

American Heart Association Novel Artificial Intelligence Approaches to Advance Cardiovascular and Cerebrovascular/Brain Health

Request for Proposals

Key Dates

RFP Posted:	Jan. 14, 2025
Required Pre-proposal Deadline:	Feb. 27, 2025
Full Proposal Deadline (invitation only):	May 1, 2025
AHA 2-Phase Peer Review:	May-June 2025
Notification of Awards:	June 2025
Award Start Date:	July 1, 2025
Webinars	
Informational Webinar:	Jan. 28 and 29, 2025
ProposalCentral Webinar:	ТВА

SUMMARY: The American Heart Association announces this funding opportunity to advance the use of Artificial Intelligence in health and health care delivery. A total of \$12 million is available to fund three investigators/investigative teams proposing novel uses of Artificial Intelligence to revolutionize cardiovascular and cerebrovascular/brain health and health care delivery.

Important Notes:

- Proposals must be received no later than 3 p.m. Central Time on the deadline date. Early submission is encouraged.
- Before beginning a proposal, review the <u>eligibility and requirements</u> that apply to all AHA research.
- The AHA believes diversity and inclusion is an essential component to driving its mission. We strongly encourage applications by women; individuals who have faced challenges or obstacles to their career due to their membership in one or more racial and ethnic groups, or due to their identification as LGBTQ+; military veterans, people with physical or mental impairment; individuals from disadvantaged backgrounds, and those who have experienced varied and non-traditional career trajectories.
- All proposals must be <u>submitted electronically via ProposalCentral</u>. The system will open at least four weeks prior to the proposal deadline to complete your pre-proposal and upload documents. You can begin to create your documents now; please refer to the <u>AHA Application Instructions</u>. All submissions require a signature from a designated institutional representative.
- Applicants must be <u>AHA Professional Members</u> at the time of proposal submission. This must be done online. Join or begin the membership process well before the deadline.
- This program will use Distributed Peer Review for the pre-proposal phase, also known as the <u>Mechanism Design Proposal Review Process</u>. In short, applicants for this program

agree to also serve as peer reviewers. Details are provided in the Peer Review Process section below.

BACKGROUND

Artificial Intelligence in Biomedical Research and Health Care

Artificial Intelligence (AI, inclusive of robotic process automation, machine learning, and generative AI), has the potential to revolutionize biomedical research and health care by enhancing data analysis, accelerating drug discovery, improving diagnostic accuracy and improving health care delivery. AI algorithms can process vast amounts of data, identify patterns, and generate hypotheses faster than traditional methods. A few examples of the potential impact of AI on healthcare include the use of AI-driven models to predict the development of novel therapeutic targets, analysis of images and datasets for disease diagnosis, and development of precision therapeutic treatments.

Artificial Intelligence in Cardiovascular, Cerebrovascular, and Brain Health Research

By 2050, cardiovascular disease (CVD) is predicted to affect more than 184 million adults in the United States and the corresponding financial burden of CVD and related diseases could triple to \$1.85 trillion.¹ Therefore, urgent need exists to accelerate and optimize the translation of discoveries into clinical practice to meet increased demand while striving for improved health care quality for all populations and deceleration of costs. AI has shown significant promise in cardiovascular, cerebrovascular, and brain health research. In CVD diagnosis and treatment, AI algorithms have shown promise in processing echocardiograms, electrocardiograms, and other imaging modalities to detect abnormalities with high accuracy.²⁻⁴ This capability potentially aids in early diagnosis, risk stratification, and personalized treatment and follow-up planning. AI applications in cerebrovascular health have shown promise in detection and management of conditions such as stroke and aneurysms.⁵ In brain health research, AI is being used to analyze neuroimaging data, identify biomarkers for neurodegenerative diseases, and develop predictive models for cognitive decline.⁶

Research Gaps and Opportunities

Many research gaps and opportunities exist in the application of AI in health care including the promise of AI use at scale to advance health and health care. A significant gap is the integration of multiple diverse datasets from a variety of sources. Since AI models require large, high-quality datasets to function effectively, improved methods for integrating data from electronic health records, diagnostic studies, biomarker and genomic data along with social determinant information to create comprehensive AI models can potentially advance the impact of AI in various aspects of healthcare. Moreover, translating AI research into clinical practice at scale will be important. Therefore, developing AI tools that can be easily integrated into clinical workflows for utility by healthcare professionals will be crucial for realizing the full benefits of AI in medicine.

