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SPECIAL ARTICLE

Implementing the National Heart, Lung, and Blood Institute's Strategic Vision in the Division of Cardiovascular Sciences—2022 Update

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ABSTRACT: Spurred by the 2016 release of the National Heart, Lung, and Blood Institute's Strategic Vision, the Division of Cardiovascular Sciences developed its Strategic Vision Implementation Plan—a blueprint for reigniting the decline in cardiovascular disease (CVD) mortality rates, improving health equity, and accelerating translation of scientific discoveries into better cardiovascular health (CVH). The 6 scientific focus areas of the Strategic Vision Implementation Plan reflect the multifactorial nature of CVD and include (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, and (6) preventing vascular dementia. This article presents an update of strategic vision implementation activities within Division of Cardiovascular Sciences. Overarching and cross-cutting themes include training the scientific workforce and engaging the extramural scientific community to stimulate transformative research in cardiovascular sciences. In partnership with other NIH Institutes, Federal agencies, industry, and the extramural research community, Division of Cardiovascular Sciences strategic vision implementation has stimulated development of numerous workshops and research funding opportunities. Strategic Vision Implementation Plan activities highlight innovative intervention modalities, interdisciplinary systems approaches to CVD reduction, a life course framework for CVH promotion and CVD prevention, and multi-pronged research strategies for combatting COVID-19. As new knowledge, technologies, and areas of scientific research emerge, Division of Cardiovascular Sciences will continue its thoughtful approach to strategic vision implementation, remaining poised to seize emerging opportunities and catalyze breakthroughs in cardiovascular sciences.

Key Words: cardiovascular diseases ■ heart failure ■ hypertension ■ social determinants of health ■ strategic vision ■ vascular dementia

Encouraged by more than a half-century of breakthroughs in cardiovascular medicine and research, the Division of Cardiovascular Sciences (DCVS) developed its plan for implementing the 2016 National Heart, Lung, and Blood Institute's (NHLBI) Strategic Vision against a backdrop of stalled progress toward improved cardiovascular health (CVH).[1,2] Successes, such as significant declines in ischemic heart disease mortality, are tempered by challenges, including decelerated improvement of cardiovascular disease (CVD) mortality rates; striking disparities in CVD morbidity and mortality; a disturbingly high proportion of maternal deaths attributable to CVD; the COVID-19 pandemic; and systemic inequities that impede efforts to combat emerging threats to CVH.[3,4]

The priorities outlined in the DCVS Strategic Vision Implementation Plan (SVIP) reflect NHLBI's resolve to reignite the decline in CVD mortality rates, improve health equity, and translate scientific discoveries into CVH by capitalizing on advances in omics technologies, data science, health informatics, cardiovascular imaging, and digital health. The DCVS SVIP emphasizes 6 scientific focus areas that map onto the NHLBI's 8 Strategic Vision objectives[1]:

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Nonstandard Abbreviations and Acronyms

AD	Alzheimer disease
BP	blood pressure
CVD	cardiovascular disease
CVH	cardiovascular health
DCVS	Division of Cardiovascular Sciences
HF	heart failure
HFpEF	heart failure with preserved ejection fraction
HLBS	heart, lung, blood, and sleep
NHLBI	National Heart, Lung, and Blood Institute
NIA	National Institute on Aging
NOSI	Notice of Special Interest
RURAL	Risk Underlying Rural Areas Longitudinal
SDoH	social determinants of health
SVIP	Strategic Vision Implementation Plan
VCID	vascular contributions to cognitive impairment and dementias

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

The SVIP focus areas reflect the multifactorial nature of CVD and emphasize a synergistic, integrative, and multidisciplinary approach to CVH promotion and CVD prevention. For example, uncontrolled hypertension is a risk factor for both heart failure (HF) and vascular dementia. Addressing social determinants of health, promoting CVH early in the life course, and enhancing resilience are avenues to reduce the risks of hypertension, HF, vascular dementia, and other CVD conditions. Since the 2016 release of the NHLBI Strategic Vision, DCVS working groups centered on SVIP focus areas have translated these priorities into Institute activities that stimulate research in CVD risk, prevention, diagnosis, and treatment. To identify research gaps and opportunities in SVIP focus areas, stimulate extramural research, and guide investigator-initiated applications, DCVS has convened numerous workshops (Table 1). DCVS has also developed or participated in numerous funding opportunities, including notices of special interest (NOSIs), and Institute-initiated funding opportunity announcements and requests for applications (Table 2). Many of these funding opportunities, particularly NOSIs, are directed toward the parent R01 funding opportunity announcements, which support basic and clinical research.

SVIP activities have leveraged the rich resources of our Institute, such as NHLBI cohort studies, which have provided rationale for addressing CVD, identified disparities, and unveiled effective intervention points. DCVS' pursuit of health equity is reflected in the many SVIP activities centered on addressing health disparities, improving population health, and training the next generation of researchers to address social determinants of CVH. For example, amid disturbing increases in CVD-related maternal morbidity and mortality, and glaring disparities therein,[3] multiple SVIP activities have centered on CVH during pregnancy and the postpartum period. Prevention and treatment of CVD across the life course features prominently among workshop topics, and a common theme among working groups is identifying factors of CVD resilience and risk. Notably, SVIP activities highlight our Institute's rapid and strategic response to COVID-19, as well as NHLBI's commitment to advancing the promise of precision cardiology.

In collaboration with the extramural research community, other NIH Institutes, Centers, and Offices, Federal agencies, nonprofit organizations, and industry, DCVS has made considerable progress towards implementing the NHLBI Strategic Vision. SVIP-centered activities conducted since the 2019 DCVS strategic plan publication[2] are found in Tables 1 and 2, with key deliverables highlighted in Table 3 and specific activities summarized below. DCVS has identified future research opportunities to engender further progress in SVIP implementation and stimulate transformative research in cardiovascular sciences (Table 4).

