Request for Applications

IMPACT Funding Opportunity Number: RFA-IMPACT-20-P02B

Pilot Grants

Pilot pragmatic clinical trials for people living with Alzheimer's disease and Alzheimer’s disease-related dementias (AD/ADRD) and their care partners

KEY DATES:

Request for Applications – Released
August 17, 2020

Letter of Intent Application – Opens
August 24, 2020

Informational Webinars
August 26, 2020 @ 2 pm ET
September 8, 2020 @ 4 pm ET

Letters of Intent Due – Required
Rolling through September 18, 2020 @ 5pm ET

Letters of Intent – Notification
October 23, 2020 @ 5pm ET

Full Proposals Due – By invitation only
January 8, 2021 @ 5pm ET
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 embedded pragmatic clinical trials (ePCTs) of non-pharmacologic interventions within health care systems to improve the care of people living with AD/ADRD and their care partners. The NIA IMPACT Collaboratory funds several one-year pilot studies annually; these are meant to generate the preliminary data necessary to design and conduct a future full-scale, Stage IV effectiveness ePCT (based on the NIH Stage Model) funded through other grant mechanisms (National Institutes of Health or other sources). The IMPACT Collaboratory encourages applications that address dementia care for people of all backgrounds and promote health equity.

The IMPACT Collaboratory provides guidance for investigators in the design, conduct, and dissemination of ePCTs through its Working Group Cores and Teams:

- Administration Core
- Pilot Studies Core
- Regulations & Ethics Core
- Technical Data Core
- Design & Statistics Core
- Health Care Systems Core
- Patient & Caregiver Reported Outcomes Core
- Dissemination & Implementation Core
- Training Core
- Health Equity Team
- Stakeholder Engagement Team

Learn more about the support provided by the Cores and Teams at http://www.impactcollaboratory.org.

Priority Areas for RFA-IMPACT-20-P02B

The IMPACT Collaboratory will consider applications for pilot ePCTs testing non-pharmacological interventions in people living with AD/ADRD and their care partners. In this grant cycle, the IMPACT Collaboratory will consider all applications that propose pilot ePCTs for people living with AD/ADRD and their care partners but will prioritize those in the following areas:

- Interventions that strive to reduce inequities in health care experienced by minority, underserved, or disadvantaged populations or in settings serving a disproportionate share of minority, underserved, or disadvantaged populations;
- Interventions that strive to address social isolation and loneliness; and
- Interventions that use telemedicine, telehealth, and remote technologies to improve health, unmet needs, quality of life and/or health outcomes.

Funding Opportunity Description

This cycle, the IMPACT Collaboratory will fund up to 5 one-year, non-renewable pilot studies. No-cost extensions are generally not allowed, and will be considered only in exceptional circumstances, will require NIA approval, and are not guaranteed.

Pilot studies should:

- Pilot test a non-pharmacological intervention targeting people living with AD/ADRD and/or their care partners using an embedded pragmatic trial design.
In addition to: Implement the intervention in two or more health care systems or sites (e.g., nursing homes, hospitals, healthcare provider practices). Randomization is NOT required.

Evaluate an intervention with a reasonable evidence-base demonstrating its efficacy as described in the Readiness Assessment for Pragmatic Trials (RAPT) Model paper. All interventions, including those addressing the priority areas of this grant cycle, must have a reasonable evidence-base demonstrating their efficacy.

Evaluate an intervention that can be implemented with a high level of fidelity. More complex interventions require ‘a priori’ evidence that they have successfully tested, well-developed, transportable training protocols and have been shown to produce intervention delivery with fidelity. However, how well intervention fidelity is maintained when implemented in health care system(s) could be assessed in a pilot study under this funding mechanism.

Be feasible within the one-year time frame.

Be no more than minimal risk to human subjects in accordance with Federal regulation 45 CFR §46.102(j).

When possible and if appropriate for the proposed research, be designed to qualify for a waiver or alteration of informed consent in accordance with Federal regulation 45 CFR §46.116(f)(3)(i.-v.). However, pilot studies may need to require informed consent to address certain research questions (e.g., collect gold-standard primary data to validate pragmatic measures).

Have a single, primary clinical outcome that can be collected pragmatically. The main purpose of delineating a primary outcome is to demonstrate the feasibility of collecting it pragmatically during the pilot study. The pilot study is NOT expected to be powered to demonstrate an effect of the intervention.

Have secondary outcomes evaluating implementation fidelity, usability and acceptability and, when appropriate, additional clinical outcomes.

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.

Include a qualified biostatistician on the research team.

Two optional informational webinars will be hosted to provide investigators with an overview of application details and support that the IMPACT Collaboratory can provide in assistance with proposal development (e.g., trial design, measurement, data extraction, etc.). Investigators will have the opportunity to ask questions. Pre-registration is required using the links below.

- **Wednesday, August 26, 2020 at 2:00 pm ET**: Register here for webinar.
- **Tuesday, September 8, 2020 at 4:00 pm ET**: Register here for webinar.

Informational webinars will be recorded and posted online at [https://impactcollaboratory.org/pilot-grants-program/](https://impactcollaboratory.org/pilot-grants-program/).

A set of frequently asked questions (FAQ) regarding this award is available online at [https://impactcollaboratory.org/pilot-grant-faq/](https://impactcollaboratory.org/pilot-grant-faq/).
Awards are for one year, up to $175,000 (direct costs), and are non-renewable. Only a single Principal Investigator (PI) is allowed, and only one application per individual PI is permitted per funding cycle.

**Institution**
- Eligible institutions include: 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.

**Principal Investigator**
- 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.

Interested applicants are required to submit a Letter of Intent (LOI) through the Brown University UFunds system at: https://ufunds.brown.edu/. LOIs may be submitted on a rolling basis but no later than September 18, 2020 at 5:00 PM ET. LOI decisions will be provided on or before October 23, 2020.

**Access to UFunds:** UFunds can be accessed using a Brown University email address or access can 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. In a given RFA cycle, the same account must be used to submit materials for the LOI and, if invited, full proposal phases. If you received access to UFunds in a previous RFA cycle, 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.**

**There is a competitive two-step application process:**

**STEP 1: LETTER OF INTENT**

The LOI application includes the following main elements, which can be accessed here:

- **Pilot Study description** not exceeding 2-pages (single spaced, 11 Arial font, 0.5" margins) including: A. Background/Rationale, B. Specific Aims, C. Design Overview, D. Setting (types and names of health care systems), E. Participants and Participant Identification Strategy, F. Intervention Structure
How to Apply continued

- Bibliography and References Cited (no more than 1-page; not included in the 2-page limit above) (PDF Upload)
- Completion of the LOI Pilot Study Pragmatic Design Worksheet (not included in 2-page limit above) (PDF Upload)
- Attestation in UFunds that Principal Investigator has read and/or viewed the following materials:
  - Viewed the video “Pragmatic Clinical Trials: How Do I Start?”
  - Read the RAPT Model paper OR viewed the IMPACT Collaboratory Grand Rounds on “Are you ready for a pragmatic trial? The RAPT Model and implementation considerations”
  - Read the PRECIS-2 paper
- Anticipated total direct costs (maximum of $175,000) and whether any subawards are anticipated.
  - Subawards (cannot exceed 2) are allowed. However, whenever feasible, purchase of services and consulting agreements are strongly preferred to subawards.
- PI's NIH Biosketch (PDF upload)

STEP 2: FULL PROPOSALS BY INVITATION ONLY

Applications selected for further consideration will be invited to submit a full proposal online that will be due no later than January 8, 2021 at 5:00 PM ET.

Full proposals must be submitted online through Brown University’s UFunds system: https://ufunds.brown.edu.

General Considerations:

Applications that do not demonstrate a substantially pragmatic design will be administratively triaged prior to review. Pilot studies for efficacy trials (e.g., Stage III on NIH Stage Model) will NOT be considered.

Applicants must submit the Pragmatic Pilot Study Worksheet (version for full proposals) based on the RAPT Model and PRECIS-2 framework and consider the elements of these frameworks in their research design and methods. The scientific review of the proposals will focus on the degree to which the proposed intervention is ready for an ePCT based on the RAPT Model and the design of the pilot study represents a pragmatic approach based on the PRECIS-2 framework. Please refer to the section above on priority areas for this pilot grant cycle. Applications for pilot ePCTs testing other non-pharmacological interventions in this population will also be considered.
Request for Applications

Proposals are expected to 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.

A description of how the pilot project considers issues related to health equity must be integrated into the Research Plan. Rationale should be provided about how aspects of the design (for example, selection of health care system location, target study population demographics, and/or tailoring of the intervention to different cultures) are and are not relevant to people from diverse backgrounds. While it may not be possible to address all issues within the limited scope of a pilot study, at minimum, a description should be provided about how the pilot project experience will inform the design of the future larger, Stage IV effectiveness ePCT in terms of its relevance to people from diverse backgrounds who are living with dementia and/or their care partners.

Proposal Contents:

Applicants invited to apply for full proposals will be sent a detailed Application Guide. Full proposals will include applicable PHS 398 Forms. Full proposals will follow the general format of an NIH R21 with IMPACT Collaboratory-specific additions, including:

- **Abstract (max 300 words)**
- **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, 2) Setting (sites/heath care systems), 3) Randomization scheme and masking when appropriate (not expected for all pilot studies), 4) Intervention structure, implementation protocol, and fidelity/adherence monitoring plan, 5) Data sources, elements, and collection protocol, and 6) Analytic plan. Health equity considerations must be integrated in the research design and methods.

The following design features are required:

- Non-pharmacological intervention that utilizes an embedded pragmatic trial design to target people living with AD/ADRD and/or their care partners.
- Intervention has a reasonable evidence-base demonstrating its efficacy as described in the RAPT Model paper. All interventions, including those addressing the priority areas of this grant cycle, must have a reasonable evidence-base demonstrating their efficacy.
- Evaluate an intervention that can be implemented with a high level of fidelity. More complex interventions require 'a priori' evidence that they
have successfully tested, well-developed, transportable training protocols and have been shown to produce intervention delivery with fidelity. However, how well intervention fidelity is maintained when implemented in health care system(s) could be assessed in a pilot study under this funding mechanism.

- Setting includes two or more health care systems or sites within health care systems (e.g., nursing homes, hospitals, healthcare provider practices). Randomization is NOT required.
- Be no more than minimal risk to human subjects in accordance with Federal regulation 45 CFR §46.102(j).
- Would likely qualify for a waiver or alteration of informed consent in accordance with Federal regulation 45 CFR §46.116(f)(3)(i.-v.). However, pilot studies may need to require informed consent to address certain research questions (e.g., collect gold-standard primary data to validate pragmatic measures).
- Feasible approach to participant identification/enrollment using existing electronic health care system data sources or infrastructures (e.g., electronic health record).
- Have a single, primary clinical outcome that can be collected pragmatically (i.e., from electronic health records, billing claims, or widely used electronic surveys such as Consumer Assessment of Healthcare Providers and Systems (CAHPS)). The main purpose of delineating a primary outcome is to demonstrate the feasibility of collecting it pragmatically. It is NOT expected that the pilot study is powered to demonstrate an effect of the intervention.
- Have secondary outcomes evaluating implementation fidelity, usability and acceptability and, when appropriate, additional clinical outcomes.
- 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.

  - **Milestones**: Specify milestones that are specific, measurable, and achievable by which your progress can be reviewed.
  - **Future Directions and Next Steps**: Specify how the pilot study will directly inform the development of a full-scale, Stage IV effectiveness ePCT (on the NIH Stage Model) application to the NIH or other funding sources and the anticipated timeline to apply for such funding.

- **Bibliography and References Cited**
- **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.
- **Pilot Study Pragmatic Design Worksheet** (To be provided)
- **NIH Biosketch** for the PI, the biostatistician, and each additional Key Personnel.

*Note: The research team must include a qualified biostatistician as co-investigator or consultant.*
• **Letters of Support.** Applicants must submit letter(s) of support from each participating healthcare system/site clearly stipulating that the proposal has high alignment with: 1) Priorities of the health care system in caring for people living with dementia and/or their care partners, and 2) Strong likelihood the intervention could be feasibly integrated and adopted into the clinical flow by frontline providers.

• **Acknowledgment Letter 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 any collaborating institution that will also be engaged in human subjects research activities. A template is available upon request.

• **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 one year, and the budget may not exceed $175,000 in direct costs. Indirect costs may be budgeted at your institution’s negotiated facilities and administrative rate.

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 (EHR), other nursing home, federal or state administrative data, and low- to no-cost smartphone or web interventions. It is expected that applicants will 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 during the pilot year.

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. Subawards are allowed (cannot exceed 2). Each subaward must have a separate budget and budget justification and at least one Key Personnel. Whenever feasible, purchase of services/consulting agreements are strongly 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.
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). Just-in-Time materials will be requested from applicants recommended for funding. These materials will be required within 2 weeks of notification of funding recommendation, including:

- Updated Human Subjects and Clinical Trial Information, if requested
- **sIRB Application:** The NIA requires that all research funded by the IMPACT Collaboratory (U54AG063546) be reviewed by the same sIRB. Thus, all awarded grants must be approved by the IMPACT Collaboratory’s overseeing sIRB (currently Advarra). The PI’s home institution must agree to cede to the sIRB that oversees all IMPACT Collaboratory-funded research. **Pls do not need to budget funds for the sIRB.**

- **Data and Safety Monitoring (DSM):** Pilot Studies will follow NIA DSM policies. The IMPACT Collaboratory DSMB will oversee all pilot studies. PIs of pilot study awards recommended for funding will be required to submit a full study-specific Data and Safety Monitoring Plan and Clinical Intervention Study Protocol (templates will be provided). A separate DSMB Charter is not required; an overarching IMPACT Collaboratory Charter is already in place.

The IMPACT Collaboratory Administration Core will assist the PI with the Just-in-Time materials.

Full proposals will be reviewed by three reviewers. Scientific merit ratings will consider the following:

**Fit within the Mission of the IMPACT Collaboratory**
- Does the intervention target people living with AD/ADRD and/or their care partners?
- Is the proposed pilot study at the proper stage in the NIH Stage Model for Behavioral Intervention Development? In other words, is this a pilot study in preparation for a full-scale, Stage IV effectiveness ePCT?

**Significance**
- Are the magnitude and prevalence of the problem clearly defined and important to address?
- Is it likely that the intervention has face validity and could affect said problem?

**Alignment with Stakeholder Priorities**
- How clear is the case that the problem and outcome measures are aligned with stakeholder priorities? Stakeholders may include health systems/organizations, clinicians, PLWD, or care partners.

**Investigative Team Qualifications**
- Does the team’s prior work support the likelihood that they can complete this study?
Scientific Merit
Review Criteria and Process continued

- Does the team include a biostatistician collaborator?
- Could this team competitively apply for a large-scale R01 or equivalent level grant?

**Intervention Readiness for a Pilot ePCT based on RAPT Model**
- Does the intervention have a reasonable evidence-base demonstrating efficacy?
- For complex interventions, has the intervention been successfully tested and shown to be deliverable with fidelity by the individuals who will be delivering it?
- Does a protocol accompany the intervention and is it clearly actionable?
- Could the intervention be performed 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?
- Can the intervention be implemented by real world staff and organizations?
- Can this study be completed in the allotted time?

**Design (Pragmatism and Scientific Validity) based on the PRECIS-2 Framework**
- Can the outcome measures be pragmatically collected?
- Are the strengths/limitations of outcome measures aligned with the goals of the study and the intervention?
- 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?
- Can subjects be identified through existing data/infrastructure, or if not through modest augmentation of existing systems?
- Are the study site(s) suited for obtaining generalizable information to inform a larger pragmatic trial (vs. highly specialized and unique)?
- Is the intervention flexible in delivery and adherence or must it be rigidly implemented and/or followed?
- Are inclusion and exclusion criteria broad and pragmatic in nature (e.g., looks like a usual care population)?
- Is the design feasible, rigorous, reproducible, and scientifically justified?

**Integration of Health Equity into the Research Plan**
- Is health equity integrated into the research plan?
- Does the study address an area where inequities currently occur (and is this addressed in the application)?
- Does the study seek to enhance health equity?
- Does the study address the biologic variable of sex or gender as it relates to populations and outcomes?
- Does the study consider diverse populations in its design and selection of settings?

**Human Subjects**
- Is this study minimal risk in nature?
Scientific Merit
Review Criteria and
Process continued

- Does it qualify for a waiver or partial waiver of informed consent and authorization (note: pilot studies may require consent for collecting gold-standard data to validate pragmatic measure)?

Milestones
- Are the milestones specific, measurable, and achievable?
- Are the milestones aligned with the project at hand?

Future Directions
- Through this award, if successful, does this pilot project have the potential to lead to external funding (i.e., an R01 or equivalent) for a full-scale ePCT?

Award recipients of the IMPACT Collaboratory Pilot Grants Program are expected to adhere to the following requirements:

1. Pilot studies must 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 for IMPACT pilot studies and can provide further guidance.

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.

4. The PI will meet with an assigned Pilot Study Core Executive Committee member for one hour every month throughout the lifecycle of the pilot. The assigned Executive Committee member will be available to help strategize and navigate challenges. To help ensure successful progress, the IMPACT Collaboratory’s Investigator Navigation Team will link PIs and their research team members with the IMPACT Collaboratory Cores and Teams, according to their pilot study’s needs.

5. 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.
   c. Attending webinar-based IMPACT Collaboratory Grand Rounds.

6. Submit required reports for study tracking and standardized data elements on a quarterly basis, as well as a final report at the end of the pilot study year.

7. Follow IMPACT Collaboratory invoicing guidelines.

8. Provide budget reports upon request and at the end of the pilot study year.
9. Adhere to the IMPACT Collaboratory publication policy and acknowledge sponsorship in all presentations, publications, and subsequent grants stemming from this pilot study. This information is required for reporting to NIA.

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

Questions?

For eligibility and research-related questions, please contact: Kathleen Unroe, MD, MHA, Associate Core Leader, Pilot Studies Core at IMPACTcollaboratory@hsl.harvard.edu.

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