

American Heart Association Strategically Focused Research Network: Disparities in Cardiovascular Disease Request for Applications

The American Heart Association (AHA) is a non-profit, voluntary health organization funded by private contributions. The mission of the American Heart Association is to build healthier lives, free of cardiovascular diseases and stroke. The Guiding Values of the organization include:

- Improving and Extending People's Lives
- Bringing Science to Life
- Speaking with a Trustworthy Voice
- Building Powerful Partnerships
- Inspiring Passionate Commitment
- Meeting People Where They Are
- Making an Extraordinary Impact
- Ensuring Equitable Health for All

A leading priority of the AHA is to fund research that increases an understanding of the causes, prevention and treatments of cardiovascular diseases and stroke. These diseases remain the No. 1 and No. 4 killers of Americans, respectively.

The American Heart Association has a tradition of support for research spanning more than 60 years. Research is the foundation of all other aspects of the AHA's lifesaving work, generating a tremendous impact on people's lives. After the NIH, the AHA is the leading funder of cardiovascular disease (CVD) and stroke research in the U.S. with over \$3.4 billion spent on research since 1949. One of the many striking outcomes of AHA's research program is the funding of 13 scientists who have gone on to be awarded the Nobel Prize.

The Strategically Focused Research Network (SFRN) is a mechanism that provides AHA an opportunity to address key strategic issues as determined by the AHA Board of Directors. This SFRN will focus on "disparities" with the AHA supporting four (4) Research Centers for a period of four (4) years. These four (4) Centers will constitute the Network and will be awarded a total of \$15 million over that period (including costs for Network oversight and administration). The goal is to select and award four (4) Disparities Centers. The desired characteristics of these Centers, the general requirements of the application and the peer review criteria are described in this Request for Applications (RFA).

Objectives of Request for Applications

The American Heart Association has adopted 2020 goals to improve the cardiovascular

health of all Americans by 20% while reducing deaths from cardiovascular diseases and stroke by 20%. Cardiovascular health is being tracked with the <u>AHA's Life's Simple 7</u> metrics (link here). Scientists and clinicians played major roles in developing the 2020 goals and in achieving AHA's 2010 goal to reduce coronary heart disease (CHD), stroke and risk by 25%.

For example, research conducted by basic scientists has identified the pathophysiologic processes underlying heart disease and stroke, revealing potential pathways for novel therapeutic interventions. Clinical scientists have helped to identify therapeutic agents and approaches that are effective in the prevention and treatment of cardiovascular diseases, and traditional and novel CVD risk factors. Population scientists have identified, among others, effective strategies for the prevention of risk factors (primordial prevention), heart disease and stroke targeted at specific populations with varying degrees of susceptibility to these diseases.

However, despite these significant advances, cardiovascular diseases and stroke remain the number 1 and number 4 killers in America, respectively, and among the leading causes of death globally. Additionally, the risk and burden of these diseases is disproportionately greater among underserved populations including both race/ethnic minority groups, those who are economically disadvantaged or who live in certain regions or environments. There are many strategies and pathways that researchers can follow to discover new knowledge that support the AHA's goal to promote healthier lives free of cardiovascular diseases and stroke.

For the intention of this particular RFA, the AHA's conceptual framework states that social characteristics of the population such as socioeconomic status, gender, race/ethnicity, language, cultural beliefs, access to care, and residential environment are powerful determinants of health and may impose disparities across the spectrum of cardiovascular disease risk factor prevalence, incidence, diagnosis, treatment, and outcomes. These disparities may be reduced by improved understanding of their biological causes (including heritable and non-heritable causes), improved lifestyle factors, and by tailored treatment modalities and systems change. Elimination of disparities requires input from cross-disciplinary investigation involving diverse approaches. Specifically, this RFA seeks to have basic, clinical and population teams from individual Centers join together and provide proposals which address the topic of cardiovascular disease disparities via their individual areas of expertise. A Center may be intra- or inter- institutional. Each Center applies for funding individually and is peer reviewed by the AHA. The most meritorious Center applications and their research projects will be combined by the AHA to form the Strategically Focused Disparities Research Network (see Illustrations 1 and 1.1).

For the purposes of this RFA, the use of data from existing longitudinal cohort studies is encouraged for the clinical and/or population portion of the Center proposal. Examples of appropriate cohort studies include, but are not limited to: MESA, IC3, REGARD, FHS and JHS.

It should be noted that the increased availability of consumer-oriented health tools and social media, among others, has created unconventional opportunities for natural experiments and novel interventions that could inform the development of effective health behavior change strategies aligned with disparities in risk factor control or patient recovery. Multidisciplinary research that takes advantage of such innovative tools also falls within the scope of this RFA. Furthermore, collaboration is encouraged with social and behavioral scientists, health policy experts, and other experts to identify programs that effectively modify an individual's lifestyle in a fashion that unequivocally reduces the risk of heart disease and stroke or improves outcomes after an event.

The AHA is committed to an investment of \$15 million to establish this Disparities Network which will provide almost \$4 million per Center. This level of investment will support fully integrated collaboration across science disciplines.

