

RESEARCH

Alzheimer's State Plan Recommendations from the Research Workgroup for the Alzheimer's Advisory Council's Review/Comments/Approval

This document was prepared by the Research Workgroup of the Alzheimer's Advisory Council. A list of the workgroup's members is included at the end of the document.

GOAL: *Advance dementia research in Massachusetts.*

BACKGROUND

With nearly six million people in the United States living with Alzheimer's disease (AD), a number projected to double by 2050 (Alzheimer's Association, 2020), the pressing need for research to answer critical questions related to the prevention and treatment of the disease continues to grow. That this research should be representative is central to the success of these efforts, ensuring that the knowledge gained is generalizable to all those affected with the illness. However, much of AD research involves mostly White individuals of higher socioeconomic status at the earlier stages of the illness. Increasing diversity of study populations, as well as approaches to studying the illness, will help address this representation gap. Increasing the diversity of AD researchers will also be necessary in this effort, as diverse perspectives and approaches often lead to innovation and discovery. Barriers to the participation of these populations in AD research are many; however, increased outreach and increased institutional support will be key means of increasing participation, ensuring dementia research that is innovative, inclusive, and equitable.

RECOMMENDATIONS

Recommendation #1: *Increase diversity in Alzheimer's disease research.*

The first recommendation of the Alzheimer's Advisory Council is to improve understanding of Alzheimer's disease and related dementias (ADRD) through increased diversity of research participants, target populations, as well as relevant research topics, environments, and methods.

Strategic Priority 1.1: Increase racial and ethnic diversity of participants in ADRD research.

If we are to develop diagnostic tools and treatments that will work for everyone, we need to ensure that diverse groups participate in the trials that evaluate their efficacy. Despite efforts to increase racial and ethnic minority groups participation in ADRD research, target populations remain underrepresented (Gilmore-Bykovskiy et al., 2019). As one example, Black participants in ADRD clinical trials demonstrate lower participation rates (4–11%) and higher rates of dropout relative to non-Hispanic Whites (Kennedy et al., 2017). Without representation in research, understanding the differences between these groups in the risk factors for, timing of diagnosis, and clinical manifestations of ADRD is severely impeded. There are many, multifaceted barriers to research participation, including lack of awareness of research opportunities and increased participant burden relative to non-Hispanic Whites. Establishing long-term relationships with communities of color is the single most important strategy for increasing participation in research studies. Further, providing infrastructure and other supports to address specific barriers, such as lack of transportation, is a critical means of increasing the ability of these individuals to participate.

Strategic Priority 1.2: Increase diversity of participants in understudied target populations.

Target populations for ADRD research should be focused toward groups that have been underrepresented and underserved with regards to ADRD prevention, awareness, and treatment. Cohorts of interest include not only those of a racial or ethnic minority but also those with a lower socioeconomic status (Gilmore-Bykovskiy et al., 2019), who often require a multi-domain approach to treatment and prevention to see statistically significant results (Imtiaz et al., 2014). Another group of interest are caregivers, who not only face specific challenges themselves (Frank, 2008), but also are directly responsible for enabling individuals with dementia to participate in the research process. It is imperative to address caregivers' concerns about the purpose of research and its direct benefit to participants, as well as the burden of participation (Connell et al., 2001). As with other underrepresented groups, community outreach is needed to encourage research participation of these individuals.

Strategic Priority 1.3: Increase diversity of the stages of ADRD that are being investigated.

The majority of current research in the Commonwealth is focused on Mild Cognitive Impairment (MCI) and mild dementia stages, driven largely in part by pharmacological interventions aimed at these populations. We want to ensure that the Commonwealth also invests in earlier and later stages of the disease. Considerable effort should be undertaken to identify individuals in the preclinical stage of ADRD and those with Subjective Cognitive Decline, as they could represent the stage of pathology that will be most responsive to treatment, thereby potentially reducing the numbers of people who go on to develop ADRD. More research is also needed in the earliest and later stages of clinically apparent dementia. Inclusive research involving individuals with early-onset, moderate, and severe ADRD will help individuals and caregivers already at these stages of the disease. Ensuring that individuals are aware of the research and opportunities across the continuum of ADRD represents an important step in equity in ADRD prevention and care.

Strategic Priority 1.4: Increase diversity of research methods used to study ADRD.

