

April 7, 2025

Martin A. Makary, M.D., M.P.H.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

RE: FDA-2024-D-4245, Study of Sex Differences in the Clinical Evaluation of Medical Products

On behalf of the undersigned organizations and university-affiliated researchers, we appreciate the opportunity to provide comments on the Food and Drug Administration (FDA) draft guidance “Study of Sex Differences in the Clinical Evaluation of Medical Products.” We commend the FDA for its ongoing commitment to ensuring the inclusion of females in clinical trials and the analysis of sex-specific data in regulatory submissions, and the draft guidance provides a valuable framework to support this work across condition and disease areas. However, we encourage the FDA to specifically consider its relevance to women at risk for or living with Alzheimer’s disease and Alzheimer’s disease-related dementias (AD/ADRD).

Currently, nearly 7 million Americans are living with Alzheimer’s disease, and this number is projected to double by the year 2060.¹ Women comprise nearly two-thirds of the Alzheimer’s disease population in the United States and account for a similar proportion of the unpaid Alzheimer’s disease caregiving population.^{2,3} Alzheimer’s disease is the fifth leading cause of death for women aged 65 and older, and women in their 60s are “more than twice as likely to develop Alzheimer’s disease” than they are to develop breast cancer.⁴

The urgent need to accelerate the development of medical products to address the growing incidence of AD/ADRD requires science that consistently examines the role of sex in the condition’s onset, progression, and overall impact. Given the higher incidence and prevalence of Alzheimer’s disease among women, we commend the FDA for prioritizing a thorough examination of sex differences in the clinical development and evaluation of medical products and raise recommendations for the agency’s consideration below.

Recommendations to FDA

We urge the FDA to implement a comprehensive framework that considers sex as a fundamental variable throughout drug and device development, approval, and post-market processes across disease and condition areas, including AD/ADRD. This should include the following recommendations:

1. **Representative Cohorts in Clinical Trials:** Ensure clinical trials recruit and retain study cohorts that are reflective of disease burden, with findings analyzed by sex and relevant social

¹ 2024 Alzheimer’s disease facts and figures. *Alzheimers Dement.* 2024;20(5):3708-3821. doi:10.1002/alz.13809

² Beam CR, Kaneshiro C, Jang JY, Reynolds CA, Pedersen NL, Gatz M. Differences Between Women and Men in Incidence Rates of Dementia and Alzheimer’s Disease. *J Alzheimers Dis.* 2018;64(4):1077-1083. doi:10.3233/JAD-180141

³ Alzheimer’s Association. Women and Alzheimer’s. *Alzheimer’s Disease and Dementia.* Published 2019. <https://www.alz.org/alzheimers-dementia/what-is-alzheimers/women-and-alzheimer-s>

⁴ Alzheimer’s Association. Women and Alzheimer’s. *Alzheimer’s Disease and Dementia.* Published 2019. <https://www.alz.org/alzheimers-dementia/what-is-alzheimers/women-and-alzheimer-s>

determinants to better understand how race, ethnicity, socio-economic status, and sex intersect in disease risk, diagnosis, and treatment outcomes.

2. **Sex Differences in Disease Risk, Progression, Prognosis, and Treatment Response:** Enhance research into how sex influences neurological disease progression and treatment responses, given the disproportionate impact on women, and explore the specific effects of life stages on brain health. In evaluating safety and efficacy of symptomatic or disease modifying therapies, rigorously assess if and how men and women respond differently.
3. **Targeted Research on Hormonal Impacts:** Focus research on the neurological impacts of hormonal changes, particularly during menopause, to develop safer, more targeted hormone therapies for women.

These recommendations are intended as a foundational starting point for understanding the role of sex differences in AD/ADRD diagnosis, manifestation, and treatment. Recognizing these differences is crucial for advancing our understanding of these conditions, and similar patterns may be observed across other diseases and health conditions. In light of this, we urge the FDA to take into account the following information, which may be valuable when considering sex-specific data in clinical evaluations.

Sex Disparities in Alzheimer's Disease Clinical Trials

The draft guidance rightly cites the historical underrepresentation of women in clinical trials for certain therapeutic areas, which remains an ongoing issue. The representation of women in Alzheimer's disease drug and device trials is more nuanced. While women are generally overrepresented compared to men in these trials, their participation still does not fully reflect the population of women living with Alzheimer's disease. Each Alzheimer's disease trial should aim for a proportion of female participants that aligns with the disease burden in the general population, acknowledging that women are at a higher risk for developing Alzheimer's disease due to factors such as age, hormonal changes, and genetics. This approach allows for flexibility in trial design, considering factors like methodology or scientific grounds that may necessitate deviations from the population-wide estimate.

The inclusion of women in clinical trials for Alzheimer's disease medical products is necessary for understanding the varied impacts of diagnostic and treatment tools. For example, women on the whole experience faster cognitive decline after the diagnosis of Alzheimer's disease mild cognitive impairment (MCI), highlighting the need for systematic study of sex-specific differences in biomarkers, risk factors, emergence and progression of symptoms, disease pathology, and treatment responses.⁵ Given the different neurobiological and hormonal factors at play, it is vital that the evaluation of diagnostic tools account for the specific ways that Alzheimer's disease presents in women.

