

ADVISORY COUNCIL ON ALZHEIMER'S RESEARCH, CARE, AND SERVICES

Virtual Meeting

January 25, 2021

Advisory Council Members in Attendance

- *Non-Federal Members Present:* Katie Brandt (Co-Chair), Allan Levey (Co-Chair), Venoreen Browne-Boatswain, Cynthia Carlsson, Debra Cherry, Robert Egge, Bradley Hyman, Matthew Janicki, Becky Kurtz, Carrie Molke, Maria de los Angeles Ordonez
- *Federal Members Present:* Arlene Bierman (Agency for Healthcare Research and Quality, AHRQ), Cheryl Schmitz (Department of Veterans Affairs, VA), Roderick Corriveau (National Institutes of Health, National Institute of Neurological Disorders and Stroke, NIH/NINDS), Elena Fazio (National Institute on Aging, NIA), Bruce Finke (Indian Health Services, IHS), Richard Hodes (National Institutes of Health, NIH), Gavin Kennedy (U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, HHS/ASPE), Shari Ling (Centers for Medicare & Medicaid Services, CMS), Erin Long (Agency on Aging, AoA), Lisa McGuire (Centers for Disease Control and Prevention, CDC), Deb Olster (National Science Foundation, NSF), Anthony Pacifico (Department of Defense, DoD), Cheryl Schmitz (Veterans Health Administration), Nina Tumosa (Health Resources and Services Administration, HRSA)
- *Advisory Council Designated Federal Officer:* Helen Lamont (ASPE)

General Proceedings

Co-Chair Allan Levey, MD, PhD, called the meeting to order at 1:00 p.m. and reviewed the agenda. Helen Lamont, PhD, conducted roll call.

Charge for Meeting

Dr. Levey noted that the COVID-19 pandemic continues to have devastating consequences for patients with Alzheimer's disease and related dementias (ADRD) and their families and caregivers. The pandemic also has impeded research on ADRD. Vaccines are a welcome development. Dr. Levey said presenters would discuss the impact of COVID-19 and vaccination efforts, racial and ethnic disparities in dementia research, and advances in biomarker research. The Council is charged with considering this timely information during discussions and when developing plans for the future. The

year 2021 marks the tenth anniversary of the National Alzheimer's Project Act, which led to the National Plan to Address Alzheimer's Disease and much of the more than \$3.1 billion annual funding for ADRD research--a more than seven-fold increase since 2011. Dr. Lamont said the 2020 National Plan Update has been released.

Update on 2020 National Research Summit on Care, Services, and Supports for Persons with Dementia and their Caregivers

Elena Fazio (NIA/NIH) summarized the planning and proceedings of the summit, which was convened virtually during July and August 2020. The summit included a Twitter poster session with live discussion. Posters, poster discussions, recordings of other summit discussions, and a summary report that discusses current gaps in research are available on the summit's website.

Legislative Updates

Robert Egge summarized recent relevant legislative activities. Congress's appropriation increased the budget for research on Alzheimer's disease by \$300 million. The appropriation also increased the Administration for Community Living's (ACL's) Alzheimer's disease programs by \$1 million. The Building Our Largest Dementia (BOLD) Infrastructure for Alzheimer's Act implementation was funded at \$15 million, a \$5 million increase. The appropriation included \$5 million annually for Healthy Brain Initiative implementation. A new IHS program to address Alzheimer's disease was funded at \$5 million, and the bill included \$15 million annually for DoD's peer-reviewed Alzheimer's disease research efforts. The Improving HOPE for Alzheimer's Act, which aims to accelerate uptake of dementia care planning benefits, was signed and passed into law. The Promoting Alzheimer's Awareness to Prevent Elder Abuse Act, which the Department of Justice will implement, also passed and was signed into law.

COVID-19

Impact of COVID on Medicare Fee-for-Service (FFS) Beneficiaries with Dementia

Dr. Lamont shared findings from recent ASPE research, which are in review for journal publication. Detailed results are not yet available for public dissemination. People with dementia are more likely to be in populations at higher risk for severe disease or mortality from COVID: older age, multiple chronic conditions, people who need personal care, nursing home residents, and people of color. ASPE collaborated with a federal contractor to analyze FFS claims data submitted from the start of the pandemic through September 2020. Data represent 28 million beneficiaries. Analyses assessed COVID diagnosis and mortality, and compared 2019 and 2020 mortality rates in order to assess COVID burden, controlling for key variables. People with dementia were significantly more likely than those not diagnosed with dementia to be diagnosed with COVID-19 and to be hospitalized for or die from COVID-19. Nursing home residents were disproportionately affected by COVID-19. Mortality rates were higher throughout 2020 than in 2019. Data indicate that this was due to the pandemic. Living in a nursing home increased risk of infection. Age is the greatest risk factor for COVID-19 mortality.

