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

Virtual Meeting

July 19, 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, Maria de los Angeles Ordonez (absent: Carrie Molke)

- *Federal Members Present*: Craig Umsheld (substituting for Arlene Bierman) (Agency for Healthcare Research and Quality, AHRQ), Ellen Blackwell (Centers for Medicare & Medicaid Services, CMS), Susan Cooley (Department of Veterans Affairs, VA), Bruce Finke (Indian Health Services, IHS), Richard Hodes (National Institutes of Health, NIH), Gavin Kennedy (Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, HHS/ASPE), Shari Ling (CMS), Erin Long (Administration for Community Living, Administration on Aging, ACL/AoA), Lisa McGuire (Centers for Disease Control and Prevention, CDC), Deborah Olster (National Science Foundation, NSF), Cheryl Schmitz (Veterans Health Administration, VHA), Joan Weiss (Health Resources and Services Administration, HRSA)

- *Advisory Council Designated Federal Officer*: Helen Lamont (ASPE)

General Proceedings

Co-Chair Katie Brandt called the meeting to order at 12:30 p.m. Eastern Daylight Time.

Welcome

Ms. Brandt welcomed the Council and introduced Tisamarie Sherry, Deputy Assistant Secretary of Behavioral Health, Disability, and Aging Policy (HHS/ASPE). Dr. Sherry thanked the Council and ASPE staff for their work, and the public for engaging with the Council.

Panel on Aducanumab

Introduction of Panel

Allen Levey said the first panel would discuss aducanumab, the first treatment approved by the Food and Drug Administration (FDA) to treat Alzheimer's disease. CMS is considering policy regarding payment for treatment with aducanumab. Dr. Levey noted that the National Plan to address Alzheimer's Disease and recent increases in federal funding have fueled impactful advances in research about causes and treatments of Alzheimer's disease and related dementias (AD/ADRD). Dr. Levey emphasized the importance of translational research on how to apply findings to improve clinical practice and prevent disease.

Impact of New/Emerging Changes in Standard Cancer Treatments on Clinical Trial Enrollment

***Meg Mooney, MD, MS**, Associate Director, Cancer Therapy Evaluation Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute (NCI)*

- The National Clinical Trials Network (NCTN) comprises five large United States groups and one Canadian partner that lead clinical trials in oncology. Trials assess investigational new drugs and comparative effectiveness. NCTN analyzes trial enrollment accrual and reasons for not achieving accrual goals. The main reason for not achieving accrual goals is challenges with randomization. Another major reason is new information that either answers questions to be addressed by the current trial or renders those questions irrelevant. New information comes from clinical trials, changes in practice guidelines, and regulatory approvals. Reviewers assess new information and decide whether to stop, amend, or continue a clinical trial. The primary endpoint for the clinical trial is a major consideration in deciding implications of new information for a clinical trial. Other considerations include patient demographics; whether the sample was local, regional, national, or global; and biomarkers. In addition, reviewers consider clinical trial design and conduct. Regardless of the decision about clinical trial continuation, patients and investigators must be informed of the new information and its potential impact on the clinical trial. FDA sometimes withdraws approval. Most changes in standard of care are responses to clinical trial results.

Discussion

- Dr. Levey said that people tend to expect cancer patients to participate in research, while this is not the case for AD/ADRD. He asked how to engage AD/ADRD patients in research. Dr. Mooney recommended outreach to all communities. It is important for research samples to be diverse and representative. Outreach should be to patients, families, medical students, interns, and residents. Outreach and dialog should be continuous.

Aducanumab: Considerations for Scientific Workforce Diversity

Marie Bernard, MD*, Chief Officer for Scientific Workforce Diversity, NIH*

- The list cost of aducanumab is $56,000 annually. The drug is administered by infusion at specialized centers. Patients must have positron emission tomography (PET) scans or cerebrospinal fluid tests to detect amyloid, then magnetic resonant imaging at baseline and periodically to monitor potential side effects. The costs of these procedures are barriers to access, which will disproportionately affect Hispanic and Black people, who have lower median annual household incomes compared to White and Asian Americans. The cost of aducanumab is high for all race/ethnic groups' median annual household incomes.