The breadth and depth of research in ADRD is vast—with key insights about the disease derived from studies of animal models, novel medications, neuroimaging, and behavioral experiments. Despite advances in ADRD research, many promising methods and research avenues remain underfunded and understudied. Challenges to research initiatives can be logistic. For example, because of the extensive duration of the disease, large-scale, long-term research may be practically or financially difficult to implement (Ritchie et al., 2015). There are several other important challenges (some named here), from topics not traditionally of interest to ADRD researchers but perhaps critically important (e.g., built environment, Calkins & Zimmerman, 2018) and those not funded at high rates (e.g., health disparities). To this, the present COVID-19 pandemic adds additional financial and practical constraints. Creative methods using new technologies, methods, and approaches should be explored and supported.

In sum, increased representation of research participants is needed across an array of different diverse groups: those of racial and ethnic minorities (1.1), individuals of lower socioeconomic status and caregivers (1.2), and individuals across the continuum of ADRD, from preclinical through severe dementia (1.3). Common across these groups are the approaches to increasing involvement: building community relationships and outreach, supporting solutions for specific barriers to participation, and bringing those with lived experience onto the research team. Increased diversity is also needed in the methods, techniques, and approaches used to study ADRD (1.4).

Recommendation #2: Increase diversity of Alzheimer's disease researchers.

Strategic Priority 2.1: Increase racial and ethnic diversity of ADRD researchers.

As with research participation, lack of representation in AD *researchers* presents a significant challenge. This phenomena is seen broadly across multiple disciplines and stages of a researcher's career, from graduate school (Hofstra et al., 2020), to early career awards (Biernat et al., 2020), and large scale grants (Ginther et al., 2011). Research *topic choice* is one main contributing factor to the disparity in representation and funding of minority groups (Hoppe et al., 2019). As one example, Black researchers are more likely to submit proposals related to community interventions and health disparities, which are funded at lower rates than are biomedical studies (Hoppe et al., 2019). Social and professional networking can support minority investigators involvement with clinical trials and further their clinical ambitions (Blanchard et al., 2019). Support is required to help advance the progress of minority groups in the field of research.

Strategic Priority 2.2: Increase gender diversity of AD researchers.

Women face a unique set of obstacles when pursuing a career in research that impacts not only their prevalence in the field, but also the ability of these researchers to obtain tenure at universities and colleges as well as mentoring opportunities (Moss-Racusin et al., 2012). Women also encounter bias when submitting to grant panels (Wittelman et al., 2019) and in the peer review process (Helmer et al., 2017), which decreases their likelihood of receiving funding for research projects and obtaining publication for their work. These challenges are further compounded by the demands of household labor, childcare, eldercare, and marriage (Malisch et al., 2020), which have been reported as contributing factors in decisions to shift career goals away from a research emphasis (Goulden et al., 2011). As such, solutions are needed for women in research concerning funding, publication, career-advancement, and mentorship opportunities.

IMPLEMENTATION STRATEGIES AND EXPECTED OUTCOMES

- **STRATEGY 1:** Engage in outreach and expand support to target populations to increase participation in research. (Advances Strategic Priorities 1.1 & 1.2.)
- **STRATEGY 2:** Provide instrumental support (e.g., funding) in the form of small research support grants to underrepresented researchers and research initiatives. (Advances Strategic Priorities 1.3, 1.4, 2.1, & 2.2.)

IMPLEMENTATION STRATEGIES AND EXPECTED OUTCOMES		
Years	Strategies	Expected Steps and Outcomes
	Strategy 1 – Increase outcomes of diversity of participants, disease stages, methods, and researchers	
1-2	<ol style="list-style-type: none"> 1. Compile data for: participants, disease stages, methods, and researchers. 2. Inform and educate industry companies and non-profit centers regarding new rules to come regarding required diversity of participants, disease stages, methods, and researchers. 3. Share our recommendations with all US states plus Puerto Rico and encourage them to set up analogous programs of their own. 	<p>Obtain data from industry companies/studies taking place in the Commonwealth (including both specific sites and overall study leadership) regarding diversity of</p> <ol style="list-style-type: none"> 1. participants’ demographic information, including race, ethnicity, and other under-represented group variables. 2. disease stages being investigated. 3. methodologies being used. 4. researchers including race, ethnicity, gender, and other under-represented group variables. <p>Obtain demographic data from non-profit centers/studies taking place in the Commonwealth regarding diversity of</p> <ol style="list-style-type: none"> 5. participants’ demographic information, including race, ethnicity, and other under-represented group variables. 6. disease stages being investigated. 7. methodologies being used. 8. researchers including race, ethnicity, gender, and other under-represented group variables. 9. By the end of calendar year 2022, both industry and non-profit variables will be

