Alzheimer's and Related Dementias Research: Tracking and Future Plans

NAPA Advisory Council Meeting

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IADRP Project Update: By the Numbers

Currently includes **35+** public, private and international funding organizations in **11** countries

Captures **7000+** unique basic, translational and health services research projects

Conducted by **4000+** researchers across**1000+** institutions

Represents **$4.7 billion+** in funding

Next Steps

- **CADRO** —
  - Collecting feedback for updating the CADRO.

- **New Federal Partners** —
  - The Federal Reporter website (https://federalreporter.nih.gov/) provides easier access to query research sponsored by other federal agencies.
  - NIA has recently identified small portfolios of AD and ADRD research supported by NASA, EPA and the Department of Agriculture.

Next Steps, cont'd

- **AD Research Milestone Database** —
  - ADRD research milestones will be added to the database and to IADRP.

- **EU Joint Programme – Neurodegenerative Diseases (JPND)** —
  - NIH is participating in the upcoming EU mapping exercise that invites 20+ countries to submit their recently funded neurodegenerative research (notably AD and ADRD).
  - JPND has volunteered to ask participating countries if the results of this exercise can also be shared, coded and uploaded into IADRP.

Visit IADRP @ http://iadrp.nia.nih.gov/

Tracking Alzheimer's Disease Research Implementation Milestones

AD Research Implementation Milestone Database

Enables users to search and track progress in funding research to address the 80+ AD Research Implementation Milestones

https://www.nia.nih.gov/alzheimers/milestones

AD Research Implementation Milestone Database

Most milestones are linked to NIH funding opportunity announcements (FOAs), special, initiatives and related activities. Users will soon be able to link to specific projects supported under targeted FOAs as they are funded.

https://www.nia.nih.gov/alzheimers/milestones

AD Research Implementation Milestone Database

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Milestone 5.A

Initiate first in human, phase I drug trials for therapeutic agents against at least 6 existing therapeutic targets. In addition to testing for safety, these trials will include assessment of target engagement.

Success Criteria:
Completion of 12, Phase I drug trials for agents against 6 existing therapeutic targets.

Time Required:
2017 to 2023

AD Research Implementation Area:
Drug Development - Existing Targets

CADRO Category:
C. Translational Research and Clinical Intervention

Activities, Funding Initiatives, and Resources:
NIH PAR-14-089: Alzheimer's Disease Pilot Clinical Trials (R01)
NIH PAR-16-365: Pilot Clincal Trials for the Spectrum of Alzheimer's Disease & Predicting Progression (R01)

Related Funded Projects (IADRP):
Category C. Translational Research and Clinical Interventions - 5. Early-stage Clinical Drug Development (Phase I and II Clinical

Relevant Recommendation(s):
2012 Summit Recommendations: 3A, 3B, 3F, and 5E

Back

Common Alzheimer's Disease Research Ontology (CADRO) codes link milestones to related funded projects and other domestic and international funding organizations currently captured in IADRP

https://www.nia.nih.gov/alzheimers/milestones

Tracking Progress – Ex.: Population Studies

Milestone 1.D: Develop state-of-the-art protocol for assessing dementia on large nationally representative samples that (a) includes racial/ethnic subsamples large enough to support disparities research and (b) is adaptable for use in comparable studies around the world [2015 AD Summit: 1B, 1.D, 3C, 3D, and 4B].

Success Criteria	Targeted Funding Opportunity Announcements (FOAs) and Special Initiatives (SIs)	Assigned CADRO Codes	Number of Funding Organizations (IADRP Partners)
Archive and share data for use by the research community. Update national estimates of the prevalence and incidence of dementia and cognitive impairment as well as address important questions about the epidemiology and population impact of dementia. Repeat national estimates in 2021 to measure trend in dementia prevalence Support research projects comparing international differences to identify potential risk and protective factors. Support research on health disparities by racial/ethnic groups.	**NIH PAR-15-349: Health Disparities and Alzheimer's Disease (R01)** NIH PAR-15-350: Emerging Directions for Addressing Health Disparities in Alzheimer's Disease (R03) NIH RFA-AG-15-015: Enhancing Cross-National Research within the Health and Retirement Study Family of Studies (R01) NIH NOT-AG-14-022: NIA Population Study of Dementia in the Health and Retirement Study	Category D. Epidemiology – 4. Multimodal Risk Factors	16

From the milestone database, CADRO-coded milestones are linked to funded projects from multiple IADRP partners.

