Implementing the National Heart, Lung, and Blood Institute’s Strategic Vision in the Division of Cardiovascular Sciences


Abstract: As we commemorate the 70th anniversary of the National Heart, Lung, and Blood Institute and celebrate important milestones that have been achieved by the division of cardiovascular sciences, it is imperative that division of cardiovascular sciences and the Extramural Research community at-large continue to address critical public health challenges that persist within the area of cardiovascular diseases. The National Heart, Lung, and Blood Institute Strategic Vision, developed with extensive input from the extramural research community and published in 2016, included overarching goals and strategic objectives that serve to provide a general blueprint for sustaining the legacy of the institute by leveraging opportunities in emerging scientific areas (eg, regenerative medicine, omics technology, data science, precision medicine, and mobile health), finding new ways to address enduring challenges (eg, social determinants of health, health inequities, prevention, and health promotion), and training the next generation of heart, lung, blood, and sleep researchers. Division of cardiovascular sciences has developed a strategic vision implementation plan to provide a cardiovascular framing for the pursuit of the institutes overarching goals and strategic objectives garnered from the input of the broader National Heart, Lung, and Blood Institute community. This plan highlights 6 scientific focus areas that demonstrate a cross-cutting and multifaceted approach to addressing cardiovascular sciences, including (1) addressing social determinants of cardiovascular health and health inequities, (2) enhancing resilience, (3) promoting cardiovascular health and preventing cardiovascular diseases across the lifespan, (4) eliminating hypertension-related cardiovascular diseases, (5) reducing the burden of heart failure, and (6) preventing vascular dementia. These priorities will guide our efforts in institute-driven activities in the coming years but will not exclude development of other novel ideas or the support of investigator-initiated grant awards. The Division of Cardiovascular Sciences strategic vision implementation plan is a living document that will evolve with iterative dialogue with the National Heart, Lung, and Blood Institute community and adapt as the dynamic scientific landscape changes to seize emerging opportunities. (Circ Res. 2019;124:491-497. DOI: 10.1161/CIRCRESAHA.118.314338.)

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these opportunities and address these challenges, DCVS initiated a process in 2017 for developing a strategic vision implementation plan based on the community input provided in the strategic vision published in 2016. This process included a landscape analysis of existing institute priorities, including support for investigator-initiated research, training, and career development, as well as other strategic investments, for example, cardiothoracic surgery, congenital heart disease, emergency medicine, HIV-related comorbidities, obesity, and women’s health. Using these inputs and iterative feedback from NHLBI’s Board of External Experts and Advisory Council, DCVS staff identified 6 scientific focus areas, all of which reflect significant opportunities across the translational spectrum for breakthroughs in knowledge and health over the next decade and interdigitate with many NHLBI strategic initiatives.

**Addressing Social Determinants of CVH and Health Inequities**

According to the World Health Organization, the social determinants of health are defined as the conditions in which people are born, grow, live, work, and age. The social determinants of health are often viewed as fundamental influences on an individual’s health and include factors such as socioeconomic status, education, neighborhoods, the physical environment, employment, social networks, and health care access. In the United States, CVD disproportionately affects racial and ethnic minorities and individuals of low socioeconomic status, including those in rural communities. DCVS has been at the forefront of supporting population-based research that has identified the important contributions of social determinants to inequities in cardiovascular disease among different segments of the US population—through cohort studies such as ARIC study (Atherosclerosis Risk in Communities), CARDIA study (Coronary Artery Risk Development in Young Adults), HCHS/SOL (Hispanic Community Health Study/Study of Latinos), JHS (Jackson Heart Study), MESA (Multi-Ethnic Study of Atherosclerosis), and the SHS (Strong Heart Study). Efforts to address the social determinants of health have included studies to identify relevant exposures, understand their biologic effects, and modify exposures like the built environment, air pollution, and other social environmental factors that are inequitably distributed. Development of an evidence base for intervening on the social determinants of CVH and health inequities is a critical challenge and compelling questions informed by the broader NHLBI stakeholder community:

1. Addressing social determinants of CVH and health inequities.
2. Enhancing resilience.
3. Promoting CVH and preventing CVD across the lifespan.
4. Eliminating hypertension-related CVD.
5. Reducing the burden of heart failure.
6. Preventing vascular dementia.