- Black and Hispanic people are more likely than Whites to have missed or delayed dementia diagnoses.

- The participants in Biogen's Phase 3 aducanumab trials were 89% White and 9% Asian. Alzheimer's disease disproportionately affects Black and Hispanic people.

- It is essential to increase drug development workforce diversity to address needs of underrepresented groups. Members of underrepresented groups are more likely to practice in underserved communities, more likely to be selected by minority patients, and are best positioned to recruit minority patients to participate in clinical research.

- The National Institute on Aging (NIA) developed a national strategy for recruiting a more diverse pool of clinical research participants. Activities include grants that support testing new recruitment approaches and developing and testing recruitment messages. NIA offers a repository of resources to recruit and retain AD/ADRD research participants.

- In response to the COVID-19 pandemic, NIH formed the Community Engagement Alliance (CEAL) to provide trustworthy information through active outreach and engagement to communities most affected.

- NIH's Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative recently issued its first funding opportunity announcement for grants for which reviewers will consider researcher identity. If successful, this effort likely will be replicated.

- NIH's UNITE initiative aims to address structural racism barriers that prevent racial/ethnic minorities from becoming researchers. Efforts target NIH research, culture, policy, and structure. The initiative led to funding "Common Fund Transformative Research to Address Health Disparities and Advance Health Equity" and a report on investigators' race/ethnicity and disability status. NIH will develop programs to spur institutional change to become more diverse and

inclusive, and will work to reduce bias and increase work with and support of historically Black colleges and universities, Tribal colleges and universities, and other minority-serving institutions. NIH published commentary on its commitment to diversity and inclusion in Cell journal, June 10, 2021.

Discussion

- Cindy Carlsson asked how academic institutions and health care systems can support efforts to diversify the research workforce and research participants. Dr. Bernard advised examining workforce composition, explicitly stating workforce diversity as an organizational value, and incentivizing actions that align with this value. Organizations should develop programs to increase diversity and should continuously measure improvement in this area. Commitment to diversity must be long term.

Aducanumab: Opportunities

Robert Egge*, Chief Public Policy Officer, Alzheimer's Association; Executive Director, Alzheimer's Impact Movement*

- Mr. Egge disclosed that the Alzheimer's Association received 0.15% of its revenue from Biogen and Eisai, and 0.89% of its revenue from the life sciences sector in 2021. Donations do not affect organizational decisions.

- News about aducanumab has increased recognition of Alzheimer's disease as a serious public health issue.

- Regardless of treatment outcomes, further study of outcomes will yield important information.

- Combining aducanumab with other treatments may result in desirable outcomes.

- The Alzheimer's Association finds the price of aducanumab to be unacceptably high and calls on Biogen to reduce it.

- A CMS national coverage decision will facilitate equitable access to aducanumab.

- Approval of treatment for early disease stages presents an opportunity to encourage people to seek screening and care in early stages.

- Alzheimer's disease care continues to be important while a definitive cure is not yet available.

- Treatment requires amyloid detection, which requires adequate workforce capacity.

Discussion

- Ms. Brandt noted that the first Alzheimer's disease survivor will be a clinical trial participant. Aducanumab offers hope for treatment, which should encourage engagement with and participation in research.

Federal Updates

Due to time constraints, federal Council members agreed to share their slide presentations on the Council website without making oral presentations at the meeting.

- **ASPE**. ASPE's new website went live Friday, July 16. Dr. Lamont will send the address to Council members.

- **CDC**. CDC issued seven grant awards through Building Our Largest Dementia (BOLD) Infrastructure for Alzheimer's Act funds. Work will commence September 30, 2021.