From IADRP, users can further filter results by
- Themes, such as **target population**
- Year
- Funding Organization

Example -
NIH PAR-15-349: Health Disparities and Alzheimer's Disease (R01)

The milestone database will soon be linked directly to **NIH Reporter** to view specific projects as they are funded under targeted FOAs along with links and access to related **publications, patents and clinical trials**

Tracking Progress – Ex.: Drug Dev.: Existing Targets

Milestone 5.B: Initiate phase II (proof of concept) drug trials for agents against 3-6 currently known therapeutic targets. Of these at least 2 will be for targets involved in at-risk asymptomatic individuals (e.g. FAD or ApoE4 carriers, Down syndrome, amyloid positive, type II diabetes etc.) These trials will be designed to provide or confirm proof of mechanism and/or evidence of target engagement for the therapeutic agent being tested. [2012 AD Summit: 3A, 3B, 3F, and 5E]

Success Criteria	Targeted Funding Opportunity Announcements (FOAs) and Special Initiatives	Assigned CADRO Codes	Number of Funding Organizations (IADRP Partners)
Completion of 3-6 phase II drug trials for agents against currently known targets, providing conclusive evidence of therapeutic mechanism/target engagement.	NIH Accelerating Medicines Partnership - AD Biomarkers Consortium **NIH PAR-16-365: Pilot Clinical Trials for the Spectrum of Alzheimer's Disease & Predicting Progression (R01)** NIH PAR-14-089: Alzheimer's Disease Pilot Clinical Trials (R01) NIH RFA-AG-13-015: Alzheimer's Disease Prevention Trials (R01) NIH RFA-AG-13-001: Alzheimer's Disease Cooperative Study (U19)	Category C. Translational Research and Clinical Interventions - 5. Early-stage Clinical Drug Development (Phase I and II Clinical Trials)	10

From IADRP, users can further filter results by
- Themes, such as **therapeutic target**
- Year
- Funding Organization

Example -
NIH PAR-16-365:
Pilot Clinical Trials
for the Spectrum of
Alzheimer's Disease
& Predicting
Progression (R01)

Tracking Progress –
Ex.: Care and Caregiver Support

Milestone 13.B: Launch research programs to develop and validate assessments of the psychological, financial, and physical health impact of caregiving. [2015 AD Summit 4B, 4D, 4H]			
Success Criteria	**Targeted Funding Opportunity Announcements (FOAs) and Special Initiatives**	**Assigned CADRO Codes**	**Number of Funding Organizations (IADRP Partners)**
Identification and validation of assessments suitable for use in a range of research contexts including observational and interventional studies and large population-based surveys. Identification and validation of at least one sensitive and robust measure for the detection of the earliest manifestations of caregiving burden and for monitoring its long-term consequences.	**NIH PAR-15-348: Research on Informal and Formal Caregiving for Alzheimer's Disease (R01)** NIH PAR-15-351: Research on Informal and Formal Caregiving for Alzheimer's Disease (R21)	**Category E. Care, Support and Health Economics of Alzheimer's Disease -** **3. Caregiver Support -** **e. Assessment and Metrics**	15

From IADRP, users can further filter results by
- Themes, such as **type of caregiver research**
- Year
- Funding Organization

Example -
NIH PAR-15-348: Research on Informal and Formal Caregiving for Alzheimer's Disease (R01)