These focus areas represent a mix of related cross-cutting topics and targeted diseases/conditions that involve complex biological, behavioral, social, and environmental interactions, thus requiring multifaceted approaches across the translational spectrum to address them effectively to create a more positive future. These areas complement the existing focus areas for strategic investments. DCVS anticipates that NHLBI’s ongoing leadership and investment in the TOPMed program (Trans-Omics for Precision Medicine), the NHLBI data (storage, toolspace, access, and analytics for big data empowerment), and the NIH data commons pilot will generate rich resources and data science platforms to enable research in new and existing focus areas.

Portfolio analyses of our funded research projects support the development of plans for workshops and potential initiatives. DCVS hosts workshops to convene external experts to identify opportunities to advance discovery to improve CVH, and sometimes, these efforts contribute to the development of Institute activities, investigator applications, or funding announcements for new research initiatives. Workshop summaries are posted on the NHLBI website (https://www.nhlbi.nih.gov/events) for the public. Our efforts to implement the strategic vision are already influencing workshop topics as shown for recent and upcoming workshops between September 2017 and December 2018 in the Table. As this process evolves, steps will include expanding portfolio analyses beyond NHLBI, exploring collaborations with other NIH Institutes/Centers/Offices (eg, All of Us Research Program, National Institute of Environmental Health Sciences, National Institute on Aging, and National Institute of Neurological Disorders and Stroke) and beyond (eg, professional societies and other research funding agencies) to leverage knowledge and resources, and proposing workshops to gather input from the external community. Current progress of the working groups is summarized below. Although not discussed in detail below, support for workforce development was a common theme across the working groups.
health inequity is an important endeavor for DCVS to support whereas continuing to support research to identify new relevant exposures and their biologic mechanisms. Evidence-based strategies that focus on effective and sustainable interventions that close the gap on health inequities in CVH must be implemented. Current efforts include partnering with the NHLBI Center for Translation Research and Implementation Science on a funding opportunity to support a community-based initiative titled disparities elimination through coordinated interventions to prevent and control heart and lung disease risk. Future efforts could include supporting development of a toolbox with common data elements to standardize data collection of social determinants across studies and supporting research to evaluate interventions, including natural experiments, addressing social determinants. These efforts would be consistent with NIH and NHLBI efforts to promote the development and adoption of common data elements in research to facilitate data harmonization, linkage, and analysis across studies.

### Enhancing Resilience

Resilience has been defined in a variety of ways and experts from our recently convened working group recommended adopting the following simple working definition: Resilience is the ability to resist and recover from a stressor. Assets and resources within the individual, their life and environment facilitate this capacity for adaptation and bouncing back in the face of adversity. Although much of the scientific research landscape has focused on the treatment and modification of symptoms, enhancing resilience may be key to achieving optimal CVH. Leveraging existing precision medicine efforts such as NIH’s All of Us Research Program, NHLBI’s TOPMed, and the National Center for Biotechnology Informations database of Genotypes and Phenotypes are critical to efforts to incorporate research on resilience into the Division’s grant portfolio by enabling a systems biology approach to understanding response and adaptation to environmental and behavioral exposures, including medications. Recommendations from our recent working group suggest future directions should include efforts in understanding resilience across the spectrum from basic science to population sciences, stimulation of big data approaches to detection of stressors and resilience enhancing factors in resources such as TOPMed, development of standardized metrics of resilience, and trials of resilience enhancing interventions.

### Promoting CVH and Preventing CVD Across the Lifespan

Despite improvements in life expectancy throughout the 20th Century, continued improvement in the overall health of the US population is threatened by the increasing incidence and prevalence rates of obesity, type 2 diabetes mellitus, and hypertension,

