



Heart Brain Connection IMPACT Award Submission Guidelines

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A. SPECIFIC PROGRAM INFORMATION

1) Rationale

The burden of heart conditions, stroke and vascular cognitive impairment on the healthcare system is immense. An analysis conducted in Heart & Stroke's 2019 (Dis)connected Report revealed that cardiovascular disease costs \$21.2 billion in direct (medical) and indirect (lost earnings) costs; stroke costs the economy \$3.6 billion and dementia \$33 billion per year in Canada. Given our aging population and the growing number of people affected by these conditions, more people will need to utilize health services in the future, driving these costs even higher. According to the 2016 census, more than six million people in Canada were aged 65 or older (16% of the population); this number is projected to grow to over 9.5 million by 2023 (23% of the population).

The heart and the brain are inextricably connected. Whether it's at the basic physiological level, in the approach to treatment and ongoing management, or the ongoing needs of people who experience heart disease, stroke or related conditions, these connections are so deep that having one condition puts one at risk for others across the lifespan. Forty percent of people admitted to hospital with a heart condition, stroke or vascular cognitive impairment will be readmitted at least once more for another similar event or a different heart, brain or mind condition. For example, people with coronary artery disease are at greater risk for having clinical depression. Depression increases the risk of developing heart disease and can even make heart disease worse. The impact of these connections on people's lives - and on the health care system - is profound. Despite growing evidence of commonalities and interactions in the underlying pathophysiology of diseases in the heart and brain, our health care system is currently designed on a "single disease" model - with different heart conditions, stroke, and vascular cognitive impairment being treated by specialists in different units or centers.

Research into the complex interactions between the brain and the heart, co-existing dependencies, and shared fundamental biological mechanisms is critically needed across prevention, care assessment, treatment, ongoing management, and system planning to make a difference in health at the individual and societal levels. In support of this key priority area, Heart & Stroke and Brain Canada are launching a multi-disciplinary, multi-institutional, integrative research competition that harnesses the power of collaboration and innovation in Canada's research community to explore the heart-brain connection. It is our goal that this competition will not only drive discovery and exploration, but build long-term capacity in heart and brain vascular research that uses an integrated approach to leverage collaboration between stakeholders to generate new knowledge and meaningful action that will directly benefit people in Canada.

Heart & Stroke and Brain Canada are making equity, diversity and inclusion an integral component of the Heart Brain Connection Impact Award. The COVID-19 pandemic has shone a revealing light on longstanding health inequities and the harsh impacts of systemic racism and other structural inequities on health and health research. Meaningful engagement of People With Lived Experience (PWLE) and awareness of the social determinants and broader contexts that influence health supports more impactful research, optimizes health outcomes, improves knowledge exchange, and can help reduce health and health care inequities. To create and sustain change in heart and brain vascular research, principles of equity, diversity, and inclusion must be integrated across research design and practices, as well as participation in the research system, including on research teams.

2) Scope

The objective of the IMPACT Award is to promote collaboration to generate new knowledge and accelerate the translation of knowledge into action for people living with diseases that impact the heart and brain, such as heart disease, stroke and vascular cognitive impairment (VCI). The Heart-Brain IMPACT Award is a multi-institutional, multi-disciplinary, multi-year, multi-partner and multi-million-dollar award to invite discovery and exploration of the heart-brain connection.

Teams will be comprised of a strong community of researchers, working in synergy across institutions and disciplines in recognizing and adopting an integrative approach to studying heart disease, stroke and vascular cognitive impairment. A successful collaborative research team must cover at least three of the four Themes of Health Research (see Section D) and will require synergies and innovative approaches to solve complex problems that cannot be solved by individual researchers or smaller-scale projects.

The knowledge gained will contribute to the cardiovascular and cerebrovascular health of the people of Canada and internationally. Research outputs must adhere to principles of open science, and knowledge exchange must expand beyond dissemination of traditional research outcomes. IMPACT Award Annual Meetings will create a unique opportunity to facilitate knowledge translation across the funded Teams, increase collaboration, engage the community and wider stakeholders, and co-create knowledge translation initiatives.

The specific objectives of this funding opportunity are to:

- Foster scientific collaboration and discovery across disciplines and institutions in Canada to investigate clearly articulated research questions within the cerebrovascular and cardiovascular systems.
- b. Develop the long-term capacity of heart and brain vascular research in Canada engaging researchers in accord with sound EDI principles, at all stages of their careers including trainees, and contribute to the training of the next generation through mentorship.
- c. Integrate consideration of variation in the determinants of health including, but not limited to, sex, gender, sexual orientation, age, race, culture, and socioeconomic status to address existing research gaps.
- d. Engage individuals with lived experience to help guide research and knowledge translation activities to benefit the health of the people of Canada.

Available Funding

The total amount available for this funding opportunity is up to \$5.8 million, to fund two teams for up to \$2.9 million each over four years, with flexibility in the annual funding profile to accommodate the needs of specific teams. There will be the possibility of extending the project period for up to 12 additional months with no additional funding.

Brain Canada will contribute up to \$2,900,000 through the Canada Brain Research Fund. Heart & Stroke will contribute up to \$2,900,000.

Brain Canada and Heart & Stroke's financial contributions for this initiative are subject to availability of funds. Should the co-funder(s) funding levels not be available or decreased due to

unforeseen circumstances, the two co-funder(s) reserve the right to reduce, defer or suspend financial contributions to grants received as a result of this funding opportunity.

3) IMPACT Award Structure

The structure of the IMPACT Award is designed to enable cutting-edge, interdisciplinary research. The IMPACT Award is comprised of two hierarchical components (see Diagram 1):

- 1. The **IMPACT Program Proposal** will detail the overarching research themes and research question(s);
- 2. **Program Modules** are subcomponents which should correspond with the major aims of the IMPACT Program Proposal and outline specific activities under each aim.

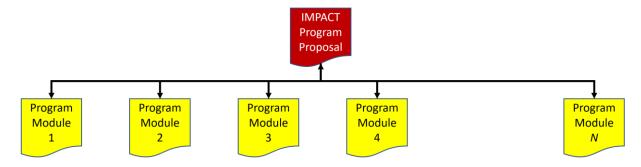


Diagram 1

One of the IMPACT Team members will be designated the **Nominated Principal Investigator (NPI)** by the Team to act on its behalf, and to be the individual responsible for submitting the IMPACT Award application in its entirety and for all communications with Heart & Stroke and Brain Canada. The NPI, and the host institution of the NPI, will be responsible for the overall budget and management of the Team, as well as delivery of the planned research program and all deliverables as described in these guidelines. The NPI is expected to be a member of one or more Program Modules.