Interview with Anthony Fauci, MD

Katie Brandt interviewed Dr. Fauci. She asked how the COVID-19 vaccine would impact people living with dementia and people who provide direct long-term care services. Dr. Fauci said healthcare providers and people living in extended care facilities have first priority for vaccination. Congregate settings increase risk of infection and deleterious consequences among patients and care providers. Ms. Brandt observed that cognitive impairment makes it challenging for people living with ADRD to follow guidelines for wearing masks and social distancing.

Ms. Brandt asked whether people with ADRD are at increased risk for adverse events caused by the COVID-19 vaccine. Dr. Fauci said this is probably not the case. However, because the immune system weakens with age, elderly patients may develop a less robust immune response to the vaccine than younger patients. Ms. Brandt noted that recent research suggests that inflammation may be a factor in triggering dementia. She asked whether inflammation caused by COVID-19 or the vaccine could precipitate or exacerbate ADRD. Dr. Fauci said there are not current conclusive research findings about this. However, acute inflammation caused by the virus could exacerbate Alzheimer's disease. Infection is associated with long-term cognitive problems, such as inability to focus. Vaccines do not trigger major inflammation and are unlikely to trigger or exacerbate ADRD. Dr. Fauci said he would not hesitate to vaccinate a patient with Alzheimer's disease. Ms. Brandt asked under what circumstances families of people with ADRD who live in nursing homes can have safe visits again, and whether it is safe for a family member who has not been vaccinated to visit a patient who has. Dr. Fauci said the vaccine does not guarantee immunity. A person who has not been vaccinated may carry the disease and put others at risk. Family members should continue to follow safety guidelines.

Ms. Brandt asked how to communicate the safety and importance of the vaccine to people who distrust the medical community. Dr. Fauci said messaging must respect skepticism and reflect understanding of reasons for skepticism. Responses to fears about unethical practice should describe safeguards, such as ethical review protocols, that protect against unethical practices. Concerns about speed of development can be addressed by explaining that fast vaccine development was possible due to recent extraordinary advances in vaccine platform technology. Concerns about safety can be addressed by explaining that clinical trials included tens of thousands of participants, and an independent data and safety monitoring board assesses data. This board reviews data before the private company developing the vaccine reviews them. The company then presents data to the Food and Drug Administration (FDA) to request an emergency use authorization. An FDA independent advisory committee, comprised of scientists and not political appointees, then conducts a review. The process is transparent.

Ms. Brandt asked Dr. Fauci whether there were lessons learned from addressing COVID-19 that are relevant to addressing ADRD. Dr. Fauci said ADRD inevitably will be very prevalent. Stakeholders should try to remain "a few steps ahead" of the acute

increase in cases, anticipating needs that will present in 3-5 years. This approach was effective for developing drugs to treat HIV.

COVID-19 Vaccine Implementation

Georgina Peacock, MD, MPH, FAAP, from the CDC presented on vaccine implementation. More than 41 million vaccine doses have been distributed and more than 21 million doses have been administered. More than 2 million long-term care facility residents and staff have received an initial vaccination. CDC posts timely, accurate information about vaccine implementation on its website. The tracker monitors and reports number of doses administered by jurisdiction. It reports total doses distributed, total doses administered, number of people who have received at least one dose, number of people who have received two doses, and number of doses administered in long-term care facilities. CDC updates data daily and also offers other information about COVID-19.

The COVID-19 vaccination is a safer way to develop immunity to the virus than natural immunity following infection, which may be long term. Risk of severe illness and death from infection outweighs benefits of natural immunity. The vaccine offers immunity without risk of severe illness. FDA has approved two vaccines, both of which proved effective in large clinical trials with diverse participants. Vaccines have been tested rigorously for safety. Both vaccines use messenger RNA (mRNA) to trigger immune response. They do not contain a live virus and do not present a risk for infection or affect DNA. Researchers do not yet know how long vaccines protect people from infection.