Likewise, the cognitive symptoms experienced by women with Alzheimer's disease can differ from those seen in men. One study evaluating sex-specific differences in verbal memory found that "women significantly outperformed men on immediate and delayed measures of verbal memory."⁶ This may lead to clinical misinterpretations of cognitive decline patterns in women, delaying critical interventions, diminishing treatment efficacy and, for some women, resulting in progression to the point of becoming ineligible to initiate treatment. Furthermore, women with Alzheimer's disease are more likely to experience mood disorders like depression, which can further complicate clinical assessment and

⁵ Ferretti MT, Iulita MF, Cavedo E, et al. Sex differences in Alzheimer disease — the gateway to precision medicine. *Nature Reviews Neurology*. 2018;14(8):457-469. doi:<https://doi.org/10.1038/s41582-018-0032-9>

⁶ Sundermann EE, Biegon A, Rubin LH, et al. Does the Female Advantage in Verbal Memory Contribute to Underestimating Alzheimer's Disease Pathology in Women versus Men?. *J Alzheimers Dis*. 2017;56(3):947-957. doi:10.3233/JAD-160716

treatment.⁷ In certain cases, “late-life depression and dementia can be indistinguishable” for clinicians. Alzheimer’s disease patients with depression tend to exhibit more severe neuropathology compared to those without depression, which may alter treatment options.⁸ Men may also show higher rates of Alzheimer’s disease related apathy or aggression.⁹

These sex-specific differences in symptomatology should be addressed in clinical trials for drugs that target behavioral symptoms or cognitive decline and should be considered in weighing the patient and caregiver reported outcomes in evaluating clinical benefits of disease-modifying and symptomatic treatments. Ensuring that trials account for the different ways in which symptoms manifest in men and women, along with any treatment response differences between men and women, is crucial for developing treatments that are appropriately titrated and effective for both sexes. Without this consideration, there is a risk that treatments may be less safe and effective for women or that their symptoms – which differ in onset, incidence, frequency, and/or intensity – may not be managed appropriately by some clinicians or in some clinical settings.

Role of Gender, Race/Ethnicity, and Social Determinants of Health in AD/ADRD

Women’s experience with AD/ADRD throughout the diagnostic and treatment process cannot be untwined from the influence of social factors, and we urge the FDA to take these experiences into account within the draft guidance.

AD/ADRD manifests differently across racial and ethnic groups, with the intersection of race, ethnicity, and sex influencing the prevalence, progression, and experience of the disease in complex ways. Black and Hispanic women, for instance, face not only the inherent risks associated with female sex but also the exacerbating effects of racial and ethnic disparities. Emerging research indicates that there may be racial and ethnic disparities in certain biomarkers of Alzheimer’s disease. For example, lower levels of total tau and phosphorylated tau181 proteins in the cerebrospinal fluid (CSF) of African American individuals seem to be influenced by a combination of race and the APOE ε4 gene. This suggests that the APOE ε4 gene may affect African American individuals differently than white individuals in relation to Alzheimer’s disease risk.¹⁰ Factors related to medical bias also contribute to observed disparities, as Black patients with Alzheimer’s disease often have to exhibit more advanced symptoms before receiving a dementia diagnosis compared to their white counterparts.¹¹ The intersection of structural sexism and racial disparities and biases exacerbates this issue, with Black women experiencing more significant memory loss and cognitive decline than white women.¹² Similar inequities are observed in other minoritized groups, such as Hispanic populations, who are up to 1.5 times more likely to develop Alzheimer’s disease and related dementias but only 18% more likely to be diagnosed.¹³

⁷ Crump C, Sieh W, Vickrey BG, Edwards AC, Sundquist J, Sundquist K. Risk of depression in persons with Alzheimer's disease: A national cohort study. *Alzheimers Dement (Amst)*. 2024;16(2):e12584. Published 2024 Apr 14. doi:10.1002/dad2.12584

⁸ Burke AD, Goldfarb D, Bollam P, Khokher S. Diagnosing and Treating Depression in Patients with Alzheimer’s Disease. *Neurology and Therapy*. 2019;8(2):325-350. doi:https://doi.org/10.1007/s40120-019-00148-5

⁹ Li XL, Hu N, Tan MS, Yu JT, Tan L. Behavioral and psychological symptoms in Alzheimer's disease. *Biomed Res Int*. 2014;2014:927804. doi:10.1155/2014/927804

¹⁰ Morris JC, Schindler SE, McCue LM, et al. Assessment of Racial Disparities in Biomarkers for Alzheimer Disease. *JAMA Neurology*. 2019;76(3):264. doi:https://doi.org/10.1001/jamaneurol.2018.4249

¹¹ National Institute on Aging. Data shows racial disparities in Alzheimer’s disease diagnosis between Black and white research study participants. National Institute on Aging. Published December 16, 2021. <https://www.nia.nih.gov/news/data-shows-racial-disparities-alzheimers-disease-diagnosis-between-black-and-white-research>

¹² Avila-Rieger JF, Adkins-Jackson PB, Hill-Jarrett TG, et al. Early life exposure to structural sexism and late-life memory trajectories among black and white women and men in the United States. *Alzheimer s & Dementia*. Published online December 18, 2024. doi:https://doi.org/10.1002/alz.14410

¹³ Race, Ethnicity, and Alzheimer’s. Alzheimer’s Association; 2020. Accessed January 27, 2025.

The draft guidance makes sparing references to race as a factor for AD/ADRD disease risk, with mentioned recommendations that sponsor reports include “the number of participants entered into the study to date tabulated by ‘age group, gender, and race,’” and requiring sponsors “to present safety and effectiveness data in the clinical data section of an NDA by ‘gender, age, and racial subgroups.’” However, the aforementioned disparities underscore the urgency for the FDA to elevate the need for strengthened proportionate racial and ethnic representation in clinical trial research, particularly in the AD/ADRD context. AD/ADRD research has been informed largely by white participants, yet African Americans, who represent nearly 20% of people living with dementia in the United States, only account for about 2% of clinical trial participants.¹⁴ Barriers to clinical trial participation are, at least in part, attributed to various social determinants of health, including medical distrust stemming from historical injustices within the medical system and lower access both to routine clinical care and research sites. Race cannot be overlooked as a factor in trials related to AD/ADRD as race and ethnicity are demonstrated to play critical roles in health outcomes, including disease onset, progression, and treatment responses for these diseases.

