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An American Thoracic Society/National Heart, Lung, and Blood Institute Workshop Report: Addressing Respiratory Health Equality in the United States

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THIS OFFICIAL WORKSHOP REPORT OF THE AMERICAN THORACIC SOCIETY (ATS) AND THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI) WAS APPROVED BY THE ATS, March 2017, AND BY THE NHLBI, OCTOBER 2016

Abstract

Health disparities related to race, ethnicity, and socioeconomic status persist and are commonly encountered by practitioners of pediatric and adult pulmonary, critical care, and sleep medicine in the United States. To address such disparities and thus progress toward equality in respiratory health, the American Thoracic Society and the National Heart, Lung, and Blood Institute convened a workshop in May of 2015. The workshop participants addressed health disparities by focusing on six topics, each of which concluded with a panel discussion that proposed recommendations for research on racial, ethnic, and socioeconomic disparities in pulmonary, critical care, and sleep medicine. Such recommendations address best practices to advance research on respiratory health disparities (e.g., characterize broad ethnic groups into subgroups known to differ with regard to a disease of

interest), risk factors for respiratory health disparities (e.g., study the impact of new tobacco or nicotine products on respiratory diseases in minority populations), addressing equity in access to healthcare and quality of care (e.g., conduct longitudinal studies of the impact of the Affordable Care Act on respiratory and sleep disorders), the impact of personalized medicine on disparities research (e.g., implement large studies of pharmacogenetics in minority populations), improving design and methodology for research studies in respiratory health disparities (e.g., use study designs that reduce participants' burden and foster trust by engaging participants as decision-makers), and achieving equity in the pulmonary, critical care, and sleep medicine workforce (e.g., develop and maintain robust mentoring programs for junior faculty, including local and external mentors). Addressing these research needs should advance efforts to reduce, and potentially eliminate, respiratory, sleep, and critical care disparities in the United States.

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The findings and conclusions in this report are those of the authors, and do not necessarily represent the views of the National Institute for Occupational Safety and Health or the National Institutes of Health.

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Health disparities can be defined as significant differences in healthcare or outcomes across groups of people who have experienced greater obstacles to health based on their: racial or ethnic group; socioeconomic status (SES); religion; sex; age; occupation; mental health; cognitive or physical disability; sexual orientation; or other characteristics historically linked to discrimination or exclusion. Such disparities explain why the approximate 9-year gain in average life expectancy in the U.S. population over the last four decades has not equally benefited all Americans (1).

Respiratory health equality, the attainment of the highest level of respiratory health for all people, is an ideal and an ultimate goal of the American Thoracic Society (ATS) and the National Heart, Lung, and Blood Institute (NHLBI). This goal is not only morally imperative, but also cost effective, as one study estimated that health equality could have saved at least 1 trillion dollars in direct and indirect healthcare costs from 2003 to 2006 (2). Moreover, efforts to attain health equality (e.g., in influenza vaccination rates [3]) can ultimately benefit all members of our society.

Because achieving equality in respiratory health entails the elimination of health disparities in diseases commonly found in pediatric and adult pulmonary, critical care, and sleep medicine (heretofore referred to as “respiratory health disparities,” for ease of exposition), a necessary step

toward equality is to identify and address the causes of such disparities (4).

Both the ATS and the NHLBI recognize the value of bringing together a diverse group of investigators to develop a consensus on research needs in respiratory health disparities, with an emphasis on racial, ethnic, and socioeconomic disparities. To encourage and facilitate state-of-the-art research on such disparities, the ATS and the NHLBI held a workshop focused on the topic on May 16, 2015.

Conceptual Framework

Respiratory health disparities can result from differences across demographic groups at any stage of the causal pathway leading to disease (Figure 1). Within this causal framework, “upstream” factors are “root causes” of an individual’s exposures to environmental risk factors for respiratory diseases. For example, racism or low SES can influence the neighborhood where a family lives. In turn, area of residence determines indoor and outdoor air quality, which can impact the development or severity of asthma (5, 6).

Environmental exposures and behavioral patterns often differ across demographic groups defined by race/ethnicity or SES, leading to most respiratory health disparities. Major risk factors for such disparities include tobacco use, air pollution, occupational hazards, and obesity (4). Racial

or ethnic groups also have different frequencies for alleles that affect the respiratory system (e.g., sickle cell disease) or are associated with sleep apnea, interact with environmental exposures in causing respiratory disease (e.g., tobacco use and severe α_1 -antitrypsin deficiency in chronic obstructive pulmonary disease [COPD]), or affect response to treatment (e.g., inhaled β_2 -agonists in asthma), all of which have implications for personalized medicine (7–9).

