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

Washington, DC

January 27, 2020

Advisory Council Members in Attendance

- *Non-Federal Members Present*: Katie Brandt (Co-Chair), Allan Levey (Co-Chair), Venoreen Browne-Boatswain, Cynthia Carlsson, Debra Cherry, Bradley Hyman, Kristine Jaffe, Kenneth Langa, Matthew Janicki, Carrie Molke, Maria de los Angeles Ordonez, Gloria Owens

- *Federal Members Present*: Arlene Bierman (Agency for Healthcare Research and Quality, AHRQ), Ellen Blackwell (Centers for Medicare & Medicaid Services, CMS), Bruce Finke (Indian Health Services, IHS), Richard Hodes (National Institutes of Health, NIH), Erin Long (Administration for Community Living, ACL), Lisa McGuire (Centers for Disease Control and Prevention, CDC), Arne Owens (Department of Health and Human Services Office of the Assistant Secretary for Planning and Evaluation, HHS/ASPE), Anthony Pacifico (Department of Defense, DoD), Marianne Shaughnessy (Department of Veterans Affairs, VA), Joan Weiss (Health Resources and Services Administration, HRSA)

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

General Proceedings, Introductions and Charge for Meeting

Co-Chair Katie Brandt called the meeting to order at 9:35 a.m.

Advisory Council members introduced themselves.

Co-Chair Allan Levey said now is an especially important time to understand the direction and implications of current research in this field.

Epidemiology/Research Sessions

Bradley Hyman explained that the day's presentations summarize current research and its potential.

What is Epidemiology and What Does it Offer for Understanding, Treating, and Preventing Alzheimer's?

Deborah Blacker presented definitions of Alzheimer's and epidemiology, and the major functions of epidemiology in the context of preventing and treating Alzheimer's. These functions are: assess and forecast the magnitude of the problem, understand risk and protective factors and their potential roles in prevention, put clinical findings in a population context, and assess and improve methods for observational studies.

It is important to understand what a person means when they refer to Alzheimer's. Dr. Blacker said that definitive Alzheimer's diagnosis is based on biomarker or autopsy evidence of pathology. Clinical diagnosis and population research often use the term "Alzheimer's" to refer only to the characterizing symptoms. The latter use is adequate for understanding the diseases and for estimating burden, including cost. Evidence of pathology is necessary for clinical trials and genetic studies. Pathology can be present, sometimes for years, without symptoms. Dementia and mild cognitive impairment (MCI) refer to functional status, which may be caused by Alzheimer's or other pathologies. However, since Alzheimer's is the most common form of dementia, the terms "Alzheimer's" and "dementia" are often used interchangeably. Alzheimer's pathology often co-occurs with other pathologies, especially cerebrovascular pathologies. These pathologies are additive and sometimes interact. Co-occurring pathologies are very common among later age groups.

Dr. Blacker presented a brief history of epidemiology, which is the study of health outcomes, including disease, prevalence and incidence in populations, and statistical associations of these outcomes with demographic factors and with risk and protective factors. Epidemiology uses quantitative measures and methods to assess trends in prevalence, incidence of outcomes, and factors that predict them. Study results can contribute to understanding disease mechanisms. Results also inform approaches to prevention and treatment, policy, and research methods and priorities. For example, identifying high-risk populations supports developing targeted interventions.

Age-specific incidence of Alzheimer's may be decreasing. However, with the aging population, prevalence is increasing. This problem is more severe in places where the change in age demographics is greater, such as China and India.

Dr. Blacker explained that research sample characteristics must be considered when interpreting results. Patients are always more impaired than non-patients because symptoms lead people to seek care (Berkson's bias). Patients are also more likely to have other illnesses and more likely to have characteristics associated with health care access, including more education and income. Biomarker data are mostly collected from clinical samples. Many studies include research volunteers, who are typically more educated, more likely to have a family history of the disease being studied, and more likely to have subclinical symptoms than the general population of people with Alzheimer's.

Epidemiology uses observational methods, not randomized controlled trials, to collect data. Therefore, researchers have developed methodological approaches to protect against drawing false or distorted conclusions from epidemiological data. Critically assessing evidence for causal relationships is necessary for making credible recommendations about how to reduce risk, particularly if recommendations involve asking people to do something unpleasant, such as give up a type of food they enjoy. Issues that can lead to biased interpretation include measurement error, sampling issues, confounding variables, and reverse causation. Measurement errors include over and underestimation, which can result from differences in likelihood of noticing symptoms. For example, people who are younger or more educated are more likely than others to notice Alzheimer's symptoms. Criteria and requirements for research participation and the definition of Alzheimer's used in a study determine the sample. As these factors vary, so does sample composition and the degree to which it represents the population of people with Alzheimer's. Confounding variables are related to both predictors and outcomes and do not explain the relationships between predictors and outcomes, but can appear to explain these relationships if research methodology does not account for them. Reverse causation occurs when an effect is interpreted as a cause.

