Charting the Future for Ethnicity and Health Research

Clinical and Population Science Insights From the MESA

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ABSTRACT

The MESA (Multi-Ethnic Study of Atherosclerosis) has been highly successful in investigating the prevalence, characteristics, and progression of subclinical cardiovascular disease (CVD) in a multiethnic American cohort of adult men and women free of CVD at baseline. MESA has also championed the use of novel biomarkers and emerging imaging techniques for the assessment of subclinical CVD and has created an extensive set of data that continues to fuel dozens of ongoing analyses. Insights from MESA include the first demonstration of ethnic differences in coronary artery calcification and its association with subclinical disease progression and incident CVD. Other findings include ethnic differences in the prevalence of pharmacological, behavioral, and lifestyle interventions for the primary prevention of CVD. MESA has also shown the association between residential neighborhood characteristics and behavioral and biomedical risk factors for CVD. This vast amount of data documenting ethnic differences in progression of subclinical CVD, diabetes, kidney disease, and pulmonary disease contrasts sharply with the relative scarcity of specific information that can pave the way for the elimination of racial and ethnic disparities. Intervention research, however, goes beyond the original objectives of MESA and other observational studies. The time has now come to build on the legacy of MESA by supporting rigorous intervention research that informs clinical and public health strategies as well as policy and environmental changes for eliminating racial and ethnic disparities in CVD and other chronic diseases and advancing the health of multiethnic communities.

By most standards of assessment, the MESA (Multi-Ethnic Study of Atherosclerosis) has been highly productive and continues to successfully address its core research mission. Initiated in July 2000 to investigate the epidemiological characteristics and progression of subclinical cardiovascular disease (CVD) in a population-based sample of 6,500 men and women ages 45 to 84 years [1], MESA successfully recruited 6,814 participants with a rich multiethnic representation of whom 38% are white, 28% African American, 22% Hispanic, and 12% Asian, predominantly of Chinese descent [2]. Through the creative use of ancillary studies and the collaborative efforts of hundreds of investigators and many active scientific working groups, MESA has also successfully built an extensive set of cohort data that is the basis of dozens of ongoing analytic studies [3]. These data include novel markers of CVD risk, including coronary artery calcification (CAC) using computed tomography [4–7], ventricular structure and function using magnetic resonance imaging [5,8–10], and carotid intima-media thickness using ultrasonography [4,5,11–14]. Additionally, MESA has amassed a wealth of phenotypic data as well as an extensive database of geographic, meteorological, and other physical and social characteristics of residential neighborhood environments of its participants [15–17].

A RICH SOURCE OF INSIGHTS AND CLINICAL EVIDENCE IN ETHNICITY AND HEALTH

As a testament to the scientific productivity of MESA investigators and collaborators, nearly 1,100 papers have been published or were in press as of mid-August 2016 [3]. This extensive source of clinical and public health insights includes the following: the first demonstration of ethnic differences in CAC [18]; the fact that CAC score is a stronger predictor of incident coronary heart disease (CHD) that shows no major differences in its predictive ability among racial and ethnic groups [19], and the fact that CAC provided superior discrimination and risk reclassification in comparison with any other risk marker in individuals at intermediate risk for incident CHD [20]. MESA also demonstrated that among persons with diabetes or metabolic syndrome, absence of CAC conferred a very low risk for incident CHD, whereas in the presence of CAC scores >400, incident CHD risk increased >10-fold [21]. Importantly, MESA also showed significant ethnic differences in the prevalence of pharmacological, behavioral, and lifestyle interventions for the primary prevention of CHD. Other evidence coming out of MESA relates to ethnic differences in dietary intake, physical activity, smoking, blood pressure, body mass index, visceral fat, and their associations with incident CHD and diabetes [22–27]. More

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recently, MESA is beginning to shed light on whether the significant Genome-Wide Association Study findings in predominantly European-descent populations are also present and associated with markers of subclinical atherosclerosis and disease progression in the multiethnic cohort of MESA [28–30].

