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### Cardiometabolic Health with a focus on Type 2 Diabetes Mellitus Strategically Focused Research Network

#### Key Dates

RFA Posted:	May 7, 2019
Letter of Intent Deadline:	June 25, 2019
Application Deadline:	Aug 13, 2019
AHA Peer Review:	Oct/Nov 2019
Notification of Awards:	Winter 2019
Award Start Date:	Jan 1, 2020

#### Award Objectives and Characteristics Announcement

The American Heart Association announces a Request for Applications for the Cardiometabolic Health with a focus on Type 2 Diabetes Mellitus Strategically Focused Research Network.

#### Purpose

A leading priority of the AHA is to fund research that increases the understanding of the etiology, pathophysiology, treatment and prevention of cardiovascular (CV) diseases and stroke. This Strategically Focused Research Network supports a collaboration of basic, clinical and population researchers from different disciplines whose collective efforts will enhance the understanding of the etiology, biological pathways and modifiable risk factors associated with cardiometabolic disorders with a particular focus on Type 2 Diabetes Mellitus (T2DM), and will lead to innovative and breakthrough discoveries for the prevention and treatment of diabetes and related cardiometabolic health disorders.

#### Topics of Interest

##### Specific Questions to be Answered by this Grant Opportunity

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 the study of cardiometabolic health and T2DM. Each Center must have two to three (2-3) research projects from two to three of these disciplines: basic, clinical, and population science. All projects must focus on cardiometabolic health and T2DM. Population studies are inclusive of projects ranging from cohort studies to translational work involving community interventions. All projects must address health and health care disparities and/or health equity.



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Note: Centers are highly encouraged, where applicable, to align with AHA initiatives focusing on cardiometabolic health and diabetes, AHA initiatives addressing the use of digital technology to improve health outcomes, or other AHA programs. These and other AHA programs can be found via [www.heart.org](http://www.heart.org).

# Example AHA Programs

Relating to Cardiometabolic Health and/or Diabetes

(This list is not exhaustive)



American Heart Association.  
Simple Cooking with Heart™



American Heart Association.  
Healthy for Good™



American Heart Association.  
Workplace Health Solutions™



American Heart Association.  
Life's Simple 7™



American Heart Association.  
Teaching Gardens™



American Heart Association.  
Check. Change. Control.  
Cholesterol™

Know **Diabetes** by **Heart**™

TARGET: **BP**™

Researchers are encouraged to use AHA metrics as their research outcomes measures. Websites for these example programs are listed at the end of this proposal.

The following are illustrative descriptions of overarching themes that could be addressed by a Center. Successful applications will provide strong evidence of synergy among the proposed projects and will address at least one of the issues below or an alternate issue of equal importance.

## Basic Mechanistic Pathways

There is an interest in gaining further insight into the key mechanistic factors associated with cardiometabolic disorders and T2DM including the underlying factors that impact the risk of atherosclerosis, coronary artery disease (CAD), endothelial dysfunction and thrombosis. A better understanding of the molecular connections and biological pathways that drive the relationships between obesity, metabolic syndrome, prediabetes, T2DM, inflammation, atherosclerosis and vascular disease risk are needed in order to learn how these pathways can be blocked or attenuated. In addition, a more in depth understanding of the mechanistic links between insulin resistance and liver and adipose tissue depots and how these affect metabolic pathways and amplify atherosclerosis risk is needed.



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### Diagnosis and Risk Assessment

A more in-depth understanding of newer biomarkers, tissue markers, cytokines, imaging modalities and non-invasive techniques is needed to better identify those at risk for CVD, stroke, chronic kidney disease (CKD) and heart failure (HF), and to help predict disease progression and improve quality of life and clinical outcomes. There are key questions regarding recent data suggesting the presence of distinct T2DM subgroups, and how these might impact cardiovascular outcomes.

### Comorbidities and Disease Progression

New strategies are needed to identify how comorbidities seen in patients with cardiometabolic disorders e.g. hypertension, dyslipidemia, obesity, CKD, among others, can impact disease progression, treatment and outcomes. Another area of interest is the relationship between T2DM and steatosis that can lead to liver disorders including non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), hepatitis, cirrhosis, and liver cancer.

