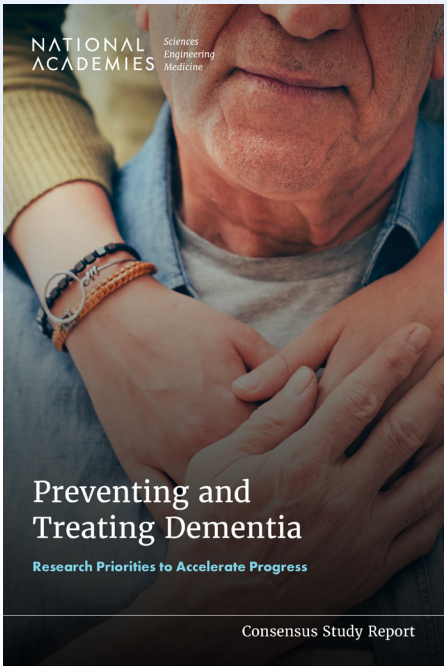
Preventing and Treating Dementia



Research Priorities to Accelerate Progress

Dementia exacts a weighty emotional and financial toll on individuals, families, and communities—one that is likely to grow due to an aging global population. Developing effective strategies for preventing and treating Alzheimer's disease and related dementias (AD/ADRD)—a collection of neurodegenerative conditions—is considered one of the most pressing needs in biomedical research. The National Institutes of Health (NIH) has invested billions of dollars in this research over the last decade, leading to a foundation of knowledge from which more can be learned. However, the pace of progress has not matched the growing needs of people living with AD/ADRD and those at risk.

To address this need and in response to a congressional request, the National Institute on Aging (NIA) and the National Institute of Neurological Disorders and Stroke (NINDS) asked the National Academies of Sciences, Engineering, and Medicine to convene a committee to examine and assess the current state of biomedical research and recommend research priorities to advance the prevention and treatment of AD/ADRD, including strategies to overcome barriers to progress on these priorities. The resulting report, *Preventing and Treating Dementia: Research Priorities to Accelerate Progress*, outlines research priorities and complementary recommendations on strategies to overcome barriers to progress.

AD/ADRD RESEARCH PRIORITIES

The report's 11 research priorities represent the committee's consensus views on the areas of scientific inquiry with the greatest promise to advance the field and improve population health (see **Recommendation 1** and Table S-1 in the report).

The research priorities detailed below are focused on advancing the science around AD/ADRD prevention and treatment, but the committee's ultimate objective was to ensure that these investments translate into improved lives for those already living with AD/ADRD and preventing many more from developing these conditions. Reflecting the prevalence of mixed pathologies in older individuals, these research priorities emphasize opportunities across the spectrum of AD/ADRD rather than focusing on gaps specific to individual dementia types. The research priorities are as follows:

- Develop better tools, including novel biomarker tests and digital assessment technologies, to monitor brain health across the life course and screen, predict, and diagnose AD/ADRD at scale;
- Implement advances in clinical research methods and tools to generate data from real-world clinical practice settings that can inform future research;
- Identify factors driving AD/ADRD risk in diverse populations, particularly understudied and disproportionately affected groups, to better understand disease heterogeneity—including molecular subtypes and disparities in environmental exposures—and to identify prevention opportunities and advance health research equity;
- Characterize the exposome and gene–environment interactions across the life course to gain insights into biological mechanisms and identify opportunities to reduce AD/ADRD risk and increase resilience;
- Elucidate the genetic and other biological mechanisms underlying resilience and resistance to identify novel targets and effective strategies for AD/ADRD prevention and treatment;
- Develop integrated molecular and cellular causal models to guide the identification of common mechanisms underlying AD/ADRD and their validation as novel targets for prevention and treatment;
- Integrate innovative approaches and novel tools into the planning, design, and execution of studies to accelerate the identification of effective interventions;
- Advance the development and evaluation of combination therapies (including pharmacological and nonpharmacological approaches) to better address the multifactorial nature of AD/ADRD;
- Evaluate precision medicine approaches for the prevention and treatment of AD/ADRD to better identify interventions likely to benefit specific groups of individuals;
- Advance the adoption of standardized outcomes for assessing interventions that are sensitive, person-centered, clinically meaningful, and reflect the priorities of those at risk for or living with AD/ADRD; and
- Evaluate the causal effects of public health approaches on overall dementia incidence and incidence in understudied and/or disproportionately affected populations.

The full report includes important additional information about these research priorities, including key scientific questions and near-term research opportunities, in Table S-1.

STRATEGIES TO OVERCOME BARRIERS TO PROGRESS ON AD/ADRD RESEARCH PRIORITIES

The report includes nine complementary recommendations focused on overcoming crosscutting barriers to progress on the recommended scientific research priorities. The landscape of proposed actions is depicted visually in Figure 1.