The AHA intends to fund four Centers that will encompass the following goals:

- Accelerate generation of important, novel ideas
- Answer significant questions addressing gaps in knowledge
- Yield important gains in knowledge and research capacity (developing new investigators is one such gain)
- Link research and training components through the program
- Prioritize multidisciplinary approaches with frequent collaborative interactions within the Center and across the Network
- Demonstrate efficacy through data collection and evaluation
- Demonstrate the effectiveness or the applicability of the findings in clinical, public health or community-based settings such as workplaces, schools, churches or other "real-life" settings.

It is anticipated that the results of the funding and formation of the AHA Strategically Focused Disparities Research Center Network and their linking in this structure will:

- Produce a cadre of new investigators who will energize the field of cardiovascular disparities research and lead to the generation of an expansion of the numbers of such investigators in later years
- Produce new research results based on the initial ideas of the funded Centers and on ideas subsequently generated by the interaction of the Centers and their investigators
- Provide insights into and report on the challenges and successful mechanisms for active collaboration
- Identify programs and policies that reduce disparities in cardiovascular disease, stroke and risk, through a variety of modalities ranging from individual lifestyle change, promotion of a healthier community / environment, and/or improved diagnosis and treatment modalities..

Although successful applicants are asked to demonstrate effectiveness of the research outcomes by articulating a plan proposing how the results could be implemented in clinical or public health settings, this does not guarantee that funds will be available for the proposed implementation. It is strongly preferred that successful applicants articulate such a plan, as it will assist the AHA furthering its mission by exploring opportunities to advance the research findings.

Examples of multidisciplinary research approaches

The intent of this initiative is to support a collaboration of basic, clinical and population researchers from different disciplines whose collective efforts will lead to new approaches to reduce disparities in heart disease and stroke risk, incidence and outcomes. Following is an illustrative list of example questions that could be addressed by a Center. The examples below display the spectrum of research that can be performed within a Center, but are not intended to represent the level of integration, from basic to population science. Successfully funded applications will provide strong evidence of synergy among the proposed projects.

Example 1: Focus on Disparities In Socioeconomic Status

Basic science questions:

- 1. What genetic/epigenetic or metabolic susceptibility differences exist based on income, education, and occupation-based indicators?
- 2. What effect does socioeconomic disadvantage *in utero* and in early childhood have on long term anatomic and physiologic effects that may lead to cardiovascular disease in adulthood?

Clinical science questions:

- 1. How can socioeconomic status influence cardiovascular disease risk prediction?
- 2. What aspects of socioeconomic state can be leveraged in the clinical setting to improve adherence to treatments?

Population science questions:

- 1. How do socioeconomic factors influence cardiovascular disease risk over the lifespan?
- 2. What novel socioeconomic markers exist to predict patient outcomes?

Example 2: Focus on Disparities in Ethnicity & Culture

Basic science questions:

- 1. What effect does immigration have on epigenetics of cardiovascular disease development?
- 2. Do molecular mechanisms of disease differ in race/ethnic groups of different geography?

Clinical science questions:

- 1. Which culturally tailored interventions are successful in improving risk factor control?
- 2. How do religious factors impact risk factor control?

Population science questions:

- 1. What programs and policies are effective in improving access to care for those with language barriers?
- 2. Should risk factor definitions differ by race/ethnicity?
- 3. Are e-health interventions equally effective in different racial/ethnicity groups?

Example 3: Focus on Disparities in the Residential Environment Basic science questions:

1. What is the impact of social stress in an animal model of atherosclerosis? How do environmental factors (social networks, pollution, etc.) influence stress response in an animal model?

Clinical science questions:

- 1. Are residential environmental characteristics associated with severity of a cardiovascular event?
- 2. Which characteristics of the social network are associated with improved

recovery after a non-fatal cardiovascular event?

Population science questions:

- Does awareness of heart disease and stroke warning signs differ by residential characteristics?
- 2. Is availability of safe public spaces associated with levels of anthropometric measures such as Body Mass Index?
- 3. Is the neighborhood built/physical and social environments influence vascular inflammation?

Additional investigative areas that would be responsive to this RFA may include, but are not limited to:

- Research aimed at identifying and characterizing therapeutic targets for different race/ethnic groups.
- Identification and evaluation of culturally effective strategies for the prevention and control of CVD risk factors
- Understanding the pathophysiology and/or improving disparities in the prevalence of CVD risk factors and cardiovascular disease within specific populations (e.g.: racial, urban vs. rural, men vs. women) across the lifespan
- Research aimed at identifying mechanisms of increased CVD event rates in certain geographic locations.
- Determining the influence of social and cultural characteristics on specific CVD risk factors, e.g. obesity, blood pressure, diabetes, etc.
- Cross-cultural approaches to prevent and control of specific CVD risk factors
- Basic, clinical, population and global health strategies to promote risk factor control
- Research aimed at understanding the cultural differences in the "image of health"
- The use of genomics and/or other "-omics" to develop stratified or precision medicine for diverse populations
- Leveraging natural experiments that use novel behavior change strategies in community-based or public settings
- Partnering with social scientists, behavioral psychologists and others to identify best practices for improving treatment compliance in diverse populations
- Investigation of the determinants of disparities in effectiveness of systems improvement programs (such as AHA's Get with the Guidelines) by race/ethnicity, region or other factors.

