Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2018	Population Studies	1.A: 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	1.B: 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.
2016-2018	Population Studies	1.C: 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.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2018-2023	Population Studies	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, 1D, 3C, 3D, and 4B].	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. Three years (2016-2018) for protocol development, implementation and archiving; four years (2016-2019) for research.
2016-2018	Research on Disease Mechanisms	2.A: 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	2.B: 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.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2018	Research on Disease Mechanisms	2.C: 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	2.D: 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.
2016-2018	Research on Disease Mechanisms	2.E: 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	2.F: 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.
2016-2020	Data Sharing and Reproducibility	3.A: 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	3.B: 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.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2017	Data Sharing and Reproducibility	3.C: 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	3.D: 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.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2019	Translational Infrastructure and Capabilities	4.A: Support the development of the next generation of animal models based on the current understanding of genetic and environmental risk and protective factors for AD and related dementias, using genome editing and other cutting-edge technologies (optogenetics/deep brain stimulation/trans-magnetic stimulation, and next-generation in vivo imaging) to facilitate assessment and validation of findings from human studies. [2015 AD Summit: 1F and 1G]	Establish a contract for storage, maintenance, and distribution of biosamples from clinical research studies on AD.
2016-2024	Translational Infrastructure and Capabilities	4.B: 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.	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	Translational Infrastructure and Capabilities	4.C: Create infrastructure/resources for extensive characterization of existing and new animal models and development of standardized and rigorous methods for preclinical efficacy testing, including web-based resources for transparent reporting of both positive and negative findings. [2012 AD Summit: 2B and 2C; 2015 AD Summit: 1H and 1I]	Create at least one translational center for animal model resources.
2016-2018	Translational Infrastructure and Capabilities	4.D: 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	4.E: 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).

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2014-2018	Translational Infrastructure and Capabilities	4.F: 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: (i) therapeutic target selection and initial target validation; (ii) predictive toxicology; and (iii) 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.
2016-2017	Translational Infrastructure and Capabilities	4.G: Establish an NIH working group to develop an expedited review track for translational AD research applications (from target identification/validation drug discovery through Phase III clinical trials). [2012 AD Summit: 2D]	New NIH policy in place for fast tracking of AD translational research application.
2014-2015	Translational Infrastructure and Capabilities	4.H: Create a national IRB. [2012 AD Summit: 3H]	Initiation of at least one multi-center clinical trial that utilizes a national IRB.
2016-2020	Translational Infrastructure and Capabilities	4.I: 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.
2017-2023	Drug Development—Existing Targets	5.A: 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.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2015-2018	Drug Development—Existing Targets	5.B: 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	5.C: Initiate Phase III drug trials for agents against at least three currently known therapeutic targets. Of these, at least one trial will be in 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 biosamples 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.
2013-2017	Drug Development—Novel Targets	6.A: Establish a searchable, open-access research database that contains all clinical, biomarker, and epidemiological data, and related genotypes and phenotypes from existing genetic studies; analyze these data to identify regions of the genome that are targets for AD therapeutics. [2012 AD Summit: 1C]	At least one novel target, pathway, or therapeutic approach identified through use of the database.
2013-2020	Drug Development—Novel Targets	6.B: 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.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2020	Drug Development—Novel Targets	6.C: 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.
2014-2020	Drug Development—Novel Targets	6.D: 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	6.E: 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	6.F: 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 AD 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.
2020-2023	Drug Development—Novel Targets	6.G: Initiate Phase II (proof-of-concept) drug trials for agents against three to six novel therapeutic targets. These trials will provide proof of mechanism and/or evidence of target engagement of the target being tested. [2012 AD Summit: 3A, 3B, 3F, and 5E]	Completion of at least six Phase II drug trials for agents against novel targets, providing conclusive evidence of therapeutic mechanism/target engagement. Of these, at least three trials should be in asymptomatic, at-risk individuals (e.g. FAD or ApoE4 carriers, Down syndrome, amyloid positive, type II diabetes etc.).

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2022-2026	Drug Development—Novel Targets	6.H: Initiate Phase III drug trials for agents against at least three novel therapeutic targets. These trials will incorporate a combination of biomarkers (fluid and imaging) and cognitive measures as outcomes, and include the collection of DNA and other bio-samples for the interrogation of responsiveness. [2012 AD Summit: 3A, 3B, 3F, and 5E]	Comprehensive success/failure analysis of data from at least three Phase III trials.