MESA has also provided important insights from social and environmental determinants of subclinical CVD and disease progression. For example, we now have a better understanding of the association between ambient air pollution and increased levels of atherosclerosis (as measured by carotid intima-media thickness) and especially how that association differs by ethnicity in the MESA communities [15]. In addition, MESA has provided a deeper understanding of the drivers of risk exposure that may inform policy and environmental interventions for CVD prevention. In a study of 5,921 white, black, Hispanic, and Chinese adults across 6 U.S. cities between 2000 and 2002, Jones et al. [16] demonstrated that air pollution exposures were significantly higher in majority Hispanic neighborhoods compared to majority white neighborhoods and that neighborhood-level segregation was importantly associated with markers of ambient air pollution. More recently, a 12-year follow-up of 5,950 adult participants of MESA [31] demonstrated that social and physical neighborhood characteristics such as the density of recreational facilities, density of healthy food stores, and measures of the availability of healthy foods, walking environment, and social environment were associated with changes in CAC. The investigators concluded that a "greater access to neighborhood healthy food resources may slow the development of coronary atherosclerosis in middle-aged and older adults" [31].

THE NEED FOR TYPES 2 AND 3 EVIDENCE IN ETHNICITY AND HEALTH

As an observational cohort study, MESA has produced a wealth of evidence that has significantly improved our understanding of the important associations between traditional and novel markers of risk and the development and progression of subclinical atherosclerosis and eventual development of overt clinical CVD and diabetes, especially in the non-white ethnic populations in the study. Rychetnik et al. [32] refer to this category of evidence as type 1 evidence or findings from "research that describes risk-disease relations, and identifies the magnitude, severity, and preventability of public health problems." Thus, type 1 evidence in ethnicity and health identifies important associations that suggests that "something should be done" [32]. In contrast, type 2 evidence identifies "the relative effectiveness of specific interventions aimed at addressing a problem" or "what should be done," whereas type 3 evidence informs us on how it should be done [32].

Relative to the wealth of type 1 evidence available, there is a real scarcity of types 2 and 3 evidence in ethnicity and health. For example, type 1 evidence from MESA and other observational cohort studies on the documented burden of subclinical and overt clinical CVD in several racial and ethnic populations is quite compelling. Although limited, type 2 evidence exists to inform us of which interventions are effective in controlling traditional risk factors such as hypertension and low-density lipoprotein cholesterol and preventing progression of subclinical atherosclerosis [33,34], very few of these interventions actually demonstrate efficacy or effectiveness in eliminating racial and ethnic disparities in CVD. For example, Mueller et al. [35] identified 39 interventions and several policy initiatives at the state and national levels that addressed reducing racial and ethnic disparities in blood pressure control. The predominant racial/ethnic group in most interventions was African American. Of the completed interventions, 27 demonstrated some improvement in blood pressure control or related process measures and 7 showed no improvement [35]. Of the 6 completed studies that specifically examined disparities, 3 reduced, 2 increased, and 1 had no effect on disparities [35].

CONCLUSIONS

As demonstrated in the articles in this special issue of *Global Heart*, the MESA investigators have made very important progress. As a result, we know more about the development, characteristics, and progression of subclinical atherosclerosis and incident CVD, especially in racial and ethnic minority populations in the United States. However, as Goethe eloquently stated, "Knowing is not enough; we must apply" [36]. The time has now come for us to apply the insights we have learned from MESA and design the appropriately rigorous and sustainable interventions that pave the way for how we eliminate racial and ethnic disparities in cardiovascular health. This challenge should not fall on the shoulders of MESA investigators and their collaborators because intervention research goes beyond the original objectives of observational cohort studies. However, observational studies will continue to play an important role using evolving state-of-the-art methodologies to make new discoveries, but all of public health should be asking when do we take action to intervene to reduce preventable death and disability and eliminate racial and ethnic disparities. Answers to these questions will be crucial in advancing ethnicity and health research, especially now as we enter the implementation phase of the National Heart, Lung, and Blood Institute Strategic Vision for the next decade [37].

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