ADDRESSING SOCIAL DETERMINANTS OF CVH AND HEALTH INEQUITIES

Social determinants of health (SDoH) are nonmedical conditions in which people are born, work, play, and live.[5] These conditions are shaped by hierarchical and multilevel federal, state, municipal, and local systems, as well as sociocultural and family practices. SDoH include socioeconomic status, health care and education access and quality, neighborhood and environmental characteristics, and social and community context. The COVID-19 pandemic and heightened awareness of structural/systemic social injustice have underscored the interplay of SDoH factors in contributing to health inequities. Widening and persistent health disparities highlight the need for continued stimulation of scientific discoveries that address and improve SDoH factors and reduce heart, lung, blood, and sleep (HLBS) inequities. A major DCVS goal is to actively mitigate—not just observe or elucidate—SDoH in promoting CVH and preventing CVD to reduce or eliminate health disparities and promote health equity.

A portfolio analysis using the SDoH Research, Condition, and Disease Categorization term[6] indicated that

Table 1. Workshops

Meeting title	Topic/research type	Links
Harnessing novel data sources and technologies for the Study of Social Determinants of Health in Heart, Lung, Blood, and Sleep Disorders, 9/2020	SDoH/population science	https://datascience.nih.gov/news/harnessing-novel-data-sources-and-technologies-study-social-determinants-health-heart-lung
Diagnostics and Disease Management Tools for Use in Underserved Populations, 4/2021	SDoH/population science	https://www.nhlbi.nih.gov/events/2021/diagnostics-and-disease-management-tools-use-underserved-populations-nhlbi-research
Food Insecurity, Neighborhood Food Environment, and Nutrition Health Disparities: State of the Science, 9/2021	SDoH/population science	https://www.nhlbi.nih.gov/events/2021/food-insecurity-neighborhood-food-environment-and-nutrition-health-disparities
Identifying research opportunities for Asian American, Native Hawaiian, and Pacific Islander Health, 3/2021	SDoH/population science	https://www.nhlbi.nih.gov/events/2021/identifying-research-opportunities-asian-american-native-hawaiian-and-pacific-islander
NHLBI Sleep 101 Symposium: Sleep Health in the Pandemic and Beyond, 9/2021	SDoH, resilience, CVH/population science	https://www.nhlbi.nih.gov/events/2021/sleep-101-symposium-sleep-health-pandemic-and-beyond
Enhancing resilience for cardiovascular health and wellness 7/2018	Resilience/basic research	https://www.nhlbi.nih.gov/events/2018/enhancing-resilience-cardiovascular-health-and-wellness
Exerkines in health, resilience, and diseases, 8/2020	Resilience/basic research	https://www.nhlbi.nih.gov/events/2020/nhlbi-and-niddk-workshop-exerkines-health-resilience-and-diseases-executive-summary
Engineering extracellular vesicles for HLBS diseases, 9/2021	Resilience/Basic Research	https://www.nhlbi.nih.gov/events/2021/engineering-extracellular-vesicles-heart-lung-blood-and-sleep-diseases-workshop
Methodological Approaches for Whole Person Research, 9/2021	Resilience/basic research	https://www.nccih.nih.gov/news/events/methodological-approaches-for-whole-person-research
Promoting cardiovascular health in early childhood (0-5 y) and transitions in childhood through adolescence, 6/2018	CVH/basic, clinical, and population research	https://www.nhlbi.nih.gov/events/2018/promoting-cardiovascular-health-early-childhood-0-5-years-and-transitions-childhood
E-cigarette prevention and cessation in youth and young adults, 4/2020	CVH/Population Science	https://www.nhlbi.nih.gov/events/2020/workshop-addresses-youth-vaping-epidemic
Pregnancy and maternal conditions that increase risk of morbidity and mortality, 5/2020	CVH/population science	https://www.nhlbi.nih.gov/events/2020/maternal-mortality-workshop
Precision nutrition: research gaps and opportunities, 1/2021	CHV/population and clinical research	https://www.nhlbi.nih.gov/events/2021/precision-nutrition-research-gaps-and-opportunities-workshop
Cardiovascular Risk Prediction for Maternal Mortality and Morbidity and Beyond, 2/2021	CVH/clinical research	https://www.nhlbi.nih.gov/events/2021/cardiovascular-risk-prediction-maternal-mortality-and-morbidity-and-beyond-workshop
Cardiovascular risk across the lifespan for polycystic ovary syndrome, 10/2021	CVH/population science	https://www.nhlbi.nih.gov/events/2021/cardiovascular-risk-across-lifespan-polycystic-ovary-syndrome-workshop
Hypertension: barriers to translation, 12/2018	Hypertension/basic and clinical research	https://www.nhlbi.nih.gov/events/2018/nhlbi-working-group-hypertension-barriers-translation-executive-summary
In the United States, why has blood pressure control declined nationally, and what solutions will improve blood pressure control?, 10/2020	Hypertension/ Population Science	https://www.nhlbi.nih.gov/events/2020/why-has-blood-pressure-control-declined-nationally-and-what-solutions-will-improve
Toward precision medicine: understanding circadian rhythms in blood pressure regulation and chronotherapy in hypertension, 10/2021	Hypertension/population science	https://www.nhlbi.nih.gov/events/2021/toward-precision-medicine-circadian-rhythm-blood-pressure-and-chronotherapy
Webinar series on research priorities in atrial fibrillation to advance population, clinical and basic research: ablation, 3/2019	HF/basic, clinical, and population research	https://nhlbi.nih.gov/events/2019/webinar-series-research-priorities-atrial-fibrillation-ablation
Improving heart failure care for older adults: Gaps and strategies to optimize care transitions, 9/2021	HF, CVH/ Population Science	https://www.nhlbi.nih.gov/events/2021/improving-heart-failure-care-older-adults-gaps-and-strategies-optimize-care-transitions
Extracorporeal CPR for out-of-hospital cardiac arrest, 8/2021	HF/clinical research	https://www.nhlbi.nih.gov/events/2021/extracorporeal-cpr-ecpr-out-hospital-cardiac-arrest
Eradication of rheumatic heart disease, 11/2021	HF/population science	https://www.nhlbi.nih.gov/events/2021/eradication-rheumatic-heart-disease-assessing-research-challenges-and-opportunities
Vascular contributions to cognitive impairment and dementia, 5/2018	VCID/basic and clinical research	https://www.nhlbi.nih.gov/events/2018/nhlbi-working-group-vascular-contributions-cognitive-impairment-and-dementia-executive
Future clinical trials to test promising approaches for reducing vascular contributions to cognitive impairment and dementia, 11/2019	VCID/clinical research	https://www.nhlbi.nih.gov/events/2019/future-clinical-trials-test-promising-approaches-reducing-vascular-contributions
Opportunities and challenges in establishing a comprehensive assessment of cognitive and dementia-like phenotypes associated with existing models of vascular disease, 9/2021	VCID/basic research	https://www.nhlbi.nih.gov/events/2021/opportunities-and-challenges-establishing-comprehensive-assessment-cognitive-and