Alzheimer's Disease and Related Dementias Research Update -- Fiscal Year (FY) 2023 Bypass Budget

***Richard Hodes, MD**, Director, NIA*

- Public Law 111-375 requires the NIH Director to submit to Congress an annual budget estimate of resources necessary to meet National Alzheimer's Plan goals. To accomplish this, NIH solicits input from academic, industry, and other organizations to develop milestones and achievement criteria and estimates of costs necessary to achieve each milestone, using the Common Alzheimer's Disease Research Ontology (CADRO) as a framework for categorizing research needs. Total projected costs for FY 2023 are $375,986,111. Additional funds needed total $225,986,111. The budget proposal narrative presents examples of recent scientific advances.

Discussion

- Dr. Levey noted the need for implementation research and dissemination efforts. He asked whether budget development includes consideration of funding for agencies that support this work. Dr. Hodes said the bypass budget is specifically from NIH. The Council considers the budget and integrates it with other information in its work. NIH supports implementation research.

Legislative Updates

Robert Egge

- The House of Representatives has called for an increase of $200 million for NIH Alzheimer's disease research, a $4.5 million increase for CDC, an increase for ACL to a total amount of $37 million, an increase of $500,000 for IHS, and level funding for the Departments of Defense and Justice.

- The Comprehensive Care for Alzheimer's Act was introduced in both houses of Congress. It has bipartisan support and would require the CMS Center for Medicare and Medicaid Innovation (CMMI) to implement and test dementia care management models.

- The Equity in Neuroscience and Alzheimer's Clinical Trials (ENACT) Act has been introduced in the House and Senate. The bill supports outreach to underserved communities, increasing diversity of clinical trials staff, and reducing participation burden.

- The Alzheimer's Caregivers Support Act has been reintroduced. It supports grants for training and support services for families and unpaid caregivers.

- The Concentrating on High-value Alzheimer's Needs to Get an End (CHANGE) Act has been reintroduced. The Act encourages early assessment and diagnosis.

- The CURES 2.0 bill has bipartisan support. It would fund the Advanced Research Projects Agency for Health and other work relevant to the Council.

- The current Administration has called for funding for community support infrastructure, including $400 billion for home and community-based services, and increasing caregivers' wages. The American Families Plan would create a national paid family medical leave plan to ensure workers remain employed while caring for themselves or a loved one with dementia.

Panel on Risk Reduction: Goals, Recommendations, Focus and Strategies

***Lisa McGuire, PhD**, CDC*
***Matthew Baumgart**, Vice President of Health Policy, Alzheimer's Impact Movement, Alzheimer's Association*
***Kelly O'Brien**, Executive Director, Brain Health Partnership, USAgainstAlzheimer's*

- The ad hoc committee on risk reduction formed with the objective of developing a national goal to reduce burden of risk factors to prevent or delay onset of AD/ADRD.

- The subcommittee included workgroups on: (1) obesity, diet, sleep, traumatic brain injury; (2) physical activity, tobacco use, alcohol; (3) social isolation, depression, hearing loss, cognitive activity; and (4) hypertension, hyperlipidemia, diabetes. Each workgroup was asked a set of framing questions: (1) Is there strong evidence, from a population health perspective, for the potential dementia risk/protective factor? (2) Are there promising or evidence-based community-level interventions for addressing the dementia risk/protective factor? (3) How would intervention affect public health and health disparities? and (4) Are there interventions or actions that individual health care providers/teams can recommend for patients in order to address the dementia risk/protective factor? Workgroups reviewed and rated scientific evidence, then developed a recommendations and strategies report. Approximately 100 external reviewers, including Council members, reviewed the report.

- The subcommittee recommends adding a sixth goal to the National Plan: "Reduce the burden of risk factors for AD/ADRD." The subcommittee recommends reducing the prevalence of 10 identified risk factors by at least 15% by 2030: unhealthy alcohol use, depression, diabetes, hearing loss, mid-life hypertensions, physical inactivity, poor diet quality/obesity, poor sleep quality/sleep disorders, tobacco use, and traumatic brain injury. Behavioral Risk Factor Surveillance System data show that approximately two-thirds (66.8%) of Americans have at least one of these risk factors. The subcommittee used a population attributable risk model to determine that 15% reductions in these risk factors per decade would likely result in 1.5 million fewer people with Alzheimer's disease in 2050.