Furthermore, women situated at the intersection of multiple marginalized identities may experience disproportionately high levels of vulnerability to AD/ADRD and disparities in diagnosis and care due to compounded socioeconomic inequities and health care disparities. This includes women residing in rural or underserved areas, particularly where health care resources are in short supply. Women of marginalized identities may encounter heightened impacts of social determinants of health, including poverty, limited access to quality health care, environmental stressors, and a legacy of medical mistrust rooted in historical injustices. The cumulative impact of these factors can delay the diagnosis of AD/ADRD and hinder access to preventive care and therapeutic interventions. This highlights the need for inclusive representation to ensure that clinical trial results are generalizable across all populations, allowing for tailored and effective treatments that meet the needs of different patient groups. The FDA must continue to push for inclusive and representative participation in clinical trials to bridge the gap in AD/ADRD research and better address the unique needs of underrepresented populations and should mitigate the barriers to clinical trial participation faced by individuals in these marginalized groups.

The relationship between environmental and lifestyle factors and AD/ADRD risk in women adds another layer of complexity, and, while there is growing interest in understanding this connection, research and evidence in this area is lacking. It remains unclear whether women are more susceptible to the adverse effects of certain lifestyles, diets, or environmental toxins compared to men, and understanding how such factors may play a role in disparities in disease prevalence could improve diagnostic and therapeutic tools. Research in other neurodegenerative disorders, such as Parkinson's disease, has shown that exposure to environmental toxins, including air pollution, can increase the risk of developing these conditions.¹⁵ Likewise, areas with higher levels of pollution, particularly in the Southeast United States and rural regions, often with socioeconomically disadvantaged populations, have been linked to an increased risk of Parkinson's and other neurodegenerative diseases. These findings suggest that similar environmental factors could potentially impact AD/ADRD risk in women, underscoring the need for further research to examine how such exposures may contribute to the disease's development.

Understanding the intersection of sex, race, ethnicity, and social determinants of health should be considered in the clinical evaluation of medical products ensures that treatments and interventions are effective across all populations. By considering these intersections, clinical trials and medical evaluations

¹⁴ Bhandari T. Equity for African Americans in Alzheimer's disease. Outlook Magazine. Published February 17, 2023. <https://outlook.washu.edu/equity-for-african-americans-in-alzheimers-disease/>

¹⁵ Murata H, Barnhill LM, Bronstein JM. Air Pollution and the Risk of Parkinson's Disease: A Review. *Mov Disord*. 2022;37(5):894-904. doi:10.1002/mds.28922

can identify any disparities in safety, efficacy, or accessibility, leading to more personalized and effective care for all populations.

Influence of Caregiving on AD/ABRD Prevalence and Outcomes

Caregiving for individuals with AD/ABRD can have profound and long-lasting effects on caregivers, especially women, who are more likely to take on these roles. Women are disproportionately represented in caregiving roles, with more than 60% of unpaid AD/ABRD caregivers being women.¹⁶ Addressing the caregiving burden on women is crucial for evaluating sex differences in clinical care because caregiving can significantly impact physical and mental health. Caregiving can be emotionally, physically and psychologically demanding, and evidence shows that caregivers experience “psychosocial and physical health effects,” with impacts being more pronounced for women caregivers and caregivers from lower socioeconomic groups.¹⁷ Caregivers can experience burnout due to the attention required to manage the complex needs of a person with AD/ABRD.

One particularly alarming aspect of caregiving is the potential for caregivers themselves to experience cognitive decline. Research has suggested that caregivers—especially those caring for individuals with dementia—are at an elevated risk for cognitive decline and, potentially, for developing dementia themselves, with one study noting that dementia caregivers have significantly greater cognitive decline compared to non-dementia caregivers, and that older adult caregivers are acutely susceptible to the psychological stress associated with caregiving.¹⁸

Women’s caregiving roles throughout the life course may have altered physiological and psychological states that potentially affect clinical trial outcomes and health care needs. Caregiving has been linked to chronic stress, which can result in hormonal changes and alterations in the brain’s function.¹⁹ Women caregivers may also be more likely to suppress their own health needs due to the demands of caregiving, delaying their own medical treatments and further exacerbating physical health challenges.

Understanding the unique physiological and psychological experiences of women caregivers is critical for improving clinical care and ensuring that medical products and treatments are evaluated in ways that account for these experiences, not only for AD/ABRD caretakers but for caretakers across condition areas. Clinical trials often fail to address how caregiving responsibilities may impact outcomes for participants, especially women. Women caregivers may experience more difficulty adhering to clinical trial protocols, may have higher dropout rates, and may exhibit different responses to treatment due to the dual stress of caregiving and their own health challenges. Clinical evaluations and practices can ultimately be improved by addressing the sex differences in caregiving and recognizing the profound impact of caregiving on health.

Evidenced Sex Differences in Alzheimer’s Disease and Hormonal Impacts

Several factors are thought to influence the apparent sex differences in Alzheimer’s disease. Age is considered the most important risk factor for Alzheimer’s disease, with most Alzheimer’s disease cases

¹⁶ Alzheimer’s Association. Women and Alzheimer’s. Alzheimer’s Disease and Dementia. Published 2019. <https://www.alz.org/alzheimers-dementia/what-is-alzheimers/women-and-alzheimer-s>

¹⁷ Sörensen S, Conwell Y. Issues in dementia caregiving: effects on mental and physical health, intervention strategies, and research needs. *Am J Geriatr Psychiatry*. 2011;19(6):491-496. doi:10.1097/JGP.0b013e31821c0e6e

¹⁸ Dassel KB, Carr DC, Vitaliano P. Does Caring for a Spouse With Dementia Accelerate Cognitive Decline? Findings From the Health and Retirement Study. *The Gerontologist*. 2015;57(2):319-328. doi:https://doi.org/10.1093/geront/gnv148

¹⁹ Whittaker AC, Gallagher S. Caregiving alters immunity and stress hormones: a review of recent research. *Current Opinion in Behavioral Sciences*. 2019;28:93-97. doi:https://doi.org/10.1016/j.cobeha.2019.02.002

becoming clinically observable after the age of 65.²⁰ In the United States, women experience greater life expectancy: 79.3 years for women compared to 73.5 years for men.²¹ Additionally, strong evidence is emerging that sex-specific differences in gene networks in the brain and hormonal factors contribute to disease onset and progression. The influence of hormones, particularly estrogen, plays a crucial role in brain health and vascular function.

