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Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
Category A. Molecular Pathogenesis and Physiology of Alzheimer's Disease			
2016-2018	Research on Disease Mechanisms	Create new research programs that use data-driven, systems-based approaches to integrate the study of fundamental biology of aging with neurobiology of aging and research on AD and related dementias to gain a deeper understanding of the complex biology and integrative physiology of healthy and pathologic brain aging. [2015 AD Summit: 1D, 2A, 3E, 3F, 3I, 3H, and 3J]	Launch at least six cross-disciplinary projects that use data-driven, systems-based approaches to integrate AD research with the study of the fundamental biology of aging/ neurobiology of aging.
2016-2018	Research on Disease Mechanisms	Establish new research programs that employ data-driven, systems-based approaches to understand the interaction between peripheral systems (in particular: immune, metabolic, microbiome) and the brain and the impact of this interaction on brain aging and neurodegeneration. These efforts should include characterizing the extent to which molecular (epigenomic, transcriptomic, and metabolomic) variation identified in peripheral tissues can be used as a proxy for inter-individual variation in the trajectories of brain aging and AD. [2015 AD Summit: 1D, 2A, 3E, 3F, 3I, 3H, and 3J]	Launch at least six cross-disciplinary projects that use data-driven, systems-based approaches aimed at understanding the interaction between peripheral organ systems and the brain and the impact of this interaction on brain aging and neurodegeneration.
2016-2018	Research on Disease Mechanisms	Create research programs on epigenetics to understand how genetic and environmental factors interact across the lifespan to influence brain aging and risk for disease and to identify potential targets for treatment and prevention. [2015 AD Summit: 1D, 2A, 3E, 3F, 3I, 3H, and 3J]	Launch at least six new projects exploring epigenetic mechanisms that underlie the heterogeneity of AD and related dementias.
2016-2018	Research on Disease Mechanisms	Create research programs in basic, translational, and clinical research aimed at comprehensive understanding of the impact of sex differences on the trajectories of brain aging and disease, phenotypes of AD risk, and responsiveness to treatment. [2015 AD Summit: 1A]	Launch at least 12 new projects exploring the impact of sex differences on the trajectories of brain aging and disease, phenotypes of AD risk, and responsiveness to treatment.

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2016-2018	Research on Disease Mechanisms	Create cross-disciplinary research programs aimed at understanding the integrative physiology of APOE and its pharmacogenetic effects on various pharmacological and nonpharmacological interventions. [2015 AD Summit: 3H]	Launch at least 10 cross-disciplinary projects aimed at developing a deeper understanding of the protective and risk factor properties of APOE and its pharmacogenetic effects on various pharmacological and nonpharmacological interventions. Of these, at least three projects should be focused on understanding the mechanisms of risk reduction by APOE2.
2016-2018	Research on Disease Mechanisms	Create new research programs aimed at understanding the integrative physiology of circadian rhythms and sleep and its impact on brain aging and the risk of AD and related dementias. [2015 AD Summit: 3J]	Launch at least six new projects focused on understanding the short-term and long-term consequences of disrupted/optimized circadian rhythms and sleep on brain aging and dementia, across all levels of biological complexity.
2013-2020	Drug Development—Novel Targets	Establish a consortium of genetics and genomics experts to develop and execute a large-scale sequencing project to analyze the genomes of a large number of well-characterized individuals, including multi-ethnic subjects, using next-generation sequencing approaches; identify a broad range of AD risk and protective gene variants in subjects with late-onset AD (LOAD). These efforts should incorporate diverse sample sets (including racial/ethnic groups, the oldest old, and other well-characterized individuals from epidemiological/observational studies) and include replication studies and data harmonization. [2012 AD Summit]	Identification of new risk and protective alleles for LOAD that lead to the identification of at least one novel therapeutic approach, drug target, or pathway for prevention.
2016-2020	Drug Development—Novel Targets	Create new research programs that use data-driven, network biology approaches aimed at understanding the (epi)genetics and complex biology of cognitive resilience in individuals with high genetic risk for dementia and in individuals with exceptional longevity. [2015 AD Summit: 2B and 3G]	Launch at least six research projects aimed at identifying molecular networks causally linked to cognitive resilience as potential therapeutic targets for disease prevention; these efforts should support the preclinical validation of the identified targets.