2016	Drug Repurposing and Combination Therapy Development	7.A: Convene an advisory meeting of experts from the pharmaceutical industry, government, academia, the FDA, and the nonprofit sector to advance rational drug repositioning and combination therapy based on translational bioinformatics and network pharmacology approaches and to explore opportunities for new public-private partnerships to facilitate drug rescue/repurposing and combination therapy. [2012 AD Summit: 4A, 4B, 4C, and 4D]	(1) Development of recommendations for rational repositioning and combination therapy development. (2) Development, negotiation, and implementation of appropriate agreements among the stakeholders involved in repositioning and combination therapy of drugs for AD. These agreements should address legal issues, intellectual property rights, and liability to expedite rigorous clinical testing of repurposed drugs.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2018	Drug Repurposing and Combination Therapy Development	7.B: 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.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2018	Drug Repurposing and Combination Therapy Development	7.C: 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.
2018-2021	Drug Repurposing and Combination Therapy Development	7.D: Initiate early clinical development for at least six existing drugs or drug combinations for the treatment or prevention of Alzheimer's dementia. [2012 AD Summit: 4A, 4B, 4C, and 4D]	Completion of at least four Phase II trials with repurposed drugs and/or drug combinations. Successful trials will provide conclusive evidence of therapeutic mechanism/target engagement.
2020-2024	Drug Repurposing and Combination Therapy Development	7.E: Initiate at least three Phase III trials with repurposed drugs or drug combinations. Of these, at least one trial will be in an asymptomatic at-risk population (e.g., mutation carriers, APOE4 positive, Down syndrome, high amyloid burden) and at least one for individuals with advanced disease. Of the trials initiated in patients with advanced disease, at least one trial will target the neuropsychiatric symptoms of Alzheimer's disease. [2012 Summit: 4A, 4B, 4C, and 4D]	Comprehensive success/failure analyses of data from at least three Phase III trials.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016	Nonpharmacologic Interventions	8.A: Convene an advisory meeting to delineate an interdisciplinary research agenda focused on: (i) advancing nonpharmacological interventions for the cognitive and behavioral symptoms of AD by nonpharmacological treatments, (ii) informing the design of therapeutic approaches combining pharmacological and nonpharmacological treatments, and (iii) identification of best practices for implementation of nonpharmacological interventions. [2012 AD Summit: 5B, 5C, 5D, and 5F]	Recommendations developed for advancing nonpharmacological interventions for AD treatment and prevention to enable successful implementation of effective nonpharmacological interventions.
2016-2020	Nonpharmacologic Interventions	8.B: 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.
2017-2021	Nonpharmacologic Interventions	8.C: 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.
2019-2023	Nonpharmacologic Interventions	8.D: Initiate clinical trials for at least three interventions combining pharmacological and nonpharmacological interventions for AD treatment or prevention. Of these, at least one trial will be a pivotal Phase III trial. [2012 AD Summit: 5B, 5C, 5D, and 5F]	At least two Phase II trials completed for interventions combining pharmacological and nonpharmacological interventions for AD treatment or prevention with conclusive evidence of therapeutic mechanism. Comprehensive success/failure analysis of data from at least one Phase III trial.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2020-2024	Nonpharmacologic Interventions	8.E: Initiate at least one clinical trial for primary prevention of AD among high-risk individuals in midlife, including a nonpharmacological treatment arm. [2015 AD Summit: 3B and 3D; 2012 AD Summit: 5.E]	Completion of at least one Phase II primary prevention trial for nonpharmacological interventions in midlife. Successful trials will provide evidence for potential therapeutic mechanisms and include the collection of biomarker data for future validation and longitudinal follow-up within the trial cohort.
2016-2018	Biomarkers	9.A: 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	9.B: 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	9.C: 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.
2017-2021	Biomarkers	9.D: Incorporate imaging and/or fluid biomarkers into Phase II (proof-of-concept) drug trials to provide proof of mechanism and/or evidence of target engagement as trials for three to six existing and three to six novel therapeutic targets are initiated. [2012 AD Summit: 1E]	Initiation and completion of five Phase II (proof of concept) drug trials using imaging and/or fluid biomarkers for proof of target engagement.