Racial, ethnic, and socioeconomic inequities in healthcare access can cause or worsen respiratory health disparities. Policies aimed to increase healthcare access have shown early potential to reduce health disparities, including those for outcomes in critically ill patients (10–13). However, health insurance does not address other barriers to care, including low health literacy, hurdles to adherence to treatment or adoption of healthy behaviors, and a profound shortage of physicians belonging to underrepresented minority (URM) groups (African Americans, Hispanics, Native Americans or Alaska natives, Hawaiian and Pacific Islanders), who were recently estimated to provide healthcare to 53.5% of minority populations (14).

Workshop Agenda

The workshop participants focused on six topics, each of which concluded with

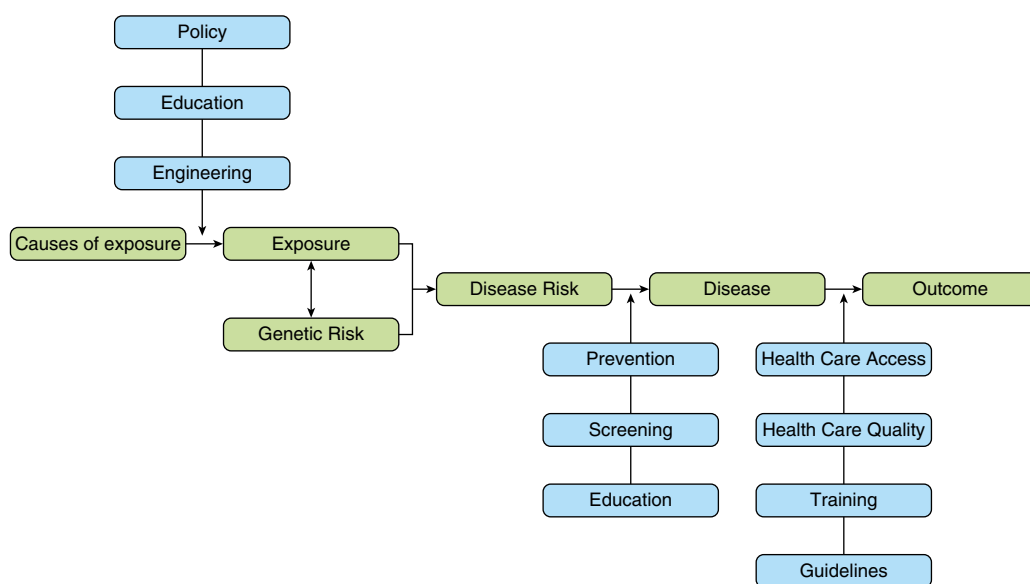


Figure 1. Causal framework for respiratory diseases. Group differences at any stage in this pathway can lead to respiratory health disparities. Reprinted by permission from Reference 4.

Table 1. Key recommendations for research on racial, ethnic, and socioeconomic disparities in pulmonary, critical care, and sleep medicine

Research Need	Recommendations	Examples	Author, Year (Reference No.)
General guidelines for assessment of race and ethnicity	Characterize broad ethnic groups into subgroups known to differ or potentially differ with regard to the disease of interest Consider measuring genetic ancestry in racially admixed populations, using AIMs	Divide Hispanics into major subgroups according to self-reported place of origin (e.g. Mexican Americans, Puerto Ricans, Cuban Americans, Dominicans) Assess continental or subcontinental ancestry (e.g., African, Native American, and European) in studies of lung function or obstructive airway diseases in African Americans and Hispanics, using AIMs Use of the McArthur sociodemographic questionnaire, which captures data on resources, prestige, and perceived social status within the community	Rosser and colleagues, 2014 (17) Kumar and colleagues, 2010 (18) Bruse and colleagues, 2011 (19) Chen and colleagues, 2014 (20) Pino-Yanes and colleagues, 2015 (21)
General guidelines for assessment of social and economic status	Assess both social and economic status (at the individual, family and community levels) using validated instruments, while also measuring chronic stressors (with the extent of assessment determined by the primary research focus)	Use of the McArthur sociodemographic questionnaire, which captures data on resources, prestige, and perceived social status within the community	www.macses.ucsf.edu/research/psychosocial/subjective.php
Examining acculturation in studies of migrant populations	Capture basic measures of acculturation in all studies of migrant populations Use comprehensive measures of acculturation for in-depth studies	Capture socioeconomic indicators at the community level (e.g. census-track poverty, violence rates, access to healthy foods) Always include place of birth, place of origin, self-reported race/ethnicity, duration of residence in the adoptive country, and fluency in English BAS, AHIMSA	Chen and colleagues, 2013 (24) Ramratham and colleagues, 2015 (25) Vangeepuram and colleagues, 2012 (26)
Characterization of modifiers of the effects of pollution on respiratory health	Estimate the effect of interactions between pollution and other risk factors on respiratory health disparities Create models integrating tobacco exposure throughout life stages and addiction risk	Psychosocial stress Indoor pollutants Extrinsic neighborhood factors Longitudinal birth cohort studies with biomarkers of both exposure to tobacco smoke and susceptibility to addiction	Sundquist and colleagues, 1999 (32) Eldeirawi and colleagues, 2005 (34) Holguin and colleagues, 2005 (35) Marin and Gamba, 1996 (109) Unger and colleagues, 2002 (110)
Better knowledge of the biologic/social basis of nicotine addiction and susceptibility to the effects of tobacco use	Study the impact of e-cigarettes, hookah or new tobacco products on respiratory diseases in underserved populations	Longitudinal studies of adolescents and young adults	Clougherty and colleagues, 2007 (37) Chiu and colleagues, 2013 (39) McCormack and colleagues, 2015 (40) Rydell and colleagues, 2016 (111)
Understanding how new modalities of tobacco or nicotine use affect the respiratory health of minorities and the poor	Incorporate basic measures of occupation and the workplace in all studies of minorities of working age, with use of more in-depth tools in studies focusing on occupation	Current and former employment status, number of hours worked, job type (using standard classifications)	Rath and colleagues, 2016 (112) Bolund and colleagues, 2015 (113)
Gaining knowledge about interactions between occupational and environmental risk factors on respiratory health disparities	Design and implement longitudinal studies of obesity and respiratory/sleep health, as well as culturally targeted interventions to prevent and treat obesity, in minority populations	Studies of obesity and obstructive sleep apnea within the large HCHS/SOL	Cade and colleagues, 2016 (9) Redline and colleagues 2014 (114)

