Request for Applications

IMPACT Funding Opportunity Number: RFA-IMPACT-21-D01

KEY DATES:

Request for Applications – Released
February 1, 2021

Informational Webinar
February 11, 2021 @ 2pm ET

Application Opens
February 15, 2021

Letter of Inquiry Email – Not Required
March 5, 2021 @ 5pm ET

Requests for Consultation from IMPACT Experts – Not Required
April 2, 2021 @ 5pm ET

Full Applications Due
April 30, 2021 @ 5pm ET

Notifications
June 2021

Demonstration Projects

Embedded pragmatic clinical trials of non-pharmacological interventions for people living with Alzheimer’s disease and Alzheimer’s disease-related dementias (AD/ADRD) and their care partners

2021
Program Overview

The National Institute on Aging (NIA) Imbedded Pragmatic Alzheimer’s Disease and Alzheimer’s Disease-Related Dementias (AD/ADRD) Clinical Trials (IMPACT) Collaboratory (U54AG063546) was established in 2019 to build the nation’s capacity to conduct pragmatic clinical trials (ePCTs) of non-pharmacological interventions embedded within health care systems to improve the care of people living with AD/ADRD and their care partners.

In 2021, the NIA IMPACT Collaboratory will fund up to two Demonstration Projects (maximum duration 24 months) designed as full-scale, Stage IV effectiveness ePCT (based on the NIH Stage Model) that test, measure and evaluate the effect of a care delivery intervention program in a health care system for people living with AD/ADRD and their care partners. The goal of the Demonstration Project is to generate evidence on effective care delivery practices that can be expanded and/or implemented in other systems. The IMPACT Collaboratory will give preference to applications for Demonstration Projects that address dementia care for populations historically marginalized or underrepresented in clinical trials and those that promote health equity.

Funding Opportunity Description

The IMPACT Collaboratory will consider applications for Demonstration Projects designed as large-scale ePCTs to test the effectiveness of non-pharmacological interventions for people living with AD/ADRD and their care partners embedded in health care systems. Under this mechanism, interventions must be linked to the needs of a health care system. The intervention will typically encompass relatively simple system changes or direct patient outreach, or successfully piloted programs ready for testing at scale. Demonstration Projects will allow health care systems and investigators to gain real-world experience integrating the intervention into clinical workflow and the delivery of health care, but in a controlled manner that provides clear information on the impact of the intervention program being tested. Demonstration Projects must be powered to detect a significant difference in the primary outcome between trial arms.

The IMPACT Collaboratory will only fund Demonstration Project applications that include a clinical trial as defined by the National Institutes of Health.

Informational Webinar

An optional informational webinar will be hosted to provide investigators and their operational or clinical partners with an overview of application details and guidance that the IMPACT Collaboratory can provide in assistance with proposal development (e.g., trial design, measurement, data extraction, etc.). Individuals will have the opportunity to ask questions. Pre-registration is required using the link below:

- Thursday, February 11, 2021 at 2:00 PM ET: Register here for webinar.

The informational webinar will be recorded and posted online at https://impactcollaboratory.org/demonstration-grants-program/.

Frequently Asked Questions

A set of frequently asked questions (FAQ) regarding this program is available online at https://impactcollaboratory.org/demonstration-projects-faq/.
Awards are for up to $500,000 (in total direct costs) budgeted over a maximum of 24 months and are non-renewable.

**Health Care System Partnerships**

Applicants must identify at least one health care system for the proposed Demonstration Project as well as a clinical or operational partner from that setting who is committed to investigating the study question and applying the results in practice. Ideally, prospective applicants would have an established productive research partnership with the health care system organization and key individuals within that health care system. Effective and sustainable partnerships with health care delivery organizations and champions within systems are critical to implementation and testing of program interventions. It is anticipated that the Demonstration Projects will be performed within electronically-supported health care systems and integrated into the clinical workflow or delivery of care to establish efficiencies. Outcomes or other metrics essential to taking a successful intervention to scale should be measurable with electronic data or as a routine part of care delivery. The partnership must facilitate the investigator’s access to all data sources relevant to the project, which may include electronic health records, inpatient, outpatient, imaging, clinical laboratory, pharmacy, and assessment data.

Alternatively, some healthcare systems may have scientifically driven demonstrations they envision proposing under this mechanism, but may not have a strong researcher to serve as a principal investigator. Healthcare systems in this situation are encouraged to contact IMPACTcollaboratory@hsl.harvard.edu. The IMPACT Collaboratory may be able to act as a bridge to finding an appropriate investigational partner for the proposed Demonstration Project.

The health care system(s) partner(s) must detail their commitment to the proposed Demonstration Project in a letter of support that clearly stipulates: 1) how the project fits with organizational priorities and will directly impact care delivery within the organization, 2) how the intervention program could be feasibly integrated and adopted into the clinical workflow by frontline providers, 3) the quality of the proposed data systems (e.g., electronic health records) for subject identification and outcome ascertainment, 4) a description of how essential data can be extracted and applied for the planned investigation and in subsequent clinical care, and 5) the commitment of information technology (IT) staff to the project.

**Institution**

- Eligible institutions include: health care organizations, colleges, universities, medical or nursing schools, or other fiscally responsible organizations within the United States (US). No research may be performed outside of the US.
- Ineligible institutions include: Foreign (non-domestic, non-US) entities including non-domestic components of US-based organizations are not eligible to apply.
Principal Investigator(s)

- Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their organization to develop an application.

- Applicants must hold a faculty or research scientist position at an eligible institution by the start date of the award or be otherwise eligible to serve as a Principal Investigator as determined by their organization.

- Applicants must be citizens or permanent residents of the United States.

- Applicants from under-represented racial and ethnic groups as well as individuals with disabilities are strongly encouraged to apply for funding.

- Multiple Principal Investigators (PIs) are allowed. Only one application per individual PI is permitted per funding cycle.

How to Apply

Letter of Inquiry: It strongly recommended that prospective applicants send a brief email describing their proposed Demonstration Project. Although a letter of inquiry is not required, the information can be helpful in determining whether the proposed project aligns with the RFA prior to a full application and whether the IMPACT Collaboratory Cores and Teams may provide useful consultation on the application. In addition, the IMPACT Collaboratory may be able to assist health care systems identify investigational partner(s) for proposed Demonstration Projects. When indicated, a discussion may be arranged with Dr. Vince Mor.

All inquiries should include the following:

- PI(s) name and affiliation
- Name of health care system(s) and partner(s)
- Brief description of intervention to be tested, including information on the target study population, control group (e.g., usual care), and primary outcome (maximum 300 words). Please review the Demonstration Project requirements specified on Page 5.

All inquiries should be directed to the IMPACTcollaboratory@hsl.harvard.edu. Prospective applicants are encouraged to email their letter of inquiry as early as possible and before March 5, 2021 at 5:00 pm ET.

Applications will be submitted through the Brown University UFunds system at: https://ufunds.brown.edu/. The application will be opened on February 15, 2021. Applications may be submitted on a rolling basis but no later than April 30, 2021 at 5:00 pm ET. Applications decisions will be provided before June 30, 2021.

Access to UFunds: UFunds can be accessed using a Brown University email address or be requested using a Gmail address ending in @gmail. The PI may request access, or someone else may request access to submit on behalf of a PI. UFunds is not a multi-user environment. If you received access to UFunds through another RFA from the IMPACT Grants Program, your credentials are still active. New users to UFunds must first request access using a Gmail address here: https://tinyurl.com/UFundsAccess. You will receive an email at your Gmail address once access to the UFunds system has been granted. Please note that the registration process can take up to 2 business days, so applicants are strongly encouraged to request access as early as possible.
Demonstration Projects should have the following features:

1. Test a non-pharmacological intervention targeting people living with AD/ADRD and/or their care partners.

2. Have design features consistent with an ePCT as guided by the domains in the PRECIS-2 framework. **Projects that do not reflect a pragmatic trial design will not be considered.**

3. Be conducted within one or more health care system(s) that has clearly stipulated its commitment and, ideally, with which the applicant has an established collaborative relationship.

4. The intervention must be well-characterized such that it could be delivered with high fidelity by health care providers and/or health care systems. The intervention(s) should be reasonably simple and not require a complex structure or excessive personnel support for implementation or monitoring. System-level interventions may be particularly suitable.

5. As in routine practice, interventions should be implemented with maximal flexibility and by all appropriate practitioners (not just those with high levels of training or competence).

6. The project must leverage opportunities within health care systems to identify the study population, and ascertain outcomes that can be captured routinely by electronic health records and/or administrative data sources, and with minimal need for adjudication.

7. The trial must enroll patients/participants based on broad eligibility criteria to maximize diversity, and minimize intentional or unintentional exclusions based on risk, age, health literacy, demographics, or expected adherence.

8. A primary outcome measure must be stipulated, and be clinically meaningful and important to stakeholders including people living with dementia/care partners, providers, and health care systems and providers. Additional outcome measures, such as use of health care services, may be included.

9. Implementation outcomes (e.g., fidelity, usability and acceptability) must be specified.

10. The trial design must incorporate a control arm, prospectively identified, preferably by randomization.

11. The proposed analytic plan must address sample size and power estimates and employ analytic strategies relevant for ePCT designs. Demonstration Projects must be powered to detect a significant difference in the primary outcome between trial arms. When relevant, power estimates should be provided for subgroup analyses.

12. The proposed project must provide detailed and definitive testing of the validity of methods used for monitoring implementation and outcome assessment.

13. The proposed project must have high alignment with stakeholder priorities. Stakeholders include but are not limited to: people living with dementia, care partners, frontline providers, healthcare systems, and/or payers.
A detailed Application Guide and other required grant application materials and resources will be available at: [https://impactcollaboratory.org/demo-required-materials-and-resources/] on February 15, 2021.

Applications will include applicable PHS 398 Forms specified in detail in the Application Guide. Applications will follow the general format of an NIH R-Level Grant with IMPACT Collaboratory-specific additions and modifications, including but not limited to:

- **Project/Performance Sites**
- **Project Summary and Relevance**
- **Specific Aims** (1 page)
- **Research Plan** (6 pages)
  - **Background and Significance**
  - **Preliminary Studies** (if applicable)
  - **Research Design and Methods**: Include the following: 1) Study population and identification strategy, 2) Setting(s) and Health Care Partnership(s), 3) Randomization scheme and masking, 4) Intervention structure, implementation protocol, and monitoring plan for fidelity and adherence, 5) Data sources, elements, and collection protocol, and 6) Analytic plan. Important considerations: Health equity must be integrated in all aspects of the research design. In addition, NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting.
  - **Milestones**: Specify milestones that are specific, measurable, and achievable by which your progress can be reviewed.
  - **Future Directions and Next Steps**: Specify how the Demonstration Project will directly inform the scalability and sustainability of the intervention.
- **Bibliography and References Cited**
- **PI/PD Leadership Plan** (only required for Multiple Principal Investigators)
- **PHS Human Subjects and Clinical Trial Information** – Form (Version F) and specific instructions will be provided. It is expected that all relevant attachments will be included.
- **Clinical Trial Milestones Plan** (Form provided)
- **Demonstration Project Pragmatic Design Worksheet** (Form provided)
- **NIH Biosketch** for the PI(s) and Key Personnel including the biostatistician. Note: The research team must include a qualified biostatistician as co-investigator or consultant.
- **Letter(s) of Support**: Include letter(s) of support from the health care system partner(s) that relates their commitment to the proposed research and clearly stipulates: 1) how the project fits with organizational priorities and directly impact delivery of health care within the organization, 2) how the intervention could be feasibly integrated and adopted into the clinical workflow by frontline providers, 3) the quality of the proposed data systems (e.g., EHR) for subject identification and outcome ascertainment, 4) a description of how essential
data can be extracted and applied for the planned investigation and in subsequent clinical care, and 5) the commitment of information technology (IT) staff to the project.

- **Acknowledgment Letters from IRB/HRPP Officials.** Applicants must submit a letter of acknowledgment from their institution’s IRB/HRPP official stating that should the study be funded, they agree to cede IRB oversight to Advarra, the central single Institutional Review Board (sIRB) chosen by the IMPACT Collaboratory. An acknowledgment letter is also required from any collaborating institution that will also be engaged in human subjects research activities. (Template provided)

- **Appendices are NOT permitted**

**Budget Considerations**

A budget detailing research-related expenses and salary support with an accompanying budget justification is required. The project period is for up to 24 months and the budget may not exceed $500,000 in total direct costs over the entire project period. Indirect costs may be budgeted at the applicant’s institutional negotiated facilities and administrative rate.

There must be an appropriate mix of time allocated for senior and junior scientists to ensure the successful conduct of the study. The investigative team must include a biostatistician. Budgeted effort of other personnel must be appropriate to the needs of the project. The budget must include personnel at all partnering HCS with expertise relevant to the project, which might include informaticists, clinical investigators and staff with expertise in the administrative aspects of clinical trials oversight. In developing the proposed budget, it is important for prospective applicants to think carefully about which costs derive from – and directly support – the research project, as opposed to those costs that would otherwise be incurred in the course of providing clinical care around which the Demonstration Project is organized. In general, the intervention should be integrated into the clinical workflow and be sustainable without research funding.

Extensive primary data collection (i.e., direct cost exceeding $30,000) is not permissible under this funding mechanism. Researchers are encouraged to use administrative data sources, such as electronic health records, federal or state administrative data, and low- to no-cost smartphone/tablet or web interventions that could feasibly become part of routine care delivery. It is expected that applicants fully describe primary data collection costs in the budget justification, when applicable.

Applicants should NOT budget for the costs of using Advarra, the independent sIRB that oversees IMPACT-funded research. These costs will be supported by the IMPACT Collaboratory.

Applicants should include costs for the PI’s travel and accommodation to one in-person 2.5-day IMPACT Collaboratory Meeting in Bethesda, Maryland in each year of the Demonstration Project.
No-cost extensions are generally not allowed. Requests for no-cost extensions will be considered only in exceptional circumstances, will require NIA approval, and are not guaranteed. Each subaward (cannot exceed 2) must have a separate budget and budget justification and at least one Key Personnel. Whenever feasible, purchase of services/consulting agreements are preferred to subawards.

 NIH grants policies as described in the NIH Grants Policy Statement will apply to the applications submitted and awards made from this funding opportunity.

 Demonstration Project applications will be reviewed by at least two non-conflicted scientific reviewers. Applications that specifically promote equity, and/or are tailored to groups traditionally marginalized or under-represented in clinical trials will be given preference. Scientific merit ratings will consider the following:

*Fit within the Mission of the IMPACT Collaboratory*
- Does the intervention target people living with dementia (PLWD) and/or their care partners?
- Is the proposed Demonstration Project a Stage IV effectiveness ePCT on the NIH Stage Model for Behavioral Intervention Development?

*Significance*
- Does the application address an important clinical or health system burden related to the care of AD/ADRD?
- Is it likely that – if the Demonstration Project is successful – the intervention could be meaningfully implemented to affect the problem?
- Would research findings from this study have the potential to inform decision making for key stakeholders? Stakeholders may include health systems/organizations, frontline providers, PLWD, or care partners.

*Alignment with Stakeholder Priorities*
- Are the problem and outcome measures aligned with stakeholder priorities? Stakeholders may include health systems/organizations, frontline providers, PLWD, or care partners.
- Does the intervention add value for the health care system(s) under investigation? How likely is it that positive findings could be of value to other health care systems, leading to implementation of changes and improvements in practice and outcomes?

*Investigative Team Qualifications*
- Does the team’s prior work and experience support the likelihood that they can complete this Demonstration Project?
- Do the investigators and health care system(s) have robust partnerships necessary for success of the Demonstration Project?
- Does the team include a biostatistician collaborator?
- Does the letter from the health care system(s) detail the level of commitment and elements necessary to support the success of the Demonstration Project including access to all data sources relevant to the project?

**Intervention Readiness for Embedding into a Health Care System**
- Is the intervention well-characterized or reasonably simple such that it could be delivered with high fidelity by health care providers and/or health care systems?
- Is the intervention reasonably simple and does it *not require* a complex structure or excessive personnel support for implementation or monitoring?
- Is the intervention flexible in delivery and adherence or must it be rigidly implemented and/or followed?
- Could the intervention be implemented and integrated into the clinical workflow of the health care system in a pragmatic fashion without extensive support of research staff (other than implementation support or technical assistance)?
- Does the intervention present a strategy that may be cost-effective?
- What is likelihood that the intervention could be implemented by real world staff and organizations?
- Is the intervention minimal risk in nature?

**Design (Pragmatism and Scientific Validity)**
- Is the design feasible, rigorous, reproducible, and scientifically justified?
- Is the project performed within electronically-supported health care systems?
- Can subjects be identified through existing data/infrastructure in a valid fashion, or if not through modest augmentation of existing systems? Are the inclusion and exclusion criteria broad and pragmatic in nature (e.g., looks like a usual care population)?
- Can subjects be enrolled in a pragmatic fashion? Would this Demonstration Project qualify for a waiver or partial waiver of informed consent and authorization?
- Does the application specify a valid primary clinical outcome that is important to stakeholders and can be collected pragmatically in both trial arms?
- Are the sample sizes and power estimates justified and based on realistic evaluations of the anticipated effect size for the primary outcome?
- Does the design and analytic plan apply appropriate methods?
- Are fidelity measures (e.g., adherence, dose, quality of delivery, acceptability to participants) collected and do they appear adequate to assess fidelity to the intervention?

**Milestones**
- Are the milestones specific, measurable, and achievable?
- Do the milestones and deliverables align with the proposed Demonstration Project?
Scientific Merit Review Criteria and Process continued

Integration of Health Equity into the Research Plan

- Are health equity considerations explicitly addressed and integrated into the research plan?
- Does the application include populations that reflect the backgrounds of people with AD/ADRD in the United States? Is there intentional representation of racial and ethnic minorities and other underserved populations?
- Does the application include a plan for monitoring differential implementation, adherence, and attrition/retention across diverse groups?
- Does the application seek to enhance health equity?
- Does the study address the biologic variable of sex as it relates to populations and outcomes?

Future Directions and Next Steps

- Does the application describe a plan for how study findings will be disseminated beyond publication in peer-review journals and presentations at national conferences?
- Does application describe how evidence that is generated from this Demonstration Project could be adopted into clinical practice and delivery of care by others?
- Does the application describe how the Demonstration Project will inform the scalability and sustainability of the intervention?

Just-In-Time

After the review committee meeting, you may be requested to submit Just-In-Time (JIT) Information for finalizing your application. This request does not guarantee anything about the ultimate funding status of your application.

Demonstration Project Grant Award Recipients

Award recipients of the IMPACT Collaboratory Demonstration Projects Grant Program are expected to adhere to the following requirements:

1. Adhere to sIRB, Data and Safety Monitoring, and Data and Resource Sharing policies. The IMPACT Collaboratory will provide a specific Data and Resource Sharing Plan approved by NIA and can provide further guidance. Human subjects research cannot commence without approval by the IMPACT Collaboratory’s overseeing single Institutional Review Board (sIRB) and Data and Safety Monitoring Board (DSMB).

2. Complete Financial Conflict of Interest (FCOI) assurance and training as detailed under their respective organization’s policy and in accordance with PHS (42 CFR Part §50.604) FCOI regulations.

3. Register with ClinicalTrials.gov in accordance with NIA guidelines. Maintain the protocol registration system (PRS) record and complete all reporting requirements, including uploading results. Grant recipients will be provided with an XML file to upload to ClinicalTrials.gov during the registration process.
4. Engage in the IMPACT Collaboratory’s scientific community, including:
   a. Participating in the academic activities of the Core Groups and Teams (e.g., writing methods articles, developing guidance documents).
   b. Attending and presenting at the in-person IMPACT Collaboratory Scientific Meeting in Bethesda, MD.
   b. Attending webinar-based IMPACT Collaboratory Grand Rounds.

5. Submit required reports for study tracking as well as a final report at the end of the project period.

6. Provide budget reports upon request and at the end of the project period.

7. Adhere to the IMPACT Collaboratory publication policy and acknowledge sponsorship in all presentations, publications, and subsequent grants stemming from this Demonstration Project. This information is required for reporting to NIA.

8. Respond to IMPACT Collaboratory queries for information after project ends.

Questions?

For eligibility and research-related questions, please email IMPACTcollaboratory@hsl.harvard.edu.

For questions related to access or use of the UFunds system please contact Faye Dvorchak at Faye_Dvorchak@brown.edu.

For questions related to budgets please contact Laura Bridge at Laura_Bridge@brown.edu.