The use of AI in health care raises several ethical, legal, and social concerns.⁷ Human oversight should remain a key element of AI deployment. It is essential to ensure that AI algorithms are transparent and unbiased, and that they are developed such that patient privacy is paramount. Maintenance of transparency of AI algorithms is challenging given that

researchers and users may not themselves be aware of data processing details. Hence, the regulatory landscape for AI must be robust. However, the regulatory landscape for AI in health care is evolving with need for clear guidelines on data protection, algorithm validation, and liability in cases of AI-related errors. Practically, the deployment of AI must consider the potential impact on healthcare workforce dynamics, patient trust, and access to quality health care. Addressing these implications requires a collaborative approach involving interdisciplinary teams of researchers, policymakers, technology companies, clinicians, patients, patient advocates and communities to ensure equitable and responsible use of AI.

RESEARCH AREAS OF INTEREST

Applicants are encouraged to submit proposals that address at least one of the following:

- Detection and diagnosis
- Classification and phenotyping
- Prevention and treatment, including personalized instruction to patients
- Longitudinal disease management
- Implementation science
- Reducing bias in diagnosis, decision making, and care delivery

Examples of general approaches for proposal submission include: In-Hospital and Electronic Health Record-Based Solutions

- AI-based, evidence-based and advanced "care-gap closure" models for key health conditions. Opportunities to improve needed prevention and treatment for patients who are under-treated based on care guidelines leveraging existing multidimensional EHR data that are both structured (e.g., imaging reports, medications and labs) and unstructured (e.g., notes, problem lists, ECG, radiology and pathology images) as source material.
- Clinical Decision Support development, validation and assessment of autonomous real-time predictive algorithms to detect impending clinical deterioration or adverse events.
- Closed loop algorithms operating in "co-pilot" mode, capable of implementing complex, personalized protocols for generating in-hospital interventions to be considered by human supervisors for modification or implementation.

Community-based Solutions

 Digital community-health – use of AI solutions to better reach and engage individuals and communities in addressing social drivers of health by leveraging consumer digital "wearable" technologies to power novel chronic disease management and/or risk factor modification strategies via remote patient monitoring (RPM) platforms.

Chronic-care Management

 Home-based chronic-condition management and rehabilitation – engagement and monitoring solutions tied to AI/ML-aided health scoring, risk stratification, predictive analytics and health management (a fully integrated secondary prevention solution for CVD patients). Applicants proposing studies using the above approaches applied to a broad array of missionrelated clinical areas and with high potential for impact are welcome and will receive full consideration. Application of the above approaches to the following clinical areas are of particular interest for this funding opportunity:

- Cardio-Kidney-Metabolic (CKM) Syndrome: CKM Syndrome provides a framework for understanding disease progression and outcomes in individuals with progressive occurrence of excess or dysfunctional adipose tissue, chronic kidney disease (CKD) and/or cardiovascular disease. The clinical impact of this condition is currently extensive and expected to grow markedly in the coming decades. Application of AI has potential to significantly improve clinical outcomes in those with CKM Syndrome and thus greatly reduce disease burden. A few examples of approaches in which AI could improve outcomes for CKM syndrome include: early detection and risk prediction; predictive analytics for monitoring of disease progression; AI-driven approaches for biomarker discovery; medication management and optimization.
- Brain Health: As noted above, several areas of promise exist for application of AI to cerebrovascular disorders/brain health. The application of AI approaches referenced above to brain health conditions might include: analysis of imaging data to improve early detection of cerebrovascular conditions and stroke and potential progression; use of AI-facilitated rehabilitation tools to personalize stroke recovery therapy.
- Food Science/Nutrition: AI offers a number of research opportunities in food science and nutrition that have strong potential to transform cardiovascular health through changes in the production, processing and use of food, including prescribed food. Examples of opportunities for application of AI tools in food science and nutrition include: AI-driven meal planning for specific cardiovascular-related conditions; predicting diet impact on cardiovascular or brain health outcomes.
- Sudden death and CPR: With survival rates from sudden cardiac arrest (SCA) hovering at approximately 10%, many opportunities exist across the chain of survival to improve outcomes. Application of AI could be instrumental in developing models for predicting susceptibility to SCA and elicitation of a coordinated response system for intervention, or use of imaging in acute coronary syndromes to help predict sudden death.
- Women's Health: The long-held misconception that women are protected from cardiovascular disease has resulted in a lack of understanding of CVD in women, along with under-diagnosis and inadequate treatment. Examples in which AI could be used to improve detection and/or monitoring of CVD in women might include development of predictive models that address women-specific conditions, such as those pregnancy-induced hypertension, preeclampsia or gestational diabetes, as well as personalized plans for management from across the spectrum of pre-pregnancy, pregnancy and post-pregnancy care based on family history and personal risk.

