NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE ON AGING

Summary Minutes

The 142nd Meeting

NATIONAL ADVISORY COUNCIL ON AGING

January 12-13, 2021

National Institutes of Health
Virtual Meeting
Bethesda, MD 20892

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Department of Health and Human Services
Public Health Service
National Institutes of Health
National Institute on Aging

NATIONAL ADVISORY COUNCIL ON AGING
SUMMARY MINUTES
January 12-13, 2021

The 142nd meeting of the National Advisory Council on Aging (NACA) was convened on Tuesday, January 12, 2021, at 3 p.m. by video conference. Dr. Richard Hodes, Director, National Institute on Aging (NIA), presided.

In accordance with the provisions of Public Law 92–463, the meeting was closed to the public on Tuesday, January 12, from 3 p.m. to 5 p.m. for the review, discussion, and evaluation of grant applications in accordance with the provisions set forth in Sections 552(b)(c)(4) and 552(b)(c)(6), Title 5, U.S. Code and Section 10(d) of the Public Law 92–463.[1] The meeting was open to the public on Wednesday, January 13, from 10:00 a.m. to 1:45 p.m.

Council Participants:
Mr. James Appleby
Dr. David A. Bennett
Dr. Shalender Bhasin
Ms. Meryl Comer
Dr. Monica A. Driscoll
Dr. Terry T. Fulmer
Dr. Alison M. Goate
Dr. Margaret Goodell
Dr. J Taylor Harden
Dr. David M. Holtzman
Dr. Stephen B. Kritchevsky
Dr. Jennifer J. Manly
Ms. Susan K. Peschin
Dr. Eric Michael Reiman
Dr. Clifford James Rosen
Dr. Amy Jo Wagers
Dr. David Weir
Dr. Keith E. Whitfield

Ad Hoc Participants:
Dr. Dedra Buchwald
Dr. Yadong Huang
Dr. Rev. Cynthia Huling Hummel

[1] For the record, it is noted that members absented themselves from the meeting when the Council discussed applications (a) from their respective institutions or (b) in which a conflict of interest may have occurred. This procedure only applied to applications that were discussed individually, not to "en bloc" actions.

Dr. David B. Reuben
Dr. Julie A. Schneider

Members of the Public Present:
Ms. Rebecca Lazeration, Rose Li and Associates, Inc.
Dr. Rose Maria Li, Rose Li and Associates, Inc.
413 live views via NIH videocast

I. REVIEW OF APPLICATIONS

This portion of the meeting was closed to the public, in accordance with the determination that it concerned matters exempt from mandatory disclosure under Sections 552(b)(c)(4) and 552(b)(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix).[2]

A total of 2,107 applications requesting $4,849,389,704 for all years underwent initial review. The Council recommended 1,105 awards for a total of $2,821,312,978 for all years. The actual funding of the awards recommended is determined by the availability of funds, percentile ranks, priority scores, and program relevance.

II. CALL TO ORDER

Dr. Hodes welcomed members to the open session of the 142nd NACA meeting and called the meeting to order at 10:00 a.m. on Wednesday, January 13, 2021.

A. Director's Status Report

Dr. Hodes reported that for Fiscal Year 2021 the NIH received a budget of $42.9 billion, which includes a 1.57% base increase for NIA to $3.899 billion. By apportionment, this budget added $40.6 million to Alzheimer's disease and Alzheimer's disease-related dementias (AD/ADRD) research at NIA and $14.9 million to non-targeted NIA research. The total NIH funding reflects a $300 million increase for AD/ADRD, as well as $500 million for All of Us, $560 million for Brain Research through Advancing Innovative Neurotechnologies® (BRAIN), and $65 million for Down syndrome research. Dr. Hodes also reported that the NIA Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) budgets have increased from $27 million in FY 2013 to an estimated $124 million in FY 2020.

NIH has established interim pay lines. For general applications reviewed by the Center for Scientific Review (CSR) and requesting less than $500,000 (direct costs) in any one year, pay lines are 8% for most applications, 11% for new investigator regular research (R01) applications, and 13% for early-stage investigator R01 applications. For CSR-reviewed applications seeking $500,000 or more, pay lines are 5% for most, 8% for new investigator, and 10% for early-stage investigator applications. Pay lines are higher for AD/ADRD-targeted applications: 28% for most, 31% for new investigator, and 33% for early-stage investigator applications. Dr. Hodes

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noted that interim pay lines for NIA-reviewed applications (e.g., program project, career development, and fellowship awards) were overall impacts scores of 15 to 20 for general applications and 35 to 40 for AD/ADRD-targeted applications.

In response to the COVID-19 pandemic, NIH implemented the Rapid Acceleration of Diagnostics (RADx) program, a $1.5 billion supplemental appropriation to speed testing innovation. The program includes RADx-Tech, which has supported technological advancements for at-home or point-of-care tests for COVID-19, narrowing the field from 686 potential testing technologies to the 22 most-promising candidates; and RADx-UP, which has supported community-engaged projects that implement strategies to enable and enhance COVID-19 testing in underserved and vulnerable populations, with 38 total awards to sites spanning the continental United States and targeting Hispanic/Latinx, Black/African American, socioeconomically disadvantaged, American Indian/Alaskan Native, underserved rural, and other minority or vulnerable populations.

Dr. Hodes next highlighted the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public–private partnership aimed at prioritizing and expediting development of the most promising COVID-19 vaccines and therapeutics. Coordinated by the Foundation for the National Institutes of Health (FNIH), ACTIV is a collaboration of NIH and its sibling agencies in the Department of Health and Human Services, including the Biomedical Advanced Research and Development Authority (BARDA), Centers for Disease Control and Prevention (CDC), and the U.S. Food and Drug Administration (FDA); other government agencies, including the Department of Defense and Department of Veterans Affairs (VA); Operation Warp Speed; the European Medicines Agency; and representatives from academia, philanthropic organizations, and numerous biopharmaceutical companies. In less than a year, the FDA issued two Emergency Use Authorizations for the Pfizer-BioNTech and Moderna, Inc. vaccines in December 2020, the latter of which was co-developed by the NIH's National Institute of Allergy and Infectious Diseases. ACTIV is also running five master clinical trial protocols targeted at identifying immune modulators, outpatient monoclonal antibodies, inpatient monoclonal antibodies, antithrombotics, and general big effect treatments for treating COVID-19 patients with all stages of disease.

To determine the impact of COVID-19 on research and development, the NIH Scientific Workforce Diversity (SWD) Office completed a survey in November 2020 of more than 200 institutions and 45,000 researchers. Dr. Hodes shared preliminary findings indicating that institutions found the following to have the greatest impact on their operations and research functions: increased expenses involved with ensuring safety of staff and students (69%), reduced access to on-site laboratories (62%), increased spending on technology (52%), loss of housing and dining revenue (47%), institutional hiring freezes (32%), and increased virtual meetings (22%). Essential priorities for restoring research operations include maintaining a healthy environment (68%), developing and implementing phased return plans (61%), and maintaining financial sustainability (60%). Among researchers, the most frequently mentioned factors negatively impacting research included the transition to a virtual environment and resulting reduced access to colleagues, the laboratory, and core facilities. In addition to performing the survey, NIH has publicized numerous resources, including a one-stop portal for COVID-19 information for both healthy and sick members of the public (combatcovid.hhs.gov).

Outside of COVID-19 work, NIH continues to engage in institution-wide efforts to facilitate the study of aging across the entire lifespan. Dr. Hodes highlighted Inclusion Across the Lifespan (IAL), a trans-NIH initiative seeking to increase the recruitment and retention of older adults and children, as well as other underrepresented populations, in NIH research. He noted that the IAL's second meeting took place in September 2020, and the full report is available online. Dr. Hodes also reported on recent changes implemented by the CSR to help study sections incorporate age and aging-related components in the scientific review process. He also mentioned the release of the final NIH Policy for Data Management and Sharing (see Section V below).

Dr. Hodes reported on various NIH staffing updates, including the recruitment of several Institute directors: Dr. Michael Chiang was named Director of the National Eye Institute and Dr. Shannon Zenk was named Director of the National Institute of Nursing Research in July 2020, and Dr. Lindsay Criswell was named Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases and Dr. Rena D'Souza was named Director of the National Institute of Dental and Craniofacial Research in August 2020. Dr. Hodes acknowledged the retirement in September 2020 of Dr. Hannah Valantine, NIH Chief Officer for Scientific Workforce Diversity (COSWD); NIA Deputy Director Dr. Marie Bernard assumed the role of acting COSWD on October 1. He also congratulated Dr. Harvey Alter, Senior Scholar in the NIH Clinical Center's Department of Transfusion Medicine, who was awarded the 2020 Nobel Prize in Physiology or Medicine for his contributions to the discovery of the hepatitis C virus.

Dr. Hodes also shared NIA updates since August 2020, including 18 professional staff hires; dissemination of NIA research progress through 21 research highlights, 15 blog posts, 5 news announcements, and 4 press releases; as well as participation by Dr. Hodes or other senior NIA staff in 13 stakeholder or advocacy group meetings, 5 professional conferences and events, and 1 congressional briefing. Dr. Hodes announced the development of the Clinical Research Operations and Management System (CROMS), which will allow the NIA to track, report, and manage extramural clinical research data, activities, and enrollment in real time. During FY21, the CROMS system will focus on grants supporting AD/ADRD clinical trials, followed by all NIA grants supporting human subjects research. Finally, Dr. Hodes announced that the 2021 Alzheimer's Disease Research Summit will be held virtually on April 19-22 and the Butler-Williams Scholars Program for junior faculty and researchers new to the field of aging will be held virtually on August 24-26, 2021.

B. Future Meeting Dates

May 11-12, 2021 (Tuesday and Wednesday), Virtual
September 14-15, 2021 (Tuesday and Wednesday), Building 45
January 25-26, 2022 (Tuesday and Wednesday), Building 45
May 5-6, 2022 (Thursday and Friday), Building 45
September 7-8, 2022 (Wednesday and Thursday), Building 45

C. Consideration of Minutes of the Last Meeting

The minutes of the September 2020 Council meeting were considered. A motion was made, seconded, and passed unanimously to approve the minutes.

III. REPORT: TASK FORCE ON MINORITY AGING RESEARCH

Co-chairs Drs. Cliff Rosen and Keith Whitfield presented updates on the Butler-Williams Scholars program evaluation and NIA's clinical research recruitment and retention initiatives. Dr. Rosen began by acknowledging the substantial efforts of their predecessors, Drs. J Taylor Harden and David Bennett, who positioned the Task Force to move forward quickly.

The purpose of the Butler-Williams Scholars program evaluation was to track the productivity of the Scholars from 2010 to 2020, measured through grants, publications, and support from other NIH Institutes, Centers, or Offices (ICOs). The evaluation team began with a list of Scholars and attempted to associate them with institution and person ID to track grant awards and publications. Reviewers were able to track 71% of Scholars with a high level of confidence.

Reviewers found that for both K and R awards, Scholars achieved a 22-37% success rate (depending on the year) on grant applications after completing the program. Dr. Whitfield noted that Scholars received grants from 23 ICOs, highlighting that scholars are producing impact outside the NIA. However, reviewers could not track nongovernment funding awards. Reviewers also found numerous publications by Scholars, noting that the average citation rate per year from 2010 to 2020 ranged from 11.5 to 19.0 citations. Based on the highly productive record of past Scholars, the NIA Council recommended that the 2020 cohort be increased from 50 to 55 scholars, and that the OSP should collect Profile ID, Commons ID, or ORCID ID from Scholars.

Dr. Rosen next presented on the importance of CROMS. He noted that despite triennial reports on recruitment and retention of NIA clinical trial participants, NIA lacks easy access to data on recruitment of minority populations. He stressed the importance of both recruiting minority individuals into trials and tracking their recruitment and retention rates. CROMS will facilitate institutional accountability for research, operational portfolio management, and data management that will eventually encompass all NIA human subject trials. Similar CROMS platforms have been used by other NIH Institutes.

The NIA CROMS project began in July 2020 with a competitive bidding process. Despite complications posed by the COVID-19 pandemic, the project is on schedule to launch its first fully operational release in July 2021 for AD/ADRD trials. Remaining trials and studies in the NIA portfolio will be added later.

CROMS includes multiple visualization features to support three types of users: leadership, program officers, and grantees. The CROMS dashboard will allow users to track recruitment and retention rates at the national and study levels and by minority populations of interest, in near real time. CROMS also allows Institute investigators to generate reports for required NIA- and NIH-level reporting.

Council members highlighted two emerging disparities that NIA should target using CROMS: (1) persistent health care disparities for gender minorities, transgender individuals, and gender

diverse individuals, and (2) increasing mortality in middle-aged white men. Council members also noted that the challenge of CROMS lies not in collecting data on minority populations, but in using the data to address the challenges to recruitment and retention of minority populations. They stressed the importance of making the data actionable at all levels, from individual grantees to NIA leadership.

IV. REPORT: WORKING GROUP ON PROGRAM

Dr. Stephen Kritchevsky, Chair of the Working Group on Program (WGOP), led the updates.

A. Recommendations from Past Meetings – None

B. Clinical Trials Advisory Panel (CTAP) Report

Dr. Kritchevsky reported that CTAP met on January 12. At that meeting, Dr. Sergei Romashkan, Chief of the Clinical Trials Branch, Division of Geriatrics and Clinical Gerontology, summarized the updates from the October 2020 CTAP meeting, during which three proposals were considered. The first proposal described a **REHAB-HFpEF Clinical Trial** to test the effect of exercise intervention on preventing rehospitalization in older adults with heart failure with preserved ejection fraction. The panel members expressed high enthusiasm for this proposal and recommended it for further consideration in the NIA planning process. Two other proposals, submitted by a small pharmaceutical company, described trials to study the effect of dietary supplementation on COVID-19 outcomes in (1) older adults hospitalized with COVID-19 (**RECOVIR-65**); and (2) outpatients with COVID-19 (**RECOVIR-AT-HOME**) with the goal of preventing hospitalization. Panel members recommended the former trial for further consideration but not the latter one because of concerns about study design and feasibility.

C. RFA/RFP Concept Clearances

Dr. Kritchevsky asked the primary reviewers to summarize the 11 concepts submitted from five NIA units: Division of Aging Biology (1), Division of Behavioral and Social Research (2), Division of Geriatrics and Clinical Gerontology (2), Division of Neuroscience (5), and the Office of Small Business Research (1). The primary reviewers had provided detailed summaries of the concepts, requested amendments or changes, and documented the WGOP decision. Although the WGOP suggested minor changes to some concepts, it approved all concepts for full Council consideration. Dr. Kritchevsky commended the WGOP for their smooth review of the concepts, noting that many Council members interacted with program staff before the meeting to increase the efficiency of the reviews. The Council members unanimously concurred with approval of the 11 concepts seeking clearance.

Development and Maintenance of a Multigenotypic Aged Mouse Colony (Renewal)

NIA supports basic biomedical research through several programs which require animals as models of the aging process. Aging mice for study of the aged brain is expensive, and many mice die during the aging process. The proposed concept will renew the funding for a barrier facility that provides an ideal environment for aging mice that can then be shipped for experiments

around the country. For two decades, the facility has already successfully supported studies of aging free of charge.

Data Enhancements and Analyses to Clarify the Relationship between Education and Cognitive Function (including AD/ADRD and Dementia)

The proposed concept will seek to clarify the relationship between education and cognitive function, including AD/ADRD, by leveraging existing datasets to follow people throughout the life course. Reviewers suggested that the proposed concept concentrate on Black, Hispanic, and Asian communities and how their differing experiences of language and culture may impact educational experiences and later-life consequences.

Screening and Intervening in Primary Care for the Maltreatment of Older & Vulnerable Adults with MCI and AD/ADRD

Older adults are less likely to report abuse at care facilities, so mistreatment of older adults is underreported. While all older adults with disabilities are at increased risk of being victims of abuse, individuals with mild cognitive impairment (MCI) and AD/ADRD are particularly vulnerable. The proposed concept will develop and validate elder abuse screening instruments or assessments for the primary care setting and effective psychoeducational and behavioral interventions to prevent and address victimization.

Data Management Coordinating Center (DMCC) and a Collaborative Research Space for Translational Research on Exceptional Longevity Leveraging Existing Large Databases and Cohorts to Better Understand the Risks and Benefits of Long-term Osteoporosis Therapy and Drug Holiday

The use, benefits, and risks of pharmacologic interventions in treating osteoporosis is unclear, with many datasets' applicability limited by the short duration of most therapeutic trials. The proposed concept will mine datasets to create an integrative platform to assist in the long-term treatment of osteoporosis.

Transformative Artificial Intelligence-based Strategies to Identify Determinants of Exceptional Health and Life Span

Based on recommendations from an NIA workshop in August 2018, the proposed concept will develop and apply artificial intelligence and machine learning to multi-omic data from NIA studies of longevity in humans and non-humans. These analyses will help discover novel targets for extending health span and delaying the onset of chronic age-related disorders including dementias.

Early- and Late-Stage Clinical Trials for the Spectrum of AD/ADRD and Age-Related Cognitive Decline (Reissue)

The proposed concept will consolidate research from early- and late-phase pharmacologic or non-pharmacologic treatment studies to emphasize timely sharing of data and biological samples. Reviewers suggested that the concept include public-private partnerships.

Elucidating the Roles of Transposable Elements in Alzheimer's Disease and Aging

Transposable elements are DNA sequences that can change position within a genome, allowing for the creation or reversal of mutations. Various lines of research have established links between TE activation and neurodegeneration, but these links have not been well studied in the AD and Parkinson's disease settings. The proposed concept will support interdisciplinary research to study the basic mechanisms of transposable elements and the roles they play in AD and aging.

High-Resolution Mapping of Biomolecules in Aging and AD Brains

The proposed concept will generate brain-specific cell-type and 3D atlases of small molecules that change in the aging brain and in AD patients. The proposal seeks to capitalize on the mass spectrometry revolution and on single-cell resolution advances to generate biomolecular maps that may be integrated with optical imaging technologies and gene expression profiles to provide comprehensive markers for a detailed brain atlas of both aging and AD brains.

Pilot Studies for the Spectrum of AD/ADRD and Age-Related Cognitive Decline (R21 Clinical Trial Optional)

PIs proposing research on early-stage age-related cognitive decline and AD/ADRD face a funding challenge: they may not have the pilot data necessary to apply for NIA support, but if they apply instead to the NIH parent R21 grant, they may submit to standing study sections that lack relevant aging and AD/ADRD clinical trials expertise. The proposed concept will help generate the pilot data needed to support competitive grant applications for pharmacological or nonpharmacological interventions focused on AD/ADRD and cognitive decline.

Role of Adaptive Immunity in Etiology of Alzheimer's Disease

Prior research has illustrated that the brain has an innate immune system; however, research to date has failed to assess the system's adaptive traits. The proposed concept will study the role of the adaptivity of the brain immune system in AD pathogenesis.

Transition to Aging and AD/ADRD Career Development Award

The proposed concept seeks to fill the gap between transitional awards that currently do not capture candidates with more than 4 years of postdoctoral experience. The award will be open to both intramural and extramural researchers who have never received major NIH funding. Applicants will work with mentors to create a submission and will have 1 year to secure a tenure-track or another secure position.

V. GUEST SPEAKER: FINAL NIH POLICY ON DATA MANAGEMENT AND SHARING

Dr. Carrie Wolinetz, Associate Director for Science Policy, reported on the Final NIH Policy for Data Management and Sharing. NIH started to develop this policy in 2016 with an initial solicitation for community input and since then has sought stakeholder input from a variety of sources (e.g., tribal consultation, government agencies) through Requests for Information (RFIs). The final policy will take effect on January 25, 2023 and replaces the 2003 policy.

The policy requires principal investigators (PIs) to submit a data management and sharing plan for all NIH-funded research that generates scientific data. The plans must specify timelines for data sharing and availability. Compliance will be tracked, and failure to follow a plan may affect future funding. However, plans can be changed as necessary during the course of the clinical trial. The goals of the policy are to foster a culture of data stewardship, to advance rigorous and reproducible research, and to promote public trust in research. Responsibly implemented and prospectively planned data sharing should be the default practice; however, researchers may designate ethical, legal, or technical exceptions (e.g., patient privacy).

Data Management and Sharing Plans will be submitted in the Budget Justification section of the protocol application and assessed by the NIH program staff. Given the extra burden involved in managing data, investigators may submit a budget request to cover costs to curate data and develop supporting documentation, preserve or share data though repositories, and manage data locally. When considering potential data repositories, investigators are encouraged but not required to use established repositories. However, ICs may choose to designate specific repositories in funding opportunity announcements.

NIH Office of Science Policy staff are engaging in outreach and engagement activities and developing supplemental materials and resources to help investigators comply with the policy, including tools to assist with estimating data management and sharing costs. They are also investigating tools and procedures to accurately track the data sharing process similar to those used to track publications via citations. Finally, they are consulting with ICs to ensure that the policy aligns with other NIH-wide or IC-specific data sharing policies (e.g., the Genomic Data Sharing Policy). Dr. Wolinetz concluded by providing the Council members with links to the policy website.

Council members asked for clarification about the PI's responsibility for long-term curation of data, citing the potential for researchers who access the data in a repository to seek additional information from the PI after a study has concluded. Dr. Wolinetz explained that NIH considers the need to comply with the Data Management and Sharing Policy to end when the award is completed, and long-term maintenance of data will not be tracked. However, investigators may have long-term data management responsibilities dictated by repository or institutional agreements. Dr. Wolinetz noted that long-term assistance to researchers extends beyond the reach of the policy. For all long-term data management issues to be thoroughly addressed, the culture of data management and storage must change at the national and international levels. Such cultural changes will occur over time with support from policies such as the NIH Data Management and Sharing Policy. The necessary changes include data harmonization and unification of data formats. Dr. Wolinetz added that repositories may need to expand, or

additional repositories may need to be established, in order to meet the increased storage demand. Such efforts are key points where new policies that facilitate harmonization can occur. Council members agreed that these critical evolutions are necessary but will require additional investments to expand infrastructure.

VI. PROGRAM HIGHLIGHTS

A. Division of Behavioral and Social Research: COVID in U.S. Nursing Homes – The Power of Data

Dr. Vincent Mor, Professor of Health Services, Policy & Practice at Brown University School of Public Health, presented updates from the NIA IMbedded Pragmatic AD/ADRD Clinical Trials (IMPACT) Collaboratory. The IMPACT Collaboratory has been operating for 16 months, 9 of which were heavily impacted by the COVID-19 pandemic. The Collaboratory responded early and quickly to assess the impact of the pandemic on vulnerable populations in nursing facilities. Dr. Mor focused his presentation on the importance of data on identifying COVID-19-related issues and designing solutions to help impacted populations.

Dr. Mor observed that the American perception of the COVID-19 outbreak in nursing facilities was shaped largely by early news reports, and the narrative tended to focus on deficiencies in facilities, regulation, infection control, and access to personal protection equipment (PPE). To counter inaccurate reports, Dr. Mor underscored a need for data to accurately track the COVID-19 virus and its impact on nursing facilities. To gather these data, Brown University formed an agreement with Genesis HealthCare to collect electronic medical records from nursing facilities in near real time. The collaboration is bolstered by weekly meetings between the Genesis clinical leadership team and Brown University investigators.

The first analysis, available in May 2020, used data collected from March and April 2020 to determine factors contributing to facility outbreaks of COVID-19. Outbreak factors included size of the facility, proportion of Black residents, and facility rating. However, investigators found that the most important factor in outbreaks was county prevalence of COVID-19 cases. Community prevalence is now accepted as the most important predictor of a COVID-19 outbreak at nursing facilities, and the CDC and CMS are interpreting the data accordingly.

Dr. Mor also described how the Genesis HealthCare data led to adjustment of the threshold fever in older populations. Geriatric patients have naturally lower temperatures than younger adults, so the CDC temperature thresholds for testing adults were originally set too high for the geriatric patient population. The collaboration provided the CDC with data on patients' temperatures and COVID-19 testing results, which ultimately led the CDC to adjust its temperature threshold for seniors from 38°C to 37.2°C.

Dr. Mor reported on the high number of asymptomatic residents with COVID-19 identified during random "sweep" testing of Genesis facilities. Facilities that performed testing in all patients found that 60% of their cases were asymptomatic, while facilities that tested based on symptoms or exposure found that only 22% of their cases were asymptomatic. These numbers suggest that facilities that do not perform random sweep testing miss a large number of asymptomatic cases. Moreover, the prevalence of asymptomatic cases suggests that the practice

of isolating symptomatic patients is not sufficient to prevent the spread of COVID-19 in nursing home facilities. As a result, Genesis facilities began broader, more frequent testing in their facilities.

The researchers also investigated mortality rates at nursing facilities, which were found to be associated with advanced age, poor physical functioning, and poor cognitive functioning. However, death due to any cause within 30 days of the first positive SARS-CoV-2 test result (i.e., 30-day all-cause mortality) decreased among residents with both symptomatic and asymptomatic cases of COVID-19 from March 2020 to September 2020. More testing is needed to determine what factors have contributed most to the decrease in mortality.

Dr. Mor presented results from an IMPACT Collaboratory supplement that studies the availability of testing and whether testing capacity differs based on the racial composition of facility residents. At Genesis facilities, the researchers found that staff testing was unaffected by resident race distribution and that resident testing was similar across resident race distributions, with slightly higher testing rates at facilities with a greater proportion of minority patients.

The researchers are also tracking adverse effects of vaccines in patients in near real time (data reported nightly) from the nursing home Data Sharing Cooperative, which consists of 12 nursing home companies (for-profit and non-profit) at about 1,000 facilities, which will serve as the basis for a Nursing Home Pragmatic Trials launchpad. The Genesis data will be the first available, with additional companies coming online to provide data nationwide. The only states not covered by this collaboration are New York, due to regulatory issues, and Oklahoma. The collaboration is seeking to remedy the gap in Oklahoma centers.

Next steps for the collaboration are to assist with the RADx-UP IMPACT supplement to combat vaccine hesitancy in nursing facility residents and staff. Only about a third of staff are willing to be vaccinated and consent processes for residents could complicate administration. Along with four nursing home companies in the Cooperative, the collaboration is randomly assigning 140 nursing facilities to receive a multi-component intervention to increase resident and staff vaccination rates. The trial is ongoing, with anticipated completion in April 2021.

Council members commended Dr. Mor on the work to change the temperature threshold for older adults, the rapid launch of this project, and the large amount of useful data gathered in a short amount of time. In response to a question about how the collaboration will target individuals with remaining vaccine hesitancy after the interventions have been implemented, Dr. Mor explained that the interventions have been designed to involve fellow staff members who are viewed as leaders in recruitment efforts to reduce remaining hesitancy among staff workers. However, one challenge is the limited number of vaccination clinics at nursing facilities. He noted that in some states, staff and patients have few alternative options to receive a vaccination if they cannot participate in a clinic when it is scheduled. Further, current data suggest inter-facility variation on vaccination rates of staff and patients. Additional data are needed to determine the causes of the variability and the interventions needed to address those causes.

VII. INTRAMURAL PROGRAM REPORT

Dr. Luigi Ferrucci, NIA Scientific Director, led the updates from the NIA intramural programs.

A. Laboratory of Clinical Investigation (LCI)

Dr. Josephine Egan, Chief, LCI, shared updates from ongoing LCI work. She noted that the LCI includes five PIs whose study of distinct aspects of the brain and variety of expertise collectively create a holistic approach.

LCI studies include attention to neuronal extracellular vesicles, which carry byproducts from brain processes (e.g., tau pathology, insulin signaling) out of the brain, and how these byproducts may be used for preclinical diagnosis of AD/ADRD and treatment response. Dr. Egan focused in part on the role of the choroid plexus in this process: the choroid plexus secretes insulin, which is critical in removing amyloid beta (Abeta) from the brain; downregulation of insulin in the choroid plexus thus results in increased brain levels of Abeta, which in turn is associated with AD/ADRD.

Dr. Egan reported on another study showing that as the choroid plexus deteriorates, it also affects other brain systems. Researchers have used MRI imaging methods to illustrate a correlation between cerebral blood flow and myelin deposits, which are normally cleared from the brain by the choroid plexus. These results illustrate that choroid plexus functioning and cerebral blood flow are highly correlated.

Dr. Egan also shared ongoing research on early brain changes that seeks to determine whether neurodegenerative effects of lipids such as APOE can be prevented.

Council members suggested pursuing research to determine whether alpha-synuclein, which has been shown to impact insulin and lipids, is involved in AD/ADRD.

B. Laboratory of Cardiovascular Science (LCS)

Dr. Edward Lakatta, Chief, LCS, reported on recent LCS research on age-related cardiovascular diseases. Dr. Lakatta explained that age-related cardiovascular diseases have three disordered domains: hemodynamics; atherothrombosis, ischemia and cell energetics; and heart rate and rhythm issues. The LCS studies these three domains by deep phenotyping in humans, studying animal models with matching phenotypes, and developing interventions in animal models for translation to humans.

LCS has been studying what happens to the aging body that causes dysfunction, such as arrhythmia, to develop. Dr. Lakatta explained that the greatest risk factor for arrythmia is aging Sick Sinus Syndrome (SSS), or the inability of the heart's natural pacemaker, the sinus node, to maintain the appropriate heart rate. SSS is a problem mainly in older populations. He observed that mice naturally experience a reduced heart rate as they age, but removal of the neuronal support for heart rate in mice decreases the heart rate dramatically. Therefore, Dr. Lakatta explained that the loss of autonomic nervous system support causes SSS in mice.

In humans, the study of heart rate reduction required scientists to conceptualize the "pacemaker," which refers to the combined cycle of events in the cell membrane system (an ensemble of electrogenic mechanisms) and the sarcoplasmic reticulum calcium system (intracellular events) that create a system of chemical and electrical clocks. Dr. Lakatta emphasized that during the

diastolic period of the pacemaker cycle, local calcium signals self-organize. These local calcium clusters are reduced over time, with older mice showing a serious decrease in clustering in older sinoatrial node tissue. He concluded that the next steps to researching local calcium signals should focus on what causes the reduction in calcium signals and how this reduction leads to cardiac disfunctions.

Council members asked whether the central locus of heartbeat regulation occurred in such a place that the spinal cord may play a role in autonomic control and whether spinal cord injury can cause autonomic instability. Dr. Lakatta responded that the field is moving toward neuro-cardiology to study such possibilities. He noted that instabilities do generate arrythmias. He described ongoing research to remove the autonomic ganglia from the surface of the heart that communicate with the spinal cord to treat these arrythmias. He added that in the course of the ongoing research the researchers hope to also show that the sinoatrial node is a little brain-like network itself.

C. Review of Intramural Research Program

This portion of the meeting was closed to the public in accordance with the provisions set forth in section 552b(c)(6), Title 5 U.S. Code and Section 10(d) of the Federal Advisory Committee Act as amended (5 U.S.C. Appendix 2).

VIII. ADJOURNMENT

The open session of the 142nd meeting of the National Advisory Council on Aging adjourned at 1:45 p.m. on January 13, 2021. The next meeting is scheduled for May 11-12, 2021.

IX. CERTIFICATION

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.[3]

Richard J. Hodes, M.D.
Chairman, National Advisory Council on Aging
Director, National Institute on Aging

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With assistance by Rose Li and Associates, Inc.

[3] These minutes will be approved formally by Council at the next meeting on May 11-12, 2021, and corrections or notations will be stated in the minutes of that meeting.