<table>
<thead>
<tr>
<th>Workshop Topic</th>
<th>Links</th>
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<tr>
<td>Diversity training support at NHLBI, 5/2018</td>
<td><a href="#">Web link pending</a></td>
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<tr>
<td>Enhancing resilience for cardiovascular health and wellness, 7/2018</td>
<td><a href="#">Web link pending</a></td>
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<td>Defining the NHLBI’s research priorities in the ethical, legal, and social implications (ELSI) of genomics 9/2018</td>
<td><a href="#">Web link pending</a></td>
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<td>The role of short-term training in HLBS workforce development, 10/2018</td>
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<td>Cardiovascular consequences of post-traumatic stress disorder, 11/2018</td>
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<td>Hypertension: barriers to translation, 12/2018</td>
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life-long effects. In 2010, the American Heart Association childhood and modifications made during this period may have CVH in US populations including current cigarette smoking, 2020 impact goal uses 7 metrics as a means for keeping track of CVH. Heart trial (Optimal MacroNutrient Intake Trial to Prevent cardiovascular disease. 25 the ECHO program (Environmental influences on Child Health Outcomes), and the CHEAR/HHEAR (Children’s Health Exposure Analysis Resource/Human Health Exposure Analysis Resource). Future efforts could include support for basic, mechanistic, and epidemiological research on biomarkers of CVH, refinement and standardization of metrics, the biologic role of stressors at different development periods on CVH, and effective age-appropriate interventions, including dietary and behavioral interventions for preserving, promoting, and restoring CVH across the lifespan.

Eliminating Hypertension-Related CVD

High blood pressure is a major risk factor for the development of CVD, including heart failure, cerebral vascular disease, and coronary heart disease, 2030. Acute decompensated heart failure continues to be the leading risk factor for mortality and disability worldwide, causing ≈9.4 million deaths per year. Attempts to mitigate high blood pressure among the general population have traditionally been centered on medications that treat individuals diagnosed as having high blood pressure. Lifestyle modifications such as exercise, reduction in salt intake, maintenance of healthy weight, and eating a diet that is rich in fruits and vegetables and low in fat and cholesterol can also decrease blood pressure in individuals diagnosed with hypertension and prevent hypertension in individuals who do not have the disease. Despite these advancements in the treatment, differences continue to exist in the incidence and prevalence of hypertension, as hypertension incidence and prevalence is particularly high in Black compared with Whites. Ground breaking hypertension clinical trials supported by the NHLBI such as the blood pressure reduction in black barbershops and the SPRINT trial (Systolic Blood Pressure Intervention) have demonstrated the need for re-examining hypertension detection, treatment, and control methods. In addition, the DASH trial (Dietary Approaches to Stop Hypertension) as well as the subsequent DASH-Sodium trial and OMNI heart trial (Optimal MacroNutrient Intake Trial to Prevent Heart Disease) demonstrated that consuming a diet rich in fruits, vegetables, and low-fat dairy products, and reduced in saturated fat and cholesterol lowers both systolic and diastolic blood pressure. Although support of research on the prevention of hypertension continues to be a priority for DCVS, research on better methods to manage high blood pressure and its impact on cardiovascular events is also important. Future efforts could include support for research on translating basic science discoveries regarding blood pressure regulation into precision treatment strategies, understanding the biologic mechanisms that influence blood pressure trajectories across the lifespan, how early pharmacological treatment should be initiated to maximize prevention of vascular and target organ damage, the biologic basis of subgroup differences in incidence of hypertension and response to treatment, and effective implementation strategies for lifestyle and pharmacological interventions to prevent and treat hypertension.

Reducing the Burden of Heart Failure

In the United States, ≈6.5 million adults are living with heart failure with total costs of care for patients with heart failure estimated to be $31 billion and expected to increase to $70 billion by 2030 as the prevalence of this disease increases. Although advances in the treatment and prevention of heart failure have resulted in lower incidence rates, the prevalence of heart failure in the US is expected to increase by 46% by 2030. Acute decompensated heart failure continues to be the primary cause of hospitalization among the elderly. NHLBI initiatives such as the heart failure network have provided valuable insights into the efficacy of heart failure treatment protocols and have demonstrated the need for continued research to improve and advance prevention and treatment of heart failure. Future efforts could include support of research to understand the role of the mitochondria in heart failure and support of resources to enable research on other mechanisms of heart failure at the cellular and molecular level. Improved phenotyping of the complex set of conditions included under the umbrella of heart failure is also needed. This latter effort is especially pertinent to heart failure with preserved ejection fraction, for which therapeutic options are limited. Improved phenotyping could facilitate development of animal models and therapeutic strategies that are more precisely aligned with the underlying causes of the various heart failure phenotypes. Future efforts might also include innovative methods for partnering with heart failure patients to facilitate clinical research efforts, including trials. Opportunities exist to leverage other programs, including the All of Us Research Program and TOPMed, to advance heart failure prevention, phenotyping, and precision medicine.