CVH indicates promoting Cardiovascular Health and preventing cardiovascular disease (CVD) across the lifespan; HF, reducing the burden of heart failure; HTN, hypertension, eliminating hypertension-related CVD; SDoH, addressing social determinants of CVH and health inequities; resilience, enhancing resilience; and VCID, preventing vascular dementia.

Table 2. Funding Initiatives

Initiative title	Topic/research type	Links
Disparities elimination through coordinated interventions to prevent and control heart and lung disease risk (DECIPHeR) (UG3/UH3 Clinical Trial Optional), March, 2019	SDoH/hypertension/ population and clinical research	https://grants.nih.gov/grants/guide/rfa-files/rfa-hl-20-003.html
DECIPHeR–Research Coordinating Center (U24 Clinical Trial Not Allowed), March, 2019	SDoH/Hypertension/ Population and Clinical Research	https://grants.nih.gov/grants/guide/rfa-files/rfa-hl-20-004.html
Native American Research Centers for Health (S06 Clinical Trials Optional), March, 2020	SDoH/population science	https://grants.nih.gov/grants/guide/pa-files/PAR-20-125.html
Notice of Special Interest (NOSI): Availability of Administrative Supplements and Urgent Competitive Revisions for Research on the 2019 Novel Coronavirus and the Behavioral and Social Sciences, April, 2020	SDoH/population science	https://grants.nih.gov/grants/guide/notice-files/not-od-20-097.html
NOSI: Emergency Competitive Revisions for Community-Engaged Research on COVID-19 Testing among Underserved and/or Vulnerable Populations, June, 2020	SDoH/population Science	https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-121.html
NOSI: Digital Health care Interventions to Address the Secondary Health Effects Related to Social, Behavioral, and Economic Impact of COVID-19, June, 2020	SDoH/population science	https://grants.nih.gov/grants/guide/notice-files/not-mh-20-053.html
Intervention Research to Improve Native American Health (R01 Clinical Trial Optional), August, 2020	SDoH/population science	https://grants.nih.gov/grants/guide/pa-files/PAR-20-238.html
Transformative Research to Address Health Disparities and Advance Health Equity at Minority Serving Institutions (U01 Clinical Trial Allowed), March, 2021	SDoH/population science	https://grants.nih.gov/grants/guide/rfa-files/RFA-RM-21-022.html
Understanding and Addressing the Impact of Structural Racism and Discrimination on Minority Health and Health Disparities (R01 Clinical Trial Optional), March, 2021	SDoH/population science	https://grants.nih.gov/grants/guide/rfa-files/RFA-MD-21-004.html
Transformative Research to Address Health Disparities and Advance Health Equity (U01 Clinical Trial Allowed), March, 2021	SDoH/population science	https://grants.nih.gov/grants/guide/rfa-files/RFA-RM-21-021.html
NOSI: Research to Address Vaccine Hesitancy, Uptake, and Implementation among Populations that Experience Health Disparities, December, 2021	SDoH/population science	https://grants.nih.gov/grants/guide/notice-files/NOT-MD-22-006.html
New Epidemiological Cohort Study among Asian Americans, Native Hawaiians, and Pacific Islanders (AsA-NHPI): Clinical/Community Field Centers (UG3/UH3-Clinical Trial Not Allowed), July, 2022	SDoH/population science	https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-23-015.html
New Epidemiological Cohort Study among AsA-NHPI: Coordinating Center (U24-Clinical Trial Not Allowed), 7/2022	SDoH/population science	https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-23-016.html
NOSI: the influence of host resilience on heterogeneity of acute respiratory distress syndrome/acute lung injury, September, 2020	Resilience/basic research	https://grants.nih.gov/grants/guide/notice-files/NOT- HL-20-814.html
NOSI: Promoting Research on Interoception and Its Impact on Health and Disease, January, 2021	Resilience/basic research	https://grants.nih.gov/grants/guide/notice-files/NOT-AT-21-002.html
NOSI: Somatic Cell Gene Editing Therapies to Improve Transplantation Outcomes, October, 2021	HF/basic research	https://grants.nih.gov/grants/guide/notice-files/NOT-AI-21-080.html
Early intervention to promote cardiovascular health of mothers and children (ENRICH) Multisite Clinical Centers (Collaborative UG3/UH3 Clinical Trial Required), February, 2021	CVH/clinical science	https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-007.html
ENRICH multisite resource and coordinating center (U24 Clinical Trial Required), February, 2021	CVH/clinical science	https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-008.html
Limited competition for the continuation of epidemiology of diabetes interventions and complications study research center (Collaborative U01 Clinical Trial Not Allowed), August, 2021	CVH/Basic Research	https://grants.nih.gov/grants/guide/rfa-files/RFA-DK-21-503.html
NOSI: promoting cardiovascular and cardiometabolic health in early stages of the lifecourse: preadolescence through adolescence to young adulthood, August, 2021	CVH/population and clinical science	https://grants.nih.gov/grants/guide/notice-files/NOT-HL-21-015.html
NHLBI Big Data Analysis Challenge: Creating New Paradigms for Heart Failure Research, February, 2020	HF/basic research	https://www.nhlbi.nih.gov/grants-and-training/funding-opportunities-and-contacts/NHLBI-heart-failure-data-challenge
Cardiovascular Biorepository for Type 1 Diabetes (U24 Clinical Trial Not Allowed), August, 2021	HF/basic research	https://grants.nih.gov/grants/guide/rfa-files/rfa-dk-21-010.html
NOSI: Improving Outcomes in Cancer Treatment-Related Cardiotoxicity, November, 2021	HF/basic research	https://grants.nih.gov/grants/guide/notice-files/NOT-CA-22-001.html
Development and Validation of Advanced Mammalian Models for Alzheimer's Disease-Related Dementias (R61/R33 Clinical Trial Not Allowed), January, 2019	VCID/basic research	https://grants.nih.gov/grants/guide/pa-files/PAR-19-167.html
NOSI: Promoting research to understand vascular contributions to cognitive impairment and dementia, October, 2021	VCID/basic research	https://grants.nih.gov/grants/guide/notice-files/NOT-HL-23-002.html
Catalyze: Enabling Technologies and Transformative Platforms for HLBS Research (R33–Clinical Trials Not Allowed), January, 2021	HLBS/basic research	https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-23-010.html

