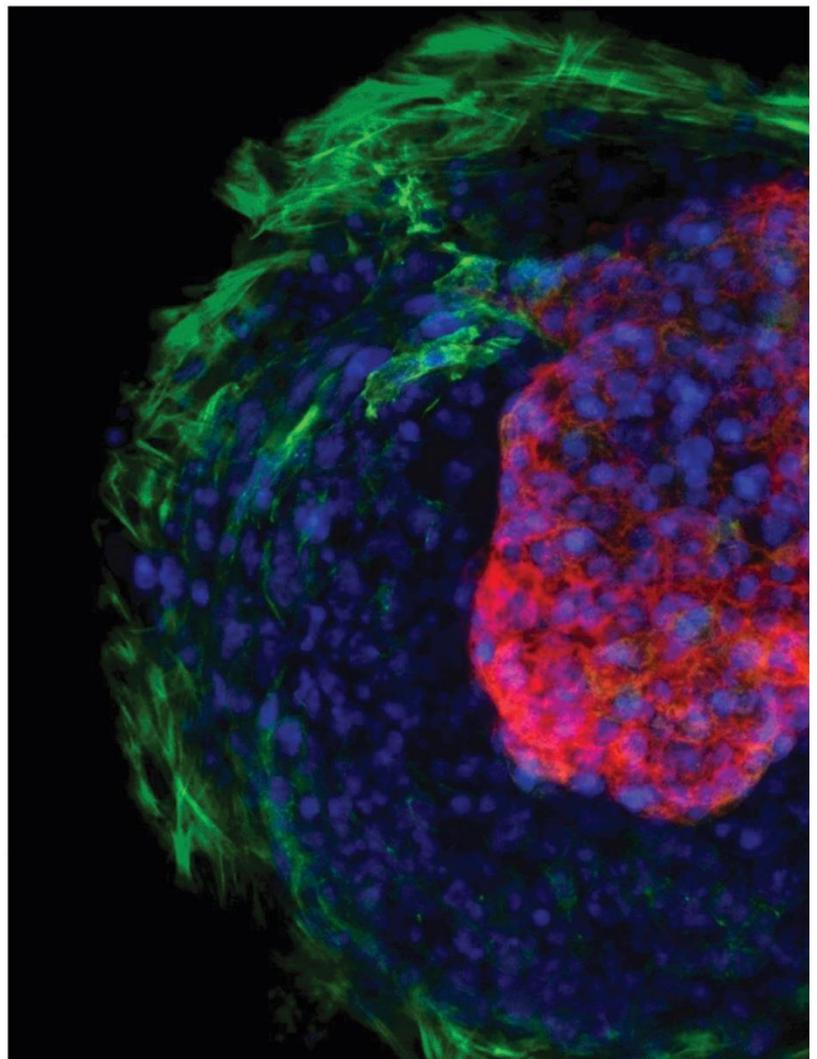
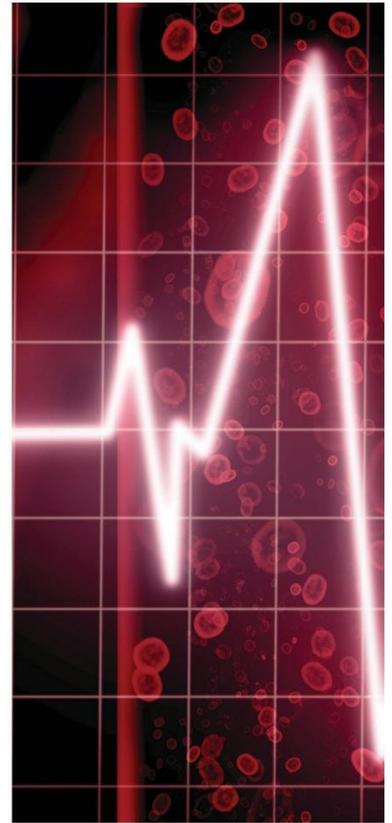


NHLBI OVERVIEW

Division of
Cardiovascular Sciences



NHLBI OVERVIEW: DIVISION OF CARDIOVASCULAR SCIENCES

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INTRODUCTION

The National Heart, Lung, and Blood Institute (NHLBI) has historically supported a robust and ambitious program of cardiovascular research comprising fundamental discovery science, early translational research, clinical investigations, and population science research through its Division of Cardiovascular Sciences (DCVS), which represents the union of two previously existing divisions, the Division of Cardiovascular Diseases and the Division of Prevention and Population Sciences in 2009. DCVS is the largest extramural division of the third largest institute of the National Institutes of Health (NIH), with an annual budget of \$1.75 billion divided among seven program branches with proportions ranging from 7 to 19 percent (Figure 1). As described in 2009,¹ these branches are distributed among three programs: the Adult and Pediatric Cardiac Research Program (APCRP), the Basic and Early Translational Research (BETR) Program, and the Prevention and Population Sciences Program (PPSP); APCRP has three branches and the other programs each have two branches. Outside these three programs, there are three offices that support the entire division (and other NHLBI divisions in some cases): the Office of Clinical Research (OCR), the Office of Biostatistics Research (OBR), and the Office of Research Training and Career Development (ORTCD), each with more than 1 percent of the DCVS budget.

Since 2009, significant advances in science and technology—like the rapidly decreasing cost and time for sequencing a human genome—and a budget trajectory that included the American Recovery and Reinvestment Act of 2009 (ARRA) and sequestration in 2013–5 have led to new areas of emphasis. These include support for pragmatic clinical trials costing less than \$2,000 per patient, streamlining large epidemiologic cohort studies, gene sequencing in well-phenotyped NHLBI epidemiologic cohorts, evaluating cardiovascular sequelae of chronic HIV infection, and most recently, an emphasis on genomic, proteomic, metabolomic, and phenotypic data in an effort to improve the prediction, prevention, diagnosis, and treatment of cardiovascular diseases (CVD) as part of the NHLBI's initiative in precision medicine. The flood of new research opportunities, in the absence of a flood of new resources, has also given rise to a new emphasis on portfolio analysis to enable DCVS to test its assumptions and direct resources to the

most needed areas.^{2–8} Finally, the recent NHLBI Strategic Visioning exercise⁹ and recommendations from specific working groups^{10–18} have made it timely to update the 2009 report.¹

In this article, DCVS provides an overview of its scientific activities in each organizational unit and describes recent major scientific contributions from its portfolio, including recently completed studies (Table 1); new and ongoing investigations (Table 2); and Trans-NHLBI, Trans-NIH, and interagency activities led or co-led by DCVS staff (Table 3). Summaries of major DCVS workshops, working groups, and scientific meetings are not listed here but may be accessed online at www.nhlbi.nih.gov/research/meetingsandreports.

ADULT AND PEDIATRIC CARDIAC RESEARCH PROGRAM (APCRP)

APCRP encompasses three branches: the Atherothrombosis and Coronary Artery Disease Branch (ACAD), the Heart Development and Structural Diseases Branch (HDSD), and the Heart Failure and Arrhythmias Branch (HFA). The scientific portfolio covers the spectrum of research from basic to clinical, as well as the lifespan from embryonic development to old age in disease conditions both common and rare. APCRP provides pediatric research leadership across NHLBI and NIH. APCRP supports three clinical networks, a pediatric cardiovascular translational research program, multiple clinical trials and registries, and hundreds of basic and translational science grants. APCRP hosts several workshops and working groups each year on topics relevant to the DCVS portfolio.

Atherothrombosis and Coronary Artery Disease Branch (ACAD)

ACAD supports integrated basic, translational, and clinical research to study the etiology, pathogenesis, diagnosis, treatment, and prevention of coronary artery disease (CAD) and

atherothrombosis, testing promising clinical interventions and innovative biomedical technologies. The CAD portfolio encompasses acute and chronic coronary syndromes and addresses the basic and clinical aspects of cardiac ischemia, myocardial infarction, and their management. The atherothrombosis portfolio includes basic and clinical research on atherosclerotic lesions in coronary arteries and other arterial beds and addresses lesion instability and thrombosis; lipoprotein metabolism; biomarker and imaging diagnostics to quantify atherosclerotic disease and its progression; and the impact of inflammation, infection, immunity, microbiome, metabolic disorders, and lifestyle variables on the development and sequelae of atherosclerotic lesions.

