



NIA IMPACT

COLLABORATORY

TRANSFORMING DEMENTIA CARE

Request for Applications

IMPACT Funding Opportunity Number: RFA-IMPACT-21-D02

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

KEY DATES:

<i>Request for Applications – Released</i>	October 4, 2021
<i>Informational Webinar</i>	October 19, 2021 @ 1pm ET
<i>Letter of Intent by Email – Required</i>	Rolling basis
<i>Letter of Intent Notifications</i>	Rolling basis
<i>Full Applications Due – By Invitation Only</i>	January 14, 2022 @ 5pm ET
<i>Notifications</i>	June 2022

2021

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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.

The NIA IMPACT Collaboratory will fund up to two Demonstration Projects (maximum duration 24 months) designed as full-scale, Stage IV effectiveness ePCTs (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 measurable results 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 was hosted on October 19, 2021 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.).

This informational webinar was recorded and is available only for viewing 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/>.

Award Information

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 health care 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. Health care 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.

Each health care system partner must detail its 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.

Eligibility

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.

Institution

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

How to Apply

There is a competitive two-step application process:

STEP 1: LETTER OF INTENT – REQUIRED

Prospective applicants must submit a letter of intent via email describing their proposed Demonstration Project. This information will 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. The IMPACT Collaboratory may also be able to assist health care systems in identifying investigational partner(s) for proposed Demonstration Projects. When indicated, a discussion will be arranged with Vince Mor, PhD, IMPACT Multiple Principal Investigator.

The letter of intent should include the following information:

- PI(s) name and affiliation
- Name of health care system(s) and partner(s)
- Brief description of the intervention to be tested, including information on the target study population, control group (e.g., usual care), and primary outcome (maximum 750 words). *Please review the Demonstration Project requirements specified below.*

Letters of intent should be emailed to IMPACTcollaboratory@hsl.harvard.edu with the subject line “Demonstration Project Letter of Intent: [Last name of the Principal Investigator]”. Prospective applicants are encouraged to email their letter of intent as early as possible. Notifications will be made on a rolling basis.

STEP 2: FULL PROPOSALS – BY INVITATION ONLY

Applications selected for further consideration will be invited to submit a full proposal that will be due no later than January 14, 2022 at 5:00 PM ET. Applications decisions will be provided before June 30, 2022.

Proposal Contents

Applicants invited to apply for full proposals will be provided with an Application Guide containing detailed guidance on the required elements. Applications will follow the general format of an NIH R-Level Grant with IMPACT Collaboratory-specific additions and modifications. An overview of the general format of the full proposal application can be found in [Appendix 1](#).

Demonstration Project Requirements

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 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. 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, health care systems, and/or payers.

Consultation from IMPACT

All applicants selected for further consideration will have the opportunity to meet with experts from IMPACT Cores and Teams. Applicants may request individual meetings with specific cores and teams throughout the proposal development process to help guide the development of the strongest application. Both the applicant and their biostatistician must attend these consultation meetings. Consultations are most helpful when the PI provides the Specific Aims page in advance of the meeting(s). This offers the opportunity for the applicant to provide clarifications, ask questions, and receive tailored guidance.

IRB Oversight

All funded Demonstration Projects must be overseen by Advarra, the central single Institutional Review Board (sIRB) chosen by the IMPACT Collaboratory. Applicants selected for further consideration 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. An acknowledgment letter is also required from each collaborating institution that will also be engaged in human subjects' research activities.

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 health care systems 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.



*Budget
Considerations
continued*

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 or 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.

**Scientific Merit
Review**

Demonstration Project applications will be reviewed by at least three non-conflicted scientific reviewers and will include a statistical review. More details on the review criteria can be found in [Appendix 2](#). Applications that specifically promote equity, and/or are tailored to groups traditionally marginalized or underrepresented in clinical trials will be given preference.

Just-In-Time

After the scientific review committee meeting, you may be requested to submit Just-In-Time (JIT) Information to finalize your application. This request does not guarantee anything about the ultimate funding status of your application. JIT materials are generally due within 2 weeks of the request. *The IMPACT Collaboratory Administration Core will assist the PI with the JIT materials.*

**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 sIRB and Data and Safety Monitoring Board.
2. Adhere to [NIH policy and guidelines regarding inclusion of women and minorities and inclusion across the life span](#) in the design and conduct of the study as mandated by [Public Health Service Act sec. 492B](#), [42 U.S.C. sec. 289a-2](#). The goal is to ensure that individuals are included in clinical research in a manner that is appropriate to the scientific question under study.
3. 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.
4. 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.
5. The PI will meet with an assigned IMPACT Multiple Principal Investigator for one hour every month throughout the lifecycle of the Demonstration Project to help strategize and navigate challenges. To help ensure successful progress, the IMPACT Collaboratory's Investigator Navigation Team will connect PIs with the IMPACT Cores and Teams, according to their project's needs.

6. Engage in the IMPACT Collaboratory scientific community, including:
 - a. Participating in the academic activities of the cores and teams (e.g., writing methods articles, developing guidance documents).
 - a. Attending and presenting at the in-person IMPACT Collaboratory Scientific Meeting in Bethesda, MD.
 - b. Attending webinar-based IMPACT Collaboratory Grand Rounds.
7. The National Institute on Aging (NIA) supports a central resource to NIA staff and extramural investigators to facilitate/support the conduct and management of clinical research. This resource, the Clinical Research Operations Management System (CROMS), is a comprehensive data management system to support the business functions, management, and oversight responsibilities of NIA grants that support the conduct of clinical research with human subjects. It is the expectation by NIA that all successful applicants will interface, integrate, or adapt their information system(s) and processes to interact with existing and future components of the CROMS as necessary.
8. Submit required reports for study tracking, an annual progress report, and a final report at the end of the project period.
9. Follow IMPACT Collaboratory invoicing guidelines.
10. Provide budget reports upon request and at the end of each project period.
11. 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.
12. Respond to IMPACT Collaboratory queries for information after project ends.

Questions?

For questions, please email IMPACTcollaboratory@hsl.harvard.edu.



Appendix 1 - General Format of Full Proposals

An Application Guide will be provided to PIs who are invited to submit a full proposal application. Applications for full proposals will include applicable [PHS 398 Forms](#) as will be specified in the Application Guide. Additional materials and resources required for the grant application will be available at: <https://impactcollaboratory.org/demo-required-materials-and-resources/>.

Full proposals will follow the general format of an NIH R21 with IMPACT Collaboratory-specific additions, including but not limited to:

- **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 considerations must be integrated in 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**
- **Clinical Trial Milestones Plan** (Form will be provided)
- [Demonstration Project Pragmatic Design Worksheet](#) (Form will be provided)
- [NIH Biosketches](#) for the PI and Key Personnel including the biostatistician. *Note: The research team must include a qualified biostatistician as co-investigator or consultant.*
- **Letters of Support.** Include letter(s) of support from each health care system partner 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 Official.** 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 each collaborating institution that will also be engaged in human subjects' research activities. (Template will be provided.)

Appendix 2 - Scientific Merit Review Criteria

The review process will consider each of the following criteria:

Fit within the Mission of the IMPACT Collaboratory

- Does the intervention target people living with dementia (PWLD) 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?

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) based on the [PRECIS-2 Framework](#)

- Is the design feasible, rigorous, reproducible, and scientifically justified?
- Is the project performed within electronically-supported health care system(s)?
- 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?

Integration of Health Equity into the Research Plan

- Are health equity considerations explicitly addressed and integrated into the design elements of the research plan?
- Does the application include populations that reflect the backgrounds of people with AD/DRD in the United States? Is there intentional representation of racial and ethnic minorities and other underserved populations?
- Does the application consider health equity in its selection of health care settings and target population demographics?
- 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 application address the biologic variable of sex as it relates to populations 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 as co-investigator or consultant?

Human Subjects

- Is this study minimal risk in nature?
- Is it likely to qualify for a waiver or partial waiver of informed consent and authorization?

Milestones

- Are the milestones specific, measurable, and achievable?
- Do the milestones and deliverables align with the proposed Demonstration Project?

Future Directions

- 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?