(Continued)

Table 1. (Continued)

Research Need	Recommendations	Examples	Author, Year (Reference No.)
Measuring the impact of increased healthcare access on respiratory health disparities	Conduct longitudinal studies of the effects of the ACA on diseases encountered in pulmonary, critical care and sleep medicine among URMIs and economically disadvantaged populations	Follow-up studies of the impact of the ACA on smoking cessation, morbidity from asthma, and treatment for lung cancer	Sommers and colleagues, 2015 (11) Sommers and colleagues, 2012 (12) Baicker and colleagues, 2013 (13)
Improve adherence and literacy in minority and economically disadvantaged populations	Develop and test culturally targeted interventions to improve adherence to treatment for pulmonary and sleep diseases in minority and economically disadvantaged populations, incorporating cultural norms and beliefs, and addressing pragmatic barriers	Clinical trials of educational interventions using plain language or teach to goal approaches in low-literacy patients	Sobel and colleagues, 2009 (73) Bailey and colleagues, 2012 (74) Bailey and colleagues, 2014 (75)
Lack of biomarkers required for personalized medicine in minority populations	Design and assess educational interventions and multimedia programs to address low health literacy	CAAPA	Kessler and colleagues, 2016 (96)
	Design and implement large pharmacogenetics studies in URMIs		
	Develop novel statistical methods to leverage both global and local genetic ancestry to increase the statistical power of genome-wide association and sequencing studies of respiratory diseases in URMIs	GALA, EVA-PR	Burchard and colleagues, 2004 (115) Chen and colleagues, 2017 (116)
Removal of barriers for participation of minorities in research studies and clinical trials	Conduct birth cohort studies of URMIs with long-term follow up, in order to develop genetic and epigenetic biomarkers of disease risk and disease severity		
	Identify culturally appropriate recruitment strategies, which consider the needs and interests of the target population	HCHS/SOL	Sorlie and colleagues, 2010 (98) Lavange and colleagues, 2010 (99)
	Use study designs that reduce participants' burden and foster trust by engaging participants as decision makers (e.g., through community-based participatory research and advisory groups)		
	Create training modules for research in respiratory health disparities		
Underrepresentation of minorities in academic (pediatric and adult) pulmonary, critical care, and sleep medicine	Development of pipeline programs in URM communities by academic institutions, establishing academic support and mentoring programs for: middle/high school, undergraduate, and medical students from URM groups	Funding from academic institutions (e.g., scholarships), the NHLBI (e.g., pre-K grants), foundations (e.g., ATS Foundation grants on health disparities) and partnerships (e.g., between the ATS and the AMFDP)	Celedón and colleagues, 2014 (4) Duncan and colleagues, 2016 (105) Arbery and colleagues, 2014 (106) Maldonado and colleagues, 2014 (107) Thakur and colleagues, 2014 (108)
	Support of junior URM faculty through new or improved funding mechanisms	Goal and metric-oriented approaches to increase the number of URMIs: (1) at the medical school, residency and divisional levels; and (2) in academic leadership positions	

(Continued)

Table 1. (Continued)