The Advisory Committee on Immunization Practices advises CDC on vaccinations. It advises efficient and equitable distribution and flexibility to respond to local need and demand. Barriers to vaccine access include cognitive decline, limited social support, disabilities and mobility impairment, lack of transportation, and lack of understanding how to use technology to access vaccines.

CDC has developed and disseminated informational materials in order to inform the general public and counter misinformation. People receive a fact sheet at the time of vaccination. Providers may provide information about how to enroll in V-Safe, a free smartphone-based tool that monitors how people feel after the vaccine and reminds patients to get a second vaccination and to continue to apply other safety measures. COVID-19 vaccines are held to the same safety standards as all vaccines. Vaccination is important, but other measures to prevent COVID-19 spread remain critical. Promoting the idea that the vaccine is safe and effective will help to counter vaccine hesitancy.

Discussion:

- Bradley Hyman, MD, PhD, asked whether V-Safe collects data on demographics and risk factors. The system does collect these data. Dr. Peacock will report to the Committee regarding data analysis and reporting. Shari Ling, MD, said the Committee is interested in information V-Safe learns about reasons for vaccine hesitancy, which could inform public health messaging. Dr. Peacock said the

Vaccinate with Confidence program, administered by CDC and partners, studies vaccine access and hesitancy. This program will offer an online forum in early February.

Dr. Hyman and other meeting participants agreed that the field should study whether COVID-19 can trigger or exacerbate Alzheimer's disease.

Racial and Ethnic Disparities

Research Update on Racial and Ethnic Disparities in Dementia

Jennifer Manly, PhD, summarized data on disparities and her team's current research on potential causes of these disparities. African Americans and American Indians/Alaska Natives are at highest risk for dementia, while Asian Americans are at lowest risk. Research shows that white matter hyperintensities are related to cognitive impairment among non-Hispanic Black but not non-Hispanic White people. Black people are more likely than White people to have white matter hyperintensities. These differences are present among people 50 to 60 years old. Hippocampal volume is related to dementia risk among non-Hispanic White but not non-Hispanic African American people. While an initial study found that t-tau levels are lower among African Americans than non-Hispanic White people, this was not replicated. Subsequent research has shown that socioeconomic status, including neighborhood characteristics, mediates racial differences in neurodegeneration. Institutional racism, reflected in policies such as redlining, leads to differences in racial composition of neighborhoods and socioeconomic disparities, and therefore is likely a causal factor in neurodegeneration and cognitive impairment risk and prevalence disparities.

Recruitment from clinical settings may lead to biased research. People from minority backgrounds may be less likely to be in these settings due to lack of access or trust in the medical system. Results from a study of participants recruited from community settings found no differences between Black, White, and Latinx participants' t-tau levels. Results showed that p-tau is the biomarker that best predicts dementia among White and Black people, but not Latinx people. Place of birth is associated with risk for dementia, even after moving. Racial disparities in cognitive functioning are associated with region where primary education occurred. Wider disparities occur in the South than other regions. These disparities persist even when people move to other regions. Counties with highest percentages of Black and Latinx people living with dementia also have the fewest neighborhood resources. Childhood education policies affect cognition later in life, with more compulsory education, longer school year, lower student-to-teacher ratio, and higher investments in elementary school associated with better cognition later. Black students experience lower school quality than other students. School quality provides less protection for Black and Latinx than White students, likely due to racism in school and employment environments.

Research must consider environmental, sociocultural, behavioral, and biological factors that affect health outcomes, including dementia. Disparities are caused by social factors

and cannot be eliminated by individuals' health behaviors. Structural racism and economic and social policies cause disparities in brain health by affecting education, neighborhoods, and wealth. Research must consider these factors and must include representative samples. Policy changes can reduce dementia disparities by repairing socioeconomic disparities.

Update on NIA's Clinical Research and Retention Initiatives

Holly Massett, PhD, said NIA is working to recruit more diverse study samples through three initiatives: Clinical Research Operations and Management System (CROMS), outreach to increase awareness of ADRD research, and developing a practitioner-based research network. NIA currently is developing CROMS to establish institute-wide informatics capability for tracking, reporting, and managing clinical enrollment, activities, and portfolios in near real time. CROMS will ensure accountability for research to include diverse participants and to respond to stakeholders' inquiries. The system will allow NIA to identify and address enrollment issues early. NIA has scheduled CROMS release for July 2021. Outreach efforts include applying best practices in health communication to develop and test materials tailored for minority audiences. In addition, NIA is developing Outreach Pro, an online tool for optimizing recruitment for clinical studies. Outreach efforts have been successful in recruiting minority participants to clinical trials. A practitioner-based research network will include providers with expertise and research interest who serve diverse communities. The network would nurture and incentivize community practitioner research. Similar networks have been successful in recruiting people from minority backgrounds to participate in clinical research.

