

ADRC Directors Meeting

Nina Silverberg, Ph.D.

Director, Alzheimer's Disease Research Centers Program

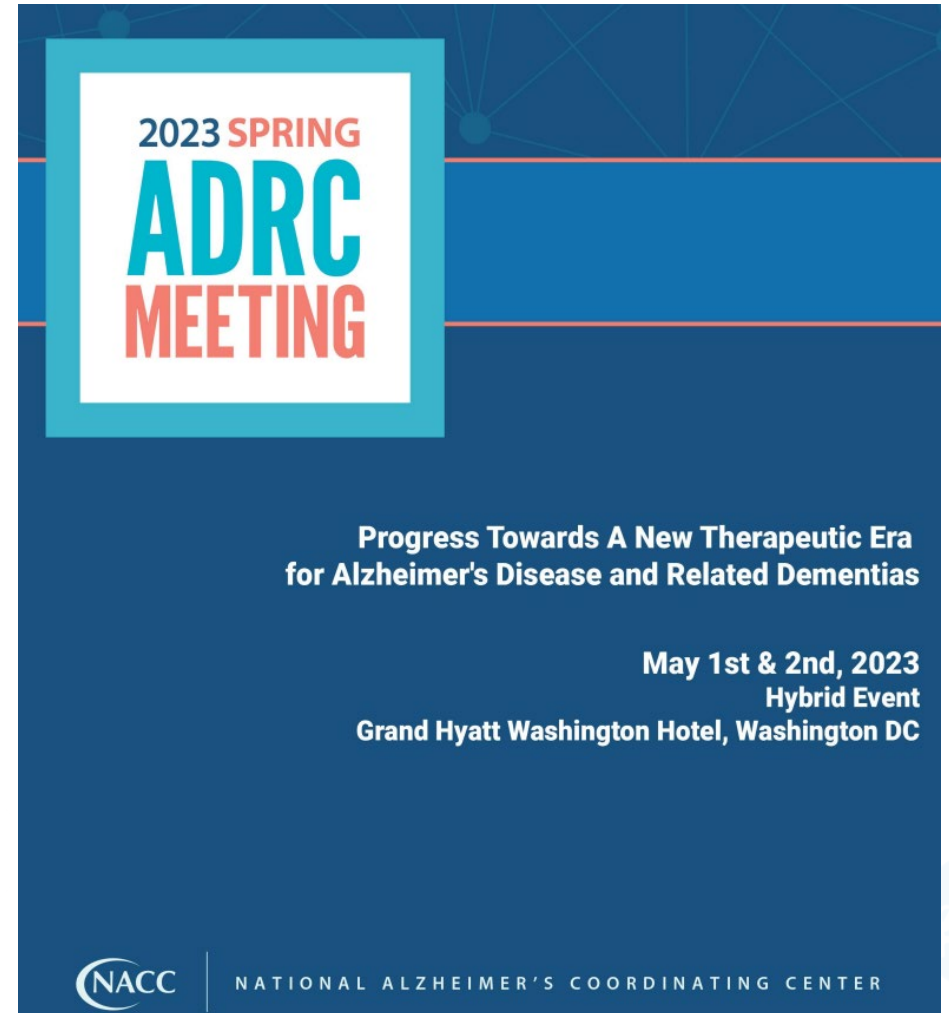
National Institute on Aging

May 1, 2023

ADRC Meeting Kudos

Thank you to:

- All the Steering Committees
- Presenters
- NACC
- CTF
- Research participants
- Survey Respondents
- NIH Staff
- In-person and virtual attendees
- NGOs