Research Need	Recommendations	Examples	Author, Year (Reference No.)
	Hold institutional efforts to recruit and retain URM faculty accountable, as reflected in decisions on federal research funding		
	Develop and implement robust mentoring programs, including local and external mentors, with at least one URM mentor	The AMFDP The NIH PRIDE	
	Include URM in decision-making bodies in the ATS (e.g., assembly and societal committees), the NHLBI (e.g., study sections) and academic institutions (e.g., leadership positions)	Inclusion of at least one URM in the ATS Board of Directors	
Evidence-based policies to address respiratory health disparities	Consider actions that might be taken based on new evidence when designing research studies	Antismoking policies based on the Surgeon's General Report	U.S. Department of Health and Human Services, 2014 (41)
	Formally train researchers in policy translation	Careful consideration of research-based evidence together with interests of stakeholders affected by new policy	

Definition of abbreviations: ACA = Affordable Care Act; AHIMSA = Acculturation, Habits, and Interests Multicultural Scale; AIMS = ancestry informative markers; AMFDP = Harold Amos Medical Faculty Development Program; ATS = American Thoracic Society; BAS = Bidimensional Acculturation Scale for Hispanics; CAAPA = Consortium on Asthma among African-ancestry Populations in the Americas; EVA-PR = Epigenetic Variation and Asthma in Puerto Ricans; GALA = Genetics of Asthma in Latino Americans; HCHS/SOL = Hispanic Community and Health Study/Study of Latinos; NHLBI = National Heart, Lung, and Blood Institute; NIH = National Institutes of Health; PRIDE = Program to Increase Diversity among Individuals Engaged in Health-Related Research; URM = underrepresented minority.

a panel discussion that resulted in recommendations for research to address “upstream” and “downstream” causes of disparities in pulmonary, critical care and sleep medicine (summarized in Table 1, which also includes relevant examples). Areas of emphasis included best practices to advance research on respiratory health disparities, risk factors for respiratory health disparities, addressing equity in access to and quality of healthcare, the impact of personalized medicine in disparities research, improving design and methodology for research studies in respiratory health disparities, and achieving equity in the pulmonary, critical care, and sleep medicine workforce. Workshop participants are listed immediately before the reference section.

Best Practices to Advance Research on Respiratory Health Disparities

Whereas race has been characterized by an individual's primary continent of origin and skin color, ethnicity is defined by a shared social, linguistic, and cultural heritage (e.g., African American, Hispanic) (15, 16). Hispanics and African Americans have varying degrees of African, European, and Native American genetic ancestry (17), and such ancestral variability has been shown to influence lung function and risk for obstructive airway diseases in these ethnic groups (18–21). Moreover, Hispanics can be further classified into subgroups by country or region of origin, and such subgroups can differ with regard to risk factors and disease burden. For example, Puerto Ricans and Mexican Americans have markedly variable morbidity and mortality from asthma (17), and smoking patterns differ across various Hispanic groups in the United States (22). Thus, combining subgroups or ignoring racial ancestry can lead to biased results of respiratory research studies in Hispanics and other racially admixed populations.

SES is often assessed using a few indicators of income and educational level. However, there is a need to better characterize social and economic status at the individual and community levels. For example, positive social factors, such as community resiliency and cohesiveness, may mitigate the negative effects of low income (23), including detrimental environmental exposures (e.g., mobilization against advertising of tobacco products). Conversely, URM and economically

disadvantaged persons may often be exposed to chronic stressors, such as racism, perceived discrimination, violence, and crime, which have been implicated in worse asthma outcomes (24–28), sleep disorders (29), and inadequate access to high-quality healthcare (30).

Acculturation is the process of cultural exchange by which immigrants modify their attitudes, beliefs, cultural norms, values, or behaviors as a result of interactions with a different culture (31). Acculturation can modify the effect of race/ethnicity or SES on respiratory health—largely by affecting environmental exposures—and is thus an important target for implementation research. The links of acculturation with environmental risk factors and respiratory health disparities may vary by birthplace, country of origin, and years of residence in an adoptive country. For example, a study of 1,000 women of Mexican descent showed that birth in the United States, years lived in the United States, and acculturation were each significantly associated with higher prevalence of cigarette smoking (32). A link between acculturation and smoking has been reported in other studies of female, but not male, Hispanic and Asian immigrants (22, 33). Similar to findings for smoking, birth in the United States has been associated with asthma among Mexican Americans (34, 35).

Recommendations

- Characterize broad ethnic groups into subgroups known to differ or potentially differ with regard to the disease of interest.
- Consider measuring genetic ancestry in racially admixed populations, using ancestry informative markers.
- Assess both social and economic status (at the individual, family, and community levels) using validated instruments, while also measuring chronic stressors (with the extent of assessment determined by the primary research focus).
- Capture basic measures of acculturation in all studies of migrant populations.
- Use comprehensive measures of acculturation for in-depth studies.