An example of measurement error in Alzheimer's research is that cognitive activity measures tend to ask about activities preferred by highly educated people, such as chess and crossword puzzles, and not about cognitive activities less educated people are more likely to engage in, such as home repairs requiring spatial and logical reasoning, cooking that requires arithmetic calculation, or games requiring probabilistic reasoning. This approach confounds education with cognitive activity. Sampling bias can include social desirability bias, leading people who engage in less cognitive activity to avoid research participation or to over-report their activity. In addition, researchers studying the relationship between cognitive activity and dementia usually focus on late-life cognitive activity. However, late-life cognitive activity may not affect dementia. It may indicate only education or be a result of early-life cognitive activity that built synapses. Few studies examine the effects of early cognitive activity. However, Alzheimer's is characterized by long-term, subtle decline, which is often unnoticed and which may be the cause, rather than effect, of decreased challenging cognitive activity. Interpreting research on Alzheimer's should include critical evaluation of the methods used. This does not require formal training in epidemiology.

Comments & Questions

- A participant asked what efforts have been made to increase sample diversity in Alzheimer's research. One approach is over-sampling some groups to ensure they are represented in research. Another is to include only traditionally under-represented groups in research samples.

Tracking the Burden of Alzheimer's Disease and Dementia in the United States: The Health and Retirement Study (HRS)

Kenneth Langa described the HRS, a longitudinal study of a nationally representative sample, conducted by the University of Michigan Institute for Social Research and funded by the National Institute on Aging (NIA) and Social Security Administration (SSA). Dr. Langa introduced his discussion with background information about Alzheimer's epidemiology and measurement complexities.

Dr. Langa explained that prevalence refers to the proportion of individuals in a defined population with a disease or condition, whereas incidence is the number of new cases of the disease or condition in this population during a specified time interval. Prevalence is a function of incidence and life expectancy. Incidence is less affected by confounding variables and is a better indicator of trends. Incidence can increase even when prevalence declines. In many countries age-specific risk of Alzheimer's has declined over the past 30 years. For example, an 80-year-old in the United States now is at lower risk than an 80-year-old in the United States in 1980. However, total number of cases of Alzheimer's in the United States (incidence) is expected to increase as the population ages. Between 2020 and 2050, the number of people younger than 5 years is expected to remain stable as the number of people older than 65 years is expected approximately to double. Now is the first time in history that older adults outnumber young children. The number of people at risk for dementia is increasing as the number of potential caretakers is decreasing.

Dementia is usually recognized when a person experiences disability. This threshold varies, making epidemiological assessment complex. In addition, people experiencing cognitive impairment frequently have difficulty answering research and clinical questions, often requiring proxies. Many people with Alzheimer's require nursing home care, which typically restrict data collection on residents. International comparisons also present challenges for epidemiological study of Alzheimer's. Language and cultural differences make it challenging to use comparable assessments. Differences in life expectancy affect prevalence rates.

Since 1992, HRS has been collecting survey data every 2 years from a sample of about 20,000 Americans who are at least 50 years old. The survey assesses health, cognition, economics, work, and family. Data are collected over the telephone or in person in participants' homes. Data are public. More than 2,000 authors have published results of analyzing HRS data in more than 4,000 publications. HRS data link to administrative records from employers, Medicare, SSA, VA, and National Death Index data. Since 2006, HRS has collected biomarker data on cholesterol, HgbA1c, C-reactive protein test, Cystatin C, blood pressure, pulse, peak air flow, balance, and gait. In 2016, HRS researchers started collecting venous blood draws. Since 2012, the study has collected single nucleotide polymorphism (SNP) genetic data. Cognitive status is assessed with the Modified Telephone Interview for Cognitive Status and tests of verbal fluency, number series, numeracy, and processing speed, as well as self-reports. Medicare data provide information regarding time of relevant medical history events. Exit interviews with family members provide end-of-life data. More than 30 countries are conducting longitudinal aging studies modeled after HRS. Comparison will provide insight about the causes of cognitive decline among older adults.

The Aging, Demographics, And Memory Study (ADAMS) is a study on dementia that supplements HRS. It was conducted with 856 HRS participants between 2001 and 2010. Data collection included intense cognitive assessment. These data were used to extrapolate estimates of dementia prevalence in the United States population. Results indicate that approximately 9% of the United States population aged 65 years and older (1.0-4.5 million individuals) has dementia, and approximately 19% (8.0-8.7 million individuals) has MCI. Dementia accounts for 30% of caregiving time and cost--a higher percentage than any other chronic disease. About two-thirds of people in the United States with dementia are women, partly due to women's longer life expectancy. The most common living arrangement for men with dementia is in the community with their spouse. The most common living arrangement for women with dementia is alone in the community. Women are more likely than men to be living in nursing homes. Average annual cost to care for dementia-specific needs is $50,000 per case, or $200,000 billion nationwide. About half of these costs are for informal care and about one-fourth of costs are for nursing home care. Dementia prevalence in the United States has declined from 11.6% in 2000 to 8.8% in 2012, a statistically significant decrease ($p<0.001$). Several high-income countries have experienced similar declines; trends are less clear in low-income countries. Increasing education levels and better control of cardiovascular risk factors are associated with declines in dementia prevalence. These results suggest that social and behavioral interventions have the potential to be effective in primary prevention of dementia.