Estrogen plays a critical role in Vascular Contributions to Cognitive Impairment and Dementia (VCID). Estrogen is thought to have neuroprotective effects, and its decline after menopause may increase women's vulnerability to both vascular cognitive impairment and other types of dementia. It is during the menopause transition, which typically occurs between the ages of 45 and 55, that women experience significant hormonal changes that impact neurological health.

From their transition into menopause through end of life, women may experience a variety of physiological changes, namely a loss in estrogen. The brain, which relies heavily on glucose as its primary fuel source, also suffers a decline in glucose metabolism during menopause. This reduction in glucose utilization—about 10-20%—is especially significant since the brain consumes a substantial portion of the body's energy. In response to this glucose deficit, the brain begins to rely on lipids as auxiliary fuel sources. This shift in fuel utilization is associated with menopausal weight gain, as the body begins to store more lipids and generate ketone bodies for energy.

One of the most notable changes during the menopause transition is the impact on brain white matter, which is crucial for facilitating fast synaptic transmissions between nerve cells. The brain is the most lipid-rich organ in the body, and this white matter plays a vital role in the efficiency of brain processes.²² However, the hormonal changes associated with menopause can interfere with the normal function of white matter, potentially affecting cognitive function. As a result, many women report cognitive complaints during menopause, including memory disruptions and difficulty concentrating.²³ In addition to cognitive symptoms, depression, autoimmune diseases, and other neurological conditions may emerge or intensify during this time, with the brain serving as the common actor for these changes. Hormone replacement therapy has been studied for its potential to reduce dementia risk in postmenopausal women and, while some studies suggest that estrogen has a protective effect on mitigating neurodegeneration, findings from others are mixed.²⁴

This decline in estrogen may also exacerbate the effects of vascular risk factors such as high blood pressure or cholesterol, increasing the likelihood of VCID and other forms of dementia.²⁵ VCID is associated with conditions like vascular dementia and cognitive decline following stroke or small vessel

²⁰ Guerreiro R, Bras J. The age factor in Alzheimer's disease. *Genome Med.* 2015;7:106. Published 2015 Oct 20. doi:10.1186/s13073-015-0232-5

²¹ QuickStats: Life Expectancy at Birth, by Sex — National Vital Statistics System, United States, 2019–2021. *MMWR Morbidity and Mortality Weekly Report.* 2023;72. doi:https://doi.org/10.15585/mmwr.mm7228a5

²² Elliott DA, Weickert CS, Garner B. Apolipoproteins in the brain: implications for neurological and psychiatric disorders. *Clin Lipidol.* 2010;51(4):555-573. doi:10.2217/CLP.10.37

²³ Weber MT, Mapstone M, Staskiewicz J, Maki PM. Reconciling subjective memory complaints with objective memory performance in the menopausal transition. *Menopause.* 2012;19(7):735-741. doi:10.1097/gme.0b013e318241fd22

²⁴ Ali N, Sohail R, Jaffer SR, et al. The Role of Estrogen Therapy as a Protective Factor for Alzheimer's Disease and Dementia in Postmenopausal Women: A Comprehensive Review of the Literature. *Cureus.* 2023;15(8):e43053. Published 2023 Aug 6. doi:10.7759/cureus.43053

²⁵ Ali N, Sohail R, Jaffer SR, et al. The Role of Estrogen Therapy as a Protective Factor for Alzheimer's Disease and Dementia in Postmenopausal Women: A Comprehensive Review of the Literature. *Cureus.* 2023;15(8):e43053. Published 2023 Aug 6. doi:10.7759/cureus.43053

disease, however, clinical understanding of the role of sex and gender in vascular dementia is limited.^{26,27} The role of cardiovascular risk factors in dementia is an area of growing interest, and some studies suggest that women more often develop cognitive impairment in “domains of attention, executive functioning, and language” after a stroke compared to men; however, more research is necessary for a holistic understanding of potential sex differences in this area.²⁸

As VCID often coexists with other dementias, including Alzheimer’s disease, particularly in the aging population, the presence of both vascular pathology and neurodegenerative pathology (e.g., Alzheimer’s or frontotemporal dementia) can lead to mixed-etiology dementia. Mixed-etiology dementia is especially difficult to diagnose and treat, as it involves multiple causes of cognitive impairment. While sex differences are not evident in the prevalence of VCID, more inclusive research could shape improved understanding around the role of how women’s longer life expectancy and higher rates of vascular risk may contribute to the development of mixed-etiology dementia.²⁹

Variations in immune response also contribute to sex-specific differences in Alzheimer’s disease. Rigorous studies demonstrate that “the immune system in females seems more robust and responsive to immune stimuli” and that “certain detrimental inflammatory responses are associated with female-biased AD risk alleles, such as [APOE ε4].”³⁰ These sex-specific differences in immune and metabolic function are critical for understanding the underlying mechanisms of Alzheimer’s disease and underscore the necessity of considering sex as a biological variable in clinical trials.