ADRC Meeting Spotlight: REC

| | |
|--|--|
| Autophagy Enables Microglia to Engage Amyloid Plaques and Prevents Microglial Senescence | Insup Choi, PhD Mount Sinai School of Medicine ADRC |
| The Implications of Apoptosis-Associated Speck-Like Protein Containing a Caspase-Recruitment Domain (ASC) Specks on Microglia Phenotype. | Kathryn Sanchez, PhD New Mexico Exploratory ADRC |
| Tunneling Nanotubes at the Microglia-Neuron Interface During Inflammation and Alzheimer's Disease | Colleen Zaccard, PhD Northwestern ADRC |
| Understanding the Role of Peripheral Inflammation in Alzheimer's Disease | Bahareh Ajami, PhD OHSU ADRC |
| Changes in the Gut Microbiome Composition May Parallel Alzheimer's disease Progression | Bernard Fongang, PhD South Texas ADRC |
| The Clinical Use of Amyloid PET: When are AD Biomarkers Most Helpful? | Jeremy Tanner, MD, MPH South Texas ADRC |
| Characterizing Relationships Between Sleep-Wake Rhythms, Neuroinflammation, and Cognition in Neurodegenerative Disease | Joe Winer, PhD Stanford ADRC |
| Reduced Microglial Function and Cholesterol Handling in Alzheimer's Disease | Oscar Munoz, PhD Candidate UC Davis ADRC |
| Cerebellar-Cortical Functional Connectivity is Associated with Alzheimer's Disease Pathology and Cerebellar Atrophy | Soyun Kim, PhD UCI ADRC |
| Scalable Plasma and Digital Cognitive Biomarkers for Diagnosis and Prognosis of Neurodegenerative Disease | Elena Tsoy, PhD UCSF ADRC |
| The Effect of Genetic Alzheimer's Disease Risk Factors on Cerebral Blood Flow Regulation During Sit-to-Stand Transitions in Older Adults | Jacqueline Palmer, PT, PhD University of Kansas ADRC |
| The Role of Area Deprivation in Language Disruption among Alzheimer's Disease Patients | Tifani Biro, PhD Penn ADRC |
| A Novel Physical Activity Metric with Cognition and Risk of Dementia | Yurun Cai, PhD University of Pittsburgh ADRC |
| Alzheimer's Disease Mortality, Access to Healthcare, Socioeconomic Status, and Rurality among American Indian and Alaska Native People | Solmaz Amiri, DDes University of Washington ADRC |
| Molecular Correlates of Stress During the COVID Pandemic in the Wake Forest AD Center Cohort | James (Trey) Bateman, MD, MPH Wake Forest ADRC |
| Examining Cerebrovascular Burden in Participants from the Wisconsin ADRC and WRAP Studies with and without Evidence of AD Proteinopathy | Leonardo Rivera-Rivera, PhD Wisconsin ADRC |

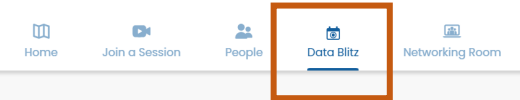
| WEDNESDAY, MAY 3rd | | | |
|--------------------|----------|---|---------------------|
| START (ET) | END (ET) | SESSION | CHAIR(S) |
| 7:30 AM | 1:00 PM | REC Mock Study Section (invite only) | Elizabeth Head, PhD |

| | |
|---|--|
| What Comes First, the Inflammasome Complex or Synaptic Dysregulation? Investigating Pathophysiological Changes Seen in the Hippocampal Formation in Post-Mortem Brain Samples with Alzheimer's Disease. | Regina Vontell, PhD 1Florida ADRC |
| AZ ADRC REC: Creating Innovative Team Science and Leadership for the 21st Century | Gerson Hernandez, MD, MPH Arizona ADRC |
| Transcranial Magnetic Stimulation Based Network Integrity Assessment in Alzheimer's disease | Recep Ozdemir, PhD Boston University ADRC |
| Social Network Typology and Cognitive Status Among Black Americans: Findings from the Health and Retirement Study | Ann Nguyen, PhD Cleveland ADRC |
| A Transcriptomic Characterization of the Locus Coeruleus in a Rat Model of Alzheimer's Disease | Michael Kelberman, PhD Emory University, Goizueta ADRC |
| Inpp5d Deficiency Increases Ab Uptake, Improves Behavioral Outcomes and Reduces Ab Pathogenesis | Adrian Oblak, PhD Indiana University ADRC |
| Synaptic Dysregulation by Tau Pathology in Aging and Alzheimer's Disease | Meaghan Morris, MD, PhD Johns Hopkins ADRC |
| Cross-Omics Integration Shows Cortex-Wide Synaptic Dysfunction at Later Stages of Alzheimer Disease | Abdullah Eteleeb, MSc, PhD Washington University Knight ADRC |
| BCG-AD: Population Health Findings and an Open-Label Interventional Trial of the Bacillus Calmette-Guérin Vaccine in Older Adults with and without Biomarker Evidence of Alzheimer's Disease. | Marc Weinberg, MD, PhD Massachusetts ADRC |
| Disparate Dementia Risk Factors Associate with Cognitive Impairment and Rates of Decline in African Americans | Christian Lachner, MD Mayo Clinic ADRC |
| Cognability: An Ecological Theory of Neighborhoods and Cognitive Aging | Jessica Finlay, PhD Michigan ADRC |