ACAD has managed influential clinical trials on the treatment of hyperglycemia, blood pressure, and blood lipids in high-risk individuals (Table 1), including Action to Control Cardiovascular Risk in Diabetes (ACCORD)¹⁹⁻²¹ and Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health Outcomes (AIM-HIGH),²² as well as trials on the diagnosis and management of coronary artery disease, such as Rule Out Myocardial Infarction by Cardiac Computed Tomography (ROMICAT II),²³ Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM),²⁶ and Trial to Assess Chelation Therapy (TACT).²⁴ In addition, ACAD incorporated the precision medicine concept in the Clarification of Optimal Anticoagulation Through Genetics (COAG) trial, examining the pharmacogenomic management of anticoagulation therapy.²⁵ ACAD's current portfolio (Table 2) includes two very large clinical trials—Cardiovascular Inflammation Reduction Trial (CIRT),⁶³ which is testing the efficacy of targeting inflammation to reduce atherosclerotic events, and International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA),^{64,65} which compares the effectiveness of an invasive versus conservative strategy of managing chronic myocardial ischemia.

Heart Development and Structural Diseases Branch (HDSD)

HDSD manages and oversees a research portfolio that includes cardiac development, congenital heart disease (CHD) in children and adults, acquired pediatric heart disease, and valvular

heart disease (Tables 1-2). The Bench to Bassinet Program spans discovery science to clinical trials in pediatric cardiovascular translational research and includes the Cardiovascular Development Consortium (CvDC), the Pediatric Cardiac Genomics Consortium (PCGC), and the Pediatric Heart Network (PHN). CvDC is characterizing the molecular networks and pathways that control heart development. PCGC uses genomic techniques to identify the genetic causes of CHD^{90,91} and determine how genes affect treatment outcomes.⁹² PHN conducts clinical research in patients with CHD and pediatric heart disease to improve outcomes and quality of life. PHN trials are funded in a number of ways, including through direct institute support, via investigator-initiated grants, and in partnership with industry.

HDSD also supports the Sudden Death in the Young Initiative, a collaborative effort between NIH and the Centers for Disease Control and Prevention to investigate the epidemiology and etiology of sudden death in infants and children. Valvular heart disease—particularly basic mechanisms of calcific aortic valve disease, genetic and acquired pediatric heart disease, and pediatric cardiac arrest—are other important research areas supported by HDSD. The branch is also a nexus for activities related to pediatric research within NHLBI, including support for the Children and Clinical Studies website,⁹³ which educates families about the importance of pediatric research.

Heart Failure and Arrhythmias Branch (HFAB)

HFAB manages a broad portfolio of basic, translational, and clinical grants that address heart failure (HF), arrhythmias, myocardial protection from ischemia/reperfusion injury, and resuscitation science. HFAB also manages a number of large scientific programs, examining fundamental mechanisms of HF, arrhythmias, and myocardial protection, including the recently concluded NHLBI Mitochondria in Heart Diseases Initiative.⁹⁴ The HFAB portfolio spans acute heart failure, heart failure with reduced ejection fraction (HFrEF), heart failure with preserved ejection fraction (HFpEF), hypertrophic cardiomyopathy, the genetics of cardiomyopathy, cardio-oncology, HIV-related HF, and fundamental aspects of HF such as hypertrophy, fibrosis, extracellular matrix physiology, and neuro-cardiovascular mechanisms. The HFAB portfolio covers a broad range of studies

that address both clinical and basic aspects of atrial fibrillation, sudden cardiac death, cardiac resynchronization therapy, and myocardial protection. Important strategic themes in HFAB include enhancing the productivity of scientific programs, optimizing stewardship of public funds, and increasing the return on research investments.

HFAB supports two large clinical trials networks (Tables 1-2). The Heart Failure Clinical Research Network (HFN) promotes innovative trial designs and novel management approaches that have culminated in several landmark HF publications.³²⁻³⁸ The Resuscitation Outcomes Consortium (ROC), which is being phased out in 2016, is another major HFAB program that has pioneered the field of resuscitation science.³⁹⁻⁴⁵ Beginning in 2017, the collaborative Strategies to Innovate EmeRgENcy Care Clinical Trials (SIREN) Network will be the platform for future resuscitation science trials. HFAB has also supported three large phase 3 trials: Aldosterone Antagonist Therapy for Adults with Heart Failure and Preserved Systolic Function (TOPCAT),⁴⁶ CABANA, and Ranolazine, late sodium current blockade in high-risk ICD patients (RAID). Finally, HFAB supports a hypertrophic cardiomyopathy registry and a newly initiated precision medicine cohort study of the genetic basis of dilated cardiomyopathy.

BASIC AND EARLY TRANSLATIONAL RESEARCH PROGRAM (BETR)

BETR encompasses two branches at the basic science end of the translational spectrum: the Advanced Technologies and Surgery Branch (ATSB) and the Vascular Biology and Hypertension Branch (VBHB). ATSB manages cross-cutting research focused on all aspects of technology development, including testing in pre-clinical models and early-phase clinical studies and trials. The branch also oversees cardiothoracic surgical activities and plays a very active role in trans-NHLBI and trans-NIH programs. VBHB has a large basic science portfolio in vascular biology and hypertension, as well as clinical trials in hypertension and peripheral arterial disease. The branch also leads trans-NIH activities in areas such as lymphatics and small-vessel biology and disease. In addition, the NHLBI Progenitor Cell

Biology Consortium (PCBC) and the Cardiovascular Cell Therapy Research Network (CCTR) are managed directly by BETR's Office of the Director.

Advanced Technologies and Surgery Branch (ATSB)

ATSB facilitates and oversees technology development from discovery and basic research through early clinical development. Its scope includes genomics/proteomics and biomarker technologies; imaging modalities/agents; early-stage drug discovery and development; tissue-, cell-, and gene-based/-guided therapies and regenerative and reparative medicine; development and evaluation of cardiovascular devices; and bioinformatics, computational systems biology, bioengineering, and nanotechnology. Recent novel ATSB technology-focused initiatives have resulted in cutting-edge advancements in tissue engineering/regenerative medicine, such as novel biomaterials and first-generation products for disease modeling.⁹⁵ These innovations should lead to improved options for drug development and surgical applications in the areas of arterial revascularization, heart valve repair, arrhythmias, and congenital heart malformations.

ATSB also supports a number of important clinical initiatives to improve cardiovascular health (Tables 1-2). The Cardiothoracic Surgical Trials Network (CTSN), a collaborative clinical trials enterprise, has successfully evaluated newer surgical techniques, technologies, devices, and innovative pharmaceutical and bioengineered products in early translational studies, observational studies, and high-impact comparative effectiveness clinical trials,⁵¹⁻⁵⁵ with more trials planned and ongoing. The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), which follows patients receiving ventricular assist devices (VADs) and artificial hearts,⁷² has been essential in assessing an observed change in risk of thrombosis in VADs over the past few years.⁹⁶⁻⁹⁸ The Pumps for Kids, Infants, and Neonates (PumpKIN) initiative has fostered the development of mechanical circulatory support devices in small children; a clinical trial will soon follow.

Vascular Biology and Hypertension Branch (VBHB)

VBHB oversees a diverse research portfolio covering all aspects of vascular biology and medicine, including the development and function of arteries, veins, lymphatics, and microcirculation; angiogenesis; cerebrovascular and peripheral vascular diseases, aortic aneurysms, and lymphatic diseases; all aspects of blood pressure regulation including central, renal, and vascular control⁹⁹; and preeclampsia. Current major programs include the National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC),⁷³ which provides clinical data and biospecimens for research to improve clinical management of thoracic aortic aneurysms, and two large clinical trials: Best Endovascular or Best Open Surgical Treatment for Critical Limb Ischemia (BEST-CLI),^{75,76} which compares the effectiveness of best surgical versus best endovascular revascularization in patients with critical limb ischemia, and Chronic Hypertension and Pregnancy (CHAP), which evaluates the effectiveness and safety of treating mild chronic hypertension in pregnancy (Table 2). In recent years VBHB spearheaded several multidisciplinary scientific inquiries to identify gaps and opportunities in understanding new potential mechanisms leading to hypertension, including the role of epigenetics,¹³ arterial stiffening, and inflammation; the contributions of sex differences in cardiovascular diseases and the contributions of small blood vessels and lymphatics within various body organs to local and systemic diseases; as well as the Claudication: Exercise Vs. Endoluminal Revascularization (CLEVER)⁵⁶ and Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL)⁵⁷ trials (Table 1).