We appreciate that the FDA draft guidance notes that “fluctuations associated with hormonal changes...may also influence clinical outcomes” and that covariates, such as pre- and post-menopause, may be responsible for the differences in safety or effectiveness for a medical product, but given the significance of the changes associated with menopause, FDA may consider highlighting this life stage in greater detail. Specifically, we encourage the FDA to provide more explicit guidance on how to account for the unique physiological and hormonal shifts during menopause when designing clinical trials or evaluating data. This could include guidance for additional stratification by menopausal status, considerations of symptom management, and incorporating menopause-related biomarkers in efficacy and safety analyses. By doing so, the FDA would help ensure that medical products are evaluated appropriately for their impact on this significant phase of life, which could lead to better tailored treatment options for individuals experiencing menopause.

Conclusion

We appreciate your consideration of these comments and look forward to working together with the FDA to deepen our understanding of sex differences in the clinical evaluation of medical products and to ensure that future research and therapies are more inclusive, effective, and tailored to the needs of all individuals. Please reach out directly to Ian Kremer, Executive Director of LEAD Coalition at ikremer@leadcoalition.org or Lindsey Miltenberger, Chief Advocacy Officer at the Society for Women’s Health Research at lindsey@swhr.org with any questions.

²⁶ National Institute on Aging. Vascular Dementia: Causes, Symptoms, and Treatments. National Institute on Aging. Published 2021. <https://www.nia.nih.gov/health/vascular-dementia/vascular-dementia-causes-symptoms-and-treatments>

²⁷ Akhter F, Persaud A, Zaokari Y, Zhao Z, Zhu D. Vascular Dementia and Underlying Sex Differences. *Front Aging Neurosci.* 2021;13:720715. Published 2021 Sep 8. doi:10.3389/fnagi.2021.720715

²⁸ Exalto LG, Weaver NA, Kuijf HJ, et al. Sex Differences in Poststroke Cognitive Impairment: A Multicenter Study in 2343 Patients With Acute Ischemic Stroke. *Stroke.* 2023;54(9):2296-2303. doi:<https://doi.org/10.1161/strokeaha.123.042507>

²⁹ Gannon OJ, Robison LS, Custozzo AJ, Zuloaga KL. Sex differences in risk factors for vascular contributions to cognitive impairment & dementia. *Neurochemistry International.* 2019;127:38-55. doi:<https://doi.org/10.1016/j.neuint.2018.11.014>

³⁰ Lopez-Lee C, Kodama L, Gan L. Sex Differences in Neurodegeneration: The Role of the Immune System in Humans. *Biol Psychiatry.* 2022;91(1):72-80. doi:10.1016/j.biopsych.2021.01.002

Sincerely,

Organizations

ACCSES – The Voice of Disability Service Providers

ACMCRM Arachnoiditis & Chronic Meningitis Collaborative Research Network

ADvancing States

AgeneBio

Alliance for Aging Research

Alliance for Patient Access

AlterDementia

Alzheimer's Association

Alzheimer's Disease Resource Center, Inc. (ADRC)

Alzheimer's Foundation of America

Alzheimer's Impact Movement (AIM)

Alzheimer's Los Angeles

Alzheimer's New Jersey

Alzheimer's Orange County

Alzheimer's San Diego

Alzheimer's Tennessee

Alzheon

American Academy of Neurology

American Association for Geriatric Psychiatry

American Brain Coalition

American Federation for Aging Research (AFAR)

American Geriatrics Society

American Medical Women's Association

American Neurological Association

American Society of Consultant Pharmacists (ASCP)

American Society on Aging

Association of California Caregiver Resource Centers (ACCRC)

Autistic Women & Nonbinary Network — AWN

The Balm In Gilead, Inc.

Benjamin Rose Institute on Aging

Biomarker Collaborative

Bone Health and Osteoporosis Foundation

The Brain Donor Project

Brain Injury Alliance of Nebraska

Bridge Builder Strategies

Brigade Health

BrightFocus Foundation

Bristol Myers Squibb

Caregiver Action Network

CaringKind, The Heart of Alzheimer's Caregiving

Center for BrainHealth at The University of Texas at Dallas

Center for Healthy Aging

Center to Advance Palliative Care

Chambers-Grundy Center for Transformative Neuroscience, Department of Brain Health, UNLV

Chronic Disease Coalition

Cleveland Clinic

Coalition of Wisconsin Aging and Health Groups

Cognitive Dynamics Foundation

Creutzfeldt-Jakob Disease Foundation

Cure Alzheimer's Fund

Danaher Diagnostics (Beckman Coulter, Cepheid, HemoCue, LeicaBiosystems, Mammotome & Radiometer)

Davos Alzheimer's Collaborative
Dementia Alliance International
Dementia Alliance of North Carolina
DigiCARE Realized Inc.
Diverse Elders Coalition
Endocrine Society
Exon 20 Group
Family Caregiver Alliance
5p- Society
Fujirebio Diagnostics, Inc.
Genetic Alliance
Georgetown University Medical Center
Memory Disorders Program
Gerontological Society of America
Global Alzheimer's Platform Foundation
Global CEO Initiative on Alzheimer's Disease
Global Coalition on Aging
Hadassah, The Women's Zionist Organization
of America, Inc.
Hannah's Hope Fund for Giant Axonal
Neuropathy, Inc.
The Hartford Institute for Geriatric Nursing,
NYU Rory Meyers College of Nursing
HealthMatters Program
HealthyWomen
HFC
Huntington's Disease Society of America
Hypertrophic Cardiomyopathy Association
ICAN, International Cancer Advocacy
Network
Infusion Access Foundation (IAF)
International Association for Indigenous Aging
Iowa State Grange
Johns Hopkins Memory and Alzheimer's
Treatment Center
K-T Support Group