Each Program Module will be led by a *Principal Investigator (PI)*. The **Program Module PI** is responsible for the intellectual direction of the proposed research and assumes administrative and financial responsibility for the Module. The NPI, working with the Module PIs, will have overall responsibility for all elements of the award including the Modules. Program Modules may include the following members:

- a. **Co-Principal Investigators (co-PI)** have major input into the intellectual direction and responsibility for a large part of the proposed research of the Module with the PI.
- b. **Co-Investigators (co-I)** contribute significantly to the research, but do not have overall responsibility and authority for the project.
- c. Collaborators provide a specialized service (such as access to equipment, provision of specific reagents, training in a specialized technique, statistical analysis, access to a patient population), but are not involved in the overall intellectual direction of the research.

d. **Knowledge Users** may be from industry, government, other non-academic sectors, international researchers, patients, family members, and caregivers.

The NPI, PI, co-PI, or co-I may not receive salary support from the award. While Collaborators and Knowledge Users cannot receive funding from the IMPACT Award, they should be listed in the application with their interaction with the team described. PWLE may be compensated as per Section C.3.f below.

Each IMPACT Program Proposal shall have at least 3 Program Modules. The number of Program Modules will be at the discretion of the Team. Program Modules should correspond to the major aims of the IMPACT Program Proposal. Each Program Module will have a budget of at least \$400,000 over the 4-year period.

4) Eligibility Criteria

Equity, diversity and inclusion (EDI) in research environments enhances excellence, innovation and creativity. Heart & Stroke and Brain Canada are committed to excellence through equity and encourage applicants from diverse and underrepresented groups to apply to our funding opportunities.

4.1 General

- a. The IMPACT Team will be comprised of a strong community of researchers, institutions, and disciplines recognizing and adopting an integrative approach to studying heart disease, stroke and vascular cognitive impairment. The NPI and Module PI are encouraged to carefully consider the membership of the Modules as well as the composition of the resulting IMPACT Team to reflect the required multidisciplinary, multi-institution and national scope of the IMPACT Award and the principles of equity, diversity and inclusion.
 - i. The IMPACT Team must cover three of the four Themes of Health Research (See Section D).
 - ii. NPI and Module PIs must be drawn from researchers located in at least three (3) institutions located in at least three (3) provinces or territories.
 - iii. The IMPACT Team must act as a cohesive unit, and not a loose collection of disparate groups. The activities within each Program Module must be linked, integrative, and build on the overall IMPACT Program Proposal objectives.
 - iv. The IMPACT Program Proposal must include a clear plan for the integration of relevant determinants of health for example, sex, gender, sexual orientation, age, race, culture, and socioeconomic status, and/or other factors into the research question, analysis, results and reporting as appropriate.
 - v. The IMAPCT Program Proposal must describe how People With Lived Experience (PWLE) are engaged as meaningful and active collaborators and as knowledge users.
 - vi. Any research applications involving Indigenous Peoples must include a knowledge user, team member or collaborator who self-identifies as Indigenous (First Nations, Inuit, and/or Métis) or otherwise provide evidence of having meaningful and culturally-safe collaboration with Indigenous Peoples.

- vii. Any research applications involving special populations must include a knowledge user or team member who self-identifies as that population or otherwise provide evidence of having meaningful and culturally-safe involvement with that population.
- **b.** All Team members who are independent researchers (NPI, Module PI, co-PI, and co-I but not Collaborators) must be based at a Canadian research institution and be eligible to receive funding from the federal granting agencies as a PI.
 - i. The NPI, Module PI, and co-PI must have an MD, PhD, PharmD, DVM, or equivalent health sciences degree with a full-time independent academic or faculty appointment (i.e., at minimum, at the Assistant or Clinical Assistant Professor level) in Canada by the Letter of Intent submission deadline.
 - ii. Teams must build capacity in brain and heart vascular research by including researchers at all stages of their careers, as well as trainees.
 - iii. Any adjunct or emeritus applicants must submit a letter from their Dean/Chair/Division Director to clarify the independent researcher nature of their specific appointment (i.e., autonomy regarding their research activities, amount of protected time available, local infrastructure in place).
 - iv. A minimum of 50% protected research time is required for the NPI and Program Module PIs.
- **c.** At the Letter of Intent stage, all independent researchers of the research team must have successfully completed:
 - Sex and Gender Considerations online training that is offered through the CIHR Institute of Gender and Health, and submit a Certificate of Completion for the module(s) most closely aligned with the type of research to be conducted.
 - ii. CIHR Unconscious Bias training module.

4.2 Other Eligibility Criteria

- a. The Host Institution/University is the institution or organization that is responsible for receiving and administering the grant/award on behalf of the recipient. It will be the home institution of the NPI. Documentation of support for the NPI and the application by the Host Institution shall be required as part of the full application process.
- **b.** Heart & Stroke and Brain Canada Foundation funds used to support research activities should principally be conducted in Canada. Justification will be required to allow for specialized service contracts at non-Canadian institution(s) who provide access to leading expertise, facilities, technologies, unique populations, and environments, research training and/or knowledge translation that is not otherwise available in Canada.
- **c.** Grants are not renewable. Teams must propose and yield results and knowledge translation within the timeframe of the four-year grant and not generate costs nor expectations beyond that period (e.g., longitudinal databases that are directly supported by this program).

5) Evaluation Criteria

This funding opportunity comprises three phases: Registration, Letter of Intent and Full Application (by invitation only).

5.1 Registration

Heart & Stroke and Brain Canada will perform a relevance and eligibility review at the Registration stage to identify applications that are relevant to and in alignment with the <u>objectives</u> and <u>research areas</u> of this funding opportunity and meet the eligibility criteria. Registrations will not be triaged at this stage. Feedback will be provided to researchers if their application does not meet criteria so that they may make appropriate changes before submitting a Letter of Intent.