The Harmonized Cognitive Assessment Protocol is a supplement to HRS to develop national estimates of dementia burden. The study collects cognitive test and informant interview data on about 3,500 HRS participants.

Nationally representative population-based studies are important resources for tracking the epidemiology of dementia.

Comments & Questions

- A participant asked which factors uniquely affect studying the epidemiology of dementia. Dr. Langa said the wide range of thresholds for dementia-related disability is one such factor. Other diseases, such as diabetes and hypertension have standardized diagnostic thresholds defined by objective measures. Another participant pointed out the need to consider issues related to screening recommendations. Dr. Langa said this will involve balancing the benefits of early identification with the costs of over-diagnosis and unnecessary treatment. A participant observed that many people live in congregate arrangements, which should be considered in analysis. She also asked if there had been issues with assessing cognitive data via telephone. Dr. Langa said results collected via telephone are comparable to data collected in person, though it is possible that some participants may "cheat" during telephone assessments. A participant noted that many studies set 65 years as the minimum age for participation, since this is the minimum age for Medicare and Social Security retirement benefits participation, while the Older Americans Act, used by many state policy makers, sets the minimum age as 60 years. It would be useful to have more data on people aged 60 years and older for state planning purposes. A participant asked for HRS data regarding needs for services and perceptions that services were helpful. Dr. Langa said several articles have been published on this topic, based on analysis of HRS data. Families have found living wills and advanced directives to be helpful in supporting care decisions. Difficulty with navigating long-term care systems and costs has been a recurring theme.

Modifiable Risk Factors for Dementia Prevention

Kristine Yaffe explained that identification of modifiable risk factors for dementia provides valuable information about brain functioning and the mechanisms for dementia development. Results identify people at risk for dementia and inform development of prevention and treatment strategies. The strongest available evidence indicates that cardiovascular factors, physical and cognitive activity, sleep quality and disorders, and traumatic brain injury (TBI) are modifiable risk factors for prevention. Dementia is the result of cumulative risk over a lifetime, yet research often focuses only on older adults. This does not allow insight into disease inception, critical windows for intervention, or thresholds for cumulative risk. It is likely that risk exposure accumulates over at least a decade, probably two decades, before symptoms appear. Preventive efforts during this period may be effective.

Cardiovascular risk factors include diabetes, hypertension, dyslipidemia, and obesity. Many studies have demonstrated that these factors increase risk for dementia, especially if they occur during mid-life. Aggressive blood pressure control has been shown to reduce risk of MCI and dementia. Hypertension in early adult and mid-life is associated with greater cognitive decline than late-life hypertension, suggesting that early intervention for cardiovascular health could reduce risk of dementia.

Physical activity promotes brain health and neuronal genesis as well as cardiovascular health. Most research on physical activity is observational. Dr. Yaffe presented results of a randomized controlled trial study she conducted which showed that exercise improves cognitive function in older adults with memory complaints. Exercise was as effective or more effective than drugs used to treat dementia. However, another randomized controlled trial found no effects of exercise on cognitive functioning or on risk for MCI or dementia. Despite some inconsistent findings, overall, research presents compelling evidence that exercise is a promising approach for reducing dementia risk. More randomized controlled trials are needed, as well as more research on whether specific types of exercise are more effective than others, and what frequency and duration are necessary for exercise to have an effect.

Research suggests that challenging cognitive activity builds “cognitive reserve,” which protects brain functioning despite neuronal damage. The protection can result in delayed impairment. For example, while low plasma A [beta] peptide levels are a risk factor for dementia, this risk level is higher among people with less education. This suggests that high-quality public education could reduce Alzheimer’s prevalence significantly. Research also has shown that cognitive training can improve cognition among older adults, but has not clearly linked intervention to dementia prevention.

Sleep quality is related to dementia risk. Older people’s sleep includes less time in deeper and rapid eye movement stages. Older people experience shifted circadian rhythms and are more likely to have sleep apnea. More research, including randomized controlled trials, is needed to understand the mechanisms of the relationship between sleep quality and dementia.

There is little awareness of TBI, including mild TBI, as a risk factor for dementia. Evidence suggests TBI history increases risk by about 60%. Researchers are exploring relationships, such as the potential effects of chronic traumatic encephalopathy resulting from TBI.

The National Academies of Sciences, Engineering, and Medicine published *Preventing Cognitive Decline: A Way Forward*, a systematic review of evidence collected from randomized controlled trials examining risk for cognitive decline with samples of at least 500 participants and data collection periods lasting at least 6 months. Very few studies met inclusion criteria, making it difficult to draw conclusions. Analysts identified cognitive training, blood pressure control, and physical activity as promising approaches for reducing dementia risk. The Lancet Commission also released a review of best evidence. This review included observational studies as well as randomized controlled trials. Analysts identified nine predictors: childhood education, exercise, social engagement, smoking, hypertension, hearing loss, depression, diabetes, and obesity. The report encouraged readers to “be ambitious about prevention.” Dr. Yaffe said that, while available evidence quality varies, researchers have a responsibility to inform the public that brain functioning can be modified, that physical health affects brain health, and that the brain continues to develop throughout the lifespan.