### Genetics and Genomics

Further exploration of the genetic, epigenetic, phenotypic, metabolomic, proteomic and molecular determinants of DM, CVD, CKD, and HF is needed in order to gauge how these determinants can be used to develop and guide the use of new diagnostics and therapeutics for these disease entities. In addition, there are questions regarding how these determinants are impacted by differences in age, gender and race, and how they relate to the progression and outcomes of cardiometabolic health disorders and DM.

### Lifestyle, Behavior, and Prevention

It is important to identify the key questions around how age, race and gender of various populations with T2DM impact the efficacy of lifestyle and behavior change strategies in primordial, primary and secondary prevention of CVD, CKD and HF. In addition, the role of hypertriglyceridemia in CV risk in T2DM and obesity is an area of interest.

### Social Determinants and Quality Of Care

A more in-depth understanding of the role of patient and family health literacy and patient and family education and its impact on CV outcomes in T2DM is needed. There is a knowledge gap regarding how the built environment, including particulate air pollution, impact adverse CV outcomes for patients with cardiometabolic disorders and T2DM. Further insight is needed to determine the optimum clinical, quality of life, economic outcomes and goals for those with T2DM.



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## Treatment

Given the limited opportunities for treatment, it is important to identify those therapeutic interventions that are most effective for prediabetes to reduce risk and delay and/or prevent progression to T2DM. A more in-depth understanding of the mechanisms underlying CV benefit from sodium glucose co-transporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP1) receptor agonists, including differences within classes is needed. In addition, there is a need for innovative pharmacologic, device and behavioral treatments that target multiple metabolic abnormalities, comorbidities and inflammatory processes which lead to cardiometabolic disorders including T2DM.

## Technology/Wearables

There is a need for the development of new and innovative technologies or wearables to address patient education, lifestyle change, disease management, screening, diagnostics and treatment adherence, and improve outcomes while minimizing the adverse events related to T2DM.

## Award Details

Duration: 4 years with the opportunity for up to a 12-month No-Cost Extension.

Award Amount: The maximum budget amount a Center applicant may request is \$3,445,000. The AHA reserves the right to determine the final award amount for competitive projects based on need and potential impact.

### Appropriate Budget Items:

- Salary and fringe benefits of the Center Director, Training Director, Principal Investigators, three named fellows, collaborating investigator(s), and other participants with faculty appointments.
- Project-related expenses, such as salaries of technical personnel essential to the conduct of the project, supplies, equipment, travel, and publication costs in accordance with institutional and AHA policies.
  - Awardees are expected to attend *two* face-to-face (F2F) meetings per year, dates/location TBD. Centers may use award dollars to pay for travel to F2F meetings and other meetings where SFRN research is presented
- Maximum of 10% institutional indirect costs may be claimed on the award.

The awardee will be responsible for overseeing the total budget for his/her grant. If awarded, the principal investigator and the institution assume an obligation to expend grant funds for the research purposes set forth in the application and in accordance



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with all regulations and policies governing the grant programs of the American Heart Association.

Sample Budget:

	Center Totals
Projects: TWO or THREE Projects at each Center for four years. <i>Maximum of \$2.6038M to be divided between the 2-3 Projects funded at the Center over the 4 years. The money does not need to be spent equally between projects or years.</i>	\$2.6038M
Fellows Three Fellows at each Center for two years each. <i>Minimum fellows' salary and fringe of \$50,000/year. Additional funds to supplement salary and fringe can come from Center Director salary, Center travel budget, Project PI budget, or additional funding sources (only if fellow's research effort is ≥75%).</i>	\$300K
Center Director One Director at each Center for four years <i>A maximum of \$50,000 per year for the Center Director. Center Director must commit at least 20% effort. If a separate Center Training Director is desired, this \$50,000 per year to be split to accommodate additional percent effort of this individual.</i>	\$200K
Center Travel Costs Covers travel for Center personnel to Center network meetings and other integration activities. <i>\$7,000 per year must be allocated to Center Travel.</i>	\$28K
Direct Costs (Total) Research Dollars	\$3.1318M
Indirect Costs AHA Policy allows for a maximum of 10% for indirect costs	\$313.18K
<b>Total</b>	<b>\$3.445M</b>

During Year 1 of the Network, the four Centers will be required to develop a Network-wide collaborative project under the direction of the Network Oversight Advisory Committee. The Collaborative project will start in Year 2. AHA has set aside money for this effort, not to exceed \$1,000,000. More details on the Collaborative project will be made available after the Centers are named.