Las Vegas HEALS
Latino Alzheimer's and Memory Disorders
Alliance
LEAD Coalition (Leaders Engaged on
Alzheimer's Disease)
Lewy Body Dementia Resource Center
Life Molecular Imaging
Linus Health, Inc.
LuMind IDSC Foundation
Lupus and Allied Diseases Association, Inc.
Medicare Rights Center
MET Crusaders
Michigan State University Alzheimer's
Alliance
Milken Institute Alliance to Improve Dementia
Care
Mount Sinai Center for Cognitive Health
National Alliance for Caregiving
National Asian Pacific Center on Aging
National Association of Activity Professionals
National Association of Social Workers
(NASW)
National Association of State Long-Term Care
Ombudsman Programs (NASOP)
National Certification Council for Activity
Professionals
National Committee to Preserve Social
Security and Medicare
National Consumers League
National Down Syndrome Society
National Hartford Center of Gerontological
Nursing Excellence
National Health Council
National Hispanic Council On Aging
(NHCOA)
National Indian Council on Aging (NICOA)
National Infusion Center Association (NICA)
National Menopause Foundation

National Minority Quality Forum
 National Task Group on Intellectual
 Disabilities and Dementia Practices
 NCBA
 Nebraska AIDS Project
 Neurotech Network
 Nevada Chronic Care Collaborative
 NFL Neurological Center
 Noah Homes
 The Ohio Council for Cognitive Health
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Scottish Brain Sciences
 Second Wind Dreams, Inc./ Virtual Dementia
 Tour
 Society for Women's Health Research
 Pat Summitt Foundation
 Synthesis Brain Health
 TauRx Pharmaceuticals Ltd.
 The Association for Frontotemporal
 Degeneration
 Trellis/ACT on Alzheimer's
 University of Chicago, Healthy Aging &
 Alzheimer's Research Care Center
 University of Kansas Alzheimer's Disease
 Research Center
 University of Rochester Alzheimer's Disease
 Care, Research and Education Program
 (AD-CARE)
 UsAgainstAlzheimer's
 Veravas
 Voices of Alzheimer's
 Volunteers of America

University-Affiliated Researchers

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Neelum T. Aggarwal, MD (Rush University
 Medical Center*)
 Benedict C. Albeni, PhD, BCMAS, CRQM
 (Nova Southeastern University*)
 Ricardo F. Allegri, MD, PhD (School of
 Medicine, Universidad de Buenos Aires*)
 Takashi Amano, PhD, MSW (Rutgers
 University Newark*)
 Halima Amjad, MD, PhD, MPH (Johns
 Hopkins University School of Medicine*)
 Liana G. Apostolova, MD, MSc, FAAN
 (Indiana University School of Medicine*)

Brian S. Appleby, M.D. (Case Western
 Reserve University School of Medicine*)
 Rhoda Au, Ph.D. (Boston University
 Chobanian & Avedisian School of
 Medicine and Public Health*)
 Laura D. Baker, PhD (Wake Forest University
 School of Medicine*)
 A.M. Barrett MD (Department of Neurology,
 UMass Chan Medical School*)
 Maryam Beigi, MD (Mary S. Easton Center
 for Alzheimer's Disease Research at
 UCLA*)

Andrew R. Bender, Ph.D. (Cleveland Clinic
Lou Ruvo Center for Brain Health*)

Tammie L.S. Benzinger, M.D., Ph.D.
(Washington University School of
Medicine*)

Soo Borson, MD (USC Keck School of
Medicine*)

Nicole Bouranis, PhD (Yale University School
of Medicine*)

Andrea Bozoki, MD, FAAN (University of
North Carolina, Chapel Hill*)

Christine J. Cliatt Brown, MD (Division of
Cognitive Neurology, University of Utah*)

Jeffrey M. Burns, MD, MS (University of
Kansas Alzheimer's Disease Research
Center*)

Goldie S. Byrd, PhD (Wake Forest University
School of Medicine*)

Ismael Calandri MD (University of Buenos
Aires*)

Christopher M. Callahan, MD (Indiana
University Center for Aging Research*)

Maria Torroella Carney, MD, FACP
(Northwell Health and Zucker School of
Medicine at Hofstra/Northwell*)

Sandra Bond Chapman, PhD (Center for
BrainHealth at The University of Texas at
Dallas*)

Joshua Chodosh, MD, MSHS, FACP (NYU
Grossman School of Medicine*)

Urvika Choksey, MD (Yale School of
Medicine, Department of Geriatric
Medicine*)

Kaitlin Casaletto, PhD (University of
California San Francisco, School of
Medicine*)

Marianne Chanti-Ketterl, PhD, MSPH (Duke-
UNC Alzheimer's Disease Research
Center*)

Anna Chodos MD, MPH (University of
California San Francisco, School of
Medicine*)

Nathaniel Chin, MD (University of Wisconsin
Alzheimer's Disease Research Center
(ADRC)*)

David G. Clark, MD (Indiana University
School of Medicine, Department of
Neurology*)

Carolyn K Clevenger, DNP, GNP-BC,
AGPCNP-BC, FAANP, FGSA, FAAN
(Emory University*)

Ann D. Cohen, PhD (Department of
Psychiatry, University of Pittsburgh, School
of Medicine*)

Tara A. Cortes, PhD, RN, FAAN, FGSA
(NYU Rory Meyers College of Nursing,
The Hartford Institute for Geriatric
Nursing*)

Suzanne Craft, PhD (Wake Forest School of
Medicine*)

Jeffrey Cummings, MD, ScD (University of
Nevada Las Vegas*)

Kirk R. Daffner MD, FAAN (Department of
Neurology, Harvard Medical School*)

Steven T. DeKosky, MD, FACP, FANA,
FAAN (University of Florida College of
Medicine*)

Peggye Dilworth-Anderson, PhD (Gillings
School of Global Public Health, University
of North Carolina- Chapel Hill*)

N. Maritza Dowling PhD (The George
Washington University School of
Nursing*)

Ranjan Duara, MD (Wien Center for
Alzheimer's Disease and Memory
Disorders, University of Florida College of
Medicine*)