Discussion:

- Dr. Levey asked whether there are critical points for investing in education. Dr. Manly said the most important change is to invest equitably. Her team will conduct research on which specific aspects of education are associated with disparities.
- Ms. Brandt observed that all citizens, not just scientists and clinicians, can help to address brain health disparities by advocating for equitable policies.

Nomenclature Update

Ron Petersen, MD, PhD said that researchers, clinicians, and public stakeholders (policy makers, advocates, research participants, and people from minority backgrounds) are stakeholders in nomenclature. The nomenclature committee has formed workgroups to focus on the needs of each of these stakeholder types. Researchers prioritize precision in nomenclature. Clinicians emphasize the need to communicate effectively with patients about science, and with scientists about patients' needs. Public stakeholders prioritize respectful language that counters stigma and encourages research participation. The nomenclature committee has developed a five-level framework to address stakeholders' interests. Level 1 is developing an umbrella term for neurological disorders that cause cognitive impairment and dementia. Level 2 is determining how to incorporate age of onset into nomenclature. Level 3 is to develop nomenclature for the continuum of severity. Level 4 is syndromic description of cognitive

and behavioral effects without addressing etiology. Level 5 describes underlying neuropathologies. People can have biomarkers for ADRD and be cognitively unimpaired. Nomenclature must address this issue. The committee will deliver a presentation on the implications of these issues to NIH on February 16, 2021.

Update on Blood-based Biomarkers for Alzheimer's Disease

David Holtzman, MD reviewed current knowledge about brain pathology characterizing Alzheimer's disease, including amyloid plaque and neurofibrillary tangles. Microglia and astrocytes are probably involved with degeneration of the brain. Amyloid plaque development begins approximately 20 years prior to symptoms emerging. Neurofibrillary tangles form a few years prior to symptoms. Alzheimer's disease biomarkers include amyloid plaques, neuronal response to amyloid, tau tangles, and neurodegeneration. Biomarkers are variables in research on the causes of Alzheimer's disease. They are used to identify Alzheimer's disease in clinical trial participants and to evaluate patients presenting with possible cognitive impairment.

Amyloid and tau positron emission tomography (PET) imaging are accurate but expensive and not covered by insurance. They are available only at major medical centers and expose patients to a small amount of radiation. Cerebrospinal fluid (CSF) biomarker imaging requires lumbar puncture, which some patients perceive to be invasive and which includes risks of headache and back pain. The procedure is also somewhat expensive and time-consuming. Blood tests are a relatively low-cost, convenient way to collect biomarker data. They could support efficient screening for clinical trials, thereby increasing speed of treatment development. Availability of a blood test would likely dramatically increase rates of screening and diagnosis of Alzheimer's disease, with more diagnosis of pathology prior to symptom development, increasing opportunity for effective prevention. The ratio of amyloid beta peptide 42 to amyloid beta peptide 40 indicates likelihood of amyloid plaque in the brain. When plasma test results are considered in combination with age and apoE genotype, they predict presence of amyloid plaque with approximately 95 percent accuracy. Current research indicates that blood plasma tests indicate pathologies earlier than CSF and PET scans. Pathology detection will be especially useful when treatments become available. The first blood test to detect amyloidosis in people with mild cognitive impairment is not available for clinical use.

Researchers are developing blood tests to screen for tau proteins. P-tau levels begin to increase about 15 years prior to onset of clinical symptoms. P-tau level increases in blood plasma predict brain atrophy in people who are amyloid positive. Therefore, p-tau tests may be useful for staging disease. Plasma neurofilament light chain (NfL) increases with brain atrophy, which sometimes occurs 5 to 10 years prior to symptom onset. NfL is not specific to Alzheimer's disease. Future blood tests likely will assess a combination of biomarkers to estimate risk for ADRD.

Discussion:

- Dr. Hyman asked whether biomarkers are likely, in the future, to quantify the degree to which specific factors cause impairment. Dr. Holtzman said this would

likely require imaging. Blood tests are more likely to detect presence of biomarkers than the extent of their contributions to pathology.