2019-2023	Biomarkers	9.E: Incorporate imaging and/or fluid biomarkers into Phase III (pivotal) drug trials to select subjects and/or provide evidence of target engagement as trials for three to six existing and three to six novel therapeutic targets are initiated. [2012 AD Summit: 1E]	Initiation of three Phase III (pivotal) drug trials using imaging and/or fluid biomarkers to select at risk subjects and/or for proof of target engagement.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2015-2019	Biomarkers	9.F: 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.
2016-2020	Biomarkers	9.G: Initiate studies to link peripheral blood-based biomarkers and central imaging and CSF biomarkers. [2012 AD Summit: 1F and 1G]	Identification of three peripheral blood-based biomarkers that have a high correlation with central imaging and/or CSF biomarkers.
2014-2018	Biomarkers	9.H: 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.
2014-2019	Biomarkers	9.I: Develop and test methods for the standardization of immunoassays and mass-spectrometry/single reaction monitoring assay or other methodologies for CSF abeta and tau and other biomarkers as they become clinically applicable. Develop and test methods for standardization of collection and analysis of MRI and PET neuroimaging data. [2012 AD Summit: 3E]	CLIA laboratory qualification in US and the equivalent certification in the EU for at least one CSF biomarker of disease pathology. For neuroimaging data, qualification of at least one biomarker for use in clinical trials by the FDA and/or the EMA.
2016-2017	Trial Design	10.A: 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.
2014-2015	Trial Design	10.B: Establish a working group to identify standard outcome measures necessary for data comparisons across secondary prevention trials. [2012 AD Summit: 5E]	Identification of at least two standard outcome measures for data comparison in clinical research.
2015-2020	Trial Design	10.C: Initiate three to four clinical research studies using common standard outcome measures. [2012 AD Summit: 5E]	Data comparisons conducted from clinical studies using common standard outcome measures.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2017-2019	Trial Design	10.D: 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.
2018-2020	Trial Design	10.E: Support research on the effectiveness of dissemination methodologies to facilitate the implementation of effective prevention strategies. [2015 AD Summit: 3L]	Launch at least three research projects evaluating the effectiveness of dissemination methodologies.
2019-2020	Trial Design	10.F: Convene an advisory meeting to evaluate how assays and best practices developed in the context of the NIH Common Fund Science of Behavior Change and other related NIH activities could be incorporated into the design of primary prevention trials for AD or for clinical trials targeting risk factors associated with increased risk of AD. [2012 AD Summit: 5E]	Meeting report recommendations that would guide the inclusion of behavioral target engagement assays and best practices in NIH-supported prevention and treatment trials for AD.
2017-2019	Enabling Technologies and Disease Monitoring	11.A: 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).
2018-2021	Enabling Technologies and Disease Monitoring	11.B: Continue to develop standard outcome measures to enable data comparisons across studies, including but not limited to cognitive functioning and physical function, and ensure that these measures are validated across a variety of educational, linguistic, and cultural groups. [2015 AD Summit: 4B]	Launch at least one large longitudinal study evaluating the validity of standard outcome measures across three or more diverse groups. The study should be sufficiently powered to enable the validation of each of the outcome measures within each of the diverse groups.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2018	Enabling Technologies and Disease Monitoring	11.C: 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	11.D: 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.
2016-2018	Recruitment and Citizen Engagement	12.A: 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	12.B: 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	12.C: 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.
2016-2017	Recruitment and Citizen Engagement	12.D: Convene a meeting with key stakeholders and organizations, including representatives from the NIH Precision Medicine Initiative, to discuss policies for streamlining and innovating patient/participant consent and data sharing. [2015 AD Summit: 5G, 5H, 5I]	Issue guidelines for streamlined electronic consenting and other consenting models that give ownership of health care data to patients and study participants.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2017-2019	Recruitment and Citizen Engagement	12.E: 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	Recruitment and Citizen Engagement	12.F: 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 or develop new crowd-powered medical research platforms for collection and/or analysis of data.
2016-2018	Recruitment and Citizen Engagement	12.G: 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	12.H: 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.
2014	Recruitment and Citizen Engagement	12.I: Establish a working group, including clinical trial recruitment experts, to dynamically evaluate and update the materials and information provided in the central resource.	Recommendations for successful recruitment methods.