- Recommended strategies are: (1) identify priorities and milestones; (2) accelerate public health action; (3) reduce risk and intervene early in clinical care; and (4) initiate and fund research to strengthen the strategies for addressing the potential risk factors for dementia, including translation and implementation scalability. A health equity framework should be used when implementing strategies.

Recommendations for identifying priorities and milestones.

- "HHS, led by CDC, should convene a biannual AD/ADRD risk reduction summit, which will provide an opportunity to obtain input from diverse stakeholders outside the Federal Government."

- "HHS and all other relevant federal agencies should identify, coordinate, and implement strategies within their current authorities and annually report on progress within the National Plan."

Recommendations for accelerating public health action.

- "Sustain and strengthen the public health infrastructure--federal, state, local, community, Tribal--for AD/ADRD to support robust efforts to address prevention of dementia risk factors."

- "Address social determinants of health that affect risk and health outcomes."

- "Develop strategies and interventions to target communities with both the highest prevalence of priority risk factors, low longevity rates, and the highest prevalence of AD/ADRD with explicit attention to the social determinants of health and strategies and interventions for historically marginalized communities."

- "Identify opportunities for collaboration with existing public and private initiatives and campaigns designed to reduce the prevalence of diseases, conditions, and other factors that are associated with risk of dementia, such as the Million Hearts Initiative and the Diabetes Prevention Program. Increase access of these programs for marginalized communities that are at high risk for dementia."

- "Align actions with those identified in CDC's Healthy Brain Initiative State and Local Public Health Partnerships to Reduce Dementia: The 2018-2023 Road Map (state and local) and Road Map for Indian Country."

Recommendations for reducing risk and intervening early in clinical care.

- "CMS, HRSA, VA, IHS, state Medicaid programs, and other public and private payers should identify a comprehensive set of actions to assess and reduce dementia risk, delay the onset of dementia, and improve early intervention, ensuring equitable reach and impact of interventions for historically marginalized populations. This should include identifying opportunities to reduce risk of mild cognitive impairment and dementia by addressing known risk factors and supporting early intervention for AD/ADRD. It also should include identifying existing benefits related to factors that can potentially reduce dementia risk, as well as coverage gaps and inequities that, if addressed, could potentially reduce known risk factors associated with AD/ADRD."

- "HHS should identify and accelerate strategies to improve access to primary care, team-based care, home and community-based care, and preventive care, including better utilization of existing benefits such as the Annual Wellness Visit."

- “CMMI should pilot AD/ADRD risk reduction interventions.”

- “HRSA should develop and broadly implement training curriculum for the primary and community care workforce to improve mild cognitive impairment and dementia risk reduction and early detection.”

- “Congress should address coverage gaps in Medicare, Medicaid, and the VA that would improve interventions for identified AD/ADRD risk factors.”

Recommendations for initiating and funding research to strengthen the strategies for addressing the potential risk factors for dementia, including translation and implementation scalability.

- “HHS should adopt an equity and inclusion framework when developing and supporting research on factors for dementia risk reduction to address biases in eligibility criteria, proportional representation, oversampling, data stratification, systemic racism, historical context, and structural factors that disproportionately affect the health of marginalized and minoritized populations.”

- “CDC should periodically update the list of key risk factors that are the focus of efforts to achieve this goal, based on the strength of scientific evidence, ripeness for public health action, and potential for impact and taking into account the needs of and potential benefits to at-risk communities.”

Discussion

- Dr. Carlsson said public health initiatives are critical for addressing risk factors.

- Brad Hyman supported the subcommittee’s development of questions with cross-cutting themes.

- Debra Cherry asked whether the subcommittee had decided to focus specifically on Alzheimer’s disease. Mr. Baumgart said this was not the case. However, the predictive model applies only to Alzheimer’s disease, since this was the only disease for which prevalence prediction data are available through 2050.