Translational potential: The opportunity to rapidly translate AI-driven advances exists in both discovery and clinical implementation realms. Thus, proposals with a feasible path for implementation, scalability and potential commercialization will be particularly competitive. Awards will be made only to eligible nonprofit institutions described in the Relevant Policies and Requirements section below. However, inclusion of subcontracted industry partners who have expertise in key areas of the proposed studies is encouraged.

Governance/Oversight: The AHA will establish an Oversight Advisory Committee (OAC) of three

to five experts who will monitor progress and foster success of all projects. The OAC will meet with awardees at least twice annually to review progress and provide input on possible opportunities and assets as available.

APPLICATION SUBMISSION

Applicant Eligibility

The PI must:

- hold an MD, PhD, ScD, PharmD, DO, DVM, DDS, or equivalent doctoral degree at time of application
- hold a faculty or staff appointment
- devote at least 10% effort to the project if funded

The PI must have and maintain one of the following designations throughout the duration of the award. Please consult with your institution's grant office.

- U.S. citizen
- Permanent resident
- Pending permanent resident

 (must have filed Form I-485 for permanent resident status and obtained an I-797C
 Notice of Action that the application has been received by USCIS and case is pending)
- E-3 Visa specialty occupation worker
- G-4 Visa family member of an international organization employee
- H1-B Visa temporary worker in a specialty occupation
- O-1 Visa temporary worker with extraordinary abilities in the sciences
- TN Visa NAFTA Professional
- DACA Deferred Action for Childhood Arrivals

Institutional Eligibility / Location of Work:

AHA awards are limited to U.S.-based non-profit institutions, including medical, osteopathic and dental schools, veterinary schools, schools of public health, pharmacy schools, nursing schools, universities and colleges, public and voluntary hospitals and others that can demonstrate the ability to conduct the proposed research. 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, except for Veterans Administrations employees.

BUDGET

Total Award Amount: \$4,000,000, including indirect costs up to 10%.

Award Duration: Three (3) years. No-cost extensions will not be allowed, and the awards are non-renewable.

Allowable Costs: The award may be used for salary and fringe benefits of the PI, collaborators, and other research personnel essential to the conduct of the project; supplies, equipment and

computers/electronics, travel; volunteer subject costs, data management; publication costs, etc.

A detailed budget is not required at the Pre-proposal stage; a comprehensive budget will be required from those invited to submit a full proposal.

REQUIRED PRE-PROPOSAL

All pre-proposals will be submitted via <u>ProposalCentral</u> and require the following three documents:

1. Research Proposal – up to 5 pages, inclusive of all sections noted below. Please address all of the following points:

- A. Concept: Summarize in general terms the overall plan to use novel Artificial Intelligence approaches to revolutionize cardiovascular and cerebrovascular/brain health research and health care. Include a description of how your proposed studies will leverage opportunities and/or develop new directions in the use of AI. Describe the potential impact and innovative nature of your proposed studies.
- B. Research Plan: Describe specific studies you will conduct in addressing the seminal question(s) you propose to pursue. Presentation of studies as a set of Specific Aims is acceptable but not required. Include:
 - A description of the technological approaches you plan to utilize and/or develop in the pursuit of your studies.
 - A description of the required datasets, images, health and other records, etc. that will be required to conduct your proposed studies, as well as your access to these resources.
 - For studies involving human subjects/human subject records, projects must include study participants/records who are under-represented and/or underserved with regard to healthcare delivery. The proportion of these individuals/records in proposed studies should be reflective, at a minimum, of their representation in the population in which these individuals/records exist.
 - An anticipated timeline for achieving key milestones over the course of this threeyear study.
 - An estimated total budget requirement and brief rationale, including the proposed number of paid staff and the approximate allocation (if applicable) between the institutions within the team.
- C. Team: Describe the research team key personnel and why they have been sought out for these studies. Include:
 - The team's experience with and/or capacity to develop new tools and methods that support creative approaches to the questions under study.
 - The lead applicant/institution's capacity to receive and manage research awards of the scale available.
- D. Ethical, Legal and Social Implications: Describe the ethical, legal and social implications that are likely to be pertinent for your proposed studies and how you will positively address them.