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Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2020	Nonpharmacologic Interventions	Initiate interdisciplinary research programs that integrate epidemiological and mechanistic research, including cutting-edge systems biology approaches to gain an in-depth understanding of the mechanisms by which various nonpharmacological interventions impact brain health and the course of AD. [2012 AD Summit: 5B, 5C, 5D, and 5F]	Identification of at least three new therapeutic targets for neuroprotection based on knowledge of mechanisms mediating the impact of nonpharmacological interventions of brain health in aging and AD. Preclinical proof-of-concept for at least three types of nonpharmacological interventions that can inform clinical trial design.
Category B. Diagnosis, Assessment, and Disease Monitoring			
2016-2018	Biomarkers	Develop and validate translatable biomarkers for their use in preclinical and clinical drug development. These efforts should include the development of pharmacodynamic biomarkers of target engagement, biomarkers of incipient disease (ocular, olfactory), and biomarkers for detection and tracking of synaptic dysfunction. [2015 AD Summit: 1I and 2I]	Develop and validate at least 12 translatable biomarkers for use in preclinical and clinical drug development.
2014-2018	Biomarkers	Initiate synthesis and testing of novel PET ligands and develop and test novel CSF/blood biomarkers for assessment of disease related to pathological burdens, such as tau, inflammation, and synaptic dysfunction. [2012 AD Summit: 1E]	Development and testing of three to five novel PET ligands and/or CSF/blood biomarkers for assessment of AD pathology.
2014-2018	Biomarkers	Initiate development of imaging and/or fluid biomarkers to demonstrate target engagement for five novel therapeutic targets for AD. [2012 AD Summit: 1E]	Identification of three imaging and/or fluid biomarkers for which there is proof of engagement of novel therapeutic targets.
2015-2019	Biomarkers	Initiate studies to develop minimally invasive biomarkers for detection of cerebral amyloidosis and other AD pathophysiology. [2012 AD Summit: 1F and 1G]	Development and testing of five biomarkers that utilize biofluids or other minimally invasive imaging, electrophysiological recording, or other methodologies to assess the burden of AD pathophysiology that could be used in community-based and epidemiological studies of AD.

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Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2014-2018	Biomarkers	Launch research programs to develop and validate sensitive neuropsychological and behavioral assessment measures to detect and track the earliest clinical manifestations of AD. [2012 AD Summit: 3D]	Development of at least one sensitive neuropsychological assessment measure that has been validated for the detection or tracking of the earliest clinical manifestations of AD.
2017-2019	Enabling Technologies and Disease Monitoring	Develop research programs aimed at evaluating a variety of technologies for in-place monitoring of individuals at all stages of disease to capture various types of patient-relevant data and caregiver-related outcomes (i.e., daily physical function, home safety, quality of life). [2015 AD Summit: 4A]	Launch at least one large multisite research platform for evaluating in-place monitoring technology and utilize the platform to evaluate at least six innovative new technologies focused on dementia assessment and care in various dwelling environments (e.g., rural, urban, assisted living, apartment dwelling, single family).
2016-2018	Enabling Technologies and Disease Monitoring	Embed wearable technologies as well as pervasive computing approaches in existing large community-based, longitudinal cohort studies as well as clinical trials to enable continuous capture of various types of participant relevant data. [2015 AD Summit: 4C, 4F, 4G, 4I]	Introduce the use of mobile/pervasive computing technologies in at least three existing longitudinal cohort studies–each study should be conducted in a different at-risk population. The studies should be designed to allow the collection of raw sensor data to enable pooling of data across studies. The sensor collection apps and data collection server infrastructure used in these studies should be built and released as open source tools.
2016-2018	Enabling Technologies and Disease Monitoring	Build cross-disciplinary teams that bring together clinical researchers with experts in mathematics, human factors design, and software engineering to develop innovative monitoring technologies for diverse aging populations. [2015 AD Summit: 4D]	Initiate at least 10 research projects focused on developing new disease-monitoring technologies.
Category C. Translational Research and Clinical Interventions			
2017-2023	Drug Development—Existing Targets	Initiate first in human Phase I drug trials for therapeutic agents against at least six existing therapeutic targets. In addition to testing for safety, these trials will include assessment of target engagement. [2012 AD Summit: 3A, 3B, 3F, and 5E]	Completion of 12 Phase I drug trials for agents against six existing therapeutic targets.