Gary Epstein-Lubow, MD (Alpert Medical
School of Brown University & Brown
University School of Public Health*)

Leslie Chang Evertson, DNP, RN, GNP-BC
(UCLA Health Geriatrics*)

D. Luke Fischer, MD, PhD (Weill Institute for
Neurosciences, University of California,
San Francisco*)

Concetta Forchetti, MD, PhD (Ascension Center for Cognitive Disorder and Clinical Research*)

Richard H. Fortinsky, PhD (UConn Center on Aging, University of Connecticut School of Medicine*)

Norman Foster, MD (University of Utah*)

Nicole R. Fowler, PhD (Indiana University School of Medicine*)

Nick C. Fox, MD (University College London, Institute of Neurology Dementia Research Centre*)

Douglas Galasko, MD (University of California San Diego, Department of Neurosciences*)

Seth A. Gale, M.D. (Brigham and Women's Hospital, Harvard Medical School*)

Michela Gallagher, PhD (Johns Hopkins University School of Medicine*)

James E. Galvin, MD, MPH (Miller School of Medicine, University of Miami*)

Sam Gandy, MD, PhD (Icahn School of Medicine at Mount Sinai*)

Joseph E. Gaugler, PhD (School of Public Health, University of Minnesota*)

David S. Geldmacher, MD, FACP (University of Alabama at Birmingham School of Medicine, Division of Cognitive and Behavioral Neurology*)

Thomas M. Gill, M.D. (Yale School of Medicine*)

Andrea Gilmore-Bykovskyi, PhD, RN

Laura N. Gitlin, PhD (Drexel University, College of Nursing and Health Professions*)

Joshua Grill, PhD (Alzheimer's Disease Research Center, University of California Irvine*)

Lisa P. Gwyther, MSW, LCSW (Duke University Medical Center*)

Christian Haass, PhD (Ludwig Maximilians University Munich*)

Duke Han, PhD (Keck School of Medicine of USC*)

Mark D. Hayward, Ph.D. (The University of Texas at Austin*)

Elizabeth Head, PhD (Center for the Neurobiology of Learning and Memory, University of California, Irvine School of Medicine*)

J. Neil Henderson, PhD (University of Minnesota Medical School*)

Vered Hermush, MD (Laniado Medical Center, Ariel University Israel*)

Patricia C. Heyn, PhD, FGSA, FACRM (Center for Optimal Aging, Marymount University*)

Nancy A. Hodgson, RN, PhD, FAAN (University of Pennsylvania School of Nursing*)

David M. Holtzman, MD (Washington University School of Medicine, Department of Neurology*)

Nikki L. Hill, PhD, RN (The Pennsylvania State University, Ross and Carol Nese College of Nursing*)

Tanisha Hill-Jarrett, PhD (University of California San Francisco School of Medicine*)

William Hu, MD, PhD, FAAN (Rutgers University*)

Ula Hwang, MD, MPH (New York University Grossman School of Medicine*)

Philip Insel PhD, MS (University of California San Francisco School of Medicine*)

Lee A. Jennings, MD, MSHS (Section of Geriatrics, University of Oklahoma Health Sciences Center*)

Katherine S. Judge, PhD (Cleveland State University*)

Amy J.H. Kind, MD, PhD (University of Wisconsin School of Medicine and Public Health*)

Fred A. Kobylarz, MD, MPH (Rutgers Robert Wood Johnson Medical School*)

Rada Koldamova, MD, PhD (School of Public Health, University of Pittsburgh*)

Walter A. Kukull, PhD (School of Public Health, University of Washington*)

Robert Jr Laforce, MD PhD (Clinique Interdisciplinaire de Mémoire, Dép. des Sciences Neurologiques, CHU de Québec*)

Debomoy K. Lahiri, PhD, Fellow AAAS, FNAI (Indiana Alzheimer's Disease Research Center, Indiana University School of Medicine*)

Cynthia A. Lemere, PhD (Department of Neurology, Brigham and Women's Hospital, Harvard Medical School*)

Michael J. Lepore, PhD (Elaine Marieb College of Nursing at University of Massachusetts, Amherst*)

Spencer W. Liebel, PhD (University of Utah School of Medicine, Department of Neurology*)

Jennifer Lingler PHD, MA, CRNP, FAAN (University of Pittsburgh, School of Nursing*)

Justin Long, MD, PhD (Washington University School of Medicine*)

Marissa Natelson Love, MD (Cognitive and Behavioral Neurology, University of Alabama at Birmingham*)

Yvonne Lu PhD, RN, FGSA, FAAN (Indiana University School of Nursing*)

Kostas Lyketsos, M.D., M.H.S. (Johns Hopkins Memory and Alzheimer's Treatment Center*)

Yannick Marchalant, Ph.D. (Central Michigan University*)

Beth Marks, PhD, RN, FAAN (University of Illinois at Chicago*)

David X. Marquez, PhD (Department of Kinesiology and Nutrition, University of Illinois at Chicago*)

Colin L. Masters, MD (The Florey Institute, The University of Melbourne*)

Richard Mayeux, MD, MSc (Columbia University, Mailman School of Public Health*)

Eric McDade, DO (Washington University School of Medicine*)

Scott M. McGinnis, MD (Brigham and Women's Hospital, Massachusetts General Hospital, Harvard Medical School*)

Michelle Mielke, PhD (Department of Epidemiology, Wake Forest University School of Medicine*)

Elizabeth Mormino, PhD (Stanford University School of Medicine*)

David G. Morgan, PhD (Michigan State University*)

Darby Morhardt, PhD, LCSW (Northwestern University Feinberg School of Medicine*)

Laura Mosqueda, MD, FAAFP, AGSF (Keck School of Medicine of USC*)