- Walter Koroshetz of the National Institute of Neurological Disorders and Stroke said addressing mid-life hypertension is very challenging. He noted that there are also benefits to addressing later life hypertension. Mr. Baumgart said nearly all identified risk factors applied across the lifespan and should be addressed early and over the life course.

- Ms. Brandt said that only non-federal Council members were eligible to vote.

- Ms. Brandt moved to make the subcommittee on risk reduction permanent. Dr. Levey seconded the motion. The motion passed unanimously among participating non-federal members.

- Ms. Brandt moved to accept all risk reduction subcommittee recommendations. Dr. Levey seconded the motion. The motion passed unanimously among participating non-federal members.

Subcommittee Recommendations

2021 Research Recommendations

Brad Hyman, MD, PhD

- Recommendation 1: “The 2021 National Plan should encourage a sense of urgency about providing a robust, comprehensive, collaborative, and transformative scientific road map for achieving the goal of preventing, effectively treating, and providing effective care and services for AD/ADRD by 2025, as well as continuous progress and improvement thereafter.”

- Recommendation 2: “A top priority remains the urgent need for Congress to continue to increase annual federal research funding sufficient to meet these goals, across biomedical, clinical, long-term services and support (LTSS), and public health.”

- Recommendation 3: “Emphasis should be given to the standardization of terminology across the spectrum of cognition in neurocognitive disorders by all agencies involved in the National Plan, to reduce ambiguity over confusing or overlapping terms, reduce stigma associated with AD/ADRD, and improve public awareness of AD/ADRD and access to relevant resources and services.”

- Recommendation 4: “A major area of emphasis by all federal agencies involved in the National Plan should be the enhancement of recruitment efforts for research involving those with, or at risk of developing, AD/ADRD.”

- Recommendation 5: “Federal agencies should develop a strategy and infrastructure to increase ethical and open sharing of, access to, and utilization of research data and samples. There should be a continued emphasis on ethics, in collaboration with academia, the pharmaceutical industry, biotech, and information system industries.”

- Recommendation 6: “All AD/ADRD research should establish the engagement of the AD/ADRD community as a standard practice in both participating in setting national research priorities for AD/ADRD and throughout all stages of clinical research and care, services, and support research.”

2021 Clinical Care Recommendations

Robert Egge

- Recommendation 1: “Educate the public about early detection and diagnosis of AD/ADRD, person-centered and family-centered care planning, and the importance of and ways to enter into research.”

- Recommendation 2: “Enhance the current and future workforce through education to better address the needs of persons living with AD/ADRD and their caregivers.”

- Recommendation 3: “Professional groups should determine a process for those groups and non-federal stakeholders to reach consensus on definitions of best practices, including the integration of new biomarkers, for comprehensive care of AD/ADRD at all disease stages.”

- Recommendation 4: “Encourage further development, evaluation, and use of health care models for AD/ADRD that align performance measures, the experience of care by people living with AD/ADRD and their caregivers, and payment.”

- Recommendation 5: “Conduct research to assess the need for eliminating the two-year waiting period for younger individuals living with AD/ADRD who have been deemed eligible for Social Security Disability Insurance (SSDI) to have access to Medicare.”

2021 Long-Term Services and Support Recommendations

Debra Cherry, PhD

- Recommendation 1: “Expand access to and utilization of affordable home and community-based services, particularly for people living with AD/ADRD who are marginalized, historically underserved, or disproportionately affected by dementia.”

- Recommendation 2: “Ensure people living with AD/ADRD and their caregivers are integral parts of the clinical care team and encourage coordination of clinical care with home and community-based services.”

- Recommendation 3: “Provide high quality person and family-centered LTSS.”

- Recommendation 4: “Develop a dementia capable LTSS workforce.”

- Recommendation 5: “Address behavioral and psychological symptoms of AD/ADRD across care settings.”