VBHB also manages two key NHLBI translational programs: the Gene Therapy Resource Program (GTRP),^{74,100} which provides U.S.-based heart, lung, blood, and sleep researchers with the resources critical to advancing investigational gene transfer products into clinical testing, and the Vascular Interventions/Innovations and Therapeutic Advances (VITA),⁷⁷ a paradigm-shifting NHLBI translational initiative specifically designed to address remaining barriers to early product development for the diagnosis and treatment of a select number of vascular diseases.¹⁰¹

PREVENTION AND POPULATION SCIENCES PROGRAM (PPSP)

PPSP encompasses two branches: the Clinical Applications and Prevention Branch (CAPB) and the Epidemiology Branch (EB), which together cover a wide range of clinical research in cardiovascular disease epidemiology and prevention. Major activities supported in the research portfolio include population-based cohort studies; studies of genetic, behavioral, and environmental influences on disease risk and outcomes; and clinical trials to prevent cardiovascular diseases and improve clinical care and public health. Additionally, PPSP supports and provides leadership across other NHLBI extramural divisions in population-, genomic-, behavioral-, and community- and clinic-based research on heart, lung, and blood diseases and sleep disorders.

Clinical Applications and Prevention Branch (CAPB)

CAPB supports both pediatric and adult research that clarifies the role of behavioral factors, broadly defined to include societal, organizational, and psychological factors in the causation, prevention, and treatment of cardiovascular disease (CVD) and elimination of CVD disparities. Recognizing the importance of translating the findings and principles of the basic behavioral sciences, CAPB supports intervention development and mechanistic studies at the interface of biology and behavior such as stress and depression. Studies of genetic markers of putative risk factors and development of precision preventive interventions for integration with precision medicine are evolving in importance. Traditional randomized clinical trials are supplemented by an increasing interest in pragmatic trials and use of electronic health records and interventions at the level of the health care system or provider. In parallel, there is an increasing interest in pragmatic trial designs of comparative effectiveness and emerging technologies for CVD prevention and for treatment with evidence-based CVD therapies in the ambulatory setting.

Many CAPB trials are relatively small or use a cluster design and target improved control of CVD risk factors such as obesity, hypertension, physical activity, and diet, largely through behavioral interventions. However, CAPB supports a few very large and highly influential trials of clinical events, such as the recently completed Systolic Blood Pressure Intervention Trial (SPRINT)⁶² and PROspective Multicenter Imaging Study for Evaluation of Chest Pain Trial (PROMISE)⁶⁰ trials (Table 1). A new, very large pragmatic trial, Women's Health Initiative Strong and Healthy Study (WHISH) (Table 2), was initiated in 2015 and uses an innovative and cost-effective design that involves embedding a trial in the Women's Health Initiative cohort. CAPB also supports "natural experiments" and policy-oriented interventions such as the Healthy Community Study,⁸⁴ which is designed to evaluate ongoing local and state programs at the community level to stem the rise of obesity.

Epidemiology Branch (EB)

To support observational research in heart, lung, blood, and sleep diseases, EB funds highly diverse population-based longitudinal cohort studies¹⁰²⁻¹⁰⁹ (Table 2); innovative genetic, functional genomic, and induced pluripotent stem-cell based studies; large nationally based population resources emphasizing research on health disparities; and new methods to take advantage of electronic health records and mobile technology.

Since 2009, EB has responded to emerging scientific opportunities and administrative needs. In innovative science and technology, EB has created a major research program (TOPMed) that uses genetic sequencing and tests the feasibility of new "omics" technologies¹¹⁰ (Table 3). EB has been a leader in performance accountability, showing how studies are enhanced through collaborative efforts and describing the productivity of specific major programs¹⁰²⁻¹⁰⁹ and the Epidemiology Program as a whole. The larger cohort studies in EB are undergoing a major administrative change in funding, with the goal of increasing the role of investigator-initiated projects in determining the cohort studies' research content. In response to recommendations from an advisory group on future directions in epidemiology,¹⁸ EB has targeted the surveillance of heart disease to attack the complex problem of using electronic health records, has integrated epidemiology studies and clinical trials with examples in the Framingham Heart Study and Women's Health Initiative, and has proposed new

models for reviewing and funding larger cohort studies. As an example of moving beyond the traditional community-based cohort studies, EB is addressing needs in unique populations such as in people with HIV (Table 3) and, in a recently organized workshop, the high risk in incarcerated and in recently released prisoners.

EXTRA-PROGRAMMATIC OFFICES

The following three DCVS Offices have responsibilities that extend across the boundaries of the NHLBI Division/Program/Branch.

Office of Biostatistics Research (OBR)

OBR contributes to the NHLBI mission by participating in the large clinical studies that DCVS and the other NHLBI extramural divisions support and in the intramural NHLBI studies conducted at the NIH Clinical Center. Members of the Office take an active role in the design, implementation, and analysis of studies in collaboration with investigators and statistical coordinating centers. OBR has statistical research interests related to NHLBI studies and publishes new methodology in the biostatistics literature. Expertise includes survival analysis, statistical design and monitoring of clinical trials, longitudinal data analysis, statistical genetics, and multiplicity problems.

Biostatisticians are involved in DCVS projects from their inception, such as with "over \$500K" teleconferences and in preparation of initiatives, thus assuring that clinical studies are well-designed and able to answer the questions posed. For example, every clinical trials network and every trial that is funded as a cooperative agreement has at least one biostatistician who contributes as part of the project team.

OBR is especially proud of the Summer Institute for Research Education in Biostatistics,¹¹¹ which will be in its 13th year in the summer of 2016. This initiative funds several universities to train undergraduate students and encourage them to pursue advanced degrees in biostatistics or related fields. More than 60 percent of participants have gone on to further related studies.

Office of Clinical Research (OCR)

OCR was established in 2013 and is responsible for facilitating staff oversight of clinical trials and other clinical studies across NHLBI. OCR provides education, expertise, and technical support to NHLBI staff and extramural investigators on topics related to the conduct of clinical research. Educational activities include an NHLBI-wide clinical research think tank and other periodic meetings to review issues in clinical trials, communications about new developments in clinical research, and maintenance of a broad array of resources for both staff and external investigators through comprehensive websites that are regularly updated. OCR staff serve as subject matter experts on clinical trial oversight and regulation for NIH and for external inquiries as well, including the media. These staff regularly give talks on pertinent topics and collaborate on internal portfolio analyses. OCR also advises on major new NHLBI clinical trial initiatives, such as new models for soliciting clinical trials. OCR responsibilities include serving as the point of contact for Certificates of Confidentiality for NHLBI and two other NIH institutes, managing NHLBI's ClinicalTrials.gov accounts, and developing and updating clinical research policies and standard operating procedures. OCR collaborates with NHLBI's information technology group to support a number of tools and resources, including systems that track data and safety monitoring boards for clinical trials and large observational studies. At present, OCR is collaborating on a clinical research database and dashboard, which will provide NHLBI staff with comprehensive information on the studies they oversee to facilitate optimal oversight, and will also provide robust reporting tools across the clinical research portfolio to support continuous improvement of DCVS clinical research activities.

Office of Research Training and Career Development (ORTCD)

ORTCD supports individual and institutional research training and career development programs across DCVS to promote development of NIH competitive R01 cardiovascular investigators. A wide variety of research training programs is available for high school students through mid-career professionals.¹¹² Currently more than 600 grants are funded, including 250 career development awards and 140 fellowships to individual investigators, and 120 T32 pre- and post-doctoral institutional grants. These programs

span the breadth of cardiovascular sciences from molecular work to clinical research and population sciences.

The office also creates K12 institutional training programs to meet areas of identified scientific need. In 2007, a K12 research training program in vascular medicine funded six centers for five years to help create NIH competitive investigators in this emerging discipline. In 2011, the office created a K12 clinical research program in emergency care research to train clinician scientists from multiple clinical specialties. Six centers were funded that, by program's end, will train 35 scholars representing emergency medicine, cardiology, critical care, pediatric emergency medicine, pediatric critical care, and trauma surgery.¹¹³ A new Trans-NIH K12 Program in emergency care research was announced this year.¹¹⁴ Participating institutes are NHLBI, the National Institute of Mental Health, and the National Institute for Nursing Research. Three centers will be awarded funding through this new program.

INTERAGENCY, TRANS-NHLBI, AND TRANS-NIH LEADERSHIP

DCVS program staff provide leadership for a number of key activities across NHLBI, NIH, and other agencies (Table 3). Within NHLBI, DCVS scientists have played key roles in programs in chronic HIV infection, whole gene sequencing studies (TOPMED), clinical epidemiology, and reparative medicine, which span heart, lung, blood, and sleep research. OCR provides leadership to rethink the clinical trial enterprise across NHLBI and enhance its operational efficiency. At the trans-NIH level, DCVS occupies leadership roles in areas including obesity, health applications of mobile technology, and small vessels and lymphatics, in addition to coordinating disease and technology-based programs. DCVS staff have played key roles in planning the new initiative in precision medicine, which will be implemented in 2016. ATSB program staff help to coordinate activities across the federal government in the areas of tissue engineering and medical device interoperability.