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Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2015-2018	Drug Development—Existing Targets	Initiate Phase II (proof-of-concept) drug trials for agents against three to six currently known therapeutic targets. Of these, at least two will be for targets involved in at-risk asymptomatic individuals (e.g., FAD or ApoE4 carriers, Down syndrome, amyloid positive, type II diabetes). 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]	Completion of three to six Phase II drug trials for agents against currently known targets, providing conclusive evidence of therapeutic mechanism/target engagement.
2017-2021	Drug Development—Existing Targets	Initiate Phase III drug trials for agents against at least 3 currently known therapeutic targets. Of these, at least one trial will be asymptomatic, at-risk populations. These trials will incorporate a combination of biomarkers (fluid and imaging) and cognitive measures as outcomes, and include collection of DNA and other bio-samples for interrogation of responsiveness. [2012 AD Summit: 3A, 3B, 3F, and 5E]	Comprehensive success/failure analysis of data from at least three Phase III trials.
2014-2020	Drug Development—Novel Targets	Identify, characterize, and complete early validation for at least six novel therapeutic targets for AD (a minimum of three targets for presymptomatic and early-stage disease and a minimum of three for advanced disease). These efforts should include therapeutic targets for the neuropsychiatric and behavioral disturbances in AD. [2012 AD Summit: 1A, 1B, 1D, and 5A]	Validation based on availability of the following for each novel target: a systems-level understanding of the gene, protein and metabolic networks within which they operate, one or more cell-based/animal models that are freely available to the research community, a quantitative assessment of the integrative response to the modulation of the target in one or more model organisms, and identification of pharmacodynamic biomarker(s) for target engagement.
2017-2023	Drug Development—Novel Targets	Initiate drug discovery efforts to develop novel therapeutic agents against at least six novel therapeutic targets (a minimum of three targets for presymptomatic and early-stage disease and a minimum of three for advanced disease). [2012 AD Summit: 1A, 1B, 1D, and 5A]	Complete preclinical development, through IND filing, of at least 12 therapeutic agents against at least three novel targets (at least one novel target should be for presymptomatic disease).
2017-2023	Drug Development—Novel Targets	Initiate first in human Phase I drug trials for therapeutic agents against at least six novel therapeutic targets. In addition to safety, these trials will provide evidence of target engagement. [2012 Summit: 3A, 3B, 3F, and 5E]	Completion of 12 Phase I drug trials for agents against six novel targets, providing conclusive evidence of safety and target engagement.

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Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2018	Drug Repurposing and Combination Therapy Development	Expand existing and develop new systems biology and systems pharmacology research programs to build multiscale models of disease that will lead to the identification of networks/sub-networks as drug targets and readouts of therapeutic activity and advance the validation of existing and novel targets, rational drug repositioning, and rational development of combination therapy. [2015 AD Summit: 1E, 2D, 2E, 2F, and 2G.]	Launch at least six cross-disciplinary research programs that bring together experts in translational bioinformatics, computational biology, genetics, epidemiology, drug discovery, and clinical research to develop a predictive model of the disease. Efforts should support: • development of computational tools and infrastructure to allow basic and clinical researchers to query model in silico and validate it by using it for patient stratification, predictions of efficacy, on- and off-target adverse effects. • identification of quantitative methods to access synergy between (1) multiple therapeutic agents and (2) pharmacological/ nonpharmacological perturbations. • development of phenotypic screens (in cell-based and/or animal models) to advance rational drug repositioning and data-driven development of combination therapy based on the ability of individual or combinations of therapeutic agents to shift the network state away from disease.

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Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2018	Drug Repurposing and Combination Therapy Development	Initiate research programs for translational bioinformatics and network pharmacology to support rational drug repositioning and combination therapy from discovery through clinical development. [2012 AD Summit: 4A, 4B, 4C, and 4D]	Identification of at least six existing drugs suitable for repurposing and/or combination therapy for AD prevention or treatment. The drugs selected for repurposing or combination therapy will be prioritized based on: • evidence that they modulate disease-relevant pathways/networks gained from computational and empirical approaches. • preclinical proof-of-efficacy in a relevant model system. • availability of biomarkers to monitor target engagement in humans. • sufficient evidence of safety for the intended target population.
2017-2021	Nonpharmacologic Interventions	Initiate clinical trials for at least three nonpharmacological interventions aimed at AD treatment and/or prevention. Of these, at least one trial will be a pivotal Phase III trial. [2012 AD Summit: 5B, 5C, 5D, and 5F]	Completion of at least two Phase II trials for nonpharmacological interventions aimed at AD treatment and/or prevention. Successful trials will provide conclusive evidence of therapeutic mechanism. Comprehensive success/failure analysis of data from at least one Phase III trial.
2016-2017	Trial Design	Convene a meeting that brings together epidemiologists, clinical trialists, clinical practitioners, representatives from industry, and patient advocates from diverse communities to formulate guidelines for defining clinically significant outcomes and methods for comprehensive analysis and interpretation of trial data. [2015 AD Summit: 3K]	Develop guidelines for defining clinically significant outcomes and methods for comprehensive analysis and interpretation of trial data.