AD Research Implementation Milestone Database

- Database will soon include the ADRD Research Milestones (once approved)

- We encourage other organizations to also post (and link) their funding announcements and activities
  - Organizations can identify strategic areas in which to invest and collaborate
  - Researchers can assess funding opportunities across multiple funders

https://www.nia.nih.gov/alzheimers/milestones

New AD Funding Opportunities

New Alzheimer's Concepts

Resource Leveraging

- Leveraging Existing Cohort Studies to Clarify Risk and Protective Factors for Alzheimer's disease and related dementias

- Validation of NIH Toolbox Instruments for Tracking and Diagnosis of MCI and early AD, and for Extension of Assessment in the Oldest Old

Caregiving and Clinical Care

- Development of Socially Assistive Robots to Engage Persons with ADRD and their Caregivers

- Pragmatic Trials for Dementia Care in Long Term Services and Support (LTSS) Settings

- Improving Quality of Care and Quality of Life for Persons with Alzheimer's Disease and Related Dementia at the End of Life

- Tools for Clinical Care and Management of Alzheimer's disease and its comorbidities

New Alzheimer's Concepts

Caregiving and Clinical Care Cont'd

- Clarifying the relationship between delirium and Alzheimer's disease and related dementias

- NIA Small Business Opportunities to Advance Alzheimer's Disease Research

- Multimorbidity in Alzheimer's Disease Impacts Choice of Ancillary Treatments

Translation

- Revision Applications to Enhance the Target and Biomarker Discovery Efforts of the AMP-AD and M^{2}OVE-AD Consortia

New Alzheimer's Concepts

Basic Research

- Understanding the Effects of APOE2 on the Interaction between Aging and Alzheimer's Disease.
- Understanding the Impact of Sex Differences on the Phenotypes of AD Risk and Responsiveness to Therapy
- Role of Exosomes in Alzheimer's Disease
- Commonalities, and Interactions Between Neurodegenerative Diseases
- Human Cell Reprogramming for Functional Genetics of Alzheimer's Disease
- Brain lymphatic system in aging and Alzheimer's disease
- Mechanisms of Selective Neuronal Vulnerability in Alzheimer's Disease

New Alzheimer's Concepts

Basic Research Cont'd

- Systems biology approaches to Alzheimer's Disease using Non-Mammalian Models
- The role of aging metabolic changes in Alzheimer's disease (AD)
- The Role of Peripheral Proteostasis on Brain Aging and on Alzheimer's Disease
- Comparative Biology of Neurodegeneration
- Dynamic interactions between Peripheral Systems and the Brain in Aging and in Alzheimer's Disease
- Complex Biology of Resilience from Alzheimer's

New Alzheimer's Concepts

Training

- Alzheimer's Disease Research Revision Awards to Institutional Training Grants

- Institutional Training Programs to Advance Translational Research for Alzheimer's Disease and AD Related Dementias

- Research Career Enhancement Award to Advance Therapy Development for AD and Related Dementias

Ways to Stay Informed and Connected

➤Visit

https://www.nia.nih.gov/research/funding

to search all active NIA funding opportunities

➤Subscribe to our blog to stay up to date with the latest from NIA
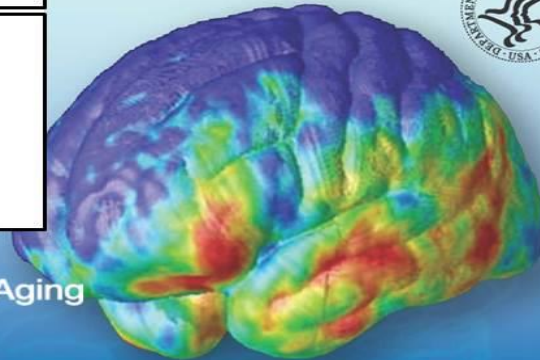
https://www.nia.nih.gov/research/blog

Save the Dates!