CVH indicates cardiovascular health; HF, heart failure; HLBS, heart, lung, blood, and sleep; NHLBI, National Heart, Lung, and Blood Institute; NOSI, Notice of Special Interest; SDoH, social determinants of health; and VCID, vascular contributions to cognitive impairment and dementias.

Table 3. Strategic Vision Implementation Deliverables

	Peer-reviewed white papers and workshop reports	Funded projects
SDoH	Suglia et al,[42] Paul et al,[43] Kanaya et al,[44] Brown et al[7]	7 projects RFA-HL-20-003
		1 project RFA-HL-20-004
		1 project RFA-MD-21-004
		2 projects NOT-OD-20-097
		1 project NOT-OD-20-120
		1 project PAR-20-238
Resilience	Gao and Galis,[14] Chow et al[15]	1 project NOT-HL-20-814
		2 projects NOT-AT-21-002
		1 project NOT-AT-21-002
CVH	Daniels et al,[18] Suglia et al[42]	7 projects RFA-HL-22-007 (ENRICH)
		1 project RFA-HL-22-008 (ENRICH)
		3 projects NOT-OD-20-104
		3 projects NOT-OD-21-071
		1 project NOT-EB-21-001
Hypertension (HTN)	Sigmund et al,[22] Commodore-Mensah et al[45]	3 projects RFA-HL-20-003 (DECIPHeR)
HF	Al-Khatib et al,[46] Delisle et al,[47] O'Donnell et al,[48] Mehra et al[49]	6 projects RFA-HL-21-015 (HeartShare)
		1 project RFA-HL-21-016 (HeartShare)
		5 projects NHLBI HF Big Data Challenge
VCID	Zlokovic et al[50] Muratoglu et al[51]	25 projects NOT-AG-18-008
		34 projects NOT-AG-18-039
		25 projects NOT-AG-20-008
		25 projects NOT-AG-20-034

CVH indicates cardiovascular health; HF, heart failure; HTN, hypertension; SDoH, social determinants of health; and VCID, vascular contributions to cognitive impairment and dementias.

only 4.3% of NHLBI applications funded within Fiscal Years 2008 to 2020 were in the area of SDoH, although the number of SDoH-funded applications increased 121% over this period.[7] Using the Healthy People 2020 SDoH subcategories,[8] the most highly funded SDoH areas were identified as Health and Health Care (62%), Economic Stability (61%), and Neighborhood/Built Environment (54%). In addition to funding SDoH-relevant research, DCVS has led multiple SDoH-related scientific workshops and participated in various funding opportunity announcements. For example, a 2020 NHLBI workshop, "Harnessing Novel Data Sources and Technologies for the Study of Social Determinants of Health in Heart, Lung, Blood, and Sleep Disorders," discussed how researchers can leverage digital technology and novel data sources to enhance SDoH research. This meeting also examined the influence of the digital divide and unintended consequences of novel technologies in widening health disparities, and implementation strategies to enhance the scientific use of novel data sources for SDoH research.

Additionally, through its Center for Translation Research and Implementation Science (CTRIS), NHLBI initiated the Disparities Elimination through Coordinated Interventions to Prevent and Control Heart and Lung Disease Risk (DECIPHeR) Alliance to test evidence-based multi-level interventions for reducing or eliminating cardiovascular and/or pulmonary disparities and improve health in high-burden communities (Table 2). This effort consists of a Research Coordination Center and Implementation Research Centers that engage diverse multidisciplinary stakeholders to effectively deliver evidence-based interventions to high-burden populations. NHLBI will also participate in Advancing Prevention Research for Health Equity, a trans-NIH research effort to develop new preventive interventions and strategies to deliver existing interventions in populations experiencing health disparities.[9]

DCVS has developed or participated in training initiatives specifically focused on SDoH and health disparities, such as a 2021 NHLBI workshop to discuss SDoH training experiences and the need for cross-institutional and interdisciplinary SDoH-training approaches. A portfolio analysis conducted as part of this workshop showed roughly 7% of NHLBI's total training awards mapped to SDoH. Workshop opportunities for advancing SDoH training included more mechanisms that protected time for mentoring and training, particularly for mid-career and senior mentors; increased networking prospects; and greater support, including infrastructure