Risk Factors for Respiratory Health Disparities

Cumulative risk refers to the aggregate risk from environmental agents and stressors to

which a population is exposed (36). Risk of adverse outcomes from pollution in asthma or COPD may be further increased by intrinsic (e.g., genetics, sex, and life stage) and extrinsic (e.g., violence, lack of community resources, and lack of access to healthcare) factors, as well as the duration of the exposure. For example, recent evidence suggests that exposures to violence and chronic stress interact with air pollution in causing asthma morbidity (37–39), and that obesity increases susceptibility to the detrimental effects of air pollution on COPD (40). Thus, there is a need to assess the biological impact of interactions between chronic exposure to air pollution and other risk factors on respiratory health in disadvantaged and URM populations.

Disparities in tobacco use and morbidity from tobacco use are due to “upstream” causes (e.g., marketing strategies of tobacco companies), factors contributing to enhanced initiation and reduced cessation rates (e.g., mental health, low education), and factors accelerating the onset or severity of respiratory diseases (e.g., comorbidities, healthcare access) (41). Because factors impacting tobacco use are also community-specific, effective tobacco control policies require customization based on objective data and consideration of the societal levels at which tobacco control measures are needed (41).

The tobacco epidemic has indeed become a series of epidemics, affecting different groups in the population to a varying extent. There are strong gradients of tobacco product use by SES indicators, and across racial and ethnic groups (41). These differences relate primarily to industry marketing (e.g., targeting menthol cigarettes toward the African American community). Among some URMs, smoking tends to be lower than in non-Hispanic white individuals (e.g., some Hispanic populations), but higher in others (e.g., many Native American tribes). Given the impact of smoking on morbidity and mortality, differences in smoking patterns and the cultural correlates of smoking are relevant to prevention of initiation, promotion of cessation, and lung cancer screening. For example, a randomized, controlled trial of proactive-care smoking cessation among U.S. veterans of war found higher rates of smoking abstinence in African American than in white individuals, a finding that may be explained by access to treatment, higher frequency of light

smoking, and self-motivation to quit among African Americans (42). Thus, there is need for research that is sufficiently rich to provide insights into topics related to smoking (including new nicotine and tobacco products) across population groups.

Occupational risk factors for respiratory disease are unevenly distributed in the population. This disparity occurs across both specific occupational diseases (e.g., pneumoconiosis) and diseases that also have nonoccupational causes (e.g., asthma). Occupational exposures should be assessed in studies of respiratory health disparities, as they may confound relationships between other risk factors and disease. For instance, relationships between poverty and lung disease may reflect respiratory hazards in low-income jobs or reverse causation from loss of income from disabling occupational disease. Moreover, relationships between air pollution and health may reflect the combined effects of occupation and area of residence, given that particulate matter exposures from outdoor air are orders of magnitude lower than those legally permitted in the workplace. Thus, there is a need to improve our understanding of the impact of interactions between environmental and occupational risk factors on respiratory health disparities.

Obesity is a major health problem that disproportionately impacts URMs. The prevalence of obesity is substantially higher in Hispanic and African American than in non-Hispanic white individuals. Obesity tracks with other risk factors for health disparities, such as poverty (43). As such, obesity is part of a set of risk factors that can synergistically cause or worsen respiratory and sleep diseases, including asthma (44) and obstructive sleep apnea (45). However, the extent to which obesity explains why URMs have a greater burden of respiratory or sleep disorders remains to be characterized. In particular, few clinical trials of weight loss management or bariatric surgery have included adequate numbers of URMs. Moreover, there is limited evidence to support culturally targeted interventions to promote respiratory and sleep health through the prevention and treatment of obesity.

Recommendations

- Estimate the effect of interactions between air pollution and other risk factors on respiratory health disparities.

- Create models integrating tobacco exposure throughout life stages and addiction risk.
- Study the impact of e-cigarettes, hookah, or new tobacco products on respiratory diseases in underserved populations.
- Incorporate basic measures of occupation and the workplace in all studies of minorities of working age, with use of more in-depth tools in studies focused on occupation.
- Design and implement longitudinal studies of obesity and respiratory/sleep health, as well as culturally targeted interventions to prevent and treat obesity, in minority populations.

Addressing Equity in Access to Healthcare and Quality of Care

Lack of health insurance is a major barrier to healthcare access and a cause of worse outcomes for respiratory diseases in URM. Uninsured individuals have higher rates of lung cancer, present with more advanced disease, and have higher mortality from lung cancer (46). Similarly, uninsured patients who are critically ill are less likely to receive common critical care procedures and have higher mortality rates (10).

The Affordable Care Act (ACA) of 2010 has significantly decreased the percentage of Americans without health insurance. Early within-state evaluations suggest that insurance expansion may increase the use of preventive services, improve health outcomes, and reduce mortality, especially among low-income and minority populations (11–13). Twenty states, however, have declined, thus far, to enact the Medicaid expansion provision of the ACA, even though some of those states have substantial URM populations (47).