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2017-2019	Trial Design	Create new research programs to implement innovative trial designs. [2015 AD Summit: 3K]	Launch at least six clinical trials using innovative trial designs such as adaptive trial design, functional challenge studies, pragmatic clinical trials, population-based cohort designs, and clinical trial/population-based cohort hybrid designs. At least three of these should stratify participant risk groups using dense "omics" and gene-environment interaction profiles.
2016-2018	Recruitment and Citizen Engagement	Provide supplemental funding for clinical research studies to build diverse community partnerships needed to increase research participation. [2015 AD Summit: 5A, 5B, 5C, 5D]	Provide supplemental funding for at least 20 clinical research studies aimed at building partnerships with diverse communities.
2016-2017	Recruitment and Citizen Engagement	Create synergies between federally funded programs such as PCORI and CTSAs to make community involvement less expensive and to learn from the various experiments of community engagement. [2015 AD Summit: 5E]	Convene an advisory meeting with representatives from relevant federally funded programs to develop strategies for enhancing community involvement in dementia research on the national level.
2016-2018	Recruitment and Citizen Engagement	Provide supplemental support for clinical research on AD and related dementias to overcome the major logistical barriers to participation, including bringing clinical trials to the participants' living environments. [2015 AD Summit: 5B]	Provide supplemental funding for at least 20 clinical research studies aimed at overcoming the major logistical barriers to participation.
2017-2019	Recruitment and Citizen Engagement	Pilot the use of electronic consent which provides participants an option for broad sharing of de-identified data in various types of clinical research on AD and related dementias. [2015 AD Summit: 1C, 5H]	Launch at least three clinical research studies with electronic consenting methods that give participants the option for broad sharing of de-identified data.
2016-2018	Public-Private Partnerships	Develop partnerships that expand the precompetitive space through clinical proof of mechanism to accelerate translational learning and to fill critical knowledge gaps in understanding the network biology of drug targets and drug-target interactions. [2015 AD Summit: 6E and 6F]	Establish at least one precompetitive partnership to validate the therapeutic targets that will be delivered by the Accelerating Medicines Partnership for AD (AMP-AD), as well as other pioneer targets, through clinical proof of mechanism/proof of concept.

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Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2017	Public-Private Partnerships	Develop a partnership among key stakeholders to implement the sharing of all data and biosamples from preclinical and clinical studies to enable the adoption of formal failure analysis across the drug development continuum. The partnership should provide resources for data hosting and curation. [2015 AD Summit: 2K]	Convene a meeting that brings together experts from industry and academia, regulatory and funding agencies, bioethics experts, patients, and patient advocates to establish the framework for a multi-stakeholder partnership aimed at enabling the sharing of all data and biosamples from preclinical and clinical studies.
Category D. Epidemiology			
2016-2018	Population Studies	Create research programs aimed at extensive molecular endophenotyping of existing, at-risk cohorts from longitudinal studies that are genetically, epigenetically, or otherwise at risk (e.g., due to cerebrovascular, metabolic, or neuroinflammatory compromise), as well cohorts and/or individuals who resist disease despite high genetic risk (e.g., Down syndrome, ApoE 4 homozygous, FAD mutation carriers). [2015 AD Summit: 1A, 2A, 2B, and 3A]. This is consistent with the longer-term goals of the Precision Medicine Initiative.	Initiate at least three programs which include dense molecular phenotyping (genomic, epigenomic, proteomic, metabolomics, microbiome) and incorporate the collection of nontraditional data modalities using wearable sensors and mobile health technologies as dimensions of health and disease. These programs should include big-data infrastructure resources to ensure that the data are made available as a public resource and support for collection, storage, and rapid distribution of biosamples including brain tissue.
2016-2018	Population Studies	Incorporate environmental context in human studies (e.g., epidemiological cohorts) and in clinical trials, such as biomarkers of environmental exposure and geocodes, to assess personal and shared environmental contribution to AD pathogenesis and response to therapy. [2015 AD Summit: 3B and 3D]	Provide supplemental funding to at least six clinical research studies to explore the impact of environmental exposure on AD pathogenesis and/or response to therapy.