ADRC Meeting Spotlight: Clinical Core Data Blitz

Mild Behavioral Impairment and Early Neuropsychiatric Symptoms

Available on Hubilo



| | |
|---|---|
| Prevalence of Neuropsychiatric Symptoms is Greater in Early Than Late-Onset Alzheimer's Disease | Angelina Polsinelli, PhD, ABPP-CN Indiana University ADRC |
| Monitoring Apathy, Depression and Anxiety Using Technology Evaluation | WanTai "Michael" AuYeung, PhD Oregon Health & Science University |
| Neural Precursors of Depressive Symptoms in Amnesic Mild Cognitive Impairment | Molly Mather, PhD Northwestern University |
| Variability in Cognition, Mood and Personality in Preclinical Alzheimer Disease and Very Mild Clinical Impairment | Andrew Aschenbrenner, PhD Washington University, St. Louis |
| Intraindividual Cognitive Variability as an Early Marker of Alzheimer's Disease | Andrea Weinstein, PhD University of Pittsburgh |
| Onset of Behaviors Characteristic of Autism Spectrum Disorder as Neuropsychiatric Symptom of Alzheimer's Disease and AD Related Dementias | Elizabeth Rhodus, PhD, MS, OTR/L University of Kentucky ADRC |
| Probing Mechanisms of Emerging Depressive Symptoms in Community-Dwelling Older Adults: A Plasma and Multimodal Neuroimaging Biomarker Study | Jennifer R. Gatchel, MD, PhD Mass General Hospital, McLean, Harvard Medical School |

| | |
|--|--|
| Digital Monitoring to Detect Autonomic Markers of Early Empathy Loss in Behavioral Variant Frontotemporal Dementia | Emma Rhodes, PhD University of Pennsylvania |
| Understanding the Role of Alzheimer's Disease Pathology in Mild Behavioral Impairment | Alexandru Iordan, PhD University of Michigan |
| Earliest Psychiatric Symptoms in Right Anterior Temporal Lobe Degeneration | Hulya Ulugut, MD, PhD University of California, San Francisco |
| Investigating Associations Between Neurodegenerative Pathologies and Behavioral and Psychological Symptoms Of Dementia (BPSDs) | Ruth Nelson University of Kentucky, Emory University |
| Speech Biomarkers and Depression Dimensions | Laili Soleimani, MD, Msc Icahn School of Medicine |
| The Association of Disinhibition and Cognitive Decline in a Multi-ethnic Sample | Amy Werry-McFarlin, PsyD South Texas ADRC |

RFA-AG-24-001: Major changes

- Almost 50% increase in Direct Costs!
- Stronger emphasis on populations at greatest risk for AD/ADRD
- Staffing for participant recruitment and engagement activities
- Time commitment requirement for core leaders
- New imaging requirement: MRI, Amyloid and Tau in ≥ 24 participants
- PEDP: Plan for Enhancing Diverse Perspectives
- Budget requirements, e.g., Cultural sensitivity and implicit bias training, Blood collection, Disclosure, sample tracking
- NIH Data Management and Sharing requirements
- All three rounds in single RFA

<https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-24-001.html>

HHS/NIH/NIA Logo Policies & Update

- NIA follows the [HHS](#) and [NIH](#) logo policies. Because of trademarking and related issues, NIH restricts use of our logos to federal (U.S. Government) usage only.
- Unfortunately, the NIA Office of Communications and Public Liaison (OCPL) recently became aware that the current ADRC logos/badges/marks, provided in 2019, are not compliant and should be removed where currently used:



- NIA OCPL is asking all ADRCs to remove these logos/badges/marks from their websites and other materials as soon as possible but no later than **June 30, 2023**.
- Grantees and other partners still are responsible for crediting the National Institutes of Health (NIH) and the National Institute on Aging (NIA) prominently in text on the product. Such as: “This Alzheimer’s Disease Research Center is funded by the National Institute on Aging, National Institutes of Health.”
- A more formal communication will be forthcoming in the coming weeks. For questions, please contact NIA OCPL Director Cindy McConnell at cindy.mcconnell@nih.gov.

NIH Application Updates

- New Forms for applications - eRA updates for applications
 - <https://grants.nih.gov/grants/guide/notice-files/not-od-22-195.html>
- Clarification and Guidance for Applicants Preparing Applications for the FALL 2023 Due Dates During the COVID-19 Pandemic
 - <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-23-067.html>
- NIH will now use the term NOFO: Notice of Funding Opportunity instead of FOA (Funding Opportunity Announcement). This is effective immediately.
 - <https://nexus.od.nih.gov/all/2023/03/02/foa-or-nofo-its-all-about-funding/>
- Cycle 1 awards need to submit an Interim RPPR in 2024 for year 5 progress
 - https://www.era.nih.gov/erahelp/commons/Commons/rppr/Interim_RPPR/interim_RPPR_overview.htm