Medical insurance does not guarantee access to high-quality care. Low SES is associated with higher odds of being denied acceptance for lung transplantation, even after adjusting for disease factors (48). Publicly insured low-income and URM children continue to receive poorer healthcare, with worsening disparities for diseases, such as asthma (49). Indeed, low-income and uninsured or publicly insured children experience longer wait times to see specialists, and report less patient-centered care (49, 50). Patients with occupational lung disease also face barriers to healthcare access, as many physicians

do not accept workers' compensation insurance (51).

Even when prescribed, low adherence to therapies for pulmonary and sleep diseases is common, particularly among African American, Hispanic, and publicly insured and low-income people (52–56). Moreover, risk factors for nonadherence to treatment differ by race/ethnicity and SES. For example, URMs with asthma are more likely to have negative beliefs about inhaled corticosteroids and to believe that God determines disease control; such beliefs may mediate the association between race/ethnicity and adherence to treatment (57, 58).

In spite of substantial evidence of barriers to adherence, few adherence intervention trials have been conducted for respiratory or sleep disorders. Although knowledge and better device skills are positively associated with adherence in asthma, simple interventions that provide education and technique training, and/or simplify regimens, do not reliably lead to improved adherence, especially in URMs (59, 60). Motivational enhancement interventions have been shown to improve adherence to continuous positive airway pressure, but these strategies have not been tested in URMs (61). Shared decision-making, setting appropriate expectations for treatment efficacy, and providing reminders may improve adherence with therapies for asthma and sleep apnea (62–66), but these interventions have not been specifically evaluated in URMs.

Health literacy, the "degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions," is usually assessed by testing reading and numeracy skills (67). Adults with low health literacy have poorer healthcare access, and greater morbidity and mortality, than those with adequate health literacy (68, 69). For example, children with asthma whose parents have low literacy are at risk for poor disease control and hospitalizations, and elderly subjects with low literacy are also at risk for asthma morbidity (70, 71). Vulnerable populations, such as URMs, those whose primary language is not English or have low SES, and elderly patients are more likely to lack health literacy skills, and thus not accomplish health-related tasks (70).

Nonadherence to medications or self-management behaviors is one mechanism

through which low health literacy may lead to poor outcomes in pulmonary and sleep diseases (72). Several interventions based on prescription packaging via standardized drug labels, educational interventions using plain language and teach-to-goal or teach-back approaches, and multimedia programs have been proposed to address the needs of patients with low literacy (73–75). However, robust evidence regarding their effectiveness in addressing respiratory health disparities is limited.

Recommendations

- Conduct longitudinal studies of the impact of the ACA on diseases encountered in pulmonary, critical care, and sleep medicine among URMs and economically disadvantaged populations.
- Develop and test culturally targeted interventions to improve adherence to treatment for pulmonary and sleep diseases in minority and economically disadvantaged populations, incorporating cultural norms, values, and beliefs, and addressing pragmatic barriers.
- Design and assess educational interventions and multimedia programs to address low health literacy.

The Impact of Personalized Medicine on Disparities Research

Precision or personalized medicine is a model for healthcare that uses individual patient characteristics, including predictive biomarkers, such as genetic and epigenetic markers, to determine the optimal treatment for an individual (76). This approach is expected to improve clinical practice through risk assessment for risk modification and tailored therapeutic interventions (77). Personalized medicine is expected to improve patient outcomes, but remains expensive and not readily accessible.

A growing field in personalized medicine research is pharmacogenetics, which analyzes gene-by-drug interactions on treatment response. Much has been learned about pharmacogenetics in respiratory diseases, such as lung cancer (78) and asthma (79). Most pharmacogenetics studies of asthma have focused on genes within the β_2 -adrenergic receptor, glucocorticoid, and leukotriene pathways (80–84).

Inclusion of multiethnic populations in pharmacogenetics studies will be critical to account for the diverse genomes of modern populations. Recently admixed populations have varying proportions of different ancestries within their genomes, due to recent gene flow between diverse populations. As a consequence, genetic variants have varying allele frequencies between different ethnic groups (8, 85, 86), which may lead to ethnic-specific differences in treatment response (8). In fact, differential responsiveness to long-acting inhaled β_2 -agonists has been observed comparing non-Hispanic white and African American individuals (82), including increased risk for life-threatening exacerbations and treatment failures in African Americans in some (7, 87), but not all (88), studies. Moreover, rare variants in the gene for the β_2 -adrenergic receptor (*ADRB2*) have been implicated in ethnic-specific response to short- and long-acting inhaled β_2 -agonists (84, 89), emphasizing the importance of evaluating ethnically diverse populations to identify novel determinants of therapeutic response.