Enhancing Longitudinal and Intervention Research

Maximize Knowledge from Longitudinal Research

Longitudinal cohort studies represent an important mechanism for developing a comprehensive view of brain health over the life course. Therefore, the report recommends that NIH prioritize investments in longitudinal research, including leveraging data from existing cohorts focused on other health conditions and

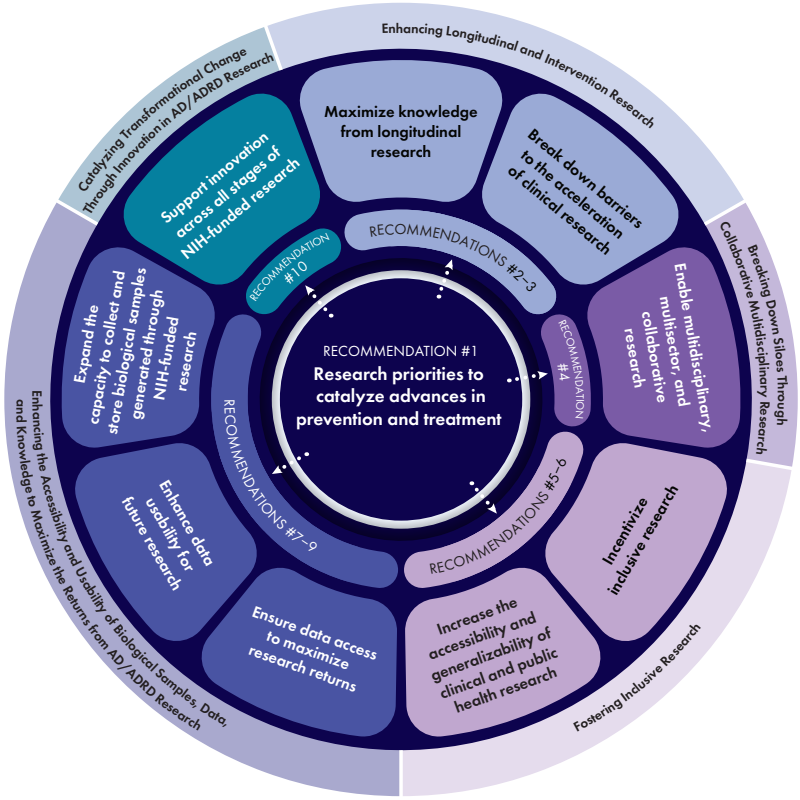


FIGURE 1 Committee recommendations for advancing the prevention and treatment of AD/ADRD.

creating new and multidimensionally diverse cohorts to address existing knowledge gaps regarding factors that influence brain health over the life course (see **Recommendation 2** in the report).

Break Down Barriers to the Acceleration of Clinical Research

Many stakeholders contribute to AD/ADRD research and increased collaboration is necessary to accelerate discovery, reduce the time to develop effective interventions, and bridge funding gaps. The report recommends that NIH continue to lead efforts across a multiplicity of relevant entities to accelerate the movement of promising interventions for AD/ADRD into clinical trials and expand the use of innovative approaches to improve the efficiency of clinical trials (see **Recommendation 3** in the report).

Breaking Down Siloes Through Collaborative, Multidisciplinary Research

The heterogeneity of AD/ADRD and disease pathways suggest that preventing and treating AD/ADRD must involve collaborative, multidisciplinary research, but numerous siloes persist, often reinforced by funding structures. Innovative funding strategies and collaboration methods are needed to address these challenges, and the report recommends that NIH expand mechanisms and leverage existing resources to break down siloes and encourage multidisciplinary and integrative AD/ADRD research efforts (see **Recommendation 4** in the report).

Fostering Inclusive Research

A comprehensive understanding of population-level differences in AD/ADRD is critical, but disproportionately affected populations are persistently underrepresented in research. Without representative study populations, findings may not be generalizable, which may exacerbate health disparities. The report recommends that NIH incentivize and guide the use of inclusive research practices and that NIH-funded investigators adopt these practices to increase the accessibility of clinical and public health research and ensure that study populations are representative of populations at risk for and living with AD/ADRD (see **Recommendation 5** and **Recommendation 6** in the report).

Enhancing the Accessibility and Usability of Biological Samples, Data, and Knowledge to Maximize the Returns from AD/ADRD Research

When data and samples are not shared, collaborative research cannot happen. The report recommends that NIH convene and support an NIH workgroup to identify and implement solutions to barriers that impede access to data from AD/ADRD research (see **Recommendation 7** in the report). However, accessibility alone is not sufficient to ensure that data from past AD/ADRD research are usable, and the report recommends that NIH invest in several strategies, which are outlined in the full report, to enable data usability (see **Recommendation 8** in the report). Lastly, the report recommends that NIA and NINDS expand support for the collection and storage of valuable biological samples from NIH-funded AD/ADRD research in a manner that maximizes opportunities for future use (see **Recommendation 9** in the report).

Catalyzing Transformational Change Through Innovation in AD/ADRD Research

Accelerating progress in AD/ADRD prevention and treatment requires truly transformational change. Therefore, the report recommends that NIH use existing funding structures and other incentives to stimulate innovation across all stages of AD/ADRD research (see **Recommendation 10** in the report).

LOOKING AHEAD

The last decade of research has seen significant progress in efforts to prevent and treat AD/ADRD—but substantial need remains. Through collaborative efforts across the biomedical research enterprise and when employing the strategies outlined in this report, it is possible to envision a future where dementia is preventable and treatable.

To learn more about this report, visit our website at nationalacademies.org/dementia-research.

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FOR MORE INFORMATION

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