PREVENTION

FUNDING OPPORTUNITY DESCRIPTION

The ADDF seeks to support precision prevention studies, combination therapy studies, and comparative effectiveness research that probe whether the use or choice of interventions may reduce the risk of Alzheimer's disease or other dementias. Studies that are not in humans will not be considered.

Clinical Populations of Interest:

- **Primary Prevention:** Primary Prevention studies include people without biomarker evidence of dementia pathology or dementia symptoms but who have specific risk factors for dementia. Relevant risk factors include: APOE4 genotype, hypertension, hyperlipidemia, type 2 diabetes mellitus, depression, obesity, hearing loss, vision loss, traumatic brain injury, postoperative delirium, postoperative cognitive dysfunction, menopause-related cognitive dysfunction, and others.
- **Secondary Prevention:** Secondary Prevention studies include people with biomarker evidence of dementia pathology who do not yet have dementia symptoms. Biomarker evidence may include PET amyloid positivity, CSF biomarkers, or blood biomarkers indicating dementia pathology. Subjects may have specific risk factors for dementia, including APOE4 genotype, hypertension, hyperlipidemia, type 2 diabetes mellitus, depression, obesity, hearing loss, vision loss, traumatic brain injury, postoperative delirium, postoperative cognitive dysfunction, menopause-related cognitive dysfunction, and others.

The Prevention RFP Supports:

1. **Precision Prevention and Risk Reduction:** In July 2024, the Lancet Commission on Dementia Prevention, Intervention and Care reported that 45% of dementia cases may be prevented by fully addressing **14 modifiable risk factors**. These modifiable risk factors include diabetes, hypertension, high LDL cholesterol, obesity, physical inactivity, depression, traumatic brain injury, hearing loss, vision loss, and others.

   Dementia risk reduction through Precision Prevention can be achieved with a targeted, mechanism-specific preventative intervention in specific populations who are at risk for developing dementia due to these risk factors and/or genetic risk factors, such as APOE4, as well as other medical conditions linked to dementia risk, including postoperative delirium/cognitive decline, menopause-related cognitive symptoms, chemotherapy-induced decline, and long COVID-19.

   The ADDF will consider funding programs that target and treat people with specific risk factors with the goal of modifying their dementia risk, as measured by outcomes related to dementia (e.g., cognitive function, neuroimaging outcomes, fluid biomarkers, and others). While interventions that are limited to lifestyle modifications alone (e.g., diet, exercise, etc.) will not be considered, studies combining a risk factor-targeted medication and/or supplement with lifestyle interventions can be considered (see "Combination Therapy Studies").

   Methods may include randomized controlled trials or epidemiologic studies. Long-term follow-up studies of successfully completed prevention clinical trials will also be considered. For clinical trial proposals, please see below detailed instructions and priorities under "Expectations and Evaluation."

2. **Combination Therapy Studies:** Combination therapies are the standard of care for the treatment and prevention of many diseases of aging. While individual interventions may have only incremental benefits, the combination of two or more drugs targeting multiple risk factors or mechanisms related to the biology of aging may exert synergistic

effects on outcomes related to dementia risk (e.g., cognitive function, neuroimaging outcomes, fluid biomarkers, and others). Randomized controlled studies testing a combination therapy of two or more agents (novel drugs, repurposed drugs, or supplements) or a combination product (containing two or more active substances within a single pharmaceutical or supplement form) will be considered. Studies combining a medication and/or supplement with lifestyle interventions will also be considered.

3. **Comparative Effectiveness Research:** For many medical conditions, physicians have a choice of prescribing clinically equivalent drugs. Some of these drugs are being investigated for repurposing to treat Alzheimer's or related dementias, due to potential disease-modifying properties that go beyond the treatment of their approved disease indication. The ADDF will consider funding research to test whether one or more clinically equivalent drugs of medical conditions is superior in protecting from Alzheimer's disease or related dementias. Priority will be given to studies that fill a gap in literature and knowledge. Methods may include randomized controlled trials or epidemiology. For clinical trial proposals, please see below detailed instructions and priorities under "Expectations and Evaluation." For epidemiological studies, those utilizing quality data from large sample sizes with detailed information on patient characteristics and relevant outcomes will be prioritized. Pooling or meta-analyzing data from multiple cohorts may also be appropriate, such as through leveraging the **Cohorts for Alzheimer's Prevention Action (CAPA)**.

Type of therapy: Novel, repurposed, and repositioned drugs, as well as natural products, supplements, and devices will be considered. The ADDF prioritizes studies of interventions with composition of matter intellectual property (IP), concrete strategies to develop novel IP, and/or a promising commercial path forward. Studies combining medications and/or supplements with lifestyle interventions will be considered. Lifestyle interventions (e.g., non-pharmacologic interventions, such as diet, meditation, and exercise) that are not combined with a study drug will not be considered.

Drug mechanisms or modes of action: Mechanisms and modes of action that target dementia risk reduction or biology of aging are considered high priority. These include, but are not limited to:

- Metabolic and mitochondrial function
- Vascular function
- Inflammation
- Neuroprotection
- Epigenetics
- Proteostatsis
- Synaptic activity and neurotransmitters
- Other mechanisms and modes of action related to the biology of aging (e.g. senescent cells)
- Other novel mechanisms or modes of action that are supported by compelling evidence demonstrating a rational biological connection to dementia risk or onset
- **Please note:** Anti-amyloid approaches (e.g., anti-amyloid aggregation, beta-amyloid vaccines, beta- or gamma-secretase inhibitors) and cholinesterase inhibitor proposals will not be considered

UPCOMING DEADLINES

ELIGIBILITY

AWARD INFORMATION

Award Amount

- Up to $5,000,000 for clinical trials based on stage and scope of research
- For studies requiring additional support, co-funding from other funding agencies or investors is encouraged
- Payment structure will be negotiated and based on milestone achievements and recruitment

Average Duration

Multi-year

Allowable costs

Only direct costs are allowed. Please review our **Funding Policies**

EXPECTATIONS AND EVALUATION

APPLICATION SUBMISSIONS

Review the **Application Instructions** for steps on applying.

LOG IN OR CREATE ACCOUNT

For inquiries, please contact:

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Alzheimer's Drug Discovery Foundation

A GuideStar-Rated Charity

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