“Global” (genome-wide) genetic ancestry has been shown to influence lung function and respiratory diseases (*see* previous text here), and thus assessing such ancestry in racially admixed populations can help epidemiologic, genetic, and pharmacogenetics studies of respiratory health disparities. Moreover, leveraging knowledge of “local” (i.e., chromosome-specific) genetic ancestry through admixture mapping may enhance identification of genes affecting treatment response or health outcomes through genome-wide association or sequencing approaches (90).

Studying genetics and pharmacogenetics in diverse populations is important, but most respiratory diseases are also influenced by social factors and environmental exposures through direct effects, gene-by-environment interactions, and environmentally induced epigenetic changes. Thus, understanding how social and environmental factors interact with genetic variants or affect epigenetic mechanisms may provide clues to molecular pathways, and be informative in assessing determinants of ethnic differences in disease pathogenesis and treatment response (91, 92). For example, DNA methylation changes have been implicated in asthma-related phenotypes (24, 93, 94) and idiopathic pulmonary fibrosis (95). In this context, there is a

critical need for longitudinal studies spanning various life stages (e.g., fetal development, early postnatal life, childhood, and adulthood) in URM subjects.

Recommendations

- Design and implement large pharmacogenetics studies in URM.
- Develop novel statistical methods to leverage both global and local genetic ancestry to increase the statistical power of genome-wide association and sequencing studies of respiratory diseases in URM.
- Conduct birth cohort studies of URM with long-term follow-up to develop genetic and epigenetic biomarkers of disease risk and disease severity.

Improving Design and Methodology for Research Studies of Health Disparities

Engaging minority participants in research studies is critically important to our understanding of common diseases encountered in pulmonary, critical care, and sleep medicine. For example, data from the Consortium on Asthma among African-Ancestry Populations in the Americas (CAAPA) (96, 97) demonstrate both the need for genetics research in URM and the potential for discoveries when conducting such research. Through sequencing over 600 genomes of African ancestry representing the African Diaspora, CAAPA discovered nearly 43.2 million variants, 48% of which are novel (not previously reported in public catalogs of variation including the Single Nucleotide Polymorphism Database (dbSNP)). Most importantly, within the CAAPA genomes, the rate of discovery of these novel alleles is significantly higher on chromosomal regions that are purely African in ancestry as compared with the regions of the genome that are purely European or Native American.

Challenges and opportunities in longitudinal, population-based studies differ from those for genetic research in URM. For example, the Hispanic Community Health Study/Study of Latinos is a longitudinal, population-based cohort study designed to assess the prevalence of common diseases (including some involving the respiratory system and sleep) and identify factors that increase or mitigate risk of such diseases (98, 99). The diverse cohort of 16,000 individuals (ages 17–76 yr) was

recruited in Miami (FL), Chicago (IL), New York (NY), and San Diego (CA) to ensure adequate representation of the major Hispanic subgroups in the United States, including Mexican Americans, Puerto Ricans, Cuban Americans, and South/Central Americans. The study’s success required strong community support at every phase of research. Sites and investigators were experienced in working within the targeted communities, sampling procedures ensured adequate representation of all groups, and instrument selection required cultural sensitivity and validity for all participants. Pilot testing evaluated the study burden to participants and the use of instructional videos. The Hispanic Community Health Study/Study of Latinos exemplifies the need to understand the impact of diversity (in lifestyle, beliefs, behaviors, exposures, ethnicity, place of origin, immigration patterns, and acculturation) on health, including opportunities to discover novel insights into disease pathogenesis, which may ultimately lead to interventions to mitigate health disparities.

More interventional studies are needed to address respiratory health disparities. Similar to observational studies, design of clinical trials in URM should anticipate potential challenges in subject recruitment within a conceptual framework that examines barriers at the level of patients, healthcare providers, and healthcare systems. From the patient perspective, these include barriers to awareness and participation in trials, as well as barriers to acceptance of participation in studies (100). Lack of trust is a frequent barrier to the decision to participate in a trial, and thus the research team’s communication skills (“cultural competence”) are essential to engage and retain URM in research. Increasingly, clinical trials are using patient navigators (nurses or trained laypersons) (101) and Web-based approaches to subject recruitment. Such approaches should be optimized when reaching out to URM, to ensure that their use does not further compromise inclusion of URM in clinical trials.

Recommendations

- Identify culturally appropriate recruitment strategies, which consider the needs and interests of the target population.

- Use study designs that reduce participants' burden and foster trust by engaging participants as decision-makers (e.g., through community-based participatory research and advisory groups).
- Create training modules for research in respiratory health disparities.