Table 4. Future Research Opportunities

	Basic	Clinical	Population
SDoH	Identify mechanisms of SDoH influence on CVD risk and pathogenesis	Develop multi-level interventions to reduce health disparities	Leverage cohort studies and novel data sources to further evaluate CVD-SDoH associations
Resilience	Identify the molecular drivers of resilience and factors that influence ARDS/ALI recovery	Develop multi-level interventions that promote resilience in vulnerable populations	In cohort studies, assess longitudinal impacts of adverse environmental conditions on resilience
CVH	Identify biomarkers in childhood, and trajectories through adolescence, to examine associations of early life environment withCVD risk	Develop interventions to improve dietary and medication adherence for older patients with HF	Elucidate impacts of adverse pregnancy outcomes on CVH trajectories
HTN	Leverage imaging and single-cell technologies to assess HTN-induced changes at cellular- and tissue-levels	Develop clinical trials for early intervention and new treatments for diverse hypertensive patient populations	Develop deeply phenotyped cohorts for improved HTN risk and treatment prediction
HF	Elucidate HF pathophysiology after onset of atrial fibrillation	Develop improved algorithms for clinical decision-making processes for advanced HF	Conduct deep phenotyping studies to define HFpEF subtypes
VCID	Develop animal models that recapitulate progressive changes in human dementia	Develop clinical trials that test efficacy of CVD interventions for VCID	Elucidate population-level differences in VCID risk and trajectory

See future research opportunities further discussed in SVIP Workshop executive summaries[52] and peer-reviewed workshop reports.[7,14,15,18,22,42–50] CVD indicates cardiovascular disease; CVH, cardiovascular health; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; SDoH, social determinants of health; and VCID, vascular contributions to cognitive impairment and dementias.

development, for less research-intensive institutions. Other training-related activities include participation in the NIH Common Fund program Community Partnerships to Advance Science for Society, which includes skill development and training curricula and aims to reduce health disparities by developing community-driven, healthy equity structural interventions.[10]

Future research directions include continued support of SDoH-related applications to reduce health inequities and advocating for clinical studies to measure SDoH. NHLBI has joined a trans-NIH SDoH Special Interest Group that will address SDoH in research by establishing interdisciplinary research teams, engaging community organizations and members in the full spectrum of research, using innovative and interdisciplinary research methods, and focusing intervention implementation in communities most affected by health inequities. NHLBI will continue to prioritize diversifying the scientific workforce and training of the next generation of scientists in SDoH, taking inspiration from past efforts such as the Diversity Training Workshop, which discussed the strengths, limitations, and gaps of current diversity-focused training mechanisms[11]; and a 2021 NHLBI workshop that discussed current challenges in maintaining a sufficient pool of physician-scientists, women, and underrepresented researchers.[12]

ENHANCING RESILIENCE

The DCVS Enhancing Resilience Working Group has been guided by the discussions at the initial 2018 NHLBI workshop on "Enhancing Resilience for CVH and Wellness" (Table 1). To facilitate a shared understanding of "resilience," attendees adopted a simplified working definition of the term: "Resilience is the ability of living systems to successfully maintain or return to homeostasis in response to physical, molecular, individual, social, societal, or environmental stressors or challenges." One workshop-identified opportunity was to pursue understanding and integration of the many facets of resilience. To this end, the Resilience Working Group collaborated with other DCVS SVIP working groups. For example, in collaboration with the HF Working Group and through NHLBI lectures, the working group examined potential contributions of mitochondrial genetics to cardiovascular resilience.[13] Invited extramural experts also discussed various aspects of resilience related to COVID-19 complications. Endothelial cell resilience has emerged as a key contributor to avoiding COVID-19-related and overall CVD morbidity, an issue highlighted in a call to action for research into the underpinnings of endothelial resilience.[14]

The Resilience Working Group has expanded to include representatives from the other NHLBI Divisions and to address topics beyond CVH, such as the role of host resilience as a critical determinant of outcomes in acute respiratory distress syndrome/acute lung injury (ARDS/ALI; Table 2). The Resilience Working Group recognized the need for effective communications and cooperation across NIH Institutes, Centers, and Offices, resulting in other NIH resilience-related initiatives. For example, in collaboration with the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK), NHLBI organized a 2020 workshop focused on the actions of exercise molecular mediators called "Exerkines." The "Exerkines in Health, Resilience, and Diseases" Workshop was attended by over 300 participants from 10 countries (Table 1). A white paper, including specific considerations about how exercise may contribute to enhancing CVH and resilience, was published.[15]

NHLBI was also one of the Trans-NIH Resilience Working Group inaugural members, which includes several

ICOs.[16] As the first order of business, NHLBI representatives proposed a shared definition of resilience. Trans-ICO collaboration during a 2020 resilience-focused NIH workshop resulted in the following statement: "NIH seeks fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability through the study of resilience. Resilience encompasses the capacity to resist, adapt to, recover, or grow from a challenge."[16] NHLBI also contributed to the development of a proposed framework for designing or identifying studies already funded by NIH that could test the contribution and mechanisms underlying resilience in various contexts. The Resilience Research Design Tool is proposed for consideration by potential applicants and NIH staff when planning research interventions to study resilience.[16] A webinar series highlighting different resilience topics related to the mission of various NIH Institutes, Centers, and Offices is ongoing.

NHLBI participates in the trans-NIH NOSI "Promoting Research on Interoception (the perception of sensations from inside the body) and Its Impact on Health and Disease" (Table 2). For this NOSI, NHLBI is interested in basic, translational, and clinical research to examine interoceptive processes and mechanisms mediating HLBS normal biological function and disease pathophysiology. Future research directions include increasing cross-collaborations to study resilience and enable training of the next generation of resilience researchers. This could help shift the current cardiovascular research paradigm from reactive to proactive by incorporating concepts of resilience from therapeutics to preventive and implementation science approaches.