Preventing Vascular Dementia

Dementia is a critical public health issue and is estimated to affect >47 million people globally. Dementia is an umbrella term that encompasses multiple disorders, often with mixed pathology and multifactorial cause. Vascular dementia, more recently known as vascular contributions to cognitive impairment and dementia (VCID), is defined as the aging neurovascular unit failing to cope with biological insults because of vascular disease, Alzheimer biology, metabolic disease, and immune affront, resulting in cognitive decline. After Alzheimer Disease (AD), vascular dementia
is the second most common dementia diagnosis, accounting for ≈20% of cases; furthermore, vascular pathology often co-exists with AD. Although dementia research is classified as being focused on AD and AD-related dementia, in clinical presentation, it is common to have both classic AD pathology and nonAD pathology, including vascular pathology together. As life expectancies continue to increase, the burden of dementia will continue to take a toll on health care systems and populations on a global basis, with costs associated with dementia in the US expected to soon surpass cancer and heart disease. Although the burden of dementia is expected to increase, there is evidence that the incidence may be decreasing, possibly due in part to more aggressive treatment of vascular risks, raising the likelihood, and promise of preventing dementia by treating vascular risk factors and diseases. In addressing the challenges faced in the prevention of VCID, a multi-pronged approach to supporting research is needed and might include: lifestyle changes, such as healthy diet, physical activity, and healthy weight, more effective treatment of CVD risk factors and disorders, a recalibration of measuring the prevalence and epidemiology of all dementia subtypes, better use of large data sets to collect and mine clinical data related to VCID, and reducing differences in VCID among racial and ethnic groups. Multiple opportunities exist to leverage efforts supported by the National Institute on Aging and the National Institute of Neurological Disorders and Stroke. Unique contributions supported by the NHLBI could include research on basic mechanisms of VCID, such as through continued support of research on vascular biology in the brain and the extension of animal models developed to study vascular disease into this research space. Other opportunities could include leveraging existing and future epidemiological studies and clinical trials to examine cognitive outcomes, including mild cognitive impairment and dementia, as has already been accomplished in studies leveraging multiple cohorts, including ARIC, CARDIA, Framingham Heart Study, JHS, MESA, and the WHI (Women’s Health Initiative), and several trials, including the ACCORD trial (Action to Control Cardiovascular Risk in Diabetes), SPRINT, and WHI.

Conclusions

The priorities described above, as informed by input from stakeholder-engagement in the strategic vision and subsequent workshops as well as dialogue with NHLBI advisory council will be used to augment our portfolio with strategically-focused institute activities or institute-solicited research programs that represent our best efforts to accelerate discovery and translation and to advance workforce development to nurture future generations of researchers. The dynamic process of implementation is ongoing in each of the areas discussed above; hence, we cannot provide detailed action plans at this time. We anticipate that reports from related workshops will provide additional information. We anticipate future reports will synthesize the output from relevant workshops and provide more detailed implementation plans. This document should be viewed as the first step in communicating this implementation plan to the community. Although not discussed above, workforce development is a theme that cuts across all scientific priorities, and an issue strongly endorsed by our investigator community. Furthermore, these priorities will inform funding recommendations for mechanisms where a payline is not specified. These priorities will not restrict development of other novel ideas for workshops and initiatives, nor restrict the investigator-initiated grant portfolio or select pay of other meritorious grant applications in DCVS' purview. DCVS will continue to capitalize on emerging opportunities, including re-evaluation of our focus areas to refresh these areas over time as appropriate. The DCVS strategic vision implementation plan is a living document that will evolve with iterative dialogue with the NHLBI community and adapt as the dynamic scientific landscape changes to seize emerging opportunities.

DCVS envisions that ten years hence, NHLBI will have fostered significant advancement of the state of cardiovascular science, the promotion of CVH, and the prevention of CVD by leveraging emerging opportunities in an informed, nimble, and collaborative fashion. We encourage the investigator community to pursue scientific advances related to the topics addressed above as well as the numerous other topics that hold promise for achieving our shared mission of turning discovery into CVH.

Appendix: NHLBI and NIH Staff Who Contributed to the DCVS Strategic Vision Implementation Plan

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Disclosures

None.