Disciplines and Expertise

Multidisciplinary teams are appropriate and desired and can be broadly defined. Basic disciplines such as cell/molecular biology, biochemistry, bioengineering/biotechnology, immunology/virology, genetics/genomics, physiology, vascular biology, geneticists and bioinformaticians among others are all appropriate. Clinical disciplines, general internal medicine, nutrition and dietetics; cardiology, pediatric cardiology, cardiovascular surgery, exercise physiology, nephrology, anesthesia, nursing, emergency medicine, kinesiology, endocrinology, neurology, psychiatry and behavioral science are all appropriate. In addition, public health disciplines including the fields of health communications, health marketing, informatics, individual and collective behavior are all of interest. Epidemiological, interventional, and behavioral science, biostatistical, and health economic approaches are appropriate to the focus of this program as well as eHealth and related technologies.

Key Requirements of the Center Application

This RFA embraces a Network "Center" concept. Thus, it would be appropriate for three (3) studies to be submitted from each Center applying to be in the Network and to have an integration of these studies within each Center. Each Center will include several components: a designated Center Director, three (3) synergistic projects related to the topic of cardiovascular disease disparities, and a research postdoctoral fellowship training component.

In addition to Centers that integrate synergistic projects, as per the three examples above, Centers can also demonstrate a high degree of collaboration by working on one comprehensive research project across all sites. For example, a Center application can be built around a comprehensive but pragmatically designed randomized trial on disparities in gender disparities in cardiovascular rehabilitation, while developing ancillary studies of a more basic/biomedical nature.

The development of each Center will be the responsibility of the Center Director, who will coordinate the projects and the training program, to ensure that they are not only complementary, but also effective in producing a greater outcome than if they were executed individually. The Director will provide administrative and scientific leadership and will be responsible for the organization and operation of the Center, and for communication with the AHA Strategically Focused Disparities Research Network Oversight Advisory Committee.

A major component of the Centers selected for funding under this initiative will be their ability to foster a successful program for the interdisciplinary training of a new generation of scientists who, from their earliest experiences in research, will collaborate with other scientists through monthly meetings with established investigators and annual meetings with other investigators participating in the Centers. An ultimate product of this program will be the creation of a report on the challenges and results of active collaboration.

The CVGPS is a collaboration among AHA, Boston University (BU) and the University of Mississippi Medical Center (UMMC), the academic coordinating homes, respectively, of the Framingham Heart Study (FHS) and the Jackson Heart Study (JHS). The Jackson Heart Study also involves Jackson State University (JSU) and Tougaloo College (TC) as partner institutions. CVGPS combines the power of long-term population studies with the precision of molecular analysis to unravel key distinctions between and within subgroups of patients. The discoveries it generates will point the way toward better-targeted, safer, and more effective treatments, based on a deeper understanding of patients' characteristics, including e.g. risk profiles and therapeutic needs.

Additional information on CVGPS can be found

at: http://my.americanheart.org/professional/Research/CardiovascularGenomePhenomeStudy-VGPS/AHA-Cardiovascular-Genome-Phenome-Study-CVGPS UCM 461668 SubHomePage.isp

In support of CVGPS, phenotypic or genetic data generated from center projects associated with the Strategically Focused Disparities in CVD Research Network will be shared within the larger framework of the CVGPS project through deposit of data, within a specified timeframe, in a data repository associated with CVGPS and approved by the AHA.

Program Structure

Each Center will:

• Conduct three (3) cohesive research projects of scope equivalent to an R01

- Provide a training program for fellows, training three (3) Center-funded postdoctoral fellows during the period of the award
- Be linked to the other Centers by interactions/meetings to accelerate exchange of ideas, encourage sharing of commonly-useful knowledge and methods, and provide networking opportunities for trainees
- Report annually on its efforts towards integration with the other centers, as well as observations on successes/challenges of such integration
- Interact as part of the American Heart Association Strategically Focused Disparities Research Network

Postdoctoral Fellowship Training Requirements:

- Each Center will provide a multidisciplinary training program to give fellows basic, clinical, population, and translational research experience.
- Each Center will train 3 fellows during the period of the award (one two-year fellowship in years one and two; one two-year fellowship in years two and three and a final two-year fellowship in years three and four).
- Each Center will provide professional, non-medical training in the form of presentation and communication skills.

Collaboration Requirements:

- Centers will be expected to meet and collaborate with each other through interactions and meetings to accelerate information exchange and ideas;
- Centers will be expected to comprise a team that meets on a regular basis and develops one or more collaborative projects;
- Centers will collaborate and participate in producing an end-of-award report about the challenges, mechanisms and successes of the Centers' collaborations;
- Centers will consider themselves part of the AHA Strategically Focused Disparities Research Network.

Collaboration Expectations

Once awarded, there is an expectation that the four (4) Centers will interact with each other, in particular to provide networking opportunities for trainees, to encourage sharing of commonly-useful knowledge and methods, and to provide a stimulating atmosphere for research collaborations. Strategies for communication and interaction among the Centers should be addressed in the proposal and could include ways to encourage interaction, augment or expand that Center's study findings, share training opportunities for fellows and junior investigators, etc. Center personnel will be expected to participate in annual meetings and visits to other centers in the network. Annual progress reports describing each Center's efforts towards integration, as well as a report on successes/challenges of such efforts, will be required.

Centers selected for funding will be expected to interact and develop new hypotheses leading to collaborative projects. The collaborating Centers are expected to share everything from "samples to ideas." The Centers will be expected to work with the AHA Oversight Advisory Committee to define the strategies for leadership in training and interdisciplinary collaboration, as well as a clear commitment to collaboration with other disciplines and other centers.