PROMOTING CVH AND PREVENTING CVD ACROSS THE LIFESPAN

Improving CVH across the lifespan, from pregnancy, infancy, early childhood, and adulthood through older adulthood, remains critical for reducing CVD burden. Understanding age-associated physiological changes and disease progression across the lifespan will inform opportunities to identify risk, address chronic diseases earlier in their development, and initiate prevention efforts to reduce chronic disease burden. It is critical to identify the factors that lead to poorer CVH, beginning in utero and at the earliest stages of life, as well as lifestyle and behavioral interventions to prevent CVD later in life. Accumulation of risk factors, including hypertension, diabetes, smoking, poor diet, and physical inactivity, contributes to adverse cardiovascular events in later life. Thus, bold new strategies, spanning medicine, public health, and health policy, are needed to combat CVD.

DCVS and the Center for Translation and Implementation Science are collaborating on major efforts to improve maternal CVH, such as the Maternal Health Community Implementation Project[17] and the "Early Intervention to Promote CVH of Mothers and Children (ENRICH)" initiative, which will investigate whether an early intervention delivered within the context of a home visiting program can enhance both maternal and early childhood CVH (Table 2). Similarly, limited metrics for ideal CVH during key pediatric developmental periods motivated publication of an initiative to define these metrics and stimulate epidemiological research on CVH trajectory during childhood (Table 2).

A 2018 workshop "Promoting CVH in Early Childhood and Transitions in Childhood through Adolescence" included interdisciplinary experts who discussed the state of the science, identified research gaps, and provided opportunities for promoting CVH in early childhood and transitions through adolescence.[18,19] Similarly, NHLBI published a 2021 NOSI, "Promoting Cardiovascular and Cardiometabolic Health in Early Stages of the Lifecourse: Preadolescence and Adolescence to Young Adulthood," to stimulate research on the mechanisms of cardiometabolic health and disease pathogenesis in vulnerable groups and to develop precision prevention interventions to address risk factors during these life stages (Table 2). Finally, in collaboration with the DCVS' Reducing the Burden of HF Working Group, a recent workshop "Improving HF Care for Older Adults: Optimizing Care Transitions" gathered experts to address gaps in treatment and care strategies underlying plateauing improvements in HF hospitalizations and the tremendous morbidity burden on older adults who are managing this disorder (Table 1).

Future research and training opportunities include elucidating the impact of early-life environmental exposures on CVD risk trajectories and integrating the life course perspective into clinician training. NHLBI is working with other ICOs including the National Institute of Child Health, NIH Office of Research in Women's Health (ORWH), and the National Institute of Aging to stimulate research across the lifespan.

ELIMINATING HYPERTENSION-RELATED CVD

Hypertension or high blood pressure (BP) is a major preventable risk factor for CVD and stroke.[20] According to the 2017 American College of Cardiology/American Heart Association Hypertension Clinical Practice Guidelines, nearly half of American adults have hypertension, defined as a systolic BP >130 mm Hg or a diastolic BP>80 mm Hg or self-reported antihypertensive medicine use.[21] A recent serial cross-sectional analysis of National Health and Nutrition Examination Survey data from 1999 to 2018 reported that hypertension control (defined as systolic BP level <140 mm Hg and diastolic

BP level <90 mm Hg) rates were stagnant during 2007 to 2014 and then worsened after 2013 to 2014.[20]

NHLBI and the Centers for Disease Control and Prevention (CDC) convened a 2020 workshop to discuss the reasons for the decline in hypertension control, barriers to regaining previous improvements, possible solutions at multiple levels, research priorities, and policy changes that might facilitate addressing this national problem (Table 1). NHLBI also organized a workshop, involving experts from varied hypertension research backgrounds, to identify barriers for the translation of basic science discoveries and knowledge of pathobiology into better hypertension treatments that can reach diverse patient populations (Table 1). Eight major challenges were identified by the workshop: (1) communication gaps among basic and clinical researchers, (2) incomplete understanding of hypertension antecedents, (3) gene-environment and gene-gene interactions to improve therapeutic decisions, (4) relevance of animal models to humans, (5) detection and reversal of patient nonadherence to hypertension medication, (6) age-related BP changes in children and young adults, (7) insufficient engagement of diverse stakeholders to enhance uptake and feasibility of clinical trials and their findings, and (8) how to bring efficacious community-based interventions up to scale.[22]

To facilitate the adoption of hypertension research findings into real-world settings, NHLBI currently supports 3 projects involving hypertension control implementation via the DECIPHeR program described above (Tables 2 and 3). NHLBI convened a workshop "Toward Precision Medicine: Circadian Rhythm of BP and Chronotherapy for Hypertension" to identify knowledge gaps related to gene-environment and gene-gene interactions in BP regulation (Table 1). Future research includes collection of BP measurements and related data through National Health and Nutrition Examination Survey to monitor trends in hypertension prevalence and control and assess the impact of future interventions. BP-related data are collected repeatedly at the clinical examinations of NHLBI-funded cohort studies, revealing longitudinal BP patterns and CVD risk trajectories. Further research into the association between long-term changes in BP levels and hypertension status and CVD outcomes will inform understanding and treatment of hypertension-associated CVD.

REDUCING THE BURDEN OF HF

HF continues to be a major public health burden and is rising in prevalence as the population ages. HF is often categorized by a single measurement, ejection fraction, that is poorly related to its pathophysiology. HF with preserved ejection fraction (HFpEF) accounts for approximately half of the ~6.5 million HF cases in the United States, involves multiple cardiac and extra-cardiac abnormalities, has a 50% mortality rate 5 years post-diagnosis, and has only recently had its first positive trial showing that empagliflozin reduces cardiovascular death and HF hospitalization.[23] Thus, there is an urgent need to improve the identification of HF subtypes through deep phenotyping to advance understanding of disease mechanisms, prevention, diagnosis, and treatment, with the long-term goal of applying personalized approaches to treat specific HF patients.