		<p>compiled.</p> <ol style="list-style-type: none"> 10. By the end of calendar year 2022, both industry companies and non-profit centers variables will be educated regarding the rules to come. 11. By the end of calendar year 2022, we will share our recommendations with all US states plus Puerto Rico and encourage them to set up analogous programs of their own. 12. By the end of calendar year 2021, \$150,000/year will be secured for personnel and oversight to compile necessary data and educate industry companies and non-profit centers. The \$150,000 will likely be in the form of a grant to a non-profit center.
<p>Strategy 2 – Research Support Grants</p>		
	<ol style="list-style-type: none"> 1. Provide sources of funding for small research support grants for increasing the diversity of underrepresented participants, disease stages, research methodologies, and researchers. 2. Secure funding and establish application mechanism. 	<ol style="list-style-type: none"> 1. By the end of calendar year 2021, application mechanism established. 2. By the end of calendar year 2022, \$100,000 funding secured for 10 grants to be awarded in years 3-4. The purpose of grants will be for seed funding that can leverage larger grants and research projects to promote recommendations.
<p>3-4+</p>	<p>Strategy 1 – Outreach</p>	

	<ol style="list-style-type: none">1. Compile data for: participants, disease stages, methods, and researchers.2. Inform and educate industry companies and non-profit centers regarding new rules to come regarding required diversity of participants, disease stages, methods, and researchers.	<ol style="list-style-type: none">1. Starting calendar year 2023, industry companies/studies taking place in the Commonwealth (including both specific sites and overall study leadership) must increase the diversity of participants including race, ethnicity, and other under-represented group variables by 1.5% per year until diversity matches catchment area.2. Starting calendar year 2023, non-profit centers/studies taking place in the Commonwealth must increase the diversity of participants including race, ethnicity, and other under-represented group variables by 3% per year until diversity matches catchment area.3. Starting calendar year 2023, industry companies/studies taking place in the Commonwealth (including both specific sites and overall study leadership) must pursue therapeutic and/or beneficial research in all disease stages, from preventative and preclinical to severe dementia. Such research may include studies of novel drugs, existing drugs for novel indications, strategies for people with dementia, strategies for caregivers, etc.4. Starting calendar year 2023, non-profit centers/studies taking place in the Commonwealth must pursue therapeutic and/or beneficial research in all disease stages from preventative and preclinical to severe dementia. Such research may include studies of novel drugs, existing drugs for novel indications, strategies for people with dementia, strategies for caregivers, etc.5. Starting calendar year 2023, industry companies/studies taking place in the Commonwealth (including both specific sites and overall study leadership) must increase the diversity of methodologies being used by 50% the first year, and 10% each year after that until the number of methodologies are at least doubled (100% increase). Such methods may include adding diverse research contexts (e.g., the built environment), diverse research aims (e.g., health disparities), diverse research approaches (e.g., new technologies), etc.6. Starting calendar year 2023, non-profit centers/studies taking place in the Commonwealth must increase the diversity of methodologies being used by 50% the first year, and 10% each year after that until the number of methodologies are at least doubled (100% increase). Such methods may include adding diverse
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		<p>research contexts (e.g., the built environment), diverse research aims (e.g., health disparities), diverse research approaches (e.g., new technologies), etc.</p> <ol style="list-style-type: none"> 7. Starting calendar year 2023, industry companies/studies taking place in the Commonwealth (including both specific sites and overall study leadership) must increase the diversity of researchers including race, ethnicity, gender, and other under-represented group variables by 1.5% per year until diversity matches catchment area. 8. Starting calendar year 2023, non-profit centers/studies taking place in the Commonwealth regarding diversity of researchers including race, ethnicity, gender, and other under-represented group variables by 1.5% per year until diversity matches catchment area. 9. Each year we will compile data on the success of these measurements. 10. Each year we will compile data regarding how many US states plus Puerto Rico have set up analogous programs of their own.
<p>Strategy 2 – Research Support Grants</p>		
	<ol style="list-style-type: none"> 1. Evaluate and fund small research support grant applications. 	<ol style="list-style-type: none"> 1. By the end of calendar year 2023, 10 \$10,000 grants will be awarded. 2. Progress reports will be required at 0.5, 1, 1.5, 2, 3, 4, & 5 years to assess the grant’s initial and legacy impact. 3. Individual grants will be evaluated for their progress toward and achievement of their individual research aims and goals at each progress report interval. 4. By the end of calendar year 2024, the overall research support grants program will be evaluated toward its overall goals of increasing diversity seeding larger grants and research projects to promote these recommendations. 5. By the end of calendar year 2024, decisions will be made to continue, discontinue, or modify the grant program depending upon its success or failure toward achieving its overall goals.