2015-2018	Recruitment and Citizen Engagement	12.J: 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.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016	Research on Care and Caregiver Support	13.A: Convene an exploratory expert meeting to delineate and prioritize an interdisciplinary research agenda focused on assessing the impact of informal and formal caregiving across the full care continuum (to include primary care, home health care, adult day care, nursing home, assisted living, hospice, etc.) on individuals, families, and society, and to inform design of new care delivery systems for individuals with dementia. [2015 AD Summit: 4K, 4B, 4J, 5D]	Definition and characterization of informal and formal caregiving, the domains of needs of caregivers and care recipients across the care continuum, the key social structural variables which contribute to variance in caregiving burden, and factors that characterize care delivery and care coordination models that reduce burden on caregivers and care recipients. Recommendations developed for research priorities on the impact of caregiving on caregivers' psychological and physical health, workforce participation, and financial security. Recommendations developed for research programs that can inform development of new care models.
2017-2019	Research on Care and Caregiver Support	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]	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.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2017-2019	Research on Care and Caregiver Support	13.C: Establish data infrastructure for the study of dementia caregiving. [2015 AD Summit: 4B, 4E, 4F]	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.
2018-2020	Research on Care and Caregiver Support	13.D: Support secondary analysis of data from population-based and intervention studies with appropriate content related to informal and formal caregiving. [2015 AD Summit 4E, 4F, 4H]	Identify predictors of high-risk caregivers. Identify economic impact of informal caregiving on families and societies. Conduct cross-national comparative research. Identify potential buffers and predictors of healthy caregivers and positive caregiving outcomes for care recipients. Identify at least one novel association, target, pathway, or intervention target or approach through use of the database.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2020	Research on Care and Caregiver Support	13.E: 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.
2017-2019	Research on Care and Caregiver Support	13.F: 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.

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2015-2019	Research on Care and Caregiver Support	13.G: 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.
2013	Public-Private Partnerships	14.A: Convene an advisory meeting focused on facilitating public-private partnerships aimed at accelerating the development and test of effective therapies for AD treatment and prevention. [2012 AD Summit: 1H, 1I, 1K, and 6C]	Established working groups on: (i) Rapid Data Sharing and Analysis, (ii) Enabling Bidirectional Translation in AD drug development, and (iii) Eliminating IP barriers for Target Validation through clinical proof of concept.
2014	Public-Private Partnerships	14.B: Convene meetings of the working groups for (i) Rapid Data Sharing and Analysis, (ii) Enabling Bidirectional Translation in AD drug development, and (iii) Eliminating IP barriers for Target Validation through clinical proof of concept. Each working group will formulate concrete steps needed to accelerate the timeframe of AD drug development. [2012 AD Summit: 1H, 1I, 1K, and 6C]	Recommendations developed on (i) the creation of an open-access, web-based resource that integrates complete, diverse multidimensional biological and chemical data that will be useful in advancing information on drug targets, including mechanistic information that will aid in the development of measures of target engagement (PD readouts); (ii) creation of computational tools for development of biological network models of AD and normal aging; (iii) creation of tools that will foster development of bio network models that provide a predictive framework for using drugs in combination or singly; and (iv) removing legal and IP barriers surrounding data sharing. One or more partnerships established to accelerate key steps in AD drug development.
2016	Public-Private Partnerships	14.C: Develop partnerships to support novel/disruptive science that would incentivize students and early-career investigators to adopt a collaborative approach to research through the use of targeted small funding schemes. [2015 AD Summit: 6D]	Establish at least one partnership to support disruptive team science by young investigators (students and early career investigators).

Alzheimer's Disease Research Implementation Milestones 2013-2025

Time Required	Research Implementation Area	Alzheimer's Disease (AD) Research Implementation Milestones	Success Criteria
2016-2018	Public-Private Partnerships	14.D: 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.
2016-2017	Public-Private Partnerships	14.E: 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.
2013-2015	Portfolio Analysis Tools and Methods	15.A: Develop a common AD research ontology, as a unified classification system for comparative analysis of research portfolios and strategic planning, and create a publicly available database that will house the AD research portfolios from AD funding agencies in the US and abroad.	Recruitment of all Federal and non-Federal funding agencies in the US as well as AD funding agencies from countries that have an AD National Plan to participate in this database.

NIH National Institutes of Health