PORTFOLIO ANALYSIS

As the flattening of the NIH budget in 2012–15 put increasing pressure on DCVS to be more strategic in setting funding priorities, DCVS has made increasing use of new tools for portfolio analysis to assess the effectiveness of its programs.²⁻⁸ In so doing, DCVS has learned of the weak and tenuous relationship between peer review scores and subsequent productivity and that most of the impact of the clinical trials DCVS funds resides in the relatively small proportion of trials that address clinical questions of direct relevance to how best to treat patients with cardiovascular disease and/or risk factors. DCVS has also learned that the papers generated by its large epidemiologic cohorts, even those written by investigators who are not supported by the cohort contracts, are significantly more highly cited than comparable epidemiologic papers generated by other data. DCVS intends to continue to expand this data-based approach of self-evaluation as it implements new strategies and programs going forward.

CONCLUSIONS

DCVS anticipates that it will continue to respond to new opportunities in many areas in the coming years. A transformation has also begun in the funding of the division's large programs, requiring stable long-term support (such as the division's epidemiologic cohorts and clinical trials networks) to separate the funding of the science—which would undergo standard peer review—from the review of the infrastructure. The Framingham and Multi-Ethnic Study of Atherosclerosis (MESA) cohort studies have already used this model. DCVS cohort studies are also prominent in the recently initiated Trans-Omics for Precision Medicine (TOPMED) project (Table 3), in which genome sequencing will be performed on heretofore unaffordably large numbers of well-phenotyped research participants. NHLBI, and DCVS in particular, has played a prominent role in planning the upcoming initiative in precision medicine and expects to be active in its implementation in 2016. On the clinical trial front, while DCVS will continue to fund a few large, traditional randomized trials like CIRT and ISCHEMIA, OCR is helping to develop a new funding announcement for clinical trials that will help align the applications with the division's focus on trials underscoring pragmatic clinical applicability over mechanism, emphasize proven

ability to accrue patients, and contain costs. DCVS also anticipates a new emphasis on the cardiovascular implications of HIV infection, which has become a chronic disease. DCVS plans to continue its recent emphasis on portfolio analysis to evaluate how well the division is achieving its objectives and to identify and address its weaknesses. Finally, DCVS eagerly awaits the release of the new NHLBI Strategic Vision, which is intended to be a living document that will help guide the division's future research efforts.

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TABLES AND FIGURES

Table 1: Examples of Completed Studies in the NHLBI DCVS Research Portfolio, 2010–2015

Program-Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
APCRP-ACAD	Action to Control Cardiovascular Risk in Diabetes (ACCORD) ¹⁹⁻²¹	Tested three complementary medical treatment strategies for type 2 diabetes, glycemia, and lipid and blood pressure control, to reduce the very high rate of major CV morbidity and mortality	Clinical Trial	NCT00000620	2010
APCRP-ACAD	Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health Outcomes (AIM-HIGH) ²²	Tested whether raising low levels of high-density lipoprotein cholesterol using niacin reduces cardiovascular event rates in patients with atherosclerotic cardiovascular disease	Clinical Trial	NCT00120289	2011
APCRP-ACAD	Rule Out Myocardial Infarction by Cardiac Computed Tomography (ROMICAT II) ²³	Determined whether the length of hospital stay was reduced in patients with symptoms suggestive of an acute coronary syndrome by the addition of a cardiac CT to the usual standard of care	Clinical Trial	NCT01084239	2012
APCRP-ACAD	Trial to Assess Chelation Therapy (TACT) ²⁴	Tested the safety and efficacy of intravenous chelation in patients with coronary heart disease	Clinical Trial	NCT00044213	2012
APCRP-ACAD	Clarification of Optimal Anticoagulation Through Genetics (COAG) ²⁵	Compared genotype-guided versus clinically guided approaches for warfarin dosing	Clinical Trial	NCT00839657	2013

Table 1: Examples of Completed Studies in the NHLBI DCVS Research Portfolio, 2010–2015

Program-Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
APCRP-ACAD	Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) ²⁶	Assessed the optimal revascularization strategy in diabetics with multivessel disease	Clinical Trial	NCT00086450	2013
APCRP-ACAD	Action to Control Cardiovascular Risk in Diabetes Follow-up Study (ACCORDION) ²⁷	Examined the long-term effects of the glycemic, lipid, and blood pressure treatments after termination of the ACCORD trial-assigned treatments	Observational Study		2016
APCRP-HDSD	PHN: Trial of Angiotensin Converting Enzyme Inhibition in Infants With Single Ventricle (ISV) ¹¹⁵	Evaluated the efficacy and safety of administering an angiotensin converting enzyme inhibitor (enalapril) to infants with a functional single ventricle	Clinical Trial	NCT00113087	2010
APCRP-HDSD	PHN: Comparison of Two Medications Aimed at Slowing Aortic Root Enlargement in Individuals With Marfan Syndrome (Marfan Trial) ²⁸	Compared losartan to atenolol to prevent aortic root enlargement in patients with Marfan syndrome	Clinical Trial	NCT00429364	2014

Table 1: Examples of Completed Studies in the NHLBI DCVS Research Portfolio, 2010–2015

Program-Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
APCRP-HDSD	Therapeutic Hypothermia after Pediatric Cardiac Arrest (THAPCA) ²⁹⁻³¹	Compared therapeutic hypothermia to normothermia in preventing morbidity and mortality after pediatric cardiac arrest	Clinical Trial	NCT00878644 NCT00880087	2015
APCRP-HFA	HFN: Diuretic Optimization Strategies Evaluation in Acute Heart Failure (DOSE-AHF) ³²	Compared response of symptoms and renal function to high versus low doses and bolus versus continuous IV infusion of diuretic in acute decompensated heart failure	Clinical Trial	NCT00577135	2011
APCRP-HFA	HFN: CARdiorenal REScue Study in Acute Decompensated Heart Failure (CARRESS) ³³	Compared weight loss in patients with acute decompensated heart failure receiving ultrafiltration versus stepped pharmacologic therapy	Clinical Trial	NCT00608491	2012
APCRP-HFA	HFN Phosphodiesterase-5 Inhibition to Improve Clinical Status And Exercise Capacity in Diastolic Heart Failure (RELAX) ³⁴	Evaluated the effect of sildenafil versus placebo on exercise capacity in patients with diastolic heart failure	Clinical Trial	NCT00763867	2013
APCRP-HFA	HFN: Renal Optimization Strategies Evaluation in Acute Heart Failure (ROSE) ³⁵	Evaluated benefits and safety of low-dose IV nesiritide and low-dose dopamine in patients with congestive heart failure and renal dysfunction	Clinical Trial	NCT01132846	2013

Table 1: Examples of Completed Studies in the NHLBI DCVS Research Portfolio, 2010–2015

Program-Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
APCRP-HFA	HFN: Using Allopurinol to Relieve Symptoms in Patients With Heart Failure and High Uric Acid Levels (EXACT) ³⁶	Evaluated efficacy of allopurinol versus placebo in relieving heart failure symptoms in patients with heart failure and high uric acid levels	Clinical Trial	NCT00987415	2014
APCRP-HFA	HFN: Functional Impact of GLP-1 for Heart Failure Treatment (FIGHT) ³⁷	Tested liraglutide, a GLP-1 agonist, to improve mortality, HF hospitalization, and time-averaged change in BNP in HFREF	Clinical Trial	NCT01800968	2015
APCRP-HFA	HFN: Nitrate's Effect on Activity Tolerance in Heart Failure with Preserved Ejection Fraction (NEAT-HFpEF) ³⁸	Evaluated effect of isosorbide mononitrate versus placebo on exercise tolerance in HFpEF	Clinical Trial	NCT02053493	2015
APCRP-HFA	ROC: Hypertonic Resuscitation Following Severe Traumatic Brain Injury (HS-TBI) ³⁹	Compared survival rates and neurologic status at six months in patients with traumatic brain injury treated with hypertonic saline (+/- dextran) versus normal saline	Clinical Trial	NCT00316004	2010
APCRP-HFA	ROC: Hypertonic Resuscitation Following Traumatic Injury (HS-SHOCK) ⁴⁰	Compared 28-day survival rates in trauma patients with hypovolemic shock treated with hypertonic saline (+/- dextran) versus normal saline	Clinical Trial	NCT00316004	2011
APCRP-HFA	ROC: Prehospital Resuscitation using an IMpedance valve	Evaluated the effect of a pulmonary impedance threshold device versus a sham device and compared an early versus	Clinical Trial	NCT00394706	2011