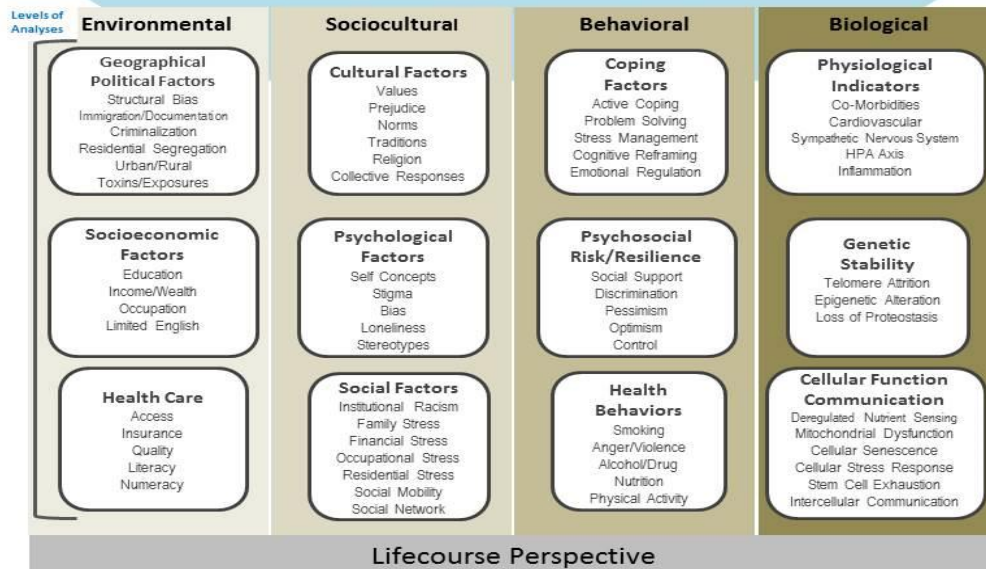AD Care and Services Research Summit **October 16-17, 2017** Bethesda, MD

Alzheimer's Disease Research Summit (III) **March 1-2, 2018** Bethesda, MD

NIH National Institute on Aging
Turning Discovery Into Health

Determinants of Disparities in Health and Life Expectancy

FUNDAMENTAL FACTORS: Ethnicity, Gender, Age, Race, Identity*

Levels of Analyses	Environmental	Sociocultural	Behavioral	Biological
	Geographical Political Factors Structural Bias Immigration/Documentation Criminalization Residential Segregation Urban/Rural Toxins/Exposures	**Cultural Factors** Values Prejudice Norms Traditions Religion Collective Responses	**Coping Factors** Active Coping Problem Solving Stress Management Cognitive Reframing Emotional Regulation	**Physiological Indicators** Co-Morbidities Cardiovascular Sympathetic Nervous System HPA Axis Inflammation
	Socioeconomic Factors Education Income/Wealth Occupation Limited English	**Psychological Factors** Self Concepts Stigma Bias Loneliness Stereotypes	**Psychosocial Risk/Resilience** Social Support Discrimination Pessimism Optimism Control	**Genetic Stability** Telomere Attrition Epigenetic Alteration Loss of Proteostasis
	Health Care Access Insurance Quality Literacy Numeracy	**Social Factors** Institutional Racism Family Stress Financial Stress Occupational Stress Residential Stress Social Mobility Social Network	**Health Behaviors** Smoking Anger/Violence Alcohol/Drug Nutrition Physical Activity	**Cellular Function Communication** Deregulated Nutrient Sensing Mitochondrial Dysfunction Cellular Senescence Cellular Stress Response Stem Cell Exhaustion Intercellular Communication

Lifecourse Perspective

*Gender, Ethnic, Racial and Sexual Identity

Adapted from: Lazarus & Folkman (1984); Pearlin (1989); Link and Phelan (1995); Jones (1997); Geronimus (2000); Williams & Collins (2001); Adler (2010); McEwen (2010); Lopez-Otin (2013)