research statement is expected to serve as a platform for discussions regarding the impact of health disparities in any population and should guide researchers to look into their country's health system for barriers to healthcare. We envision that another research statement could be prepared with the collaboration of professionals from around the globe. ■

This official statement was prepared by an *ad hoc* subcommittee of the Pulmonary Circulation Assembly.

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