- E. Development/commercialization Plan: Should your studies be successful, describe the opportunity for their development and potential commercialization. A full business plan is not required. However, applicants should address the following:
 - What is the market opportunity for the anticipated product/technology/service that could result from your research and what is a reasonable timeline for development and commercialization?
 - Following conclusion of the studies as proposed, what additional resources financial, business development expertise, etc. – might be needed, and what are possible opportunities/venues for identifying and securing these resources?
- 2. <u>Biosketch</u> (Principal Investigator only, NIH format, max. 5 pages)
- 3. Literature Cited (two page limit)

NO OTHER UPLOADS ARE PERMITTED at the Pre-Proposal stage.

Format/Type Requirements

You must comply exactly with the AHA's format/type requirements and page limits. Failure to comply will result in the administrative withdrawal (disqualification) of the pre-proposal.

- Documents must be single-spaced. No more than 15 characters per inch (cpi) or an average of no more than 15 cpi (cpi includes symbols, punctuation, and spaces).
- No less than ¾" page margins on all four sides.
- Maximum of 50 lines per page.
- Arial Font style, 12-point font size for Windows users; Helvetica Font style, 12-point font size for Macintosh users.
- Only Portable Document Format (PDF) files are accepted.

Note: The ProposalCentral electronic system will reject a document that exceeds the page limit.

PEER REVIEW

Peer Review Criteria:

- Investigator/Investigative Team: Is the investigator(s) appropriately trained and wellsuited to conduct the proposed studies? Does the investigative team bring complementary expertise to the project (if applicable)?
- Significance: Does this proposal address an important problem directly related to areas of interest as described in the RFP? If the aims of the application are achieved, how will scientific knowledge or clinical practice be significantly impacted? Will there be an effect on the concepts, methods, and technologies that drive this field?
- Innovation: Does the proposal have the potential to lead to major conceptual and/or technological innovations that will accelerate improvements in health care?

- Impact: Does the proposal have a high probability of sustainable influence on the research field(s) of study?
- ELSI: Has the investigator/investigative team identified pertinent ethical, legal and social implications that may impact one or more aspects of the proposed studies, and opportunities to address and/or optimize as appropriate?
- Opportunity for Development: Has the applicant identified a clear market need and considered a potential path for development and/or commercialization for the product or service that is the focus of the proposed studies?

Peer Review Process:

The peer review process will have three stages.

• The first stage of review will evaluate the pre-proposal using the criteria listed above and the distributed peer review approach, also referred to as <u>Mechanism Design Proposal</u> <u>Review Process</u>.

Distributed peer review relies on the principles of a traditional peer review panel: academic integrity, rigor, transparency, and a desire to advance the best science. As opposed to traditional peer review, distributed peer review capitalizes on the expertise of the applicant pool and incentivizes timely review in fairness to all applicants.

All applicants who submit a proposal will be required to serve as a peer reviewer within this program and will be assigned five to seven proposals for review. By agreeing to the program terms at the time of proposal submission, the principal investigator agrees concurrently to serve as a peer reviewer within this program and meet all peer review expectations and requirements. Principal investigators must declare conflicts of interest and will only be assigned proposals for which they do not have an institutional or individual conflict; PIs (reviewers) are bound by all other requirements associated with peer review. PIs will be provided approximately three weeks to complete review and scoring of the proposals to which they are assigned.

Only peer reviewers who complete their assigned reviews and record their scores in a timely fashion will in turn have their own proposal evaluated for advancement. Narrative critiques are not expected although bulleted strengths and weaknesses are suggested. Principal investigators who have not completed their reviews nor submitted their scores by the stated deadline will have their proposals withdrawn and returned as not in compliance with the program announcement, and they will not receive scores should any have been completed for their proposal. Peer review will require submission of scores using ProposalCentral; there will be no peer review panel discussions or meetings. All other <u>AHA Peer Review</u> processes apply. Additional details of the application and review process will be shared at upcoming webinars related to this program.

• A second stage proposal ("full proposal") will be invited from those submitting the highest ranked pre-proposal submissions. Those invited to submit a full proposal should plan to develop a 12-page research plan, detailed budget and additional information associated with a proposal of this type, including, for example: a description of the research environment(s), assurance(s) related to ethical use of animal and/or human

subjects and tissues, a data sharing plan, an expanded development/commercialization plan, etc. Additional details for full proposal submission will be communicated in detail when applicants are notified of their advancement.

• Following review of invited full proposals by a convened study section, top applicants ("finalists") will be invited to present their proposal in person to a convened expert panel. Detailed information required for this final stage will be communicated to finalists at time of notification.

Applicants are prohibited from discussing proposals with 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 AND REQUIREMENTS

Use of AHA's Precision Medicine Platform:

Awardees are encouraged to make use of AHA's <u>Precision Medicine Platform</u> (PMP), powered by Amazon Web Services.