Number of Awards: Cardiometabolic Health with a focus on Type 2 Diabetes Mellitus Strategically Focused Research Network will be comprised of four (4) Center grants\*. Awards will be selected based on scientific merit and how each group aligns with AHA's mission and goals.

\*The AHA reserves the right to determine the final number of awardees.



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Subjects/Study Cohorts: All Network studies must include under-represented racial and ethnic groups (UREG), which is congruent with AHA's mission. All Centers must address any rationale for the non-use of UREGs in their subject populations.

For clinical and/or population projects enrolling human subjects, it will be important to design studies that incorporate both realistic recruitment goals and sufficient statistical power to ensure valid results.

Institutional Partnership Policy: Each Center applicant must partner with at least one non-research-intensive institution and their scientists and include them in a substantive manner in the scope of the center and projects.

What is a non-research-intensive institution? To be considered a non-research-intensive, an institution must meet the following:

- Only domestic accredited public or non-profit institutions of higher education are eligible. Federal government institutions are not eligible.
- The institution must grant baccalaureate or advanced degrees in the biomedical or behavioral sciences. For example, a four-year liberal arts college.
- To be eligible to apply for this AHA award, the applicant's institution may not have received more than \$6 million per year in NIH support in each of four of the last seven years.

NIH no longer maintains a list of ineligible institutions; therefore, there is no mechanism to verify if an institution does not qualify. Instead, an institution must meet all criteria above and submit a letter from the Dean of Research or Provost (or equivalent) stating as such.

For more information, please refer to the Organization Eligibility section of the [NIH Research Enhancement Award \(R15\)](#) page. AHA follows NIH's guidelines.

Interim Assessment: Awardees must report progress on a minimum annual (once per year) basis. Progress may take the form of a required written report in addition to video conferencing, phone calls, and/or face to face visits. Reporting will be focused on achievement of stated milestones as indicated in the project timeline. The Oversight Advisory Committee reserves the right to request additional updates, site visits, or reporting.

## Peer Review

Each PROJECT within a Center application will be scored individually according to the criteria below.

Projects – Potential impact of the project on research in the field of the designated research topic; strengths of applicant investigators (qualifications, expertise and productivity); potential for collaboration or synergy of projects; scientific content;



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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? *For all applications that include vertebrate animals or human subjects, applicants must explain how relevant biological variables, such as sex, are factored into the research design, analysis and reporting. Furthermore, strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex.*
- Innovation: 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?
- Investigator: 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)?
- Significance: 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?
- Environment: 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?
- Impact: How does the project relate to and support the mission of the AHA – *To be a relentless force for a world of longer, healthier lives?*
- Synergy: How does this project enhance the Center and the two additional science projects? How does this project allow the Center and two additional science projects to out-perform were it to be a standalone project? Only projects that demonstrate synergy will move forward to Phase II.





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- Lay Summary: How well written is lay summary in explaining to lay audience what research work is intended to do and its importance? Does the Lay Summary adequately:
  - explain the major health problem being addressed by this study
  - provide specific questions and how each Center will answer them
  - provide the long-term biomedical significance of the proposed projects and the expected advances the projects will lead to?

CENTER application scoring is based on the criteria below.