- Recommendation 6: “Improve and expand LTSS emergency preparedness to better address the needs of the AD/ADRD community.”

Discussion

- Ms. Brandt moved to adopt all recommendations. Dr. Levey seconded the motion. The motion passed unanimously among participating non-federal members.

Public Comments

- Arnold Beresh, a person with mild cognitive impairment and early onset dementia, noted that the FDA rejected aducanumab twice. Current approval was based on ability to remove amyloid protein, not prevent cognitive decline. The drug has not been tested on patients with comorbid conditions. Some hospitals refuse to administer aducanumab. The cost is prohibitive.

- Beth Nolan of Positive Approach to Care said patients, caregivers, and clinicians are confused about aducanumab. She asked the Council to demonstrate leadership by using consistent nomenclature and by changing its name to refer to dementia rather than Alzheimer’s disease. Ms. Nolan asked the Council to advocate for funding to identify best practices for building infrastructure for disease modifying protocols.

- Sue Bunning of Medical Imaging and Technology Alliance (MITA) said it is important to determine whether patients have amyloid plaque before treating them with aducanumab. The Imaging Dementia--Evidence for Amyloid Scanning (IDEAS) Study was the largest study of Alzheimer’s disease ever conducted. The study included amyloid PET detection, which resulted in a disease management change for more than 60% of participating patients and a diagnosis change for 26% of patients. CMS does not currently cover amyloid detection. MITA encourages CMS to open the non-covered treatment consideration request submitted September 2020 to prevent delays in patients’ access to the first disease-modifying treatment. New targeted diagnostic radiopharmaceuticals are a financial liability for hospitals. This has been a barrier to enrollment in the new IDEAS study, which examines Alzheimer’s disease in minority populations.

- Seth Keller, developmental neurologist, chair of the American Academy of Neurology Adult Intellectual and Developmental Disabilities section, said early onset Alzheimer’s disease is very prevalent among people with Down’s syndrome. This group should be included in clinical research.

- Chris Leibman, Alzheimer’s disease researcher at Biogen, said the development of aducanumab is likely to spark other innovative treatments. The field should focus on access to care and innovation.

- Hannah Mamuszka, chief executive officer of Alva10, which creates economic models to incentivize development of diagnostics, said currently available tests do not differentiate types of Alzheimer's disease or indicate whether a condition is likely to respond to a specific class of drugs. Insurance does not cover many tests. It important to invest in and pay for diagnostic tools to define and subtype dementias.

- Brandy Matthews, behavioral neurologist of Eli Lilly and Company, said patients must have timely, equitable access to diagnostics and therapies. CMS should pay for Alzheimer's disease diagnostics.

- Dr. Lamont read comments from Kathryn Pears, co-vice president of the National Task Force on Intellectual Disabilities and Dementia Practices, which calls for more research on Alzheimer's Disease among people with autism spectrum disorder (ASD). People with ASD disproportionately experience risk factors for Alzheimer's disease. The organization also calls for development of evidence-based interventions for Alzheimer's disease for people with ASD and education for care providers about issues related to aging with ASD.

- Matt Sharp of the Association for Frontotemporal Degeneration said his organization supports adding the risk reduction committee's proposed sixth goal to the National Plan and Council recommendations. The Association calls for more research on risk factors for non-Alzheimer's dementias.

- Angela Taylor, senior director for research and advocacy, Lewy Body Dementia (LBD) Association, said people with LBD often experience side effects that are uncommon among people with Alzheimer's disease. Clinical trials are needed to determine whether aducanumab is safe and effective for this population. She called for trials that include participants with a broad range of dementia types.

Concluding Remarks

Dr. Lamont reminded the Council that its next meeting will focus on LTSS and is currently planned for October 25, 2021. She adjourned the meeting at 4:26 p.m. EDT.

Minutes submitted by Helen Lamont (ASPE).

All presentation handouts are available at https://aspe.hhs.gov/collaborations-committees-advisory-groups/napa/napa-advisory-council/napa-advisory-council-meetings.