Current research includes estimating the proportion of disease incidence that can be attributed to specific risk factors (population attributable risk). Population attributable risk is associated with how common the risk factor is as well as how strongly it is related to disease occurrence. Recent research by Dr. Yaffe and others suggests that about one-third of dementia risk is attributable to physical activity, smoking, depression, mid-life hypertension, mid-life obesity, low education, and diabetes. Reducing these risk factors could significantly reduce dementia prevalence. Improved education and blood pressure control may be partly responsible for recent reductions in prevalence. Conversely, current trends toward increased obesity and sedentary lifestyles may increase prevalence.

Four multi-domain trials assessing effectiveness of interventions targeting multiple potential predictors have been published. Three found no benefits for cognitive functioning and one found small but significant benefits. Dr. Yaffe is currently conducting a multi-domain personalized intervention.

Research indicates that low-cost, low-risk interventions could reduce dementia risk. However, evidence quality is not yet optimal and conclusions are somewhat controversial. More research is needed, including life course studies, more randomized controlled trials, and more multi-domain intervention evaluations, including studies that assess effects of both lifestyle and medication. It is likely that dementia prevention and management, as with other chronic diseases, ultimately will include lifestyle choices and medication.

Comments & Questions

- A participant cited a recent study conducted in Wisconsin that found living in a disadvantaged neighborhood increased risk for hippocampal atrophy. He asked what research is being conducted on social determinants and dementia. Dr. Langa said HRS collects data on quality of participants' schools. Other studies are assessing effects of pollution on brain health. Dr. Yaffe said social determinants affect all health outcomes at every stage of life. Research has shown income uncertainty affects mid-life cognitive functioning. Socioeconomic status has been shown to be a reason for higher prevalence of dementia among African Americans. Dr. Blacker said people often assume the reason education reduces dementia risk is that it improves brain function. The relationship is probably also because more education predicts greater income, living in a safe environment, and access to health care.

- A participant asked what level of evidence should be required for developing and delivering public health messages. Lisa McGuire said that, based on current promising evidence, CDC is working to tailor risk reduction messages that have already been effective to communicate information about brain health. Factors associated with reducing dementia risk have already been demonstrated to have other health benefits.

- A participant asked if researchers have identified a window for intervention. Dr. Yaffe said this has not yet happened. It is challenging to identify an intervention window because typically there is little cognitive change in mid-life, and cognitive function measures are not very sensitive. However, it would be useful to study this issue.

- A participant asked if substance use has been shown to be a risk factor for dementia. Dr. Yaffe said the effects of alcohol have not been studied adequately. She noted that alcohol is associated with earlier mortality. In general, substance abuse is associated with increased risk for dementia.

- A participant asked Dr. Yaffe to discuss co-morbidities found in her study of veterans' retirement home residents. Dr. Yaffe said comparison of older veterans with and without TBI showed that those with TBI had more behavioral problems and poorer cognitive functioning. A participant said the study showed substance abuse was prevalent and co-morbid with TBI.

- A participant observed that the research findings presented indicated a need for more research on people in mid-life and on social determinants of health. She noted that policies affect social determinants and that it is critically important to try to improve health through policy.

Public Comments

- ***Jane Boyle*** shared the story of her sister, who had Down syndrome and died from Alzheimer's at age 52. Ms. Boyle had been her sister's legal guardian and caregiver. It was difficult to obtain a diagnosis. Little information and support and few resources were available for dealing with co-occurring Down syndrome and Alzheimer's. Systems were not designed and providers were not trained to serve patients with both disorders. Down syndrome is a risk factor for early onset Alzheimer's. Ms. Boyle asked the Council to consider the needs of people with both Down syndrome and Alzheimer's, and of their caregivers in the Council's work.

- ***Patricia D'Antonio***, Vice President of the Gerontological Society of America (GSA), advocated for improved recognition of neuropsychiatric symptoms of dementia. These symptoms are associated with more severe dementia outcomes, such as impaired activities of daily living, earlier institutionalization, and accelerated mortality. Neuropsychiatric symptoms include dementia-related psychosis, which can be stigmatizing and require long-term residential care. In August 2019, GSA published *Dementia-Related Psychosis: Gaps and Opportunities for Improving Quality of Care*, summarizing experts' recommendations for best practices. Key recommendations in the report are: (1) develop better ways for clinicians to document diagnosis of dementia-related psychosis in order to support appropriate care planning; (2) provide better training to health care providers about effective communication with people with dementia and their informal caregivers about symptom progression and coping; and (3) support more research to inform evidence-based treatment.

  Ms. D'Antonio invited the Council to read the report, which is available on the GSA website at https://www.geron.org/programs-services/alliances-and-multi-stakeholder-collaborations/dementia-related-psychosis. She thanked the Council for their work.

- ***Gary Epstein-Lubow***, a geriatric psychiatrist at Butler Hospital and associate professor at Brown University, presented comments prepared with David Reuben, professor of medicine and Chief of the Division of Geriatrics at University of California, Los Angeles. Dr. Epstein-Lubow said that ASPE and this Advisory Council must address payment reform for dementia care and treatment. There are currently six models of dementia care associated with improved clinical outcomes for people living with dementia and their caregivers. These models of care also lower costs. However, care based on these models is not widely available. The Hartford Foundation and Hebrew Senior Life supported the "Payment Models for Comprehensive Dementia Care" conference in Washington, DC, on November 7, 2019. More than 50 clinicians, researchers, advocates, payers, and other experts on dementia care convened to discuss payment reform and approaches to accelerating use of currently available payment models associated with better quality care and lower costs. Conference proceedings will be published in 2020. Drs. Epstein-Lubow and Reuben recommend that HHS advance payment reform by: (1) continuing to examine models of dementia care; (2) convening at least one work group to address payment reform for comprehensive dementia care; and (3) monitoring how inclusion of dementia as a risk adjustment modifier in the CMS hierarchical condition category coding affects definitions of populations of people living with dementia, quality of care, types of care received, and health outcomes. The recommendations align with the National Plan to Address Alzheimer's Disease Strategy 1.E, "translation of findings into medical practice and public health programs," and all strategies for achieving Goal 2, "enhance care quality and efficiency."

- ***David Ervin***, Chief Executive Officer of the Jewish Foundation for Group Homes, said that service providers are ill equipped to serve people living with developmental and intellectual disabilities as well as Alzheimer's. People living with developmental and intellectual disabilities are now living longer than at any other time in history. They also tend to experience Alzheimer's at significantly younger ages than people with neurotypical development. Funding and policies are not structured to serve these patients or to support their aging in place. Research designed with input from this population is needed to determine how best to serve them. Research must assess efficacy of support and care, and inform development of a community of care for this population. Standards of care must be defined for accreditation and licensing for long-term services tailored for this population's needs, and be integrated with the general health care system.

- Helen Lamont read comments from ***Mary Hogan***, a friend of Ms. Boyle. Ms. Hogan emphasized the importance of lifelong high quality of life for all people. Ms. Hogan's brother had Down syndrome and died of Alzheimer's complications when he was 49 years old. Ms. Hogan said people should recognize that everyone has something of value to contribute. Support for research and training, policy, awareness of this special population's needs, and advocacy have increased over the past decade and should continue over the next decade.

- Helen Lamont read comments from ***Leone Murphy***, the mother of a woman with Down syndrome and Alzheimer's. When her daughter was born her life expectancy was sometime in her 40s. Medical care providers did not know how to prepare the family for their current situation. People with Down syndrome are living longer, but there are not services available to support them as they age prematurely and develop Alzheimer's. Ms. Murphy started a support group for families of people with intellectual disabilities and Alzheimer's in January 2019.

After 1 year, group membership has grown to 40. Ms. Murphy asked the Council to consider this population in its planning and service development.

- Dr. Lamont read comments from ***Michelle Murphy***, as a 46-year-old person with Down syndrome who has lost four of her eight close childhood friends to Alzheimer's when they were in their early 50s. Ms. Murphy said she is afraid of what the future holds for her and her family. She asked the Council to consider the needs of people with Down syndrome in their planning and programs.

- ***Angela Taylor***, Senior Director of Research and Advocacy for the Lewy Body Dementia Association, recently attended the CDC-hosted "Neurological Surveillance Summit," where CDC's National Neurological Conditions Surveillance System (NNCSS) was discussed. The system was pilot tested to collect data on multiple sclerosis and Parkinson's disease. CDC solicited input on which other diseases could be monitored with the system. Ms. Taylor said there is little research on dementias other than Alzheimer's. She recommended that CDC include all forms of dementia in the surveillance system. She said the project is underfunded, and she encouraged the Council to recommend a funding increase to support NNCSS. Inclusion of additional diseases in the system will require efforts of advocates and experts. Ms. Taylor asked the Council to consider asking CDC to prioritize dementia for inclusion in NNCSS.

- ***Matthew Sharp***, Program Manager for the Association for Frontotemporal Degeneration (AFTD), said there is little epidemiological data on frontotemporal degeneration (FTD), partly because the average age of onset is about 60, which excludes people with FTD from many research studies. FTD diagnoses include progressive supranuclear palsy, corticobasal syndrome, all types of primary progressive aphasia, and behavioral variant frontotemporal dementia. Prevalence and incidence are uncertain. AFTD estimates a minimum of 60,000 cases in the United States. This is likely an underestimate since FTD is often undiagnosed. It may not be a single disease; it has multiple pathologies, including tau and TDP-43 protein pathology, and C9orf72 genetic mutations. FTD commonly co-occurs with amyotrophic lateral sclerosis. AFTD advocates for research to identify biomarkers for diagnosis and prediction of FTD over the next 2-7 years. In 2016, AFTD launched the FTD Biomarkers Initiative, which has supported 13 grants to develop FTD imaging tests to determine biomarkers.

- ***Debbie Yobs***, President of the Creutzfeldt-Jakob Disease Foundation, said that Creutzfeldt-Jakob disease (CJD) is always fatal. She asked for the Council's support in raising awareness of prion disease as a related dementia in the category of Alzheimer's disease and related dementias (AD/ADRD). CJD is a rapidly progressive dementia caused by prions, which are normal proteins that misfold in the brain, causing diseases similar to AD/ADRD. The disease symptoms and mechanisms as well as patient and caregiver experiences are similar. Research breakthroughs for any protein misfolding disease are likely to inform progress in others. Prion diseases occur in animals and are transmissible under certain circumstances, making them the protein misfolding disease with the most valid animal models. Excluding prion diseases from the AD/ADRD category does not serve patients, caregivers, or researchers.

Congressional Updates

Robert Egge reported that the 2020 Appropriations Bill allocates $350 million in new funding to NIH for AD/ADRD research, for total annual funding of $2.8 billion. Funding includes $10 million to support the Building Our Largest Dementia (BOLD) Infrastructure for Alzheimer's Act. In October 2019, the House of Representatives passed three Bills that await Senate action: Palliative Care and Hospice Education and Training Act, Lifespan Respite Care Authorization Act, and the EMPOWER for Health Act of 2019. In addition, the House passed the Younger-onset Alzheimer's Disease Act, which extends support to people younger than 60 years who are living with Alzheimer's, and the Improving HOPE for Alzheimer's Act; both are making progress through the Senate. Mr. Egge reported that CMS has chosen a new risk adjustment model to calculate Medicare Advantage plan payments, which includes codes for dementia with and without complications. This should support better resource allocation and more accurate payment for complex beneficiaries. Mr. Egge reported that, in response to an HHS request for information about modifying HIPAA rules to improve coordinated care by allowing adult children to access treatment records of parents with early onset dementia, the Council recommended that "Congress, federal agencies, and states must…address reimbursement, training, and HIPAA policy and practice barriers to enable health care providers to provide care planning with family caregivers".

National Institute of Neurological Diseases and Stroke (NINDS) and Alzheimer's Disease-Related Dementia (ADRD) Summit 2019 Report

Roderick Corriveau provided the annual update. A current and ongoing priority is to train the next generation of researchers. Researchers are exploring multiple potential pathways to dementia. NINDS collaborates closely with NIA on AD/ADRD. NIA is responsible for Alzheimer's disease research and leading implementation of the National Plan to Address Alzheimer's Disease. NINDS leads research on AD/ADRD and convenes ADRD summits. Efforts support progress toward the goal to prevent and treat AD/ADRD by 2025. Dr. Corriveau said that research on dementias that NIH does not identify as Alzheimer's-related is eligible for special funds. Triennial summits shape research priorities. Congressional funding for research has increased steadily since 2013. Funds support research that responds to relevant initiatives and investigator-initiated research. Projects include:

- Mark VCID, a national consortium with a goal of identifying biomarkers of vascular contributions to cognitive impairment and dementia (VCID) by conducting clinical trials on potential biomarkers that are already used in the field.

- Detect CID, a national consortium to develop paradigms for detecting cognitive impairment in primary care settings.
- Tau Center without Walls, a multidisciplinary research team working to identify and validate molecular mechanisms that contribute to tau toxicity associated with FTD.
- Lewy Body Dementias Biomarker Initiative to discover Lewy body biomarkers.
- Natural history studies of FTD to determine clinical, genetic, and biomarker profiles.
- Workshops on vascular contributions to cognitive impairment.

Dr. Corriveau provided an example of investigator-led research that demonstrated that tau toxicity facilitates “jumping gene” activity, which accelerates pathology at the cellular level. The study identifies transposable element regulation as a potential pharmacological target for treatment. Dr. Corriveau said this study illustrates the importance of supporting scientific creativity.

NINDS has issued a funding opportunity announcement for research on white matter lesion etiology of dementia, including in populations affected by disparities, and another announcement of funding to support clinical trials planning for symptomatic vascular contributions to cognitive impairment and dementia. Both of these opportunities are active.

The purpose of the ADRD summits is to solicit input from diverse stakeholders to draft research recommendations for consideration by NINDS and this Council. Approved recommendations become National Plan implementation milestones and inform bypass budgets to support implementation. The Federal Advisory Council at the 2019 ADRD Summit approved 47 research recommendations, assigned priorities to these recommendations, and developed timelines for their implementation. Recommendations for research topics include: biomarkers and risk profiles, resource infrastructure, training and workforce needs, and nomenclature. The Council recognized the need for basic, clinical, and translational research. Top priorities include developing and improving cognitive assessment tools for populations affected by AD/ADRD disparities, and increasing availability and utilization of culturally and linguistically appropriate assessment tools in research studies. The top priorities for Lewy body dementia research were clinical trials to treat or prevent the disease as well as biomarker development. The top priorities for FTD were defining disease pathways and mechanisms. For vascular contributions to cognitive impairment and dementia, priorities were to develop next generation experimental models and translational imaging methods, and to develop, validate, and track biomarkers.

Dr. Corriveau reiterated Dr. Blacker’s point that definitions of AD/ADRD vary and that clinicians and researchers must communicate their meaning clearly in order to be effective in clinical, research, training, and public settings.

Comments & Questions

- A participant suggested a more integrated approach to addressing AD/ADRD, including convening one summit that focuses on both. Richard Hodes said that originally this was too much to address in one summit, but NIH is working toward better integrating efforts. A participant said that focusing on distinctions between syndromes increases families' sense of isolation. It is important for practitioners to recognize this and offer their support.

Congressionally Directed Medical Research Programs: Peer-reviewed Alzheimer's Research Program (PRARP) Overview

Anthony Pacifico described the DoD programs, which aim to explain the association between TBI and AD/ADRD, and to reduce burden on patients and caregivers, especially among military members and veterans. He reiterated data summarizing Alzheimer's prevalence and impact. He said that TBI disproportionately affects military members. PRARP administrators conduct market research to set research priorities, which currently include basic research, family care and support, diagnostics and prognostics, clinical studies, quality of life issues, and epidemiology. PRARP currently funds more than 100 projects. Examples include: a study demonstrating that glia mediate a prolonged neuro-inflammatory response to TBI, which is made worse by over-expressed amyloid; research on the role of the glymphatic system clearing waste from the brain during sleep; research assessing co-morbidity of TBI and post-traumatic stress disorder; exploring psychiatric co-morbidities of TBI and Alzheimer's; and exploring ways to improve caregiver quality of life. PRARP researchers are working to find methods other than surveys, including imaging technologies, to assess quality of life. This could provide biomarker data on how exercise affects the brain. PRARP award mechanisms include: Convergence Science Research Award to support innovation in research resources, Innovation in Care and Support Award to improve quality of life for people living with symptoms of TBI and dementia and their caregivers, Research Partnership Award to facilitate research collaboration, Accelerating Diagnostics for Traumatic Brain Injury Research Award to support development of diagnostic and prognostic TBI biomarkers as they pertain to AD/ADRD, and the Leveraging Approaches for Innovation in Care and Support Award (LEAP-InCASA) to support multi-institutional collaboration to address quality of life and care issues.

Comments & Questions

- A participant asked what the challenges are for measuring TBI. Dr. Pacifico said current approaches rely too much on self-report, not enough prospective data, and that there are not enough large sample studies that can support identification of risk factors.

Federal Updates

Helen Lamont explained that federal representatives would provide updates on their agencies' activities during the past quarter, with a focus on epidemiological topics.

- ***NIA***. Richard Hodes said NIH's budget for fiscal year (FY) 2020 is $41.7 billion. The budget includes $500 million for the All of Us program, $500 for the BRAIN program, and $60 million for Down syndrome research. The NIA budget is $3.54 billion. The National Alzheimer's Project Act was enacted in 2011. In 2012, NIH budgeted $50 million for AD/ADRD research. In 2016, the budget was dramatically increased to $350 million. Between FY 2015 and FY 2018, research budgets for AD/ADRD research more than doubled for every disease type. NIA has invested in infrastructure to support progress from basic through translational research. The agency currently supports 229 AD/ADRD studies, including 37 early-stage and 9 late-stage clinical drug development trials, 108 non-pharmacological interventions, 8 projects to develop clinical therapy to treat neuropsychiatric symptoms, and 67 interventions to improve formal and informal care. Current epidemiology initiatives include opportunities for research on epidemiology of AD/ADRD and cognitive resilience, Centers on the Demography and Economics of Alzheimer's and ADRD, and High-priority Behavioral and Social Research Networks in Alzheimer's and ADRD. HRS is an NIA project. Dr. Hodes noted that the Research Summit on Dementia Care will be held at NIH in Bethesda, MD, on March 24-25, 2020. NIH's Inclusion Across the Lifespan Workshop will be held September 23, 2020, at NIH.

- ***CMS***. Ellen Blackwell said that CMS aims to reduce overprescribing of antipsychotic medications in nursing homes. National prevalence has decreased 39% since 2011 Q2 to 14.6% in Q4 2018. In October 2019, CMS updated the State Performance Standards System nursing home safety inspection process. Changes include increased monitoring, new performance measures for timeliness and accuracy, and increased state agency access to CMS data.

- ***IHS***. Bruce Finke said that IHS's Public Health Nursing Program is collaborating with the VA to increase caregiver support in Indian Country. Training will be pilot tested with the San Carlos Apache Tribe in late January 2020. IHS has identified five strategies to improve native elder health, four of which are related to national priorities for addressing AD/ADRD. Dr. Finke said that interventions are only successful when built on a foundation of strengths, resources, and cultural capital. Change must be systemic.

- ***AHRQ***. Arlene Biermann said that AHRQ is collaborating with the National Institute on Diabetes and Digestive and Kidney Disorders (NIDDK) to develop an electronic care plan for people with multiple chronic conditions. The project is funded by ASPE to contribute to infrastructure for supporting patient-centered outcomes research. Patients with multiple chronic conditions who transfer to new settings often have missing data in their records. The electronic care plan aims to address this problem. Dr. Biermann said the electronic care plan is being designed to support research as well as clinical practice. AHRQ and NIDDK are currently in the process of developing the electronic care plan. The plan will be an application using the SMART platform. It will meet Fast Healthcare Interoperability Resources standards for interoperability with multiple electronic health records. Developers are currently identifying data elements to include in the plan. Data elements will include treatment goals and social risk factors. Dr. Biermann invited input on the data element selection process. Developers plan to complete initial development by fall 2020, at which time they will test it in ambulatory and hospital settings in a large health system. Debra Cherry said that cognitive care planning has distinct requirements and must be the foundation of all health care planning for people with cognitive impairments. Dr. Biermann agreed and said that is why she was soliciting input from this Council.

AHRQ is also developing an Opioids and Older Adults Initiative. The agency is interested in drug-disease interactions and drug-drug interactions. The initiative supports development of a technical brief on prevention, diagnosis, and management of opioids, opioid misuse, and opioid use disorder in older adults to inform AHRQ's research agenda. The initiative also supports a project to identify and test strategies for primary care practice management of opioid use and misuse in older adults, and a project to improve management of opioids and opioid use disorder in older adults. Joan Weiss said that HRSA would be interested in the results of these projects.

- ***VA***. Marianne Shaughnessy said the VA now has a directive for a system of care for veterans with dementia. This system is an integrated service delivery network that provides primary and specialty care. Caregiver staff at all VA facilities have received training to provide REACH-VA individual and support group interventions for veterans' caregivers. The VA now is conducting a national randomized controlled trial to test the effectiveness of combining REACH-VA with a DoD App, Virtual Hope Box, to improve caregivers' well-being and management of veteran concerns and safety. VA's Office of Rural Health is supporting several geriatrics, extended care, and dementia-related projects. The VA offers dementia education and resources to geriatric scholars. The VA is implementing Staff Training in Assisted-living Residences (STAR-VA), a person-centered, interdisciplinary behavioral approach to managing challenging behaviors among people with dementia in residential care. Veterans with behavioral problems are not always welcome in nursing homes. So, training staff to care for these patients is a high priority. In STAR-VA, a mental health professional and registered nurse work with a team to teach realistic expectations, effective communication, problem-solving, and focus on pleasant events. Training includes an intensive virtual workshop and 6 months of consultation. The VA is evaluating STAR-VA's impact on psychotropic prescribing, staff injuries, distress indicators, and sustainability facilitators.

- ***ACL***. Helen Lamont relayed a message from Erin Long that ACL, will issue a funding opportunity announcement in the next few weeks for the Alzheimer's Disease Program Initiative program, which is expected to support 24 grants for between $400,000 and $1,000,000 annually. ACL's RAISE Family Caregiving Advisory Council is requesting information on developing goals, objectives, and recommendations for a report to Congress on national family caregiving strategy. Its next advisory council meeting will be held February 11-12, 2020. ACL is hosting a series of dementia-related webinars in 2020.

- ***CDC***. Lisa McGuire said CDC has developed infographics tailored to specific target audiences, including African Americans, Hispanics, and Asians and Pacific Islanders. The agency has translated informational products into Spanish. CDC collaborated with the Alzheimer's Association and Emory University to update the curriculum, *A Public Health Approach to Alzheimer's and Other Dementias*. CDC published "The public health road map to respond to the growing dementia crisis" in *Innovation in Aging*, and "Comorbid chronic conditions among older adults with subjective decline, United States, 2015-2017" in the same journal. CDC extended its podcast series, "Aging and Health Matters," which is available in Spanish. The Healthy Brain Research Network published seven fact sheets before the project ended in 2019. CDC issued the National Healthy Brain Initiative to support organizations in developing public health strategies and to support populations disproportionately affected by AD/ADRD. The BOLD Infrastructure for Alzheimer's Act directs CDC to establish Alzheimer's and Related Dementias Centers of Excellence, award funding to public health departments, and increase data analysis and timely reporting. Funding opportunities for Centers of Excellence on caregiving, risk reduction, and early assessment and diagnosis will be released by the end of February 2020. CDC also will issue a funding announcement for developing public health programs as part of uniform public health infrastructure for AD/ADRD.

- ***ASPE***. Helen Lamont discussed three methods for identifying dementia and their implications for the National Plan, which includes "ensure a timely and accurate diagnosis" as a strategy and "improve data to track progress" as goals. Methods include asking the patient or a proxy, assessing cognition, and reviewing administrative data such as Medicare claims. Appropriate diagnosis is critical for linking to appropriate services. Many people are undiagnosed or have not been informed of their diagnosis. In 2009, 38% of patients with dementia were not aware of the diagnosis. ASPE conducted a study to determine how many older adults were misdiagnosed or not told about a diagnosis of dementia. A total 14.8% of participants were identified as having dementia by at least one method; 4.3% were identified by all three methods. Results indicate a need to improve diagnostic assessment, communication with patients about diagnosis, and data collection that support tracking progress toward reaching goals defined by the National Plan.

Concluding Remarks

Helen Lamont adjourned the meeting at 4:15 p.m.

Minutes submitted by Helen Lamont (ASPE).

All presentation handouts are available at http://aspe.hhs.gov/daltcp/napa/.