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Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2018	Population Studies	Create new cohorts to accelerate the identification of genomic variants and other risk and protective factors contributing to the heterogeneity and multifactorial etiology of dementia. [2015 AD Summit: 1B and 3C]. This is consistent with the longer-term goals of the Precision Medicine Initiative.	Establish at least three new cohorts for extensive endophenotyping with participants of African, Native American, Asian, and mixed ancestry, e.g., Latinos as well as younger cohorts (midlife and younger participants). The phenotyping should include cognitive, behavioral, imaging, exposome measurements, multidimensional "omics" data, and multiple types of physiologic measurements that can be used for systems biology and gene-environment interaction studies. These programs should include big-data infrastructure resources to ensure that the data are made available as a public resource and support for collection, storage, and rapid distribution of biosamples including brain tissue.
2015-2018	Recruitment and Citizen Engagement	Increase awareness of large-scale registries that encompass the spectrum of the disease from healthy and at-risk asymptomatic to symptomatic individuals from early midlife to late life, willing to participate in clinical research aimed at AD prevention and treatment.	A central repository of AD related registries and cohorts created and publicized.
Category E. Care and Caregiver Support			
2017-2019	Research on Care and Caregiver Support	Launch research programs to develop and validate assessments of the psychological, financial, and physical health impact of caregiving. [2015 AD Summit: 4B, 4D, 4H]	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.

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2017-2019	Research on Care and Caregiver Support	Establish data infrastructure for the study of dementia caregiving. [2015 AD Summit: 4.B, 4.E, 4.F]	Identification of existing cohorts of nationally representative and cross-national samples and determination of the need for data collection in new cohorts. Establishment of standard protocols for harmonizable survey data collection and data infrastructure. Supplement existing national panel studies to collect data on formal and informal caregiving. Support archiving of data from population-based and intervention studies with appropriate content related to informal and formal caregiving.
2016-2020	Research on Care and Caregiver Support	Partner with community organizations to support a research agenda that will lead to the development of a national framework for dementia caregiver support in the community. [2015 AD Summit: 4K, 4I, 5B, 5C, 5D, and 5F]	Support research projects that will inform the design of cost-effective, community-based, informal caregiving interventions tools that address unmet psychological and physical health needs of caregivers and which ensure a safe home environment, to enable individuals with AD to remain in their homes for as long as possible. Identify or develop effective in-home, in-community, off-the-shelf intervention programs and tools to support caregiver well-being and health that aid in the integration of formal and informal care.

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2017-2019	Research on Care and Caregiver Support	Partner with insurers (including CMS) to conduct comparative effectiveness research to determine which existing evidence-based interventions to reduce burden in caregivers are effective if implemented as an adjunct to primary care in nonresearch settings across the full care continuum, including patients in a variety of settings (home, nursing home, assisted living, hospice). [2015 AD Summit: 5B, 5C, 5D, and 5F]	Conduct cluster randomized trials comparing interventions stemming from contact with caregiver dyads in primary care, with insurers supporting intervention costs and enrolled participants agreeing to allow researchers to link the data obtained in the study with billing data, to allow researchers to follow longer-range health effects of caregiving and effective interventions. Identification of programs that work best for different stages of the care continuum. Identification of which programs work best with different population subgroups (racial, ethnic, geographic, socioeconomic). Development of new models of care that can be adopted by insurers.
2015-2019	Research on Care and Caregiver Support	Leverage existing palliative care research networks to develop and advance interventions for palliative and hospice care of persons with advanced dementia and their families. [2012 AD Summit: 5E, 5G; 2015 AD Summit: 2J, 4B, 4D, 4H, 4K, 4L, and 6A.	Launch cross-disciplinary projects to design and test clinical interventions and models of palliative and hospice care for persons with advanced dementia and their families. These programs should address needs across diverse cultural subgroups, care settings, and rural/urban locales.
Category F. Research Resources			
2016-2020	Data Sharing and Reproducibility	Provide resources to make datasets from existing and legacy clinical research studies on AD and related dementias widely accessible and ensure their adequate annotation and curation to maximize their usability.	Provide funding to make datasets from publicly funded clinical research studies on AD and related dementias, annotated, curated, and made widely available via web-based resources.
2016-2019	Data Sharing and Reproducibility	Provide support to establish/improve the interoperability among relevant biomedical data repositories.	Provide supplemental funding to establish/improve the interoperability among relevant biomedical data repositories funded by NIH or other funding agencies.