Risk Reduction Goal: Subcommittee Update

Lisa McGuire, PhD, said the Steering Committee is forming the Risk Reduction Subcommittee, which is charged with developing a national goal to reduce burden of risk factors to prevent or delay ADRD onset. The subcommittee will include two members with expertise in each key area: public health, clinical care, innovation/industry, and research. Members will have extensive experience and training in diverse fields of discipline. The Steering Committee has invited potential subcommittee members and is awaiting their responses. The subcommittee will form workgroups and develop recommendations, which will require review. Dr. McGuire invited Council members interested in serving on workgroups or as reviewers to contact her.

Public Comments

- Beth Nolan, representing Positive Approach to Care, said nomenclature should acknowledge that addressing patients' needs includes not only prevention and treatment, but also rehabilitation, compensation to address skill loss, and comfort and palliative care. This is an essential perspective for individual care planning.
- Kate Gordon of Research Triangle Institute (RTI) International said RTI has provided technical assistance to ACL's dementia initiatives since 2004. Grantees have provided services during the COVID-19 pandemic through telemedicine services that comply with the Health Information Portability and Accountability Act.
- Susan Bunning, Industry Director for PET for the Medical Imaging and Technology Alliance (MITA), said precision radiopharmaceuticals make important contributions to diagnosis and management of Alzheimer's disease. They detect changes in pathology early. Medicare does not cover use of these technologies outside of clinical trials for purposes other than oncology. Results of the Imaging Dementia-Evidence for Amyloid Screening (IDEAS) Study, with more than 18,000 patients, demonstrated value of PET for amyloid screening. Current CMS payment policy makes administering the tests a financial liability for hospitals. Ms. Bunning asked Council members to support changing this policy.
- Kristin Lees Haggerty, PhD, of the Education Development Center presented comments developed with Dr. Gary Epstein-Lubow of Brown University and Dr. David Reuben of the University of California, Los Angeles. She urged ASPE and the Council to improve access to comprehensive dementia care through payment reform. National experts recommend several approaches to payment reform. One potential approach is for the CMS Innovation Center to create and test an alternative payment and care model for people with dementia. The Alzheimer's

Impact Movement and Alzheimer's Association recently published a report entitled "Dementia Care Management," which proposes an alternative payment model framework. Drs. Epstein-Lubow and Reuben contributed to this report. Alternative payment models will increase access to effective, comprehensive dementia care. Dr. Haggerty encouraged the Council to develop strategies for advancing the work discussed in the report; continue its work in examining models for dementia care; convene at least one workgroup to address payment reform for comprehensive dementia care; and monitor and report on how the inclusion of dementia as a risk adjustment modifier in the CMS hierarchical condition category coding affects definitions of populations living with dementia, the quality and types of care they receive, and their health outcomes.

- Scott Turner, Director of the memory disorders program at Georgetown University, said there are currently three FDA-approved diagnostic radiopharmaceutical procedures for PET brain imaging to determine amyloid plaque density and other causes of cognitive decline associated with aging. CMS reimburses for these procedures only when there is evidence of disease development. The IDEAS study showed that PET test results caused providers to change treatment for 60 percent of patients with mild cognitive impairment. Diagnosis changed for 36 percent of patients. The New IDEAS study is beginning and aims to enroll more African American and Latinx patients than the original IDEAS study. Dr. Turner encouraged the Council to support CMS reimbursement for appropriate use of PET imaging for diagnosis of Alzheimer's disease.
- Kendra Kuehn conveyed comments on behalf of David Baldrige, Executive Director of the International Association for Indigenous Aging. The CDC awarded a Healthy Brain cooperative agreement to the association to create and coordinate federally-recognized Tribes' national response to ADRD. The association serves as evaluator for two ACL Alzheimer's Disease Program Initiative grants. COVID-19 disproportionately affects Tribal populations, which often have had to discontinue dementia care in order to respond to the pandemic. Ms. Kuehn asked the Council to consider Tribal people in all actions and recommendations. The International Association for Indigenous Aging is interested in collaboration with Council members' organizations.

Concluding Remarks

Dr. Levey reminded the Council that the next meeting is scheduled for May 2021. He adjourned the meeting at 4:28 p.m. Eastern time.

Minutes submitted by Helen Lamont (ASPE).

All presentation handouts are available at <https://aspe.hhs.gov/advisory-council-alzheimers-research-care-and-services-meetings>.