Catherine Mummery, PhD FRCP (Dementia Research Centre, Institute of Neurology, University College London*)

Daniel L. Murman, MD, MS (University of Nebraska Medical Center*)

Neelesh K. Nadkarni, MD, PhD, FRCPC (University of Pittsburgh School of Medicine, Department of Medicine (Geriatric Medicine) and Neurology*)

Aanand Naik, MD (Institute on Aging at the University of Texas Health Science Center at Houston*)

Adrian L. Oblak, PhD (Indiana University School of Medicine*)

Esther Oh MD, PhD, AGSF (Johns Hopkins University School of Medicine*)

Kenjiro Ono, PhD, MD (Department of Neurology, Kanazawa University Graduate School of Medical Sciences*)

Rik Ossenkoppele, PhD (Amsterdam University Medical Center and Lund University*)

Miguel A. Pappolla, MD, PhD (University of Texas Medical Branch, Department of Neurology*)

Monica W. Parker, MD (Goizueta Alzheimer's Disease Research Center, Emory University*)

Rachel Peterson, PhD, MPH, MA (University of California, Davis*)

Henry Paulson MD, PhD (Michigan Alzheimer's Disease Center, University of Michigan Medical School*)

Anton P. Porsteinsson, MD (University of Rochester School of Medicine Alzheimer's Disease Care, Research and Education Program*)

Katherine Possin, PhD (University of California San Francisco, Memory and Aging Center*)

Daniel C. Potts, MD, FAAN (University of Alabama Department of Psychology and Alabama Research Institute on Aging*)

Anupam Raina, PhD (University of Alabama at Birmingham, Department of Pathology*)

Vanessa Rayment, MBChB, MSc, MRCPsych (University of Oxford*)

Dorene M. Rentz, PsyD (Brigham and Women's Hospital, Harvard Medical School*)

Alaine Reschke-Hernandez PhD, MT-BC (University of Kentucky College of Medicine, Sanders-Brown Center on Aging*)

David B. Reuben, MD (David Geffen School of Medicine at UCLA*)

Emma Rhodes, PhD (University of Pennsylvania, Department of Neurology, Frontotemporal Degeneration Center*)

Justina Avila-Rieger PhD (Columbia University Irving Medical Center, Department of Neurology*)

Craig W Ritchie, MD, PhD (University of St. Andrews*)

Emily Rogalski, PhD (University of Chicago, Healthy Aging & Alzheimer's Research Care Center*)

Theresa Rohr-Kirchgraber, MD, FACP, FAMWA (Augusta University/University of Georgia Medical Partnership*)

Takaomi C Saido, PhD (RIKEN Center for Brain Science*)

Quincy Miles Samus, PhD, MS (Johns Hopkins School of Medicine*)

Jacqueline Sandoval, MPH (Yale School of Medicine*)

Elizabeth J. Santos, MD, MPH, DFAPA, DFAAGP (University of Rochester Medical Center, Division of Geriatric Mental Health & Memory Care*)

Andrew J. Saykin, PsyD, ABCN (Indiana Alzheimer's Disease Research Center, Indiana University School of Medicine*)

Saurabh Sharma, MD (Georgetown University Memory Disorders Program*)

Suzanne Schindler, MD, PhD (Washington University School of Medicine, Department of Neurology*)

Dennis J. Selkoe, MD (Brigham and Women's Hospital, Harvard Medical School*)

Leslie M. Shaw, PhD (Perelman School of Medicine, University of Pennsylvania*)

Hom Lal Shrestha, MA/PhD (Laurentian University*)

Amanda G. Smith, MD (University of South Florida Byrd Alzheimer's Institute*)

Peter J. Snyder, Ph.D. (Department of Biomedical and Pharmaceutical Sciences, The University of Rhode Island*)

Alan B. Stevens, PhD (Texas A&M Health Science Center*)

Shana D. Stites, PsyD, MA, MS (Penn Memory Center, University of Pennsylvania*)

Donald Sullivan, MD, MA, MCR (Oregon Health and Science University*)

Erin Sundermann, PhD (University of California, San Diego, Department of Psychiatry*)

Malú Gámez Tansey, PhD (Indiana University School of Medicine*)

Pierre N. Tariot, MD (University of Arizona College of Medicine*)

Carmela Tartaglia, M.D., FRCPC (Tanz Centre for Research in Neurodegenerative Diseases, University of Toronto*)

Megan Thomas Hebdon, PhD, DNP, RN, NP-c (University of Utah*)

Debra F Tomasino, MA, CDP (NYU Langone Health, Grossman School of Medicine*)

Taisuke Tomita, PhD (The University of Tokyo*)

Elena Tsoy, PhD (Department of Neurology, University of California, San Francisco*)

R. Scott Turner, MD, PhD (Georgetown University Memory Disorders Program*)

Stella L. Volpe, PhD, RDN, ACSM-CEP, FACSM (Virginia Tech*)

Keith Vossel, MD, MSc (Mary S. Easton Center for Alzheimer's Disease Research,

David Geffen School of Medicine at UCLA*)

Lindsey Walsh, B.A. (Framingham Heart Study, Boston University School of Medicine*)

Qing Wang, PhD (Washington University School of Medicine*)

Nancy Wilson, MA LCSW (Baylor College of Medicine*)

Charles Windon MD (Weill Institute for Neurosciences, University of California, San Francisco*)

Jennifer Wolff, PhD (Johns Hopkins Bloomberg School of Public Health*)

Benjamin Wolozin, M.D., Ph.D. (Boston University Chobanian & Avedisian School of Medicine*)

Mia Yang MD MS (Wake Forest School of Medicine, Department of Internal Medicine - Section on Geriatric Medicine & Gerontology*)

Julie M. Zissimopoulos, PhD (University of Southern California, Price School of Public Policy*)