To better understand HF pathophysiology, NHLBI issued a "Big Data Analysis Challenge: Creating Paradigms for HF Research" competition to solicit innovative, open-source models that can define HF subtypes and generate new research hypotheses (Table 2). The recently awarded NHLBI HeartShare Program will also define HF subtypes based on biological mechanisms through deep phenotyping, imaging, and omics of patients with HFpEF (Table 2). HeartShare's objectives are to (1) analyze large datasets from diverse HFpEF patients, including those in NHLBI cohorts; (2) relate biological measurements with clinical outcomes; and (3) create and validate HF diagnostic algorithms that can be used by clinicians. The long-term goal is to better understand HFpEF pathophysiology and identify treatment targets with the ultimate aim of precision medicine trials. Efforts are ongoing for HeartShare's expansion with a public-private partnership between the NIH and industry as a HF Accelerated Medicines Partnership (HF AMP) to improve understanding of HF disease pathways and facilitate better selection of treatment targets.[24]

Recent relevant NHLBI workshops have examined the circadian mechanisms underlying sudden cardiac death; the molecular, immunologic, and pathological pathways underpinning myocarditis; the pathophysiology, prevention, treatment, and role of SDOH in combatting atrial fibrillation; and reducing readmissions and improving transitions of care in older HF patients (Table 1). Future research includes exploring artificial intelligence approaches in cardiovascular imaging toward improved clinical implementation and precision medicine, developing better animal models for HFpEF, and prevention and treatment of chemotherapy-induced HF in cancer patients.

PREVENTING VASCULAR DEMENTIA

Dementia is a public health crisis and an umbrella term that describes loss of cognitive function, including thinking, remembering, and behavioral abilities, that is severe enough to interfere with one's daily life. Alzheimer's disease (AD) is the most common dementia diagnosis, but AD as a clinical syndrome has mixed pathology and multifactorial etiology. Having biomarker evidence of AD is not the equivalent of AD clinical syndrome. Individuals with AD pathology (amyloid-β deposition and pathological tau) might not develop dementia without underlying vascular dysfunction or other co-existing conditions.

Human pathology findings suggest that over 50% of clinical AD patients have vascular injuries. The presence of cardiovascular risk factors, such as hypertension, obesity, diabetes, and smoking, particularly earlier in adulthood, has been associated with dementia and faster cognitive decline. The lack of an effective treatment for dementia underscores the urgency to identify and test treatment for modifiable risk factors. Notably, the results of the Systolic BP Intervention Trial-MIND substudy (SPRINT-MIND) were published since the 2019 publication of the SVIP and demonstrated that intensive treatment of systolic BP can reduce the incidence of mild cognitive impairment.[25]

To understand research gaps and opportunities in basic, translational, and clinical research in vascular dementia, NHLBI, in collaboration with the National Institute of Aging and the National Institute for Neurological Disorders and Strokes, organized three workshops from 2018 to 2021 (Table 1). The first workshop sought to identify research opportunities in basic and epidemiological research toward understanding vascular contributions to cognitive impairment and dementias (VCID). In 2019, a second workshop examined lessons learned from recently completed VCID trials, the promise of ongoing trials, and opportunities for additional clinical trials that deliver more effective interventions. In 2021, NHLBI convened the third workshop focused on establishment of a comprehensive assessment of neurological phenotypes, including cognitive deficiencies, associated with existing vascular disease animal models that have been used to study cardiovascular disorders (Table 1).

NHLBI joined an National Institute for Neurological Disorders and Strokes-led Funding Opportunity Announcement to support the Development and Validation of Advanced Mammalian Models for Alzheimer's Disease-Related Dementias in 2019 (Table 2). Although no meritorious applications were funded by NHLBI from this Funding Opportunity Announcement, there was considerable interest from the research community in this topic, and the unmet needs for VCID animal models persist. Researchers interested in developing and/or validating VCID animal models may consider applying through one of the NHLBI "Catalyze: Enabling Technologies and Transformative Platforms for HLBS Research" funding opportunity announcements (Table 2). Recently, NHLBI, with participation from National Institute for Neurological Disorders and Strokes and National Institute of Aging, published a NOSI to encourage collaborative and multidisciplinary research in VCID driven by investigators' interests that may require studying multiple organs and systems in the same grant (Table 2).

In addition to future VCID research described in the 3 workshop reports/executive summaries (Tables 1 and 3), there are numerous other research opportunities, including many that synergize with other SVIP focus areas, such as promoting CVH across lifespan and addressing SDoH. For example, further exploration of the association of childhood and early adult adverse CVD risk factors with VCID is required, as is identifying SDoH factors that contribute to VCID. NHLBI cohort study procedures feature cognitive assessments, and ancillary studies (eg, Multiethnic Study of Atherosclerosis-MIND and Atherosclerosis Risk in Communities-Neurocognitive Study) have also been established. Future work in these and other cohort studies will further unearth links between CVH and cognitive function. Regardless of the scientific areas, collaboration among researchers from various disciplines and across the translational research spectrum will be critical to advance VCID research.

UNDERSTANDING, PREVENTING, AND TREATING ACUTE AND POST-ACUTE (LONG) COVID-19

The serious cardiovascular, pulmonary, and hematologic complications of COVID-19 have placed NHLBI at the forefront of combatting the pandemic. NHLBI's multi-pronged strategy spans the research spectrum and includes initiating and participating in COVID-19 research funding opportunities that reflect its commitment to addressing COVID-19 cause, outcomes, and disparities (Table 2).[26]

A pillar of NHLBI's pandemic response is leveraging its research infrastructure, including clinical trial networks and cohort studies, to rapidly conduct research on COVID-19. For example, as part of the trans-NIH Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Initiative, NHLBI's Collaborating Network of Networks for Evaluating COVID-19 and Therapeutic Strategies (CONNECTS) leverages NHLBI networks to investigate COVID-19 risk factors and identify potential therapies.[27] The Collaborative Cohort of Cohorts for COVID-19 (C4R) study leverages NHLBI's population-based cohorts to investigate long-term COVID-19 effects and identify factors of risk and resilience.[28] In addition, the Long-Term Outcomes After the MUSIC (Multisystem Inflammatory Syndrome in Children) Study leverages the NHLBI Pediatric Heart Network to understand multisystem inflammatory syndrome in children (MIS-C), a COVID-19-related condition that disproportionately affects Black and Latinx children.[29] NHLBI is addressing Long COVID through participation in the NIH Researching COVID to Enhance Recovery (RECOVER) initiative, which aims to understand, prevent, and treat Long COVID.[30]

Community engagement is central to NHLBI's strategy for reducing COVID-19 disparities. With the National Institutes on Minority Health and Health Disparities (NIMHD), NHLBI co-leads the NIH Community Engagement Alliance (CEAL) against COVID-19. disparities.[31] This initiative fosters partnerships with

communities disproportionately burdened by COVID-19 to address mistrust and misinformation, increase COVID testing and vaccination, and promote inclusion in clinical trials. NHLBI also participates in Rapid Acceleration of Diagnostics-Underserved Populations (RADX-Up), community-based projects that evaluate and expand COVID-19 testing, and implement culturally tailored testing, in underserved and vulnerable populations.[32]

TRAINING THE NEXT GENERATION OF CARDIOVASCULAR SCIENTISTS

Training the next generation of HLBS researchers is critical for advancing DCVS SVIP goals, hence NHLBI leadership in several training and career development opportunities.[33] Among these are opportunities to recruit and retain researchers from diverse backgrounds, which is a high NHLBI priority. NHLBI's commitment to inclusive excellence is reflected in the many diversity-related funding opportunities in which the Institute has initiated or participated,[34] including the NHLBI Programs to Increase Diversity Among Individuals Engaged in Health-Related Research (PRIDE); the Helena Mishoe Fellowship for Underrepresented Scientists; and the NHLBI Mentored Research Scientist Career Development Award to Promote Faculty Diversity in Biomedical Research (K01).

NHLBI participates in the Support for Research Excellence (SuRE) Award programs to develop and sustain research excellence at institutions that receive limited NIH support and serve students from groups underrepresented in biomedical research.[35,36] NHLBI also participates in the Faculty Institutional Recruitment for Sustainable Transformation program, an NIH Common Fund initiative to recruit and support a diverse cohort of new research faculty.[37] In addition, NHLBI participates in the Maximizing Opportunities for Scientific and Academic Independent Careers program, which supports the career transitions of postdoctoral researchers from diverse backgrounds.[38]

NHLBI supports women in science through participation in the Office of Research in Women's Health (ORWH) Supplements to Promote Research Continuity and Retention, which help sustain research during critical life events, including childbirth. NHLBI will also participate in the ORWH Research Education Program (R25), supporting skills development and curriculum/methods development on topics relevant to sex/gender influences on HLBS diseases/disorders. Future directions include enhancing opportunities for transition of K awardees into independent research positions, stronger integration of data science into our training portfolio, and expanding research opportunities for physician-scientists.

CONCLUSIONS

The activities described herein emphasize a vision of enhanced CVH for all, encompassing concepts, areas of research, and emerging opportunities that can stimulate cutting-edge, transformative research in cardiovascular sciences. DCVS SVIP implementation has resulted in development of nearly 50 workshops/seminars and nearly 30 research funding opportunities (Tables 1 and 2). These activities span the research spectrum, offer avenues through which health equity can be achieved, leverage scientific and technological advances, and present a multi-pronged research strategy for tackling COVID-19. Key deliverables include peer-reviewed white papers, workshop executive reports, and NHLBI-funded projects (Table 3). SVIP implementation has also stimulated partnerships within NHLBI and with other NIH Institutes. Examples include collaboration with the Center for Translation Research and Implementation Science on hypertension and maternal well-being; partnerships with various ICOs, such as ORWH, National Institute of Aging, National Institute of Child Health, NIDDK, and National Institute for Neurological Disorders and Strokes; the Trans-NIH Resilience Working Group; the Trans-NIH SDoH Interest Group; trans-HHS partnerships (ENRICH), and public-private partnerships (HF AMP).

Giving shape to a vision of enhanced CVH for all requires forethought in an ever-evolving landscape in which new knowledge, areas of research, and technologies emerge. Thus, DCVS has identified opportunities for future research in pursuit of this vision (Table 4). Examples include leveraging the NHLBI Trans-omics for Precision Medicine Program (TOPMed)[39] and BioData Catalyst[40] to facilitate a systems-based understanding of CVD. Importantly, 60% of sequenced TOPMed participants are of non-European ancestry, ensuring health equity in the age of precision medicine. NHLBI will continue to stimulate research and training in data science, bioinformatics, and omics technology that address the complexity and heterogeneity of disorders such as HF.

Since the 2019 DCVS SVIP publication, NHLBI has developed 2 new cohort studies: The RURAL (Risk Underlying Rural Areas Longitudinal) cohort study[41]; and an epidemiological cohort study among Asian Americans, Native Hawaiians, and Pacific Islanders (Table 2). Future research in these cohorts will extend NHLBI's legacy of addressing CVH disparities and identifying factors of CVD risk and resilience in different populations. We will continue to address COVID-19 development, outcomes, and disparities, applying elements of NHLBI's pandemic response (eg, platform trial and "network of networks" approaches) to CVD prevention and treatment.

Just as the NHLBI SV, on which the DCVS SVIP is predicated, engaged the extramural community in its development, DCVS has sought input from extramural

researchers in achieving SVIP goals. DCVS will continue this engagement through NHLBI-organized workshops, in which extramural researchers participate to help identify gaps and barriers in research and recommend new research opportunities. DCVS will also continue inviting extramural researchers to present at the DCVS Strategic Vision Webinar Series. NHLBI frequently issues Requests for Information, through which the extramural community can contribute to strategic visioning efforts. Though much remains to be done to turn discovery into CVH, reignite the decline in CVD mortality, and close the equity gap in CVD and CVH, future DCVS endeavors and those discussed herein lay the groundwork for success.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

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