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2016-2017	Data Sharing and Reproducibility	Convene an advisory meeting of relevant stakeholders to develop a consensus regarding eliminating barriers to sharing, integrating, and reuse of data needed to build predictive models of disease. [2015 AD Summit: 1A, 2C, 3A, and 6A]	Develop recommendations for new policies and incentives to enable open, reproducible, and translatable research. These should address: • removing barriers to combining data from multiple sources and sharing processed data with other investigators. • generating combined and harmonized datasets that can be shared between investigators. • providing genetic and other patient-level data on a common-access cloud site where researchers can perform large-scale computational tasks without the need to download and store large datasets. • providing access to sponsor-level data from clinical trials to revisit those that failed to demonstrate efficacy. • supporting electronic consenting and other consenting models that give ownership of health care data to patients and study participants.
2016-2017	Data Sharing and Reproducibility	Convene a meeting with administrators from academic institutions (deans, chancellors, department chairs), representatives from NIH and other funding agencies, journals, and public advocates to develop recommendations for alternative recognition and attribution methods that would foster large-scale team science and increase the transparency and reproducibility of federally funded research. [2015 AD Summit: 1K and 6B]	Develop recommendations for new metrics for recruitment, career advancement, and publication attribution.
2016 -2024	Translational Infrastructure and Capabilities	Provide support for storage and rapid distribution of biosamples from relevant NIH-funded clinical research studies to ensure that biosamples generated from federally funded research can be maintained and made available to all qualified researchers after the funding cycle ends.	Establish a contract for storage, maintenance, and distribution of biosamples from clinical research studies on AD.

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2016-2018	Translational Infrastructure and Capabilities	Support the development of standardized, cost-effective, high-throughput methods to isolate neural and glial cells for "omics" profiling and drug-screening. [2015 AD Summit: 1G and 2H]	Develop standardized high-throughput methods for isolation and "omic" profiling of relevant neural and glial cell types.
2016-2018	Translational Infrastructure and Capabilities	Develop improved iPSC protocols for all relevant cell types and human-based organoid model systems. [2015 AD Summit: 2H]	Develop and make widely available standardized protocols for the generation of hiPSC for the major cell types (neurons, astrocytes, microglia, oligodendrocytes, pericytes).
2014-2018	Translational Infrastructure and Capabilities	Create a network of translational centers that bring together expertise and technology needed for integration of multimodal data analysis, mathematical modeling, and empirical testing, and apply a systems biology/systems pharmacology approach to the most challenging aspects in preclinical therapy development, such as: (1) therapeutic target selection and initial target validation, (2) predictive toxicology, and (3) rigorous preclinical efficacy testing and development of translatable, preclinical biomarkers. The centers will also provide training programs for the new generation of translational scientists. [2012 AD Summit: 2A and 2B]	Creation of at least three translational centers that will apply the principles of quantitative and systems pharmacology to AD drug development.
2016-2020	Translational Infrastructure and Capabilities	Create new integrative training programs for junior neuroscience researchers (predoc, postdoc, and junior faculty) that include training in aging biology, systems biology, geriatrics, all aspects of data science, as well as traditional and emerging drug discovery disciplines. [2015 AD Summit: 1J, 4D, and 4E]	Establish new training programs as well as fellowship and career development programs to develop a new translational and data science workforce.
2016-2018	Recruitment and Citizen Engagement	Support projects that use citizen science to accelerate collection of relevant data and data analyses. [2015 AD Summit: 5G]	Launch at least three citizen science projects that use existing data or develop new crowd-powered medical research platforms for collection and/or analysis of data.