NACC Subaward Usage for Data Core

- [RFA-AG-21-014](#) instructs NACC to provide sufficient resources to support data and sample collection at ADRCs as well as assuring secure transmission of de-identified data from ADRCs to NACC
- The annual NACC \$25K Subaward is to be used for by the Data Management and Statistical Cores to facilitate collaborations between and among Centers and with NACC and the broader research community.
 - **1.43 calendar months is the average support for data personnel**
- There is a lack of timely invoice submissions to NACC for this subaward to be used by the end of the fiscal year. We are instructing NACC to prepare timelines and communications in fiscal year 23 (6/1/23 – 5/31/24).
 - If the deadlines for invoicing are missed by ADRCs in FY23, there will be no carryover of funds for the subawards to the Center.
- Large available balances are concerning regarding effective use of the Subaward. The following activities may be partially supported by the subaward:
 - Electronic Data Capture Workgroup
 - SCAN Data Coordination
 - NACC Data submissions

Unobligated Balances

- NIA Leadership is considering the balances of the parent grants for administrative supplements and will require a spend down plan and an explanation for your balance with your requests.
- NIH Prior approval for carryover is required of P30/P20 ADRCs and this requirement is included in your Notice of Award.
 - The NIH Grants Policy Statement (Section 8.1.2.4) outlines the information the AOR should submit in requesting approval for carryover of unobligated balances
 - ✓ A detailed budget by direct cost category with the F&A cost information (base and rate) for the proposed use of the carryover funds.
 - ✓ A scientific justification for the use of funds.
 - ✓ The reason for the unobligated balance.
- The NIH Grants Policy Statement (Section 8.4.1.5.4) states using the principle of “first in-first out,” unobligated funds carried over are expected to be used before newly awarded funds.
 - If the funds available exceed the NIH share of the approved budget for the current budget period, the GMO may select one of the following options: In response to a written request from the recipient, revise the current NoA to authorize the recipient to spend the excess funds for additional approved purposes. Offset the current award or a subsequent award by an amount representing some or all of the excess.

Neuroimaging Implementation Challenges

Equipment

- Scanner acquisitions delays
- Aged equipment
- Shared ownership
- Usage capacity/availability

Communication

- MR and PET Certifications
- MR and PET Protocols
- SCAN Start up – January 2021

Participant Recruitment

- Participant Education
- Scheduling
- Slow to recruit
- Diversity

Parallel Initiatives

- Conflation of recruitment success

Staffing

- Schedulers
- Imaging Technicians
- Turnovers and shortages
- Imaging shutdown

PET Imaging

- Lacking institutional infrastructure for adoption
- Varied level of prioritization

Radiotracer

- Procurement delays
- Production failures
- Radiopharmacy limitations

COVID

- Varied operational dates

Upcoming Workshop: LATE

Gaps and Opportunities Related to Clinical Detection of Limbic-predominant Age-related TDP-43 Encephalopathy (LATE)

- Thursday, May 25th from 10 AM to 6 PM ET
- Available virtually on Zoom
- There will be a series of presentations related to clinical detection of LATE, including:
 - What are the gaps and opportunities for developing criteria for diagnosis of LATE in people during life? These will include considerations of diversity and health equity.
 - What are the gaps and opportunities related to the clinical detection of LATE both on its own and in conjunction with Alzheimer's Disease and Related Dementias?
 - What is the state of the science on the clinical manifestations of LATE and biomarkers for the detection of LATE?
 - What are preliminary considerations for features that may help guide diagnosis, and use of these criteria in clinical trials?

<https://www.nia.nih.gov/research/dn/workshop-gaps-and-opportunities-related-clinical-detection-limbic-predominant-age>

CTF Technology Workgroup Restructure

Goal: Expanded and richer data collection with less burden on participants and staff

CTF Tech WG Parent: Sets governance for workgroup and teams, approves charters, provides guidelines

Leads:

- **ADRC Co-Leads:** Rhoda Au, Spencer Low
- **NACC Co-Leads:** Sarah Biber, Sean Mooney

Other Members:

- Nina Silverberg, Bud Kukull, Alan Lerner, Sudeshna Das, Hiroko Dodge, Erin Abner, Greg Jicha

Teams (ADRC co-leads)

In-Clinic UDS Digital Instruments

- **Co-leads:** Kate Possin, Teresa Gomez-Isla, Hiroko Dodge, NACC co-lead TBA
- **Overview:** Cognitive and non-cognitive; TabCAT; and other UDS digital instruments used in the clinic



Standard UDS Done Virtually

- **Co-leads:** Sudeshna Das, Zach Beattie, Melissa Lamar, NACC co-lead TBA
- **Overview:** Cognitive and non-cognitive; Virtual version of standard



New Non-UDS Digital Instruments

- **Co-leads:** Jeff Kaye, Jason Hassenstab, Kate Papp, NACC co-lead TBA
- **Overview:** Cognitive and non-cognitive; new digital instruments not currently included in UDS; in-clinic or out of clinic; including survey



ClinicoPath Conference (CPC) survey - REC

Thank you to Liz Head and Claire Nelson!