- Synergy – A clear vision of scientific direction is expected. A Strategically Focused Research Center should be viewed as a group of interrelated research projects, each of which is not only individually scientifically meritorious, but also complements the other projects and contributes to an integrating theme. Describe the rationale for the total program. Explain the strategy of achieving the objectives of the overall program and how each individual project relates to the strategy. Describe the synergies and interactions among projects and their investigators. Is there evidence of synergy among the projects and training component of the Center?
- Collaboration – History of collaboration, as well as the ability and commitment to collaborate with other institutions, investigators and within the applicant institution as well as within the awarded Network. Defined and detailed process for collaboration with other sites in addition to within and among the proposed 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. What collaborations do you envision between investigators working on individual projects?
- Interaction Plan within and among this Network and other AHA Networks (if appropriate) – Plan for and commitment to sharing 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. Centers proposing clinical projects must document that they have sufficient volume of patients to assure that robust studies may be conducted.
- Training component – A detailed plan for developing and implementing a postdoctoral training program that includes clinical (M.D.) or Ph.D. training in research in the field outlined by the RFA; 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.





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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 researchers in the appropriate research topic.

- Center Team – Qualifications of the Director to provide scientific and administrative leadership for the Center; experience and commitment of the nominated Director; quality of research team; qualifications of investigators and co-investigators; experience in the field of study outlined by the RFA; training experience. Applicants should comment on the gender/racial/ethnic composition of the proposed research teams, in keeping with AHA’s core values of diversity and inclusivity.
- 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. Documented evidence of willingness to collaborate with others outside their institution to share ideas, science, etc. to progress the field of research as outlined in the RFA.
- Investigator team – Qualifications of each PI to provide scientific and administrative leadership for their respective projects; demonstrated commitment of each PI, and experience with studies in the field outlined by the RFA; quality of interdisciplinary research team; qualifications of co- investigators; training experience.
- 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.

Process:

Peer Review of Submitted Applications

Two phases of face-to-face Peer Review for submitted applications will be conducted, approximately 4-5 weeks apart.

- Phase I includes a written review of the science/projects



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- Phase II includes a reverse site visit of a limited set of applicants, with the review focused on the overall vision of the center, synergy and collaborative possibilities, and the training plan and environment

For more information on Peer Review of submitted applications, including information on reverse site visits, see the Peer Review section of the [SFRN General Information](#) page on the [AHA SFRN website](#).

*An applicant is prohibited from contacting AHA peer reviewers. This is a form of scientific misconduct and will result in removal of the application from funding consideration and institutional notification of misconduct.*

Relevant Policies:

Public Access: The AHA's public access policy requires that all journal articles resulting from AHA funding be made freely available in PubMed Central (PMC) and attributed to a specific AHA award within 12 months of publication. It is the responsibility of the awardee to ensure journal articles are deposited into PMC.

Open Data: Any factual data that is needed for independent verification of research results must be made freely and publicly available in an AHA-approved repository within 12 months of the end of the funding period (and any no-cost extension). We also strongly encourage awardees to post their data to AHA's Institute for Cardiovascular Precision Medicine Precision Medicine Platform (<https://precision.heart.org/>).

For more information on the above policies, see AHA's [Open Science Policy](#) webpage.

Other: 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. Visit the Research Programs Awards Policies page for more information on this topic: [AHA Policies Governing All Research Awards](#)

Award Selection and Other Policies

Final funding recommendations will be approved by the AHA. For all other relevant policies and Frequently Asked Questions, please see the [SFRN website](#).

Application Submission

Applications must be submitted using the AHA's online submission portal available at [Grants@Heart](#). For explicit Application Instructions, visit the [AHA SFRN General Application Information](#) page.



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### Example AHA Programs

For more information on the AHA programs listed in this RFP, please refer to their individual webpages.

#### Simple Cooking with Heart

<https://recipes.heart.org/en/collections/programs/simple-cooking-with-heart>

Healthy for Good <https://www.heart.org/en/healthy-living>

Workplace Health Solutions <https://www.heart.org/en/professional/workplace-health>

Life's simple 7 <https://www.heart.org/en/healthy-living/healthy-lifestyle/my-life-check--lifes-simple-7>

Teaching gardens <https://www.heart.org/en/professional/educator/teaching-gardens>

Check.change.control.cholesterol <https://www.heart.org/en/health-topics/cholesterol/cholesterol-tools-and-resources/check-change-control-cholesterol-program>

Know Diabetes By Heart <https://knowdiabetesbyheart.org/>

Target Blood Pressure <https://targetbp.org/>