The registration process collects information on the proposed research project, including:

- a. Nominated Principal Investigator (NPI), PI(s), any co-PI(s) and collaborators
- **b.** Host institution (home institution of NPI)
- c. Language of Application: E or F
- d. Areas of research
- e. Research themes (see Section D)
- f. Research descriptors (up to 10 key words)
- **g.** Brief description of how the proposed research meets the Heart-Brain Connection IMPACT award objectives
- h. Proposed Major Aims

5.2 Letter of Intent (LOI link to be available by end of March 2021)

Letters of Intent (LOI) will be evaluated by a subcommittee of the HSFC Scientific Review Committee (SRC) Peer Review Heart-Brain Connection IMPACT Award panel using the following criteria:

- a. Research question and approach, including:
 - i. Innovation and originality of the proposed research
 - ii. Feasibility of the timeline and associated milestones
 - iii. Translatability and potential impact of the research
 - iv. Adoption of appropriate open science strategies.
- b. Quality of the multi-disciplinary aspects of the team and research proposal, including partnerships in the health system, such as with patient(s)/family/caregiver(s). Composition of the team in accordance with sound EDI principles.
- **c.** Sound considerations of relevant determinants of health including sex, gender, sexual orientation, age, race, culture, socioeconomic status, and/or other factors to the research design, methods, analysis and interpretation, and/or dissemination of research findings, as appropriate.
- d. Relevance and transformation assessment by People With Lived Experience (PWLE).

e. Budget justification for grant development funds (up to \$10,000 per team).

The highest ranked LOIs will be invited to the Full Application stage. The teams invited to submit a full application will be provided with an application planning grant of up to \$10,000 per team to develop their full application. A budget justification for these grant development funds will be submitted with each LOI.

5.3 Full Application (by invitation only)

Full Applications will be evaluated by the HSFC SRC Peer Review Heart-Brain Connection IMPACT Award panel using the following major criteria to support the strategic objectives of this funding opportunity. In addition, the individual Program Modules will be evaluated by the appropriate SRC Peer Review panel (see Section A.10.3 for more information).

a. Research Approach

- i. Clarity of the research question and its relevance to the objectives of this funding opportunity, with an integrative approach that must cover at least three of the four Themes of Health Research (see Section D).
- ii. Clarity of rationale for the overall research approach and methodology in the IMPACT Program Proposal.
- iii. Clarity of rationale for the Program Modules and how each contributes to the overall research question and approach. Use of appropriate research methodology for the proposed research.
- iv. Sound considerations of relevant determinants of health such as sex, gender, sexual orientation, age, race, culture, socioeconomic status, and/or other factors are considered and integrated into the proposal, as appropriate, including in the research design, methods, analysis and interpretation, and/or dissemination of research findings.
- v. Appropriateness and inclusion of People With Lived Experience (PWLE) in the proposal with meaningful engagement.
- vi. The extent to which any ethical, social, and/or legal implications are raised and addressed by the application of the research findings from the research project. Applicants are encouraged to consult the CIHR Ethics in Research: A Science Lifecycle Approach workbook.
 - Any research project involving special populations must follow relevant ethical principles and guidelines. For applications undertaking research with Indigenous communities:
 - Community-based research experience, track record, relevance of past experience, including expertise related to Indigenous living experience(s)
 - Evidence of a track record of working with First Nations, Inuit or Métis Peoples in a manner consistent with the Tri-Council Policy Statement (TCPS 2) Chapter 9 and principles of Indigenous community leadership and data possession

- Demonstrated adherence to OCAP® (Ownership, Control, Access and Possession) principles regarding data standards.
- vii. Application of open science principles for research outputs to be FAIR: Findable, Accessible, Interoperable, and Reusable.
- viii. Teams are encouraged to link and coordinate with, to utilize, and to build on existing platforms, cohorts, and collectives such as data repositories and datasharing systems, tissue banks, etc. if applicable. Examples include: the Canadian Open Neuroscience Platform (CONP), Canadian Consortium on Neurodegeneration in Aging (CCNA), Canadian Longitudinal Study on Ageing (CLSA), or CanPATH.
- ix. Knowledge translation (KT) plan specifying KT activities to be undertaken by the team, if successful, and proposing how Heart & Stroke and Brain Canada may be engaged as knowledge users and KT partners.

b. Team Composition

- Appropriateness and inclusion of team members in relation to the objectives of this funding opportunity. The team members must cover at least three of the four Themes of Health Research (See Section D).
- ii. Qualification of the NPI, PI and co-PI, including training and experience in the proposed area of research and with the proposed methodology. Ability of the team to effectively implement and deliver the proposed research project.
- iii. Application of sound equity, diversity and inclusion principles to team assembly. The role of mid- and early-career researchers as well as trainees in the project, including plans for mentorship and training.
- iv. Quality of the collaboration and partnership(s) between team members.
- v. Quality of the inclusion and engagement of patient(s)/family/caregiver(s), in the research program, knowledge exchange and translation plan.
- vi. Innovation and Originality of the Proposed Research.
 - Degree to which the proposed research, while grounded in/informed by evidence, involves innovative strategy and/or offers transformative advances or new approaches to studying heart disease, stroke and vascular cognitive impairment, and the linkages between these entities.
 - Extent to which the research proposal addresses a critical barrier, significant need or gap in our understanding of the heart-brain connection.
- vii. If international collaborators are included, explanation of how their training and experience are required and complement the team.

c. Feasibility of the Proposed Research

- Availability and accessibility of personnel, facilities and infrastructure required to conduct the research including any in-kind or financial support from public, private or not-for-profit organizations.
- ii. Suitability of the environment(s) to conduct the proposed research.
- iii. Suitability of the environment (milieu, project and mentors as applicable) for the training and mentoring of trainees.
- iv. Feasibility of the timeline, and associated milestones, to be completed within the budget and term of the grant including a detailed project plan detailing key milestones.
- v. Plan for strong project management to ensure deliverability and accountability.
- **d.** Impact and Translatability of the Proposed Research
 - i. Potential for translation of research outcomes into measurable impacts for People With Lived Experience.
 - ii. Appropriate consideration given to diverse groups that reflect the diversity of culture and conditions, taking into account relevant determinants of health such as sex, gender, sexual orientation, age, race, culture, socioeconomic status, and/or other factors where applicable.
 - iii. Appropriateness and adequacy of the proposed plan to mobilize knowledge generated through this work, including knowledge dissemination and exchange.
 - iv. Expected health and societal benefits, including but not limited to the size of these impacts or their accessibility to less well-served communities.
 - v. Potential for Heart & Stroke and Brain Canada to be engaged as knowledge users and KT partners.

6) Timelines

January 29, 2021 Pre-announcement

March 4, 2021 Announcement and Launch of Competition

April 8, 2021 Registration

April 15, 2021 Feedback to applicants

May 13, 2021 Letter of Intent submission deadline

May 2021 IMPACT SRC Peer Review of Letter of Intent May 27, 2021 Notifications of short list for full applications

June 2021 Publication of the short-listed teams

June – September 2021 Grant development period to refine proposals

August 26, 2021 Program Application Due Date

December 2021 SRC Peer Review of Program Modules **January 2022** SRC Peer Review of Full Application

January – March 2022 Post-panel Processes
March 2022 Decision to Fund

Decición to i ana

March – May 2022 Finalize Research Grant Agreement

May 2022 Public announcement of successful Teams

7) Application Process and Deadlines

7.1 Registration Letter

The NPI must complete and submit the registration form to Heart & Stroke by **16:00 ET on 8 April 2021** via email to research@heartandstroke.ca.

<u>Registration Forms</u> submitted after the deadline will NOT be accepted. There will be no appeal process for late submissions.

7.2 Letter of Intent

The NPI must complete and submit the Letter of Intent to Heart & Stroke by 16:00 ET on 13 May 2021 via email to research@heartandstroke.ca. Letters of intent submitted after the deadline will NOT be accepted. There will be no appeal process for late submissions.

Requirements for the Letter of Intent are found in Section A.5.2. The LOI form will be available by the end of March 2021. Please check back at this space.

7.3 Full Application by Invitation ONLY

The NPI must complete and submit the IMPACT Award application to Heart & Stroke by **16:00 ET on 26 August 2021**. Details of how to submit the IMPACT Award will be made available in the LOI notification letters and posted on the Heart & Stroke website "For researchers" section.

Applications received after the deadline will NOT be accepted. There will be no appeal process for late submissions.

A complete Full Application must include:

- An IMPACT Award application (on provided forms), and
- Three or more Program Modules (each completed using CIRCUlink)

Instructions for completing these components are provided in the following two Sections.

8) IMPACT Award Application Format

The IMPACT Program Proposal will detail the overarching research themes and question(s). This component of the application process is intended to provide a high level description of the project including its aims, hypothesis and/or research questions; an assessment of the originality of the research and its relationship to past research; clear articulations of the research undertaken in the Project Modules (including any interdependencies), and the knowledge exchange plans; and a description of the leadership group and overall project management strategy.

a. Impact Statement

A clear, 300-word description of the project for lay audiences that describes its potential to transform, to address a significant gap/need, to make a difference, and to translate into measurable impact for People With Lived Experience.

This Impact Statement should be written for a patient, carer or community member audience so that it is easily understood by a non-technical audience. It should inspire and speak to relevance and meaningfulness of the work and to the desired outcomes. Authors are advised to use one of the commercially available tools to ensure readability at a maximum of a grade 9 level.

b. Research Leadership Team Details

List the names and affiliations of the NPI, PIs and Co-PIs, as well as their role in the proposed research. Indicate which Aim the PI and/or Co-PI will manage. Provide a URL to their institutional or personal webpage.

For each Research Leader, provide a HSFC Common CV Module outlining each team member's qualifications and achievements. See Common CV here.

c. IMPACT Award Proposal

A 10-page description, excluding references, of the proposed IMPACT Award program research, team composition/roles, and implementation plan. The research proposal must include the following:

- i. Title of Research Proposal;
- ii. Research aims of the study and/or hypothesis to be tested and/or research question to be addressed:
- iii. Knowledge to date;
- iv. Methods to be used;
- v. Anticipated results and/or findings, and conclusions;
- vi. Anticipated challenges and potential solutions;
- vii. Address any ethical, social, and legal implications that may be raised by the application of neuroscience and cardiovascular research findings from the research project;
- viii. Clear plan for KT demonstrating strong linkages with knowledge users across relevant health research themes and supporting translation of the research findings into action. The plan must explain the relevance of anticipated or expected research findings to knowledge users such as other researchers, policy makers, health professionals, and community-based groups and with Heart & Stroke and Brain Canada, as well as outline strategies to ensure dissemination and uptake of the findings.
- ix. Clear plan for integrating consideration of variation in determinants of health including, but not limited to, sex, gender, sexual orientation, age, race, culture, and socioeconomic status can help to ensure that research projects lead to better outcomes and are beneficial for all people living in Canada.
- x. Cultural considerations (including Indigenous knowledges); and
- xi. Pertinent references.

d. Letter of Institutional Support

A letter from the Vice President Research or institutional equivalents from the Host Institution, must be submitted confirming institutional commitment from the NPI and adherence to the eligibility requirements, and from the Dean and Department Heads for all PI and co-PI's institution confirming institutional commitment and adherence to the eligibility requirements (please refer to Section A.8.g for acceptable forms of signatures).

e. Budget Request Summary

Availability of funds is valued at a maximum of \$2,900,000 for up to four (4) years, with the possibility of extending the project period for up to 12 months with no additional funding, and with flexibility in the total amount up to the stated maximum, and annual funding profile to accommodate the needs of specific projects. Rigorous justification of all proposed spending must be provided and will be thoroughly reviewed by Heart & Stroke. Failure to provide detailed information and appropriate justification may result in budget cuts that could adversely affect the final budget awarded for the program. Further information about budget requests and justification can be found in Section C.3. Funds may not be used as salary support for the NPI, Principal Investigators, Co-Principal Investigators or Co-Investigators.

Note: Detailed budget justification of all proposed research spending for each Program Module is required.

f. Confirmation of Health Research Training

CIHR Institute of Gender and Health online training module certificate(s): Integrating Sex & Gender in Health Research. Confirmation of completion of CIHR Unconscious Bias Training Module.

g. Signature(s)

Heart & Stroke will accept either original signatures, a scanned copy of the original signatures, or electronic signatures. Note: The expectation is that an electronic signature will hold the same weight as an original (wet) signature.

9) Program Module Proposals

The Program Module will provide the details of research effort associated with each research aim. At least three distinct Program Modules must be submitted to complete the IMPACT Award process. Individual Program Modules should be able to stand alone and should avoid references to activities in other modules. They will be reviewed by the appropriate SRC Peer Review panel and by the HSFC SRC Peer Review Heart-Brain Connection IMPACT Award panel.

a. Program Module

Proposals for each subcomponent Program Module must include:

- i. Description of how the Module contributes to the overall IMPACT Program Proposal;
- ii. Research aim of the study and/or hypothesis to be tested and/or research question to be addressed;
- iii. Knowledge to date;

- iv. Methods to be used;
- v. Anticipated results and conclusions;
- vi. Possible problems; and
- vii. Pertinent references.

Further information about formatting and organization of the proposed research program can be found in Section C.1.

b. Budget Request and Justification

Each program module must request a minimum of \$400,000 over up to four (4) years, with the possibility of extending the project period for up to 12 months with no additional funding. There is flexibility in the total amount requested provide the minimum number of Program Modules is 3 or more, and the total funding request for the IMPACT Award does not exceed \$2.9 million. Rigorous justification of all proposed spending proposed in the Program Module must be provided and will be thoroughly reviewed. Failure to provide detailed information and appropriate justification may result in budget cuts that could adversely affect the final budget awarded for the Award. Further information about budget requests and justification can be found in Section C.3. Funds may not be used as salary support for the NPI, Principal Investigators, Co-Principal Investigators or Co-investigators. Budget justification will be reviewed by the program module peer review panel.

10) Review Process

10.1 Registration Review

The participating partners (Heart & Stroke and Brain Canada) will perform a relevance and eligibility review at the Registration stage to identify applications that are relevant to and in alignment with the objectives and research areas of this funding opportunity and meet the eligibility criteria. Registrations will not be triaged at this stage. Feedback will be provided to researchers if their application does not meet criteria so that they may make corrections before submitting Letters of Intent.

10.2 Letter of Intent Review

All relevant and eligible Letters of Intent will undergo peer review by a Heart and Brain Connection IMPACT Award Panel convened in accordance with the Heart & Stroke Scientific Review Committee (SRC) policies and procedures, which may include expert reviewers, People With Lived Experience, and knowledge users. Expert reviewers may include international members as well as reviewers from Canada. External reviews may be sought to bring additional expertise to support the review process.

10.3 Full Application Review

Full Applications will be evaluated using a two-stage review process. In the first stage, Program Modules will be reviewed by the appropriate SRC Peer Review panel. In the second stage the IMPACT Award and Program Modules will be reviewed by the HSFC SRC Peer Review Heart-

Brain Connection IMPACT Award panel. Full Applications will be reviewed using the criteria set out in Section A.5 to support the strategic objectives of this funding opportunity.

Individual IMPACT Program Modules will be assigned for review to the appropriate SRC panel. The standing peer review panels include:

- Clinical cardiovascular and cerebrovascular research: Mechanistic studies and clinical trials/health services research. Areas and expertise include: Mechanistic studies focusing on human studies, clinical trials (therapeutic and surgical), health services, and health care delivery.
- II. Integrative studies: Genetic manipulations/imaging/bioengineering. Areas and expertise include: Integrative studies in animal models, diagnostic and imaging technology development in animals and humans, and novel therapeutic strategy and device development in animals, including regenerative approaches.
- III. **Basic science stroke/neurophysiology/neuroregulation**. Areas and expertise include: Stroke, neurophysiology and neural cell biology, and neuroregulation.
- IV. **Cellular biochemistry, pharmacology, and electrophysiology.** Areas and expertise include: Cardiovascular physiology and pathophysiology, cell biology, cell signaling, cellular biochemistry, pharmacology, and electrophysiology. Specifically, the three sub-panels are:
 - a. Molecular, biochemical and cellular physiological approaches to cardiovascular health and disease, vascular disorders.
 - b. Cardiac arrhythmias, cardiac mechanics, electrophysiological approaches to cardiovascular health and disease, ischemia related disorders.
 - c. Cardiovascular complications associated with obesity/diabetes, metabolism, and cardiac development/remodelling.
- V. **Molecular basis of cardiac and vascular function.** Areas and expertise include: Inflammation, immunology, transplantation, and vascular pathology.
- VI. Thrombosis/lipid and lipoproteins/fundamental nutrition research. Areas and expertise include: Coagulation, bleeding disorders, thromboembolism, lipid and lipoprotein metabolism, atherogenesis, atheroma, and its degenerative consequences, and nutritional contribution to atherogenesis, thrombophilia or bleeding disorders.

VII.

- a. Health services and Public Health. Areas and expertise include: research that examines the influence, delivery and management of health care services, evaluates and assesses outcomes of health care services, and health services policy and regulation. Research examining influences, predictors, trends, socio-cultural influences on public health and population level health, including health services provision and targets, health equity, access to services and policies affecting public health. Population health interventions.
- b. Health behaviour; health psychology. Areas and expertise include: research that examines influences and precursors, including social and environmental influences, on behaviours and on the relationships of behaviours to health outcomes including social, environmental and health psychological factors predicting health status, health behaviours, health outcomes, and the relationships among them. Interventions targeted at

specific individuals or sub-populations based on behavioural or psychological manipulations.

Heart and Stroke reserves the right to combine and divide panels in response to submission levels.

11) Final Competition Results

Official letters will be sent to the applicants in March 2022.

12) Monitoring Progress

A progress report, which will be shared with partners, must be submitted to Heart & Stroke by each funded Team no later than no later than 30 days following the one-year anniversary date. the duration of the grant. The progress report template will be available on the Heart & Stroke website in the "For researchers" section. In addition to the progress report, each funded Team will have bi-annual check-in meetings with representatives of Heart & Stroke and Brain Canada. Release of subsequent funds will be dependent on successful completion of the expected deliverables. Ongoing dialogue between each funded Team and the co-funders will aim to problem-solve and support timely resolution of issues.

13) Annual Meeting

As this IMPACT Award is translational in nature, an Annual Meeting will be convened with the two funded Teams, Heart & Stroke and Brain Canada, and other stakeholders. The Annual Meeting will be organized by Heart & Stroke and Brain Canada, working with the Awardees to facilitate knowledge exchange between the funded Teams, to increase community engagement, and for co-funders to monitor progress.

- Objectives:
 - Review of the overall progress for the past year (i.e., discussing the submitted yearly progress report) and plans for the coming year
 - Provide a forum to disseminate the latest research findings and convene researchers with the co-funders and other invited stakeholders
 - Identify opportunities for the co-funders to support the translation of the findings into action, leverage their resources and align their priorities and actions for the coming year
 - Enable problem-solving and information-sharing
 - Develop any joint KT strategies and activities for the coming year (e.g., presenting at conferences, publication of articles, meeting with stakeholders).
 - Identify opportunities to leverage the funding provided by this program into other concurrent relevant programs
 - Identify opportunities to leverage this funding to gain access to additional funding, for example through provincial matching programs

14) Final Report

A final report that will be shared with funding partners must be submitted to Heart & Stroke no later than six (6) months after completion/termination of the grant. The final report template is available on heartandstroke.ca in the "For researchers" section. Once received, a final meeting will be held between the co-funders and the NPI, PIs and Co-PIs to optimize dissemination and knowledge translation of the findings.

B. RESEARCH INTEGRITY POLICY

The primary objective of Heart & Stroke's Research Integrity Policy is to protect and defend the integrity of the research process and to deal with allegations of scientific misconduct in a timely and transparent fashion. Responsibilities of researchers, institutions and the Heart & Stroke with respect to research integrity are outlined in the Heart & Stroke: Responsible Conduct of Research

.

As a condition of funding, all Heart & Stroke grant and award recipients agree to comply with the Principles and Responsibilities set out in that policy, and the research misconduct provisions below.

Heart & Stroke defines research misconduct to include actions that are inconsistent with "integrity" as defined by the Framework, and to include such actions as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.¹

Heart & Stroke will deal with allegations of scientific misconduct in the following manner:

- Any allegation of scientific misconduct will be initially reviewed by the Heart & Stroke to determine
 whether an investigation is warranted. If it is felt that an investigation is required, the Heart &
 Stroke may request that this be conducted by the host institution of the individual considered to
 have performed the alleged misconduct. In allegations specifically related to the peer review
 process, the investigation may be conducted jointly by the institution and the Heart & Stroke.
- Heart & Stroke will not act on verbal allegations of misconduct. All allegations must be submitted
 in writing. Although the confidentiality of persons who submit an allegation of scientific
 misconduct will be protected as much as possible, it must be recognized that due process will
 often result in the identity of this person being released to the investigating institution.
- The institution will be required to submit a written report upon conclusion of the investigation. This
 report will summarize the findings of the investigation and any future actions that will be
 undertaken by the institute as a result of the findings.
- In cases where misconduct is concluded to have occurred, the Heart & Stroke may apply sanctions against the individual(s) implicated. These sanctions will range from a reprimand letter to a ban from applying for or holding Heart & Stroke funds for a set period of time.

¹ Wording adopted from the US Department of Health and Human Services, Public Health Service Policies on Research Misconduct, Final Rule. May 17, 2005. Definitions are available from. https://ori.hhs.gov/definition-misconduct

C. APPLICATION INFORMATION

1) Program Module Guidelines

a. Formatting

- Text must be single-spaced, 12-point Times New Roman or 11-point Arial (including labels and descriptions, accompanying figures, tables, charts, photographs, etc.)
- Margin of 2 cm (3/4 inch) around the entire page.
- Header:
 - "Program Module" (left corner)
 - PI Name (right corner)
- Footer:
 - Number pages consecutively
 - Page numbers must be centered

B. Organization

- The Research Proposal should be predominantly text and is limited to ten (10) pages. The number of pages should reflect the size and scope of the proposed research. Pages beyond the ten (10) page limit will NOT be evaluated by the reviewers
- Within the allotted 10 page limitation applicants may submit figures, charts, tables and photographs. These portions of the submission count towards the ten (10) page limit.
- References should be placed at the end of the research proposal and will not count toward the ten (10) page limit.
- Additional supporting documentation such as questionnaires, more detailed explanations of RCT methods, and consent forms may be attached as a separate document (there is no page restriction and these will not count towards the 10 page limit).

Failure to adhere to the guidelines above risks the application being deemed unacceptable and removed from the competition.

2) Multi-Centre/Site/Communities Applications

Benefit must be demonstrated to all centres/sites involved in the research project. It is the responsibility of the applicant to ensure that applications demonstrate the following:

- A high probability of informing policies, practice, programs and/or future research questions.
- Significant "value-added" to perform a particular project across centres/sites/communities.
- A research design reflecting work done in each centre/site.

3) Budget Guidelines

The minimum funding request for a Program Module is \$400,000 over 4 years. The annual funding profile should accommodate the needs of the specific research proposal over the term of the grant.

a. Salaries and Benefits (excluding those of the PI/co-PIs,co-Is and collaborators)

Under no circumstances can operating funds be used to support the salary or benefits of the NPI, nor any principal investigators/applicants.

Benefits for eligible salaries are allowable within the funding envelope to a maximum of 30% of the salary cost.

Provide names (if known), categories of employment and proposed salaries (including non-discretionary benefits) of all personnel identified in the budget. Attach a copy of the institutional guidelines relating to requested benefit levels. Briefly describe the percentage of dedicated time and responsibilities of each position for which support is requested and attach a brief CV as an appendix for those positions for which an individual has been identified.

Inclusion of salary support for an experienced project manager (minimum 0.5 FTE) is strongly encouraged.

Salaries for unnamed project manager, research assistants, technicians, and research associates should also conform to those of the institution in which the individual is carrying out the research, subject to the approval of Heart & Stroke and Brain Canada. The costs of salary/benefit increases must be accommodated for within the approved budget.

b. Summer Students/Graduate Students

Heart & Stroke and Brain Canada encourage junior trainees (particularly doctoral students) to be included in the proposed research with a defined and clearly written role (within the project submitted). Stipend levels must be aligned with Heart & Stroke guidelines. Stipend levels are listed below:

- Doctoral Level Trainees (PhD): \$21,000
- **Post-Doctoral Level Trainees** who hold a health professional degree at a doctoral level (e.g. MD, PharmD, DVM; or other regulated accredited health professionals who have a PhD) who hold a license to practice in a province or territory of Canada: \$50,000.
- Post-Doctoral Level Trainees who hold a PhD degree or applicants with a health professional degree at a doctoral level (e.g. MD, PharmD, DVM; or other regulated accredited health professionals who have a PhD) who do not hold a license to practice in a province or territory of Canada: \$40,000

Where comparable values do not exist (e.g. summer students, undergraduate, master's level), stipend levels must be aligned with institutional guidelines. However, support will not be provided for benefit costs of summer students, undergraduate students, graduate students, and/or post-doctoral fellows.

c. Research Equipment (including maintenance and facility)

Budget requests for research equipment and/or services amounting to more than \$50,000 cumulative across the entire program over the span of four (4) years **will not be accepted**.

Research equipment is defined as any item (or interrelated collection of items comprising a system) that meets all three (3) of these conditions:

- Non-expendable tangible property;
- Useful life of more than one (1) year; and
- A cost of \$2,000 or more.

For example: A laptop computer that costs less than \$2,000 would be considered as materials or supplies even though it is a non-expendable tangible item with a useful life of more than one year.

For equipment or service contracts greater than \$10,000:

A detailed cost quotation must be provided.

Provide a breakdown and justification of the items requested. Give details of models, manufacturers, prices and applicable taxes. In addition, for maintenance and/or equipment items listed, indicate:

- The availability and status of similar equipment.
- The anticipated extent of utilization.
- The reasons for choice of specific type, model or service contract, in relation to alternatives.
- Where applicable, the necessity for upgrading existing equipment or service contracts.

All equipment and contracts must meet relevant institutional requirements for sourcing; for items greater than the institutional threshold multiple quotations will be required.

d. Materials and Supplies

Provide specific details and justify / explain major items (ex. costs for purchasing cell lines, primary cells, global estimates for disposables including reagents, kits, etc.). Do not simply list items.

e. Payments to Study Subjects

Heart & Stroke allows well justified and reasonable reimbursements for required travel, parking, childcare, honoraria, or other items that would reduce barriers to participation.

f. Payments to People With Lived Experience (PWLE)

Heart & Stroke and Brain Canada believe that providing financial compensation to acknowledges the valued contributions of PWLE representatives and helps to remove barriers to participation. Offering compensation, reduces power hierarchies caused by the fact that others at the table receive a salary related to their role and ensures that PWLE Representatives who cannot afford to volunteer their time are able to participate. PWLE include individuals with personal experience of a health issue and informal caregivers, including family and friends.

PWLE representatives will be fairly compensated for their participation in any aspect of the IMPACT award research program. Please reflect these costs in the budget grid (Module and/or Program).

g. Service Contracts

Provide justification / explanation for each item listed (ex. Biostatistical time, access to administrative databases, etc.). Justification is required to allow for specialized service contracts at non-Canadian institution(s) who provide access to leading expertise, facilities, technologies, unique populations, and environments, research training and/or knowledge translation that is not otherwise available in Canada.

h. Travel

Travel to Conferences/Academic Meetings: Up to \$10,000 per year can be requested in support of travel to conferences and other academic meetings across the entire program. Proper justification and a brief explanation of how each activity relates to the proposed research are required. The purpose and estimated cost (up to a maximum of \$10,000 per year) of such travel must be given.

Travel to Annual Meeting: A budget for travel to the Annual Meeting will be allocated out of the \$25,000 per year per Awarded Team will be used the Annual Meeting, which will be organized by Heart & Stroke and Brain Canada and the funded Teams. The estimated cost must be budgeted for in their program budget.

Cost for Engagement with Indigenous Communities

J. Financial Contributions from Other Sources (if applicable)

Provide a brief explanation of any financial (not in-kind) contribution from other sources (if applicable).

Private sector or industry partners may be included in the proposal, but are not required, and their involvement will not be factored into the review of the application. Any private sector or industry involvement must be free of conflict of interest.

Contact Information:

Research Department Heart & Stroke 110-1525 Carling Avenue Ottawa, Ontario K1Z 8R9

Tel: (613) 691-4041 Fax: (613) 569-3278

E-mail: research@heartandstroke.ca

Website: http://www.heartandstroke.ca/research

D. GENERAL INFORMATION

Ethical Requirements

By signing and submitting applications to Heart & Stroke, applicants undertake the responsibility to ensure the research that results from this initiative be acceptable to the institution on ethical grounds and comply with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans and the host institution research policies, as applicable.

Heart & Stroke requires a copy of all ethics/safety review board approval forms. In the full application, please indicate the status of such forms (e.g., "Included", "Form to be Sent", "Not applicable") as they apply to the research proposal. If the full application is successful, funds will be encumbered pending receipt of all required forms. Further, in applying applicant and institutional signatures to this application, applicants are confirming to the Heart & Stroke that the proposed research will not be undertaken until it has been endorsed as ethical and safe – initially and throughout the term of the project, as needed – by the appropriate review body(ies).

Heart & Stroke reserves the right to periodically request additional approval forms during the term of the project. Forms included with the application must be valid at least 30 days beyond the start date of the award.

Applicants must provide acceptable documentation for human and/or animal ethical approval, and biohazard and safety approval as outlined in the Heart & Stroke guidelines.

Applicants must ensure all experiments comply with the following guidelines and host institution research policies, as applicable:

- Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans².
- Good Clinical Practice (GCP).
- Good Laboratory Practice (GLP).
- In the case of laboratory animal experimentation, the guiding principles and standards enunciated by the Canadian Council on Animal Care³.
- Guidelines and standards for biological and chemical hazards as outlined in the Public Health Agency/Canadian Food Inspection Agency's Canadian Biosafety Standards and Guidelines⁴.
- Any research involving human pluripotent stem cells must adhere to the CIHR
 Guidelines for Human Pluripotent Stem Cell Research⁵. The institution must notify the
 Heart & Stroke as to the results of the review by the CIHR's Stem Cell Oversight
 Committee.

Four Themes of Health Research

Applicants must estimate what proportion of the proposed research and proposed project budget falls under the four health research themes. This data is gathered for Heart & Stroke's and Brain Canada's use only.

² See http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default for details.

³ See http://www.ccac.ca/en_/standards/guidelines

⁴ See http://canadianbiosafetystandards.collaboration.gc.ca/index-eng.php for details.

⁵ See http://www.cihr-irsc.gc.ca/e/15255.html for details.

The four (4) themes of health research are:

Basic Biomedical (I)

Research with the goal of understanding normal and abnormal human function, at the molecular, cellular, organ system and whole body levels, including the development of tools and techniques to be applied for this purpose; developing new therapies or devices which improve health or the quality of life of individuals, up to the point where they are tested on human subjects. Studies on human subjects that do not have a diagnostic or therapeutic orientation.

Clinical (II)

Research with the goal of improving the diagnosis and treatment (including rehabilitation and palliation) of disease and injury; improving the health and quality of life of individuals as they pass through normal life stages. Research on, or for the treatment of, patients.

Health Services/Systems (III)

Research with the goal of improving the efficiency and effectiveness of health professionals and the health care system, through changes to practice and policy. Health services research is a multidisciplinary field of scientific investigation that studies how social factors, financing systems, organizational structures and processes, health technologies, and personal behaviours affect access to health care, the quality and cost of health care, and ultimately Canadians' health and well-being.

Social, cultural, environmental and population health (IV)

Research with the goal of improving the health of the Canadian population, or of defined sub-populations, through a better understanding of the ways in which social, cultural, environmental, occupational, and economic factors determine health status.

Incomplete/Unacceptable Applications

- All applicants are strongly cautioned to carefully *read* and *follow* the instructions and requirements outlined in this guideline document.
- In order to maintain the principle of fairness to all applicants, regulations *must* be adhered to in the preparation of the application. *Any* infraction of the rules will lead to the truncation or immediate rejection (without appeal) of the application.
- Heart & Stroke reserves the right to decline incomplete applications.

Indirect Costs

Heart & Stroke and Brain Canada support only the direct costs of research. No funding is to be used for indirect costs of research. The definition of indirect costs of research for the purposes of this policy is costs which cannot be directly associated with a particular research program or operating grant including costs associated with the general operation and maintenance of facilities (from laboratories to libraries); the management of the research process (from grant management to commercialization); and regulation and safety compliance (including human ethics, animal care and environmental assessment).

Non-Employee Status

The granting of an award is deemed to establish neither an employer-employee relationship nor a partnership between the grantor and the grantee.

Open Access to Research Outputs policy

Heart & Stroke and Brain Canada require that all researchers supported in whole or in part through Heart & Stroke and Brain Canada make their research outputs publicly available as soon as possible but no later than 12 months after the final publication or availability of results. In this policy, Heart & Stroke and Brain Canada defines research outputs as peer-reviewed journal publications, research data, and the results of clinical trials that will not be published in peer-reviewed journals (even if negative or not the desired outcome). Compliance with the Open Access to Research Outputs policy is a condition of acceptance of all Heart & Stroke research funding. Please see the Heart & Stroke's Open Access to Research Outputs.

People With Lived Experience (PWLE) in Peer Review

Heart & Stroke incorporates PWLE as lay reviewers on its Scientific Review Committee (SRC) panels in order to increase accountability and transparency of the review process and to ensure that the research is aligned with its goals and mission and relevant to its constituents. The Heart-Brain Connection IMPACT Award peer review process will include PWLE at the LOI and Full Application stages. The co-funders place a high priority on ensuring appropriate Impact Statements are submitted as part of each application. PWLE will be evaluating the Impact Statements, as well as commenting on the relevance and transformational potential of the proposals. They will evaluate these elements and contribute to the scoring of an application. full members of the panel.

Public Information

Successful applicants need to be aware that the title of their research project and the lay summary may be placed into the public domain or included in Heart & Stroke and/or Brain Canada publications without notification. Applicants are cautioned not to disclose information that could endanger a proprietary position in these sections.

We would like to encourage applicants to help us communicate the importance of research to Heart & Stroke donors and to the general public. In this increasingly difficult economic climate, raising funds to support research is becoming progressively more difficult. More than ever, we need to let our donors and the public know that their donations are being used to support world class research. You are one of the best representatives to explain to the public the role of research in increasing heart and brain health and reducing the burden of heart disease and brain related diseases/disorders, such as stroke.

Publications and presentations

A Principal Investigator must acknowledge the support of Heart & Stroke and Brain Canada in all scientific publications and presentations related to their grant with the following wording as applicable:

"This work was supported by funding from Heart & Stroke and the Brain Canada Foundation through the Canada Brain Research Fund, with the financial support of Health Canada."

To facilitate the implementation of Heart & Stroke and Brain Canada programs for knowledge transfer and exchange, Heart & Stroke and Brain Canada MUST be notified in advance of the publication date of any major publications and/or press releases arising from research funded by Heart & Stroke and Brain Canada.

Any proactive media planning and outreach, such as digital communications, press releases or press conferences must be approved by Heart & Stroke and Brain Canada, jointly released and presented with at least 20 days prior notice to any public announcement. The co-funders must be involved and present, if they are available, along with the investigators and the relevant institutions. Any infraction will result in withholding of remaining funds.

To maximize the knowledge translation and communications, any abstracts and presentations must be shared in advance.

A copy of publications and presentations must be submitted with each progress and final technical report.

Status of Publications

Manuscripts may not be attached unless they have been published or the manuscripts have been submitted or accepted for publication. Any manuscript included with an application, but not yet published must be accompanied by documentation from a journal verifying that the manuscript has been submitted, is accepted for publication or is in press. Heart & Stroke will not accept letters indicating confirmation of acceptance for publication of a paper after 01 December 2020.

Appendix 1: List of Partners

Funding Partners



Heart & Stroke Life. We don't want you to miss it. That's why Heart & Stroke leads the fight against heart disease and stroke. We must generate the next medical breakthroughs, so Canadians don't miss out on precious moments. Together, we are working to prevent disease, save lives and promote recovery through research, health promotion and public policy.



Brain Canada Foundation is a national non-profit organization that develops and supports collaborative, multidisciplinary, multi-institutional research across the neurosciences. Through partnering with the public, private and voluntary sectors, Brain Canada connects the knowledge and resources available in this area to accelerate neuroscience research and funding and maximize the output of Canada's world-class scientists and researchers.