Table 1: Examples of Completed Studies in the NHLBI DCVS Research Portfolio, 2010–2015

Program-Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
	and Early vs Delayed analysis (PRIMED) ^{41,42}	later rhythm analysis strategy on survival to hospital discharge patients with cardiac arrest			
APCRP-HFA	ROC: Hypotensive Resuscitation versus Standard Resuscitation in Patients with Hemorrhagic Shock after Trauma (HypoResus) ⁴³	Compared hypotensive to standard resuscitation protocol with regard to volume of fluid given and 24-hour survival in shock patients with blunt trauma or penetrating wound	Clinical Trial	NCT01411852	2014
APCRP-HFA	ROC: Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPPR) ⁴⁴	Tested safety and effectiveness of transfusing patients with severe trauma and major bleeding using plasma, platelets, and red blood cells in a 1:1:1 ratio compared with a 1:1:2 ratio	Clinical Trial	NCT01545232	2015
APCRP-HFA	ROC: Trial of Continuous or Interrupted Chest Compressions During CPR (CCC) ⁴⁵	Compared safety and efficacy of continuous chest compressions versus interrupted chest compressions in patients with non-trauma related cardiac arrest	Clinical Trial	NCT01372748	2015
APCRP-HFA	Aldosterone Antagonist Therapy for Adults with Heart Failure and Preserved Systolic Function (TOPCAT) ⁴⁶	Evaluated effectiveness of spiro lactone versus placebo in improving major cardiovascular outcomes in HFpEF	Clinical Trial	NCT00094302	2014

Table 1: Examples of Completed Studies in the NHLBI DCVS Research Portfolio, 2010–2015

Program-Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
BETR	CCTR: Use of Adult Autologous Stem Cells in Treating People 2 to 3 Weeks After Having a Heart Attack (LATE-TIME) ⁴⁷	Evaluated the effect of bone marrow-derived mononuclear cells (BNP) delivered via coronary catheterization two to three weeks post-myocardial infarction on cardiac function	Clinical Trial	NCT00684060	2011
BETR	CCTR: Use of Adult Autologous Stem Cells in Treating People Who Have Had a Heart Attack (TIME) ⁴⁸	Evaluated the effect of bone marrow-derived mononuclear cells delivered via coronary catheterization three or seven days post-myocardial infarction on cardiac function	Clinical Trial	NCT00684021	2012
BETR	CCTR: Effectiveness of Stem Cell Treatment for Adults With Ischemic Cardiomyopathy (FOCUS) ⁴⁹	Evaluated the effect of bone marrow-derived mononuclear cells (BNP) delivered via intracardiac injection on cardiac function in chronic heart failure	Clinical Trial	NCT00824005	2012
BETR-ATSB	PCSP: Pediatric Circulatory Support Program ⁵⁰	Developed novel circulatory support devices for children with medically refractory heart failure	Device Development	BAA-NHLBI-HV-04-01	2009
BETR-ATSB	CTSN: Management Practices and the Risk of Infections Following Cardiothoracic Surgery	Identified management practices that put patients at risk for infections post-cardiothoracic surgery	Registry		2010

Table 1: Examples of Completed Studies in the NHLBI DCVS Research Portfolio, 2010–2015

Program-Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
BETR-ATSB	Innovative Technologies for Engineering Small Blood Vessels	Applied recent advances in biomaterials, tissue engineering, and nanotechnology toward the development of small-diameter (<5.0 mm inner diameter) functional blood vessels for clinical evaluation	Translational Study		2011
BETR-ATSB	CTSN: Exploring the Effect of Intramyocardial Injection of Mesenchymal Precursor Cells (MPCs) on Myocardial Function, Stage (LVAD) ⁵¹	Compared a single, low dose of MPCs to sham (cryoprotective media) injected into native myocardium of left-ventricular assist device recipients	Clinical Trial (pilot)	NCT01442129	2013
BETR-ATSB	CTSN: Evaluation of Outcomes Following Mitral Valve Repair/Replacement in Severe Chronic Ischemic Mitral Regurgitation (SMR) ^{52,53}	Compared mitral valve repair to replacement among patients with severe ischemic mitral regurgitation	Clinical Trial	NCT00807040	2014
BETR-ATSB	CTSN: Surgical Interventions for Moderate Ischemic Regurgitation (MMR) ⁵⁴	Compared mitral valve repair to no repair among patients with moderate ischemic mitral regurgitation undergoing coronary grafting bypass surgery	Clinical Trial	NCT00806988	2014

Table 1: Examples of Completed Studies in the NHLBI DCVS Research Portfolio, 2010–2015

Program-Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
BETR-ATSB	CTSN: Surgical Ablation versus No Surgical Ablation in Patients with Atrial Fibrillation Undergoing Mitral Valve Surgery (AFib) ⁵⁵	Compared MVS alone to MVS + ablation in patients with persistent or longstanding persistent atrial fibrillation undergoing mitral valve surgery	Clinical Trial	NCT00903370	2015
BETR-ATSB	New Strategies for Growing 3D Tissues	Improved understanding of how cells respond to their environment into engineering systems that support tissue formation, either in vitro or in vivo	Translational Study		2015
BETR-VBHB	CLaudication: Exercise Vs. Endoluminal Revascularization (CLEVER) ⁵⁶	Compared optimal medical therapy, supervised exercise, and arterial stent placement in patients with claudication	Clinical Trial	NCT00132743	2013
BETR-VBHB	Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) ⁵⁷	Compared medical therapy plus stenting of hemodynamically significant renal artery stenosis versus medical therapy alone in patients with systolic hypertension and renal artery stenosis	Clinical Trial	NCT00081731	2013
PPSP-CAPB	Counseling African Americans to Control Hypertension (CAATCH) ⁵⁸	Evaluated the effectiveness of a multi-level, multi-component, evidence-based intervention compared to usual care in improving BP control among hypertensive African Americans who receive care in community health centers	Clinical Trial (Cluster)	NC00233220	2014

Table 1: Examples of Completed Studies in the NHLBI DCVS Research Portfolio, 2010–2015

Program-Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
PPSP-CAPB	Effects of High vs. Low Glycemic Index of Dietary Carbohydrate on Cardiovascular Disease Risk Factors and Insulin Sensitivity (OmniCarb)	Compared effects of four diets with differing glycemic index on glycemia and CV risk factors	Clinical Trial (Crossover)	NCT00608049	2014
PPSP-CAPB	Lampert et al., 2009 ⁵⁹	Examined relationship of anger-induced T-wave alternans to future ventricular arrhythmias in patients with cardioverter-defibrillators	Observational Study		2014
PPSP-CAPB	PROspective Multicenter Imaging Study for Evaluation of Chest Pain Trial (PROMISE) ⁶⁰	Compared anatomic versus functional diagnostic testing strategies in symptomatic patients with suspected coronary artery disease	Clinical Trial	NCT01174550	2015
PPSP-CAPB	Cell phone InTervention for You (CITY) ⁶¹	Compared effects of behavioral weight loss intervention using mobile phone versus personal coaching versus usual care in young adults	Clinical Trial	NCT01092364	2015
PPSP-CAPB	Obesity Related Behavioral Intervention Trials (ORBIT)	Five NHLBI trials (and two in other institutes) that developed, tested, and refined novel interventions based on principles from basic research on human behavior	5 Clinical Trials (4 registered in ClinicalTrials.gov)	NCT01198990 NCT01307683 NCT01350531 NCT01778712	2015
PPSP-CAPB	Systolic Blood Pressure Intervention Trial (SPRINT) ⁶²	Compared standard hypertension treatment to a more intensive treatment strategy among non-diabetic patients at high risk for CVD events	Clinical Trial	NCT01206062	2015
*Type of study; #Year of study/registry initiation					

Table 2: Example of New and Ongoing Studies in the NHLBI DCVS Research Portfolio, 2010-2015

Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
APCRP-ACAD	Cardiovascular Inflammation Reduction Trial (CIRT) ⁶³	Compares low-dose methotrexate (a potent anti-inflammatory agent with no lipid effects) versus placebo to prevent cardiovascular events in patients with stable coronary artery disease and either type 2 diabetes or metabolic syndrome	Clinical Trial	NCT01594333	2011
APCRP-ACAD	International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA) ^{64,65}	Compares the effectiveness of an invasive strategy employing early coronary angiography (usually leading to revascularization) versus a conservative strategy employing only optimal medical therapy to prevent cardiovascular events in patients with moderate to severe inducible myocardial ischemia	Clinical Trial	NCT01471522	2011
APCRP-ACAD	ISCHEMIA-Chronic Kidney Disease Trial (ISCHEMIA-CKD) ⁶⁶	A parallel trial to ISCHEMIA trial in patients with advanced chronic kidney disease and inducible myocardial ischemia	Clinical Trial	NCT01985360	2013
APCRP-HDSD	Congenital Heart Disease Network Study (CHD GENES)	A PGC-led multi-center, prospective, observational study whose goal is to acquire phenotypic data and source DNA from participants, parents, and affected family members	Observational Study	NCT01196182	2010
APCRP-HDSD	Pregnancy as a Window to Future Cardiovascular Health (nuMoM2B-HHS)	An observational cohort study following women for cardiovascular health two to three years after their first pregnancy	Observational Study	NCT02231398	2014
APCRP-HDSD	Sudden Death in the Young Case Registry (SDY)	Surveillance system and registry of cases of sudden death in young people in 10 states	Registry		2015
APCRP-HDSD	PHN: Dyslipidemia of Obesity Intervention in Teens Trial (DO-IT)	Will determine if treatment with two years of oral pitavastatin will improve LDL-C with acceptable safety among adolescents with combined dyslipidemia of obesity	Clinical Trial		2016

Table 2: Example of New and Ongoing Studies in the NHLBI DCVS Research Portfolio, 2010-2015

Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
APCRP-HDSD	PHN: Fontan Udenafil Exercise Longitudinal Assessment Trial (FUEL)	Will determine if six months of Udenafil improves exercise performance in adolescents following the Fontan procedure for single-ventricle congenital heart disease	Clinical Trial		2016
APCRP-HFAB	Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation Trial (CABANA)	Tests safety and efficacy of catheter ablation versus anti-arrhythmic therapy for chronic atrial fibrillation	Clinical Trial	NCT00911508	2009
APCRP-HFAB	RAzolazine, late sodium current blockade in high-risk ICD patients (RAID)	Tests safety and efficacy of ranolazine to decrease ventricular arrhythmias	Clinical Trial	NCT01215253	2010
APCRP-HFAB	ROC: Amiodarone, lidocaine or placebo for out-of-hospital cardiac arrest due to ventricular fibrillation or tachycardia (ALPS) ⁶⁷	Compares safety and efficacy of amiodarone versus lidocaine in cardiac arrest	Clinical Trial	NCT01401647	2013
APCRP-HFAB	Hypertrophic Cardiomyopathy (HCM) Registry: Novel Markers of Prognosis in HCM	Characterizes phenotypes and clinical outcomes of HCM	Registry		2013
APCRP-HFAB	HFN: Oral Iron Repletion Effects On Oxygen Uptake in	Evaluates the benefit of oral iron versus placebo on functional capacity in HFREF patients with iron deficiency	Clinical Trial	NCT02188784	2014

Table 2: Example of New and Ongoing Studies in the NHLBI DCVS Research Portfolio, 2010-2015

Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
	Heart Failure (IRONOUT)				
APCRP-HFAB	HFN: Aldosterone Targeted Neurohormonal Combined with Natriuresis Therapy (ATHENA-HF)	Tests safety and efficacy of high-dose aldosterone antagonism in acute HF	Clinical Trial	NCT02235077	2014
APCRP-HFAB	Precision Medicine for Dilated Cardiomyopathy in European and African Ancestry	Examines the genetic basis for dilated cardiomyopathy	Cohort Study		2015
BETR	PCBC: NHLBI Progenitor Cell Biology Consortium ⁶⁸	Identifies and characterizes progenitor cell lines, directs the differentiation of stem and progenitor cells to desired cell fates, and develops new strategies to address the unique challenges presented by the transplantation of these cells	Consortium		2009
BETR	CCTR: Patients With Intermittent Claudication Injected With ALDH Bright Cells (PACE) ⁶⁹	Tests whether autologous aldehyde dehydrogenase bright (ALDHbr) cells injected into affected calf and thigh muscles will improve blood flow and/or peak walking time in patients with claudication	Clinical Trial	NCT01774097	2013
BETR	CCTR Combination of Mesenchymal and C-kit+ Cardiac Stem Cells as Regenerative Therapy for Heart Failure (CONCERT-HF) ⁷⁰	Assesses feasibility, safety, and effect of autologous bone marrow-derived mesenchymal stem cells (MSCs) and c-kit+ cardiac stem cells (CSCs) both alone and in combination (Combo), compared to placebo as well as each other, administered by transendocardial injection in patients with ischemic cardiomyopathy	Clinical Trial	NCT02501811	2015

Table 2: Example of New and Ongoing Studies in the NHLBI DCVS Research Portfolio, 2010-2015

Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
BETR	CCTRN: Stem Cell Injection in Cancer Survivors (SENECA) ⁷⁰	Assesses safety and feasibility of delivering allogeneic human mesenchymal stem cells (allo-MSCs) by transendocardial injection to cancer survivors with left ventricular (LV) dysfunction secondary to anthracycline-induced cardiomyopathy (AIC)	Clinical Trial	NCT02509156	2016
BETR	PCTC: NHLBI Progenitor Cell Translational Consortium (to be funded in Autumn 2016) ⁷¹	Will translate advances in progenitor cell biology using progenitor cell-based disease models to understand disease mechanisms; develop novel therapies; and apply cell-based therapies for heart, lung, and blood disease treatment	Consortium		2016
BETR-ATSB	Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) ⁷²	National audited registry for patients receiving FDA-approved mechanical circulatory support device therapy to treat advanced heart failure	Registry		2006
BETR-ATSB	Pumps for Kids, Infants, and Neonates (PumpKIN)	Develops and does pre-clinical testing of promising pediatric circulatory support devices and runs the prospective multicenter RCTs to evaluate the safety and benefit of devices that receive IDE from FDA	Device Development, Clinical Trial	NHLBI-HV-09-14(2) & NHLBI-HV-12-03	2010
BETR-ATSB	Development of molecular imaging agents and methods to detect high risk atherosclerotic plaque	A translational research program for the development of target-specific molecular imaging agents to detect high-risk atherosclerotic plaque	Translational Study		2014
BETR-ATSB	CTSN: Rate Control Versus Rhythm Control for Postoperative Atrial Fibrillation (POAF)	Compares rate control versus rhythm control among cardiothoracic surgery patients developing atrial fibrillation and/or atrial flutter after surgery but during hospitalization	Clinical Trial	NCT02132767	2014

Table 2: Example of New and Ongoing Studies in the NHLBI DCVS Research Portfolio, 2010-2015

Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
BETR-ATSB	CTSN: Safety & Efficacy of Intramyocardial Injection of Mesenchymal Precursor Cells (MPCs) on Myocardial Function in LVAD Recipients (LVAD-MPC 2)	Evaluates safety and efficacy of a single high dose of MPCs versus sham (cryoprotective media) injected into the native myocardium of LVAD recipients	Clinical Trial	NCT02362646	2015
BETR-ATSB	CTSN: Neuroprotection in Patients Undergoing Aortic Valve Replacement	Evaluates efficacy and safety of commercial embolic protection devices to reduce ischemic brain injury in patients undergoing surgical aortic valve replacement	Clinical Trial	NCT02389894	2015
BETR-ATSB	Registry Evaluation of Vital Information for VADs in Ambulatory Life (REVIVAL)	Characterizes clinical outcomes, quality of life, and functional impairment in ambulatory patients on evidence-based therapy with advanced chronic systolic heart failure who may benefit from VAD therapy	Registry	NCT01369407	2015
BETR-ATSB	Bioreactors for Reparative Medicine	Supports the development of complex, 3D biomimetic culture systems for heart, lung, or bone marrow tissues	Technology Development		2015
BETR-ATSB	Percutaneous Deliverable Biomaterial for treating Myocardial Infarction	First-in-man clinical trial that seeks to translate a novel catheter deliverable biomaterial therapy for treating myocardial infarction	Clinical Trial		2016

Table 2: Example of New and Ongoing Studies in the NHLBI DCVS Research Portfolio, 2010-2015

Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
BETR-ATSB	NHLBI Exploratory Bioengineering Research Grants	Supports basic, translational, and clinical proof-of-concept research projects that are needed for the advancement of bioengineering approaches for heart, lung and blood diseases	Technology Development, Translational Research		2017
BETR-VBHB	National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC) ⁷³	A data and biospecimen registry established to improve the clinical management of these conditions by providing resources at no cost to qualified investigators worldwide	Registry	NCT01322165	2006
BETR-VBHB	Gene Therapy Resource Program (GTRP) ⁷⁴	A translational research program to provide resources critical to advancing investigational gene transfer products into clinical testing	Translational Resource Program		2007
BETR-VBHB	Best Endovascular or Best Open Surgical Treatment for Critical Limb Ischemia (BEST-CLI) ^{75,76}	Compares the effectiveness of best surgical compared to best endovascular revascularization in patients with critical limb ischemia	Clinical Trial	NCT02060630	2013
BETR-VBHB	The Vascular Interventions/Innovations and Therapeutic Advances (VITA) ⁷⁷	An R&D translational research program to address remaining barriers in the way of early product development for the diagnostic and treatment of a select number of vascular diseases	Translational Research Program		2013
BETR-VBHB	Chronic Hypertension and Pregnancy (CHAP)	Evaluates the effectiveness and safety of pharmacologic treatment of mild chronic hypertension in pregnancy	Clinical Trial	NCT02299414	2014
PPSP-CAPB	Systolic Blood Pressure	Compares cognitive/dementia and renal outcomes in non-diabetic hypertensive patients at high risk for CVD events who	Clinical Trial	NCT01206062	2009

Table 2: Example of New and Ongoing Studies in the NHLBI DCVS Research Portfolio, 2010-2015

Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
	Intervention Trial MIND Study (SPRINT-MIND)	were treated with standard versus a more intensive hypertension treatment strategy			
PPSP-CAPB	Childhood Obesity Prevention and Treatment Research (COPTR) ⁷⁸⁻⁸³	Four trials testing approaches to attenuate weight gain in preschoolers and reduce weight in obese adolescents by targeting the home, community, and primary care settings in low-income and ethnically diverse neighborhoods	Clinical Trials	NCT01316653NC T01514279 NCT01606891NC T01642836	2010
PPSP-CAPB	Healthy Community Study (HCS) ⁸⁴	Prospective evaluation of community-level interventions to prevent childhood obesity. Assesses associations of community program characteristics and policies with BMI, nutrition, and physical activity	Observational Study		2010
PPSP-CAPB	VITamin D and Omega-3 Trial (VITAL) ⁸⁵	Evaluates the efficacy of vitamin D and/or Omega-3 fatty acids (EPA and DHA) for prevention of cancer and major cardiovascular events in 20,000 adults over seven years	Clinical Trial	NCT01169259	2010
PPSP-CAPB	Guiding Evidence Therapy using Biomarker Intensified Treatment (GUIDE-IT) ⁸⁶	Compares biomarker-directed care (NT proBNP-care) with usual care in low systolic-ejection heart failure patients	Clinical Trial	NCT01685840	2012
PPSP-CAPB	Effect of Exercise and Weight Loss on Cardiovascular Health (HEART HEALTH)	Compares the effects of diet plus high versus moderate versus no-exercise program on weight loss in persons enrolled in a comprehensive weight loss program	Clinical Trial	NCT01500356	2014
PPSP-CAPB	Women's Health Initiative Strong and Healthy Study (WHISH)	This pragmatic trial embedded in the Women's Health Initiative cohort evaluates the benefits of a physical activity program in 50,000 elderly women	Clinical Trial	NCT02425345	2015

Table 2: Example of New and Ongoing Studies in the NHLBI DCVS Research Portfolio, 2010-2015

Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
PPSP-CAPB	Influenza Vaccine to Effectively Stop Cardio Thoracic Events and Decompensated heart failure (INVESTED)	Will test whether high-dose (versus standard-dose) influenza vaccine will reduce all-cause death and cardiopulmonary hospitalization in adults at high cardiovascular risk	Clinical Trial		2016
PPSP-EB	Framingham Heart Study (FHS)	Cohort study of three generations, emphasis on risk factors, life course, health aging, longevity, family studies genetics, clinical and subclinical outcomes, social networks, pulmonary Generation 1 (5,209 participants) Generation 2 (5,124 participants) Generation 3 (4,095 participants)	Observational Study	NCT00062777	1948 1971 2002
PPSP-EB	Coronary Artery Risk Development in Young Adults (CARDIA)	Cohort study of 5,115 participants, black and white, ages 18–30 at entry, emphasis on diet, obesity, young adult risk factor changes, subclinical disease, early CVD, pulmonary function, sleep	Observational Study	NCT00005130	1985
PPSP-EB	Atherosclerosis Risk in Communities (ARIC)	Cohort study of 15,792 participants, black and white, ages 45–64 at entry; emphasis on biomarkers, subclinical CVD, CHD, heart failure, cognitive change, community surveillance, pulmonary function, sleep	Observational Study	NCT00005131	1987
PPSP-EB	Cardiovascular Health Study (CHS)	Cohort study of 5,888 participants, black and white, ages 65+ at entry, emphasis on aging, stroke, heart failure, genetics, vascular dementia, comorbidities, pulmonary function	Observational Study	NCT00005133	1989
PPSP-EB	Strong Heart Study (SHS)	Cohort study of 4,549 participants, all Native American, ages 45–74, emphasis on diabetes, microalbuminuria, obesity, metabolic syndrome, subclinical disease, diabetes, CVD	Observational Study	NCT00005134	1989

Table 2: Example of New and Ongoing Studies in the NHLBI DCVS Research Portfolio, 2010-2015

Branch	Study	Description	Type*	ClinicalTrials.gov Identifier	Year#
PPSP-EB	Women's Health Initiative (WHI)	Cohort study and clinical trial of 161,808 participants, all women, white, black, Hispanic, Asian, Native American, observational emphasis on post-trial risks, aging and CVD, multiple phenotypes, biomarkers, genetics, proteomics	Post-trial observational study	NCT00000611	1993
PPSP-EB	Jackson Heart Study (JHS)	Cohort study of 5,301 participants, all African American, ages 20–95 at entry, emphasis on hypertension, diabetes, cardiac function, psychosocial factors, families, genetics, pulmonary	Observational Study	NCT00005485	2000
PPSP-EB	Multi-Ethnic Study of Atherosclerosis (MESA)	Cohort study of 6,814 participants, white, black, Hispanic, Chinese, ages 45–84 at entry, emphasis on subclinical CVD, multiple ethnic comparisons, neighborhoods, air pollution, family and genetics, pulmonary	Observational Study	NCT00005487	2000
PPSP-EB	Hispanic Community Health Study/Study of Latinos (HCHS/SOL)	Cohort study of 16,000 participants ages 18–74 at entry; of Mexican, Puerto Rican, Cuban, Central American, South American, or Dominican descent; emphasis on diabetes, diet obesity, sleep, liver function, renal function, occupation, physical activity, health care, cognitive function, psychosocial factors, acculturation, and pulmonary	Observational Study	NCT02060344	2008
*Type of study; #Year of study/registry initiation					

Table 3: Examples of Inter-Agency, Trans-NIH, and Trans-NHLBI Activities Led or Co-Led by DCVS

Branch	Study	Description
Trans-NHLBI		
DCVS	NHLBI AIDS Program	Multidisciplinary program with a dedicated budget to support HIV-related heart, lung, blood, and sleep research. Research priorities include HIV-related co-morbidities, prevention, and cure. A key program is the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE), the largest HIV-related cardiovascular disease trial in history
APCRP-ACAD	Point of Care Initiative	Supports research using advanced technologies to develop novel POC devices or use existing technologies in a clinical setting to guide diagnosis and therapy
APCRP-ACAD	Secondary Dataset Analysis Initiative	Designed to test innovative hypotheses using existing human datasets via R21 grants (PAR13-009) ⁸⁷
BETR-ATSB	Bioreactors for Reparative Medicine	Supports the development of complex, 3D biomimetic culture systems for heart, lung, or bone marrow tissues
PPSP	PRSG: Populations Research Strategy Group	Developing an implementation plan for the recommendations from the Working Group of the NHLBI Advisory Council and Board of Extramural Experts on the Future of Population Sciences and Epidemiology ¹⁸
PPSP-EB	TOPMED: Trans-Omics for Precision Medicine	Seeks to discover factors that influence disease risk, identify subtypes of disease, and develop more targeted and personalized treatments, coupling Whole Genome Sequencing, other Omics, and phenotype data
OCR	CSSC: Clinical Studies Coordinating Committee	Provides an opportunity for NHLBI staff to learn about and discuss current issues in clinical research through internal and external presenters
OCR	OCTET: Optimizing the Clinical Trials Enterprise Team	Provides a unified framework for coordination of clinical research oversight activities, identification of new policy directions, and providing trans-NHLBI input on proposed NIH and other governmental policies related to clinical trials