RISKS TO IMPLEMENTATION AND SUSTAINABILITY, AND RISK RESPONSE STRATEGIES

1. Industry companies and non-profit centers may not wish to share information with us regarding the diversity of their participants, disease stages, methodologies, and researchers.

RESPONSE: To encourage participation we can either use incentives (such as less rapid implementation of mandated guidelines) or penalties (such as financial or other penalties).

2. Other US states and territories may not be interested in our recommendations and may choose not to set up analogous programs.

RESPONSE: We can explain that such recommendations are important both for the benefit of the science as well as for the citizens of each state and territory.

3. Industry companies and non-profit centers may not wish to implement the mandated guidelines regarding the diversity of their participants, disease stages, methodologies, and researchers.

RESPONSE: To encourage participation we can use incentives (such as sharing outreach and recruitment materials and strategies to increase diversity) or penalties (such as financial or other penalties).

4. Industry companies and non-profit centers may complain that the new mandated guidelines make it more difficult to operate in Massachusetts and may threaten to leave.

RESPONSE: We can work to ensure similar guidelines are in place in many US states and territories. We can also work to help companies and centers to achieve guidelines painlessly.

RESPONSIBLE ORGANIZATIONS

The Commonwealth, its Alzheimer's Advisory Council, and Alzheimer's Advisory Council's Research Workgroup.

COSTS/ RESOURCES

Associated costs include funding for personnel, outreach materials and costs, and funding for the small research support grants to support the Recommendations and Strategic Priorities outlined above. Specifically:

Year 1: \$150,000 grant to non-profit for personnel and oversight of this entire program. This will be a yearly recurring cost, termed "\$150,000 Personnel Grant."

Alzheimer's Advisory Council

11/15/20

Year 2: \$150,000 Personnel Grant

Year 3: \$150,000 Personnel Grant plus \$200,000 Research Grant (includes overhead monies that range from 15% to 79%). Note: Any additional Research Grant funds available will be used to fund additional grants until all monies are exhausted. Total Year 3: \$350,000.

Year 4: \$150,000 Personnel Grant

Year 5: \$150,000 Personnel Grant plus \$200,000 Research Grant (if the Research Grant program is continued). Total Year 4: either \$350,000 or \$150,000 depending upon whether the Research Grant program is continued.

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Research Workgroup Members

Andrew Budson, MD

Workgroup Lead and Council Member

Chief of Cognitive & Behavioral Neurology, Associate Chief of Staff for Education, and Director of the Center for Translational Cognitive Neuroscience at Veterans Affairs (VA) Boston Healthcare System
Associate Director for Research at Boston University Alzheimer's Disease Center
Lecturer in Neurology at Harvard Medical School
Medical Director of the Boston Center for Memory

Jonathan Jackson, PhD

Council Member

Founder and Executive Director
Community Access, Recruitment, & Engagement (CARE)
Research Center
Massachusetts General Hospital
Instructor in Neurology at Harvard Medical School

Renée DeCaro, PhD

Postdoctoral Research Fellow
Center for Translational Cognitive Neuroscience
Boston Veterans Affairs | Boston University
Alzheimer's Disease Center

Anna Marin

PhD Student, Behavioral Neuroscience, Boston University School of Medicine
Center for Translational Cognitive Neuroscience,
VA Boston Healthcare System