Achieving Equity in the Pulmonary, Critical Care, and Sleep Medicine Workforce

In 2010, only 8% of faculty in U.S. medical schools (an engine for healthcare and research) were URMs (102). Moreover, all U.S. scientific research faculty (beyond those in medical schools) include relatively low percentages of URMs, estimated as follows: 4% African American; 4% Hispanic; 0.2% Native American; and 0.1% Hawaiian or Pacific Islander (103). This narrow pool of physicians and scientists partly explains why few URMs are engaged in pulmonary, critical care and sleep medicine research. Of 6,973 ATS members surveyed between 1998 and 2000, 3.9% were Hispanic, 1.5% were African American, and 0.2% were Pacific Islander, Native American or Alaskan Native (104).

Recognizing the need for workforce diversity in academic pulmonary, critical care, and sleep medicine, both the ATS and the NHLBI have further increased their existing efforts to develop new approaches to achieve such diversity (4, 105–108). Participation and retention of URMs in the practice of research on respiratory diseases is influenced by factors encompassing continuous or overlapping stages in professional development, ranging from high school to a position as academic faculty member (105, 107). Thus, there is broad consensus on the need for multipronged approaches to address this issue, involving nongovernmental and governmental funding agencies, academic institutions, professional organizations, such as the Accreditation Council on Graduate Medical Education, professional societies, community organizations, and society at large (4, 105–108).

A recent NHLBI workshop that included early-stage investigators identified key issues facing URM trainees, including lack of exposure to science at a young age, financial barriers (e.g., cost of living), family obligations (e.g., lack of parental leave support, child care issues), restricted

research directions during a postdoctoral fellowship, difficulties in obtaining extramural funding, and lack of external mentors (105). Although some of these issues are also relevant to nonminority trainees, salient issues for URMs include scarce exposure to science during childhood and limited access to external mentors from similar cultural/ethnic backgrounds (105).

Institutional leadership is critical to achieving workforce diversity (107). Academic faculty and academic leaders may not actively oppose diversity efforts, but are often passive or skeptical about the likelihood of success. Skepticism often emanates from the perceived limited pool of qualified applicants, scarcity of resources to support these efforts, and challenges in sustaining improvement in URM student, resident, and faculty diversity. Institutional leadership is highly influential in making progress to achieve workforce diversity. If academic leadership (e.g., the division chief, department chair, and dean) is not willing to make diversity a priority, improvement in academic diversity—at all stages of career development—remains incremental at best. For example, the division chief may not convey an emphasis on diversity to residency or fellowship program directors, and thus diversity metrics may not be monitored in a transparent manner (107). Noninclusion of qualified midcareer and senior URM faculty in key decision-making bodies (e.g., promotion committees, leadership positions) may be an additional obstacle to retention and career advancement of URMs (105).

The Harold Amos Medical Faculty Development Program (AMFDP), funded by the Robert W. Johnson Foundation, is an example of a successful approach to increasing workforce diversity in academic medicine (106). Of the 256 alumni of the AMFDP in 2013, greater than 80% were in academic medicine, with 18 in pulmonary medicine (105). Graduates from the AMFDP include 72 associate professors, 65 professors, 3 National Institutes of Health directors, 4 deans of medical schools, and 10 members of the National Academy of Medicine (106). Consistent with some of what is outlined previously here, the success of the AMFDP has been attributed to several factors: a committed group of advisors, three levels of mentorship (a mentor from the National Advisory

Committee of the AMFDP, a mentor at the trainee's local institution, and an external mentor—with at least one URM mentor), 4-year funding (to support 70% protected time for research effort and a research grant), and an excellent program for career development (106).

Recommendations

- Development of pipeline programs in URM communities by academic institutions, establishing academic support and mentoring programs for: middle/high school, undergraduate, and medical students from URM groups.
- Support of junior URM faculty through new or improved funding mechanisms.
- Hold institutional efforts to recruit and retain URM faculty accountable, as reflected in decisions on federal research funding.
- Develop and implement robust mentoring programs, including local and external mentors, with at least one URM mentor.
- Include URMs in decision-making bodies in the ATS, the NHLBI, and academic institutions.

Conclusions and Future Directions

Eliminating racial, ethnic, and socioeconomic disparities in respiratory health will remain aspirational without a concentrated effort by all stakeholders. Using best practices in health disparities research, considering how research impacts policies affecting minority and economically disadvantaged populations, and developing new approaches to engage and fund trainees and clinical investigators to conduct high-quality research on disparities in pulmonary, critical care, and sleep medicine is essential. In order for all Americans to attain optimal respiratory health, it will be necessary to improve our understanding of the evolving role of personalized medicine and risk factors for respiratory health disparities. The participants at the ATS/NHLBI Workshop on Respiratory Health Equality created a forum to discuss these issues and propose key recommendations. Addressing these recommendations may potentially reduce—and/or eliminate—racial, ethnic, and socioeconomic disparities

in respiratory health in the United States. We hope that this workshop will motivate similar efforts to examine other causes of respiratory health disparities, including sex, sexual orientation, and cognitive and physical disabilities. ■

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