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2016-2018	Recruitment and Citizen Engagement	Establish a partnership among NIH and other federal agencies to develop a national public education campaign (K-12) to eliminate the stigma of aging and dementia and provide accurate evidence-based information on environmental and lifestyle factors associated with the development and maintenance of a healthy brain and cognition. [2012 AD Summit: 6A]	Launch a national public education campaign for K-12 students focused on eliminating the stigma of aging and dementia and providing accurate, evidence-based information on environmental and lifestyle factors associated with the development and maintenance of a healthy brain and cognition.
2015-2018	Recruitment and Citizen Engagement	Increase knowledge among research scientists of best practices for recruitment and retention of research participants.	Central resources for both references and tools, including videos and presentation materials created and available.
Category H. Alzheimer's Disease-Related Dementias			
2017-2022	**ADRD 1: Multiple Etiology Dementias** **Focus Area 1:** Differential Diagnosis	Develop clinical algorithms for detection of neurodegenerative dementias and vascular contributions to cognitive impairment and dementia (VCID) in (a) primary care, (b) general neurology, and (c) general psychiatry outpatient settings; and clinical algorithms for referral to specialists in appropriate cases that also might involve consultations using novel technologies.	Develop and/or apply clinical algorithms for detecting primary dementias in outpatient general neurology. The algorithms should also be applicable to a primary care setting and should yield appropriate referral guidance. Include a training component to support high quality clinical training for physicians and nonphysicians.
2017-2020	**ADRD 1: Multiple Etiology Dementias** **Focus Area 2:** Epidemiology	Conduct population-based studies of dementia prevalence and incidence in diverse ethnic groups and age ranges using imaging and fluid biomarkers.	Initiate at least one research study using biomarkers or contributing to biomarkers discovery within a health disparities population that specifically examines dementia prevalence and incidence.
2017-2021	**ADRD 2: Health Disparities** **Focus Area 1:** Recruitment	Initiate and leverage ongoing longitudinal, community-based cohort studies of incident dementia in diverse populations incorporating imaging, fluid biomarkers, and autopsy.	Maximize diverse representation in dementia research by embedding sample collection (e.g., blood, CSF, and autopsy tissue) and clinical data in high-impact research cohorts among those identified. To increase the range of comorbidities represented, when possible, collection should emphasize samples based on the community or population, rather than memory clinics or other specialized medical settings. Facilitate wide sharing of the samples and clinical data for biomarkers discovery and other research.

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2017-2022	**ADRD 2: Health Disparities** **Focus Area 1:** Recruitment	Initiate and leverage ongoing longitudinal, community-based cohort studies of incident dementia in diverse populations incorporating imaging, fluid biomarkers, and autopsy.	Enhance the power of diversity community-based research studies of middle-age and older adults by developing, within the identified research cohorts, assessment tools for cognitive impairment and dementia and for neuropsychiatric status in diverse populations (guided by evidence from mixed methods studies to evaluate and improve population appropriate measures). These efforts should contribute to and be informed by leading edge development of best practices for assessing cognitive function, cognitive impairment, and dementia in diverse populations.
2017-2023	**ADRD 2: Health Disparities** **Focus Area 2:** Advancing Treatment and Prevention Strategies	Enhance the design of all trials of vascular health interventions to improve their application to diverse populations.	(1) Develop and make widely available guidelines for brain health assessments in clinical trials of vascular interventions in diverse populations. These guidelines will include standardized outcome measures relevant to cognitive outcomes in diverse populations (e.g., clinical, imaging, neurological, cognitive, and vascular) that will facilitate meta-analyses of intervention studies of vascular health in diverse populations, and will draw from expertise in related fields, e.g., stroke, lipid metabolism, cardiovascular intervention, and immune function. The guidelines should provide tiers of vascular, cognitive, and other relevant assessments that are optimized for resources, such as caregiver time, and technology available at sites relevant for cognitive impairment and dementia research in diverse populations. Guidance should also include best practices for recruitment in diverse populations. (2) Implement and validate, in vascular health intervention studies that include diverse populations, assessments of standardized outcome measures relevant to AD and ADRD.