Goals:

- Offer cross center and outside center educational opportunities
- Opportunity to share unique/rare or difficult cases
- Share expertise

Overall high enthusiasm and interest (87% of centers responded, all cores)

Concerns about privacy/confidentiality, consent, specifics

Options on how to proceed

Plans: Will share all results and convene working group



Offers of Payment to Research Participants

Group Members:

- Emily Largent, U Penn, Chair
- Andrea Denny, Wash U
- Crystal Glover, Rush U
- Josh Grill, UCI
- Margot Kushel, UCSF
- Gladys Maestre, UTRGV
- Jessica Mozersky, Wash U
- Aimee Pierce, OHSU

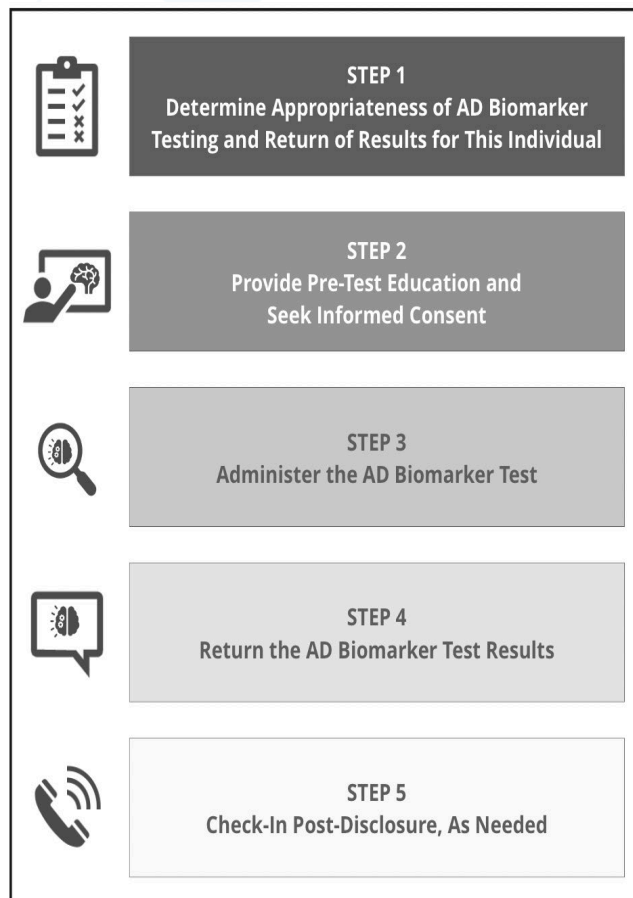
- **Background:** Payment to research participants and study partners may be appropriate and effective for facilitating equitable research participation.
- **Purpose:** Guide each Center's consideration of payment and payment-related practices for ADRC-affiliated research projects.
- **Content:**
 - Functions of Payment – *Why do we offer payment?*
 - Designing Payment – *How do we design the amount, timing, and method of payment to account for both study features and participant needs?*
 - IRB Approval and the Common Rule – *What are the ethical and regulatory considerations when offering payment?*
 - Taxation and Benefits Eligibility – *How might payment affect participants' tax liability or eligibility for government benefits programs?*
 - Other Legal Considerations – *What other issues should we be aware of?*

<https://nacccdata.org/adrc-resources/best-practices>

Disclosure Guidance

Group members

- Melissa Armstrong, U of Florida
- Jasmeer Chhatwal, MGH/Harvard
- Kacie Deters, UCLA
- Joshua Grill, UC Irvine
- Jason Karlawish, U of Pennsylvania
- Fred Ketchum, U of Wisconsin
- Emily Largent, U of Pennsylvania
- Jennifer Lingler, U of Pittsburgh
- Beth Mormino, Stanford U
- Annalise Rahman Filipiak, U of Michigan
- Malia Rumbaugh, Indiana U
- Suzanne Schindler, Washington U



Largent et al., Testing for Alzheimer Disease Biomarkers and Disclosing Results Across the Disease Continuum, *Neurology* 2023

<https://nacccdata.org/adