# Request for Applications

**IMPACT Funding Opportunity Number: RFA-IMPACT-21-P03A**

## 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:

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Request for Applications – Released</td>
<td>February 1, 2021</td>
</tr>
<tr>
<td>Letter of Intent Application – Opens</td>
<td>February 8, 2021</td>
</tr>
<tr>
<td>Informational Webinars</td>
<td>February 9, 2021 @ 2 pm ET</td>
</tr>
<tr>
<td></td>
<td>February 22, 2021 @ 4 pm ET</td>
</tr>
<tr>
<td>Letters of Intent Due – Required</td>
<td>Rolling through March 5, 2021 @ 5pm ET</td>
</tr>
<tr>
<td>Letters of Intent – Notification</td>
<td>April 2, 2021</td>
</tr>
<tr>
<td>Full Proposals Due – By invitation only</td>
<td>June 18, 2021 @ 5pm ET</td>
</tr>
</tbody>
</table>
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-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 10 Cores and Teams. Learn more at http://www.impactcollaboratory.org.

Funding Opportunity Description

The IMPACT Collaboratory will consider applications for pilot ePCTs that test non-pharmacological interventions embedded in health care system(s) for people living with AD/ADRD and their care partners. All applications should make a convincing case that the pilot ePCT proposed can be scaled up to a full-scale Stage IV effectiveness ePCT as the next step. Required features of the study design are delineated on Pages 6-7. In this cycle, up to five 1-year, non-renewable pilot studies will be funded. No-cost extensions are generally not allowed, will be considered only in exceptional circumstances, will require NIA approval, and are not guaranteed.

Informational Webinars

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.

- **Tuesday, February 9, 2021 at 2:00 pm ET**: Register here for webinar.
- **Monday, February 22, 2021 at 4:00 pm ET**: Register here for webinar.

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

Frequently Asked Questions

A set of frequently asked questions (FAQ) regarding this award is available online at https://impactcollaboratory.org/pilot-grant-faq/.

Award Information

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.

Eligibility

**Institution**

- Eligible institutions include: colleges, universities, medical or nursing schools, healthcare systems or settings, 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.

How to Apply

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 March 5, 2021 at 5:00 PM ET. LOI decisions will be provided on or before April 2, 2021.

Access to UFunds: UFunds can be accessed using a Brown University email address or 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, submission of the full proposal application. 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 (access templates 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 and Implementation Strategy, and G. Outcome Definitions and Collection Methods. (PDF Upload)
- Bibliography and References Cited (no more than 1-page; not included in the 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
How to Apply continued

- Completion of the LOI Pilot Study Pragmatic Design Worksheet (not included in 2-page limit above) (PDF Upload)
- 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 June 18, 2021 at 5:00 PM ET.

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

Full Proposal Requirements

General Considerations:

Applications must be for pilot ePCTs testing non-pharmacological interventions in people living with dementia and/or their care partners.

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.

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.

Scientific review will also focus on the degree to which health equity considerations are addressed in preparation for the full-scale ePCT. Learn more about achieving health equity in the design of ePCTs. A description of how the pilot project considers issues related to health equity must both be integrated into the Research Plan and discussed in a separate 1-page section of the application (not included in page limits). Rationale should be provided about how aspects of the design address the needs of people from diverse backgrounds. If a project does not meet this expectation, provide
a compelling rationale for why the design does not address issues of health equity and how the results of the proposed pilot study might support a subsequent ePCT that does address health equity issues. For example:

- selection of health care system(s)
- target study population demographics
- tailoring of the intervention to different backgrounds, languages, cultures
- monitoring differential implementation, adherence, attrition/retention
- assessing outcomes

While it may not be possible to address all issues within the limited scope of a pilot study, at minimum, the proposal should address how the pilot project experience will inform the design of the future larger, Stage IV effectiveness ePCT in terms of its relevance to people with AD/ADRD from diverse backgrounds and/or their care partners.

Proposal Contents:

Applicants invited to apply for full proposals will be sent a detailed Application Guide. Applications for full proposals will include applicable PHS 398 Forms specified in detail in the Application Guide. Full proposals will follow the general format of an NIH R21 with IMPACT Collaboratory-specific additions, including but not limited to:

- **General Audience Summary:** Provide a consumer-friendly overview of the proposed research for people who are not trained in the sciences. This summary will be reviewed by key stakeholders (people living with dementia, care partners, and health system leaders) and will be considered when selecting applications for funding (see Stakeholder Review Criteria and Process below). The summary should be written in language understandable to the general public. Concisely describe the background, significance, target population, intervention to be studied, information to be obtained, and the potential impact of your proposed pilot study (max 500 words).

- **NIH 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, 2) Setting (sites/health 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 as described above.**
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 must have a reasonable evidence-base demonstrating their efficacy.

- Evaluate an intervention that can be implemented with a high level of fidelity.
  - Pilot ePCTs evaluating relatively simple interventions that have a greater likelihood of being implemented with fidelity are encouraged.
  - More complex, multicomponent interventions must have well-developed, transportable training and implementation protocols with ‘a priori’ evidence (e.g., from a stage 2 or 3 study) demonstrating the training programs work and the intervention can be delivered with fidelity.
    - It could be appropriate to use this pilot funding to better assess intervention fidelity when the intervention is scaled up for implementation within a health care system.

- Setting includes two or more healthcare systems or sites within healthcare systems (e.g., nursing homes, hospitals, healthcare provider practices).

- The number of sites and subjects should be maximized to provide a convincing foundation to support the feasibility, generalizability, and scalability to a full-scale ePCT as the next research step. Randomization is NOT required.

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

- When possible and if appropriate, 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.). Informed consent may be needed 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.

• Addresses biologic variable of sex as it relates to populations and outcomes.
  - 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

• Health Equity: Describe how health equity is addressed in the proposed study and will be considered in the future ePCT. Rationale should be provided about how aspects of the design address the needs of people from diverse backgrounds as described on Page 4-5. If a project does not meet this expectation, provide a compelling rationale for why the design does not address issues of health equity and how the results of the proposed pilot study might support a subsequent ePCT that does address health equity issues. This section may be up to one page in length.

• 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 (to be provided)

• Pilot Study Pragmatic Design Worksheet (to be provided)

• NIH Biosketch 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. 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.

• Appendices are NOT permitted
Full Proposal Requirements continued

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, 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 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.

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.

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.

Full proposals will be reviewed by at least two non-conflicted scientific reviewers. Scientific merit ratings will consider input from the stakeholder review in addition to 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, frontline providers, PLWD, or care partners.

Investigative Team Qualifications
- Does the team’s prior work support the likelihood that they can complete this study?
- 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 can 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
- Are health equity considerations integrated into the research plan?
- Does the study consider health equity in its selection of health care settings and target population demographics?
Scientific Merit Review Criteria and Process continued

- Does the study address an area where inequities currently occur (and is this addressed in the application)?
- Does the study include a plan for monitoring differential implementation, adherence, and attrition/retention across diverse groups?
- Does the study seek to enhance health equity?
- Does the study address the biologic variable of sex as it relates to populations and outcomes?

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? *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?

Stakeholder Review Criteria and Process

The general audience summary will be reviewed by members of the stakeholder community. Stakeholders may include people living with dementia, care partners, or other healthcare system stakeholders. Stakeholders will have familiarity with caring for people living with dementia, but may have little to no formal research or clinical training. Stakeholders will consider the following:

- How important and relevant is the intervention to people living with dementia and care partners?
- How well does this proposal address a weakness or need that people living with dementia or care partners experience in health care systems?
- How well does this study fill an important gap in dementia care, making a difference in the real-world for people living with dementia, care partners, and health care systems?

Just-in-Time

After the scientific 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. Just-in-Time materials are generally due within 2 weeks of the request.

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

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: Ab Brody, PhD, RN, FAAN, Pilot Studies Core Leader at IMPACTcollaboratory@hsl.harvard.edu.

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