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2019-2025	**ADRD 3: Lewy Body Dementias** **Focus Area 1:** Establish Longitudinal Cohorts with Common Measures, Culminating in Autopsy Studies	Initiate clinical trials for DLB and PDD using existing and newly developed symptomatic therapies that address key symptoms that impact patient function and the burden put on caregivers.	Initiate at least one new clinical trial that leverages an existing clinical network infrastructure and one or more FDA-approved drugs for symptomatic improvement of one or more of the core clinical features of DLB and PDD.
2017-2022	**ADRD 3: Lewy Body Dementias** **Focus Area 4:** Model Disease Processes to Develop Potential Symptomatic and Disease Modifying Therapies	Recognizing the importance of α-synuclein and AD pathophysiologic processes in DLB and PDD, new animal, cellular, and in vitro models are needed that recapitulate key features of these disorders with the ultimate goal of identifying strategies that can be carried forward into clinical trials.	(1) Establish basic research studies focused on developing a better understanding of the basic science of LBD, e.g., but not limited to, alpha synuclein biology and how it is related to LBD, and beta-amyloid and alpha synuclein interactions. (2) Develop one or more new animal models that fit known molecular pathology of DLB and PDD. Optimally, new animal model/s will be informed by human-based systematic mapping of DLB and PDD, and by results of biomarker studies.
2017-2021	**ADRD 4: FTD and Related Taupathies** **Focus Area 2:** Clinical Science—FTD Clinical Discovery, Tools, and Cohorts	Expand efforts to genotype patients with FTD and identify new genes.	Initiate at least one new large study to discover new genes and risk alleles for FTD. Where appropriate and synergistic, these efforts should include amyotrophic lateral sclerosis (ALS) kindreds in gene discovery studies.

FY 2017 Alzheimer's Disease Bypass Budget Milestones

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2017-2023	**ADRD 4: FTD and Related Taupathies** **Focus Area 1:** Basic Science **Focus Area 2:** Clinical Science—FTD Clinical Discovery, Tools, and Cohorts	Develop better FTD in vivo and cell-based model systems. Develop FTD biomarkers for diagnosis and disease progression.	(1) Generate in vivo and cell-based models of TDP-43/FUS, GRN haploinsufficiency, and C9ORF72 expansion models that recapitulate key biochemical, neuropathological, and functional aspects of FTD, and can contribute to therapeutic development. (2) Develop and validate in vivo functional assays and neuropathological endpoints for mammalian models that are aligned with FTD anatomy. (3) Initiate at least one new large study focused on development, testing, and pathological confirmation of novel PET ligands and/or CSF/blood biomarkers for the molecular diagnosis of FTLD-tau, -TDP and -FUS. (4) Develop and test sensitive, systems-level surrogate biomarkers (e.g., MRI/fMRI/PET/EEG/clinical) to detect and monitor prodromal FTD and progression during early-stage disease; the goal is to inform early in disease clinical proof-of-concept studies, complement clinical outcome measures in Phase III CT, and lay the foundation for endpoints on which drug registration can be based.
2017-2022	**ADRD 5: Vascular Contributions to ADRD—Small Vessel Disease and AD/Vascular Interactions** **Focus Area 1:** Basic Mechanisms and Experimental Models	Develop next-generation experimental models of VCID.	(1) Establish new animal models that: (i) reproduce small vessel disease and other key pathogenic processes thought to result in cognitive impairment, or (ii) are easily applicable to both VCID and AD research for advances in mixed dementias, or (iii) address vascular contributions to dementia via both white matter and grey matter. (2) Develop tools for cell- (endothelial, smooth muscle, pericyte, etc.) and region- (gray vs. white matter, cortex vs. striatum, etc.) specific characterization of the effects of altered cerebrovascular and neurovascular unit (glia, immune cells, etc.) function.

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Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2017-2022	**Topic 5: Vascular Contributions to ADRD—Focus on Small Vessel Disease and AD/Vascular Interactions** **Focus Area 2:** Human-based Studies	Develop and validate noninvasive markers of key vascular processes related to cognitive and neurologic impairment.	Development: (1) Identify neuroimaging or biochemical biomarker(s) that independently correlate with the presence and severity of advanced small vessel disease (SVD) in at least two human SVD cohorts. (2) Identify a neuroimaging marker for the vascular pathology of arteriolosclerosis. Validation: (1) Establish a direct link from in vivo imaging to ex vivo imaging to histopathology for biomarker(s) identified in the Development Phase. (2) Establish a link between the presence or progression of the biomarker(s) identified in the development phase and cognitive/neurologic impairment or decline in at least two SVD cohorts.