- The PMP supports cloud computing in a secure and private workspace and enables investigators to collaborate and analyze data securely. Each Project will receive Amazon Web Services computational credits to offset the cost of using the platform during the award period.
- Data analysis is enabled in secure workspaces by a friendly web user interface that allows researchers to code in various languages, including R and Python and use statistical software including but not limited to SAS and R studio. The most up-to-date machine learning and artificial intelligence software available from Amazon Web Services is also included. Researchers are also able to install their own tools if they are compatible with the workspace.
- To learn more about the Precision Medicine Platform and how it can enable your research, please review the information at the following links.
 - AHA Precision Medicine Platform Getting Started
 - o <u>AHA Precision Medicine Platform Uses</u>
 - <u>AHA Precision Medicine Platform Tools & Features</u>
 - o AHA Precision Medicine Platform Security Information

Interim Assessment (if awarded):

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 the achievement of stated milestones as indicated in the project timeline. The named Oversight Advisory Committee reserves the right to request additional updates, site visits, or reporting.

Open Science Policy Statements for AHA Funded Research

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 as soon as possible, and no later than the time of an associated publication or the end of the award period (and any no-cost extension), whichever comes first. For more information on the above policies, see AHA's <u>Open Science Policy</u> webpage.
- Preregistration: AHA requires preregistration for any funded clinical trials and encourages preregistration for any studies that make an inferential claim from a sampled group or population, as well as studies that are reporting and testing hypotheses. After a project is completed, protocols and preregistration analysis plans can be used in conjunction with the final study and analysis by researchers seeking to replicate, reproduce, and build upon findings. See AHA's preregistration information.

Intellectual Property

Any inventions, intellectual property, and patents resulting from this funding are governed by the AHA Intellectual Property Policy for Research Funding (the "IP Policy"); provided that the IP Policy is modified as follows:

- The definition of Net Income in the IP Policy is replaced in its entirety with the following language:
- "Net Income" means all Gross Income received related to commercialization of Intellectual Property resulting, in whole or in part, from an Award, less third-party, out-of-pocket expenses related directly to costs associated with application and registration required to establish ownership rights in or protection of the Intellectual Property. All other costs, including Unrecovered Indirect Costs and Internal Distributions, are not deductible when calculating Net Income.
- Section V, Paragraph D of the IP Policy is replaced in its entirety with the following: language
- Institution shall pay the AHA annually a percentage of the Net Income derived from Intellectual Property conceived or reduced to practice in the performance or as a result of an Award, regardless of the amount of Net Income actually received, equal to AHA's portion of support (expressed as a percentage) for the work or research giving rise to the Intellectual Property. In no event shall the application of the foregoing result in either AHA or Institution receiving less than 15% of Net Income.
- A new Section V, Paragraph F is added to the IP Policy with the following language:

The AHA wishes to support and accelerate the commercialization and deployment of the results from Inventor's research. Because AHA wishes to rapidly advance mission-aligned concepts to impact, and to help Institution(s) and Inventor(s) create more opportunities to bring funded Intellectual Property of Institution and Inventor to market as quickly as possible, Institution and Inventor shall inform AHA of any offer to license, commercialize or invest in the Intellectual Property, and grant to AHA the opportunity to match said offer.

Overlapping Work

The projects described can have no scientific or budgetary overlap with other funded work.

Compliance with AHA Policies

The applicant/awardee and institution are responsible for compliance with all AHA 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: <u>AHA Policies</u> <u>Governing All Research Awards</u>.

References

- 1. Joynt Maddox, KE et al., Circulation. 2024;150:e65-e88. DOI: 10.1161/CIR.00000000001256
- 2. Sun, X et al. Eur J Med Res. 2023;28:242 doi.org/10.1186/s40001-023-01065-y
- 3. Armoundas, AA et al., Circulation. 2024;149:e1028-e1050. DOI:10.1161/CIR.000000000001201
- 4. Hanneman, K., et al., Circulation. 2024;149:e296-e311. DOI:10.1161/CIR.00000000001202
- 5. Kim, H-W et al., Stroke Vasc Interv Neurol. 2023;3:e000938. DOI: 10.1161/SVIN.123.000938
- 6. Lee, H et al., Nat Biomed Eng. 2019 Mar;3(3):173-182 doi: 10.1038/s41551-018-0324-9
- 7. Adedinsewo, D., Circulation. 2024;150:174-176 DOI: 10.1161/CIRCULATIONAHA124.068113