Table 3: Examples of Inter-Agency, Trans-NIH, and Trans-NHLBI Activities Led or Co-Led by DCVS

Branch	Study	Description
Trans-NIH		
APCRP-ACAD	Molecular Transducers of Physical Activity in Humans Consortium	Common Fund initiative designed to assemble a comprehensive map of the molecular changes that occur in response to exercise and develop a database accessible to researchers
APCRP-ACAD	In Silico Modeling of Biomarkers of Atherosclerosis	A public-private partnership facilitated by the Foundation for NIH designed to build a model to predict cardiovascular outcomes from a change in a panel of biomarkers
APCRP-ACAD	Mobilizing Research: A Research Resource to Enhance mHealth Research	Supported the development of a research resource to allow researchers to evaluate mobile and wireless (mHealth) technologies and to develop an infrastructure that works with wireless carriers to create a registry of potential research participants
APCRP-HDSD	Gabriella Miller Kids First Research Program	Common Fund integrated data resource of well-curated phenotype and genomic sequence data for the pediatric research community, enabling identification of genetic pathways underlying structural birth defects and childhood cancer. NHLBI is a lead IC in the management of the program.
BETR-ATSB	LINCS: Library of Integrated Network-Based Cellular Signatures	Trans-NIH activity to coordinate centers identifying and categorizing molecular signatures occurring when cells are perturbed
BETR-VBHB	GTRP: Gene Therapy Research Program	Facilitates translational research by providing U.S.-based heart, lung, blood, and sleep researchers with the resources critical to advancing investigational gene transfer products into clinical testing, and also provides services to other NIH institutes

Table 3: Examples of Inter-Agency, Trans-NIH, and Trans-NHLBI Activities Led or Co-Led by DCVS

Branch	Study	Description
BETR-VBHB	Trans-NIH Lymphatics Coordinating Committee	Advances research on the lymphatic system, including its role in function and diseases of organs in the body
BETR-VBHB	Trans-NIH Small Blood Vessel Biology and Disease Working Group	Shares and integrates existent knowledge and resources related to the normal function and malfunction of small blood vessels throughout the body currently administered by many different NIH institutes, and to foster collaborative extramural research
BETR-VBHB	KOMP2: Knockout Mouse Phenotyping Program	Provides broad, standardized phenotyping of a genome-wide collection of mouse knockouts generated by the International Knockout Mouse Consortium
PPSP-CAPB	Obesity Research Task Force (ORTF)	Multi-institute established in 2003 to accelerate progress in obesity research across the NIH. ORTF is co-chaired by the directors of NHLBI, NIDDK, and NICHD and meets semi-annually
Interagency		
APCRP-ACAD	CART: A Working Group to Investigate Innovative In-Home Monitoring Technologies to Enhance Health While Aging in Place	Working group composed of members from FDA, CMS, NSF, VA, HUD, ACL, and NIH that assesses the present state and identifies challenges in the development and application of technologies for in-home care for assisting older adults and people with chronic diseases to live independently. The working group is also in charge of establishing committees that will oversee the CART FOA ⁸⁸
BETR-ATSB	MATES: Multi-Agency Tissue Engineering	Coordinates federal funding, scientific meetings, regulatory guidance, standards development, funding efforts, and other key issues related to tissue engineering science, enabling coordination among federal agencies

Table 3: Examples of Inter-Agency, Trans-NIH, and Trans-NHLBI Activities Led or Co-Led by DCVS

Branch	Study	Description
	Science Working Group	
BETR-ATSB	Federal Forum on Medical Device Interoperability Working Group	Coordinates activities in standards, policies, and research in Medical Device Interoperability. Participating federal government agencies include FDA, NSF, NIST, DoD, TETRC, Navy, Air Force, and the VA
PPSP-EB	National Health and Examination Survey (NHANES), IAA with NCHS, CDC ⁸⁹	The NHLBI supports incorporation of measures of interest, such as measurements and questionnaires on blood pressure, lipids, pulmonary function, and sleep, in NHANES
PPSP-EB	National Longitudinal Mortality Study (NLMS), IAA with the Census Bureau	The NHLBI has funded major portions of this large national database to elucidate the role of demographic, social, and economic disparities to overall and cause-specific mortality. This study is now completed
PPSP-EB	Mortality Disparities in American Communities, IAA with the Census Bureau	New project using the Census Bureau's very large American Communities Survey to elucidate disparities in mortality (using the NCHS National Death Index) and medical care (using Medicare and Medicaid databases)

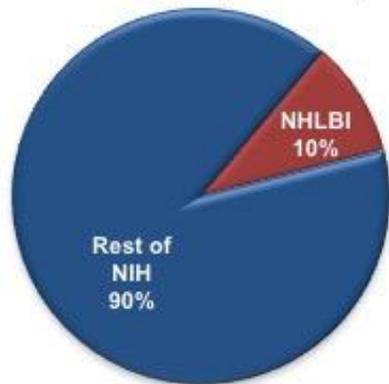
Figure 1: Resource Allocation Among DCVS Branches (2014)

The proportion of NIH funds going to NHLBI, the proportion of NHLBI funds going to DCVS, and the proportions of DCVS funds going to each office and branch. Note that the Women's Health Initiative branch was absorbed into EB in 2015 and is therefore merged with EB in this figure.

Abbreviations: NIH = National Institutes of Health; NHLBI = National Heart, Lung and Blood Institute; DCVS = Division of Cardiovascular Science; APCRP = Adult and Pediatric Cardiac Research Program; BETR = Basic and Early Translational Research Program; PPSP = Prevention and Population Sciences Program; ACAD = Atherothrombosis and Coronary Artery Disease Branch; HDSD = Heart Development and Structural Diseases Branch; HFAB = Heart Failure and Arrhythmias Branch; ATSB = Advanced Technologies and Surgery Branch; VBHB = Vascular Biology and Hypertension Branch; CAPB = Clinical Applications and Prevention Branch; EB = Epidemiology Branch; WHI = Women's Health Initiative; OBR = Office of Biostatistics Research; OCR = Office of Clinical Research; ORTCD = Office of Research Training and Career Development; FY 2014 = Fiscal Year 2014 (October 1, 2013 through September 30, 2014).

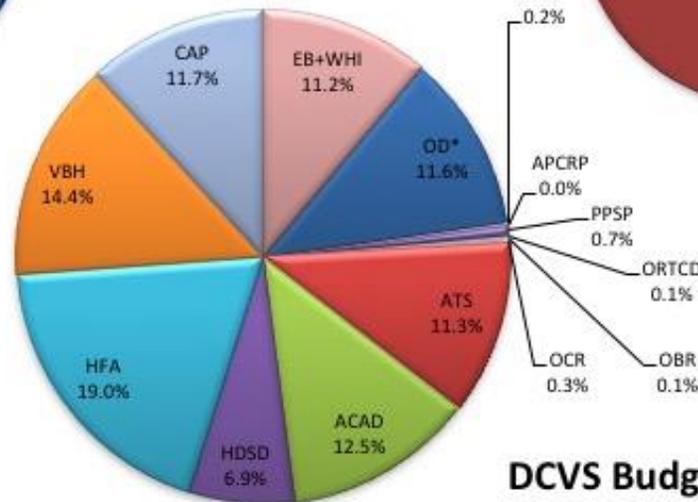
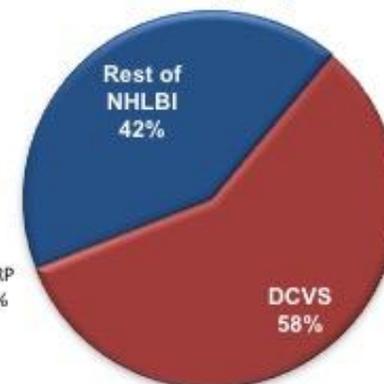
Figure 1. Percentage Share of the National Institutes of Health Total Budget Allocated to NHLBI, DCVS, and DCVS Branches, Fiscal Year 2014

NHLBI Percentage Share of NIH Total Budget (FY 2014)



**NIH FY 2014 Total Budget
\$30.07 Billion**

DCVS Percentage Share of NHLBI Total Budget (FY 2014)



DCVS Budget by Branch

* Trans-NHLBI initiatives funded through DCVS are reflected in the Office of the Director total

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