Eligible Institutions and Investigators

Awards are limited to non-profit institutions in the United States, such as universities and colleges, public and voluntary hospitals, laboratories, research institutes, and other non-profit institutions that can demonstrate the ability to conduct projects and organize a center.

Applications will not be accepted for work with funding to be administered through any federal institution or work to be performed by a federal employee with the exception of Veterans Administration employees.

The Centers are not transferable to other institutions. An institution may submit only one AHA Strategically Focused Disparities Research Network Center application for this competition. Individuals at the applicant institution who are not participating in their institution's center application (and/or its three project applications) may participate in another separate institution's center application. Individuals participating in their institution's center application, other than the Center Director or Center Training Director, may participate in a separate institution's center application. The application may include individuals and/or projects at more than one institution provided there is evidence for a successful close personal and geographical interaction among research and training personnel.

It is the responsibility of the *submitting institution* to ensure that only one proposal is submitted for the institution or to coordinate across several institutions to create a single application. The Center Director's institution will maintain fiscal responsibility for the entire award. The appropriate Institutional Officer should sign off on the proposal in AHA's online grants management system, Grants@Heart.

Directors and Principal Investigators of projects of the Centers must possess an M.D., Ph.D., D.O., D.V.M., or equivalent doctoral degree at time of application, and have a faculty or staff appointment. Directors and Principal Investigators of projects at the Centers may hold another AHA award simultaneously. The Center Director may also serve as a Project PI on the Center application. There is a 20% minimum effort requirement for the Director and a 10% minimum effort requirement for Principal Investigators (PI) of Center projects. Director and Project PI salary requested must be proportional to the percent effort devoted to the Center. An individual who holds a Director position within the Center application (Center Director or Center Training Director) may not serve in a director capacity on another institution's application.

The Center Director must demonstrate expertise in the area of disparities in cardiovascular disease research, with demonstrated ability to build a Center team. The Director should ideally demonstrate a successful history of leadership in a research project team and in career development. A clear demonstration of the Director's commitment to integration with the other Centers is required. Experience in multi-institutional collaboration is encouraged.

The responsive application will demonstrate a history of successful post-doctoral fellowship training with a plan to continue the program or a strong plan to develop a successful program. In addition, training in clinical outcomes research and translational research concepts as well as collaborative research should be described in the application. Collaborative interdisciplinary training programs are encouraged.

A viable source for identifying and recruiting trainees must be presented in the application and while trainees are not required to be named at the time of the application submission, the first set of fellows must be identified by July 1 of 2015. The trainee fellows must possess an M.D., Ph.D. or equivalent doctoral degree at the time of participation in the program. Collaborative interdisciplinary training programs are encouraged.

Citizenship Requirements for Directors, Principal Investigators and Fellows

Directors must have one of the following designations:

- U.S. citizen
- Permanent Resident
- Pending Permanent Resident (must have applied for permanent residency and have filed Form I-485 with the U.S. Citizenship and Immigration Services and have received authorization to legally remain in the U.S., having filed an Application for Employment Form I-765)
- G-4 Visa family member of employee of international organizations and NATO Principal Investigators of proposed projects must have one of the following designations:
 - U.S. citizen
 - Permanent Resident
 - Pending Permanent Resident (must have applied for permanent residency and have filed Form I-485 with the U.S. Citizenship and Immigration Services and have received authorization to legally remain in the U.S., having filed an Application for Employment Form I-765)
 - E-3 Visa specialty occupation worker
 - H1-B Visa temporary worker in a specialty occupation
 - O-1 Visa temporary worker with extraordinary abilities in the sciences
 - TN Visa NAFTA professional
- G-4 Visa family member of employee of international organizations and NATO

Named fellows of the Centers must have one of the following designations:

- U.S. citizen
- Permanent Resident
- Pending Permanent Resident (must have applied for permanent residency and have filed Form I-485 with the U.S. Citizenship and Immigration Services and have received authorization to legally remain in the U.S., having filed an Application for Employment Form I-765)
- E-3 Visa specialty occupation worker
- H1-B Visa temporary worker in a specialty occupation
- O-1 Visa temporary worker with extraordinary abilities in the sciences
- TN Visa NAFTA professional
- J-1 Visa exchange visitor
- F-1 Visa student
- G-4 Visa family member of employee of international organizations and NATO

All awardees must meet the citizenship criteria throughout the duration of the award.

Fellowship Qualifications

Named fellows of the Centers at U.S. institutions must hold a Ph.D., M.D., D.O., D.V.M. or equivalent doctoral degree and commit 75% effort to research training. Center fellows may commit a minimum of 70% effort if justification is accepted by the AHA Oversight Advisory Committee. A named fellow may not hold another fellowship award, although the institution may provide supplemental funding. Fellows may not hold a faculty or staff appointment, with the exception of M.D.s or M.D./Ph.D.s with clinical responsibilities. These fellows may hold a title of instructor or similar due to their patient care responsibilities, but must devote at least 75% effort to research training. A named fellow may have been a recipient of an AHA fellowship, but may not hold an AHA affiliate fellowship or AHA Fellow-to-Faculty Transition Award at the same time as an AHA Strategically Focused Disparities Research Network fellowship.

Other Relevant Policies

The Center awards are not transferable to other institutions. The projects described can have no scientific or budgetary overlap with other funded work. Any inventions, intellectual property, and patents resulting from this funding are governed by the AHA Patent, Intellectual Property

and Technology Transfer Policy. The applicant/awardee and institution are responsible for compliance with all American Heart Association research award policies and guidelines for the duration of any awards they may receive. Go to Policies Governing All Research Awards to review AHA policies.

Application Submission Process

Only one Center proposal, including multiple research project proposals, may be submitted from an institution. Each Center application should have only one (1) Center Director. Co-Directors will not be recognized on official documents or publications. The completed application must include the primary Center application, three individual research project applications, and the overall training plan. The components of the application are described below.

Application instructions for the AHA Strategically Focused Disparities Research Centers will be available on the American Heart Association's <u>website</u> approximately mid-September 2014. Applications will only be accepted through AHA's online research system – Grants@Heart.

Components of Application

Primary Center Application

The Director of the proposed Center must submit an umbrella application which consists of the following components:

- 1) Center Science Vision and Synergy (a clear, unifying central theme to which each research project application relates); a center should be viewed as a group of interrelated research projects that are complementary and synergistic.
- 2) Information regarding the Director
- 3) Information regarding any current disparities in cardiovascular disease research programs and any history of successes in disparities research
- 4) A detailed description of the multidisciplinary training program for the AHA Strategically Focused Research Center two-year fellowships (basic, clinical and translational research exposure), including information regarding the selection of prospective fellows and how funded fellows' ongoing progress will be guided via an individual development plan (IDP) and evaluated at least annually. In addition to participating in annual SFRN Center meetings, Centers are expected to incorporate collaboration with established investigators at other Disparities Research Network Center institutions through regular meetings and/or Center-to-Center visits
- 5) Information on current training programs and training grants within the Center institution and affiliated institutions relative to the research being proposed (if appropriate)
- 6) Information regarding other faculty/staff members at the Center institution and affiliated institutions (if appropriate) who will be submitting research projects
- 7) Information on research funding available to the Director and proposed Principal Investigators on Center research projects
- 8) Information on existing collaborative research teams within the Center institution and affiliated institutions (if appropriate) and their ability to share information and methodologies with other institutions. Documented evidence that other collaborations have produced synergistic results.
- 9) Information on facilities available to support the Center and affiliated institutions' (if appropriate) research projects
- 10) An overview of the estimated four-year budget for the Center
- 11) Information regarding the identification of a faculty/staff member at the Center institution

or affiliated institutions (if appropriate) with the leadership skills to bring team-building and professional/organizational development to the collaborative process

Center Research Project Applications

A Center research application must include three (3) synergistic research projects related to disparities in cardiovascular disease research. Each project should demonstrate importance and relevance of the research to the field of disparities in cardiovascular disease. The projects proposed by a Center will be reviewed as a group. Submitted projects must be feasible within the budget described. American Heart Association research funds will not be awarded to supplement or duplicate any work which is being supported by other funding agencies.

The Principal Investigator of each proposed research project must submit an application which consists of the following components:

- 1) Required application forms
- 2) Investigator's qualifications
- 3) Specific project aims
- 4) Background and significance
- 5) Preliminary data on same or related problems
- 6) Contemplated methods of approach to problem
- 7) Evidence of successful collaboration with other Center members
- 8) Ethical and human subject aspects

Peer Review Process

Review of the applications will be conducted by the American Heart Association and will occur in two phases. For the first phase, a peer review committee of volunteer scientists will be assembled to review all the submitted Center applications. Appropriate scientific expertise will be sought to review the applications received. Each application will be reviewed in depth by a minimum of three (3) peers and more than likely four (4) reviewers will be analyzing each aspect of the submission, i.e. Center, Projects, Training Program and Collaboration. These reviews will be presented to a peer review panel of 12 or more. At the discretion of the review committee, and based upon the preliminary scores assigned to an application by the assigned reviewers, a streamlined review may be conducted for any application. After discussion of each Center proposal, each panel member will score each application, using the current AHA review scoring system. The Centers and their projects will be ranked, based upon the average merit scores and percentile ranking of the panel members' scores.

A second stage of the review will then be conducted with only the highest ranked Center applications, and will include a "reverse site visit" presentation to the AHA review group by the Center Director and select members of the Center team. A minimum number of participants, to be decided by the AHA, will be invited to the reverse site visit. Reviewers will score the Centers as a whole following the presentations, with the average of the reviewers' scores providing the final ranked list of applications. The ranked list will be reviewed by the AHA Research Committee. The four Centers with the highest rank will be funded, contingent upon resolution of any policy concerns.

Peer Review Criteria

The following major factors will be considered in the evaluation of each Center. These factors are intended to assist applicants in determining the appropriateness of candidacy. All of these factors will be entered into the deliberations of the peer review committee. These factors are not listed in any specific order of priority.

- **I. Projects** Potential impact of the project on disparities in cardiovascular disease research; strengths of applicant investigators (qualifications, expertise and productivity); potential for collaboration or synergy of projects; scientific content; background; preliminary studies; detailed specific aims; approach detail; analytical plan; sample size; data management; significance; innovation; individual project scientific merit; and total project coordination (within and among projects). Projects will be rated on the following areas:
 - Approach: Are the conceptual framework, design, methods and analyses adequately developed, well integrated, well-reasoned and feasible (as determined by preliminary data) and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?
 - <u>Innovation</u>: Is the project original and innovative? For example: Does the project challenge existing paradigms and address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?
 - <u>Investigator</u>: Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?
 - <u>Significance</u>: Does this study address an important problem broadly related to cardiovascular disease or stroke? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods and technologies that drive this field?
 - <u>Environment</u>: Does the scientific environment in which the work will be done contribute
 to the probability of success? Do the proposed studies benefit from unique features of
 the scientific environment, or subject populations, or employ useful collaborative
 arrangements? Is there evidence of institutional support?
 - <u>Impact</u>: How does the project relate to and support the mission of the American Heart Association to **building healthier lives**, free of cardiovascular diseases and stroke?
 - Relationship to other Center projects: Does the project complement other aspects of the proposed Center, including other Center projects? Is there evidence of synergy among the projects and training component of the Center?
- **II. Training component** A detailed plan for developing and implementing a postdoctoral training program that includes clinical (M.D.) or Ph.D. training in disparities in cardiovascular disease research; qualifications and characteristics of current and anticipated trainees; didactic and practicum training opportunities; plan for the selection of prospective fellows and how funded fellows' ongoing progress will be guided via an individual development plan (IDP) and evaluated at least annually. Plan for involving fellows in annual Center meetings and Center-to-Center visits, along with identifying opportunities for fellows to work with established investigators at other network Centers; ability to track trainees; conferences and meeting participation for trainees; documentation of a ready supply of fellows; and history of successful fellowship training for disparities in cardiovascular disease researchers.
- **III. Center Team** Qualifications of the Director to provide scientific and administrative leadership for the Center; experience and commitment of the nominated Director; quality of disparities in cardiovascular research team; qualifications of investigators and co-investigators; experience with disparities in cardiovascular disease-related studies; training experience.
- **IV. Environment** Institutional commitment, resources and facilities to sustain the Center; institutional resources available to complete the project; analytical resources available to the project; letter from Center Director's Department Head assuring the department and institution's support of the Center along with confirmation that the Center Director will devote at least 20%

effort towards the Center. Other Center personnel may be appointed to assist the Director in the administration of the Center. However, the Director will be required to devote 20% effort to the Center.

V. Interaction Plan within and among Centers—Plan for and commitment to sharing of commonly-useful knowledge and methods, providing a stimulating atmosphere for research collaborations, and providing networking opportunities for trainees. Cited strategies for communication and interaction among the Centers.

Peer Review Scoring Criteria

- I. Projects Potential impact of the project on disparities in cardiovascular disease research; strengths of applicant investigators and collaborations (qualifications, expertise and productivity); scientific content; background; preliminary studies; detailed specific aims; approach detail; analytical plan; sample size; data management; proposed productivity; significance; innovation; individual project scientific merit; and total project coordination (within and among projects).
 (30%) of total evaluation
- **II. Training component** A detailed plan for developing and implementing a training program that includes clinical (M.D.) training in translational research and Ph.D. training in disparities in cardiovascular disease research investigation; opportunities for non-medical training including communication and presentation skills; didactic and practicum training opportunities; ability to track trainees; conferences and meeting participation for trainees; documentation of a ready supply of fellows; qualifications and characteristics of any current or anticipated trainees and history of successful fellowship training for clinicians and academic researchers.

(20%) of total evaluation

- III. Collaboration History, ability and commitment to collaborate with other institutions, investigators and within the applicant institution. Defined and detailed process for collaboration with other sites in addition to within and among the proposed different projects; plans to actively participate in a collaborative network. Evidence of formal training in leadership skills with an emphasis on collaborative leadership will be favorably reviewed. (25%) of total evaluation
- IV. Center Director Demonstrated ability to lead others, along with experience and commitment to the success of the Center, the projects contained within, and the Network as a whole. Documented evidence of willingness to collaborate with others outside their institution to share ideas, science, etc. to progress the field of disparities in cardiovascular disease research.

 (10%) of total evaluation
- **V. Investigator team** Qualifications of each PI to provide scientific and administrative leadership for their respective projects; demonstrated commitment of each PI, and experience with disparities in cardiovascular disease studies; quality of interdisciplinary research team; qualifications of co- investigators; training experience. **(10%) of total evaluation**
- VI. Environment Institutional commitment, resources and facilities to sustain the Center; institutional resources available to complete the project; analytical resources available to the project. (5%) of total evaluation

Reverse Site Visit Expectations

If a Center application is selected to move to the 2nd phase of review, they will have the critiques and committee member comments available electronically at the time of notification. The Center Director and key personnel will have approximately 3-4 weeks to prepare for the reverse site

visit. The committee members will listen to the presentation in response to the critiques, plus any additional information that is presented. There will be a question and answer period, so the actual presentation should not be more than 30 minutes, which will allow for responses and follow-up questions from the panel. The entire reverse site visit will last approximately 45 minutes.

Human Subjects and Ethical Considerations

All applications are expected to adhere to American Heart Association research program policies and standards including those regarding the ethical treatment of human subjects, as well as the policy addressing inclusiveness of study populations relative to gender, race, age and socioeconomic status. Institutional review board approval will be handled on a "just in time" basis and will be required by the date of the first quarterly payment made to the institution. Funding is contingent upon institutional review board approval initially and for the duration of the award. Any ethical concerns identified via the review process shall be forwarded to the AHA Research Committee for consideration.

Oversight Advisory Committee

Once the Centers are selected, the AHA Strategically Focused Disparities Research Oversight Advisory Committee will provide external oversight for the Centers and serve in an advisory capacity to the Centers. Anyone who applies to the Program and is funded will not be considered for membership on the Advisory Committee. Center Directors and project Pl's will report to and meet with the Advisory Committee regularly. The Oversight Advisory Committee also will offer advice to the AHA Research Committee on the progress of the Centers and any issues that arise in their administration.

Responsibilities of the Oversight Advisory Committee include:

- Monitoring the scientific progress of the Centers and Center Projects
- Overseeing and annually evaluating the program, including an evaluation of the progress of the trainees, making recommendations regarding continuation to the AHA Research Committee
- Monitoring and encouraging interaction efforts within and among Centers. The Advisory
 Committee will encourage Centers to change traditional culture by rewarding interaction
 and will request an annual report on the successes and challenges resulting from efforts
 to interact
- Making recommendations to the AHA Research Committee regarding management of the program

The Advisory Committee will include:

- Leading established investigators in disparities in cardiovascular disease research who are not funded by the program
- Investigators experienced in multidisciplinary approaches
- at least one (1) member who is a specialist in (bio)statistics
- at least one (1) member who is a specialist in epidemiology
- at least one (1) member who is a specialist in economics and social science
- at least one (1) member of the request for applications (RFA) writing group
- a representative from the AHA Research Committee

Network Membership Responsibilities

One of the key objectives of this initiative is to encourage interaction among the Strategically Focused Research Network Centers, both in training and research efforts. An important component of the initiative is a multi-disciplinary approach both within and among Centers that comprise the Network. The structure of the Network will include sufficient components to maximize the interaction and collaboration among the Disparities in Cardiovascular Disease Centers. The AHA Oversight Advisory Committee will track and encourage interactive and collaborative activities, and develop and implement a plan for regular dialogue among the Center participants. The entire network should operate as a team.

The initiative will begin with a meeting of all key staff from the Centers and the Oversight Advisory Committee. This meeting, among other things, provides a forum for determining the nature and extent of interactions, collaboration and information sharing. Subsequent meetings, teleconferences, and other interactions among the Centers will occur throughout the duration of the initiative. The institutions in which the Centers are located must provide assurance that no barriers exist to thwart collaboration and sharing of ideas. A minimum requirement of the Centers within the Network is that they agree to change any local data collection system to a common one appropriate to the network. Technological support for this multi-site program with an emphasis on collaboration will be provided to facilitate all the required interactions/meetings in an effective and convenient manner.

Program Evaluation

Preliminary measures of the success of the initiative have been identified. Each Center will be required to provide an annual interim report, as well as a final written scientific report of progress. Progress made and plans for the coming year shall be addressed in these annual reports. In addition to the annual and final report of progress from each Center, funded Centers will be asked to report on the following measures:

- Productivity of Centers track publications and citations; document outcomes of research projects; document other funding resulting from the current initiative
- Transfer of intellectual property to the marketplace
- Impact of the fellowship training experience on career development: track trained fellows over a five-year period for such measures as percent of time in research, publications, other funding, and promotions
- Report on the interaction among the Centers and lessons learned, including measures
 of level of collaboration, such as heterogeneity of co-authors of papers (number of
 academic departments represented among co-authors)

Budget

The Program will have a total budget of approximately \$15 million. The funding will be allocated as follows:

	Network Totals	Center Totals
<u>Projects</u>		
Three projects at each of four Centers for four years Maximum of \$711,000 per year to be divided among the Projects funded at the Center. PI must commit at least 10% effort to project. While there is not a stated maximum on Project PI salary and fringe, these items must be commensurate with percent effort devoted to the project.	\$11,376,000	\$2.844M/Center
Fellows		
Three Fellows at each Center for two years each	\$ 1,200,000	\$0.3M/Center
Ossilan Dimentan		
Center Director One Director at each Center for four years A maximum of \$50,000 per year for each Director. Center Director must commit at least 20% effort	\$ 800,000	\$0.2M/Center
Center Travel Costs Covers travel for Center personnel to Center network meetings and other integration activities. \$7,000 per year must be allocated to Center Travel.	\$ 112,000	\$28,000/Center
Direct Costs (Total)		
Research Dollars	\$13,488,000	\$3.372m/Center
Indirect Costs AHA Policy allows for a maximum of 10% for indirect costs	\$ 1,348,800	\$0.3372M/Center
Total	\$14,836,800	\$3.7092M/Center

The total amount requested per Center, *including* 10% indirect costs, annually may not exceed approximately \$3.7 million for the 4-year award.

The Center Director will be responsible for overseeing the total budget for his/her Center within the Network. If awarded, the Director and the institution assume an obligation to expend grant funds for the research purposes set forth in the application and in accordance with all regulations and policies governing the grant programs of the American Heart Association, Inc.

The AHA is currently paying all research payments quarterly on or around the 17th of the month following the end of the calendar quarter. Payments are made to institutions on behalf of the Director. If activated on April 1, the first payment to the Center would be sent on or around July 17th (and in October, January, April and July thereafter).

Timeline

Activity	Date
Promotion of program	March 2014
Request for Applications Published	September 2014
Application instructions on AHA web site	September 2014
Letter of Intent deadline	October 30, 2014
Center and Center Projects Deadline	January 30, 2015
Review of proposals (two phases)	March/April 2015
Funding decisions made by AHA Research Committee / Applicants Notified	May 2015
Centers conduct research, train fellows, interact, report results	June 2015 – June 2019

Letter of Intent

Prospective applicants are invited to submit a Letter of Intent for the AHA Strategically Focused Research Network on Disparities in Cardiovascular Disease on or before **October 30**, **2014**. The letter should include the following information:

- Name, institution, address, telephone, and e-mail of proposed Center Director
- Name, institution, address, telephone, and email of proposed Center Training Director
- Names, institutions, addresses, telephones, and e-mails of proposed Principal Investigators for Center Research Projects
- Names, institutions, addresses, telephones, and emails of other Key Personnel collaborators, consultants, etc.
- Information on any additional participating/affiliated institutions not listed above
- Brief overview of the 3 proposed projects please label project "Basic" "Clinical" or "Population." Include a maximum 1-2 paragraph project summary on each project along with the proposed project title.

While a Letter of Intent is requested, it does not enter into the review of said subsequent application. The information provided in a Letter of Intent allows AHA staff to estimate the potential peer review workload and to avoid potential conflicts of interest in the peer review process. It also allows AHA to provide applicants with updated information about the application process if necessary.

The Letter of Intent should be submitted electronically via Grants@Heart between September 15th and October 30th, 2014. <u>Instructions for the Letter of Intent</u> are available online.

Inquiries

Inquiries regarding this RFA may be sent to:

Phone 214-360-6107

Glossary of Terms

Dania Onione	The study of five descentables are a Thirty was a forest with its
Basic Science	The study of fundamental life processes. This type of research is
	often purely theoretical with the intent of increasing our
	understanding of certain phenomena or behaviors but is not
0	directly aimed at solving a specific prevention or treatment issue.
Center	A Center is comprised of a Center Director, Center Training
	Director and multiple Project Pls. These individuals may be
	located at the same or separate institutions as long as there is
	evidence of past and/or current collaboration. Centers will work
	together to move research forward in the area of study.
Center Director	The Director serves as the leader of his/her Center. This
	individual is renowned as an expert in the science topic being
	proposed and provides leadership, training and collaboration
Cantan Fallow	experience.
Center Fellow	A Center Fellow has a post-baccalaureate doctoral degree (MD,
	PhD, DO, DVM, PharmD). These individuals will be highly
	involved in the work being proposed by the Center and will be
	encouraged to collaborate with fellows across the network. The
	Center Fellows will work closely with the Center Training Director
	and Center Director on their individualized multidisciplinary
Clinical Science	training plan. Addresses important questions of normal function and disease
Clinical Science	using human subjects (or on material of human origin such as
	tissues, specimens, and cognitive phenomena) wherein an
	investigator or colleague directly interacts with human subjects. It
	includes research on mechanisms of human disease, therapeutic
	interventions, clinical trials, and development of new
	technologies, but does not include in vitro studies using human
	tissues not linked to a living individual.
Collaboration	Collaboration is defined as a process where two or more
Conaboration	individuals or organizations work together to complete a task and
	achieve shared goals - a deep, collective, determination to reach
	an identified objective — by sharing knowledge, learning and
	building consensus.
Letter of Intent	The Letter of Intent is used by the AHA to gather information on
	prospective applicants – quantity of expected applications,
	projects being proposed, etc.
Multidisciplinary	Multidisciplinary Research brings different disciplines together to
Research	explore a topic from different perspectives. Collaboration across
	the disciplines is key to create new approaches, ideas,
	knowledge base, etc.
Oversight Advisory	A group of scientific volunteers in the named strategic area
Committee	tasked with supervising the progress and direction of the Centers
	in the Network to ensure that the goals of each project, each
	training program, cross-center collaboration, etc. are met and
	accomplished during the life of the Network.
Population Science	The science and art of studying the distribution and determinants
-	of health status as influenced by social, economic and physical
	environments, human biology (including genetics and genomics),
	health policy and services and of preventing disease, prolonging
	life and promoting health at the population level. Population

	health research may include epidemiologic and behavioral
	, ,
	studies, outcomes research, and health services research.
Project PI	A Project PI is an independent investigator responsible for
	carrying out the scientific research project proposed in their
	application. They must provide evidence of successful research
	accomplishments and their ability and commitment to collaborate
	and share knowledge with others.
Reverse Site Visit	A reverse site visit occurs during the second phase of peer
Reverse Site visit	
	review for the Strategically Focused Research Network
	applications. The visit consists of an in-person presentation by
	the proposed Center Director and Project Pls, to the AHA Peer
	Review Committee. The reverse site visit is held at a neutral
	location and will consist of a brief oral presentation followed by a
	question and answer period.
Strategically Focused	A Network is composed for multiple Centers, each at different
Research Network – aka	institutions, coming together to study a common topic determined
Network	by the AHA to encourage collaboration and move the science
Network	community forward.
Symonor	
Synergy	Synergy is the ability of a group to produce something greater
	than the sum of its parts; the ability of the group to outperform
	even its best individual member.
Training Director	The Training Director is responsible for the direction and
	execution of the training program of the center postdoctoral
	fellows. This program should include multidisciplinary approach
	to training and developing the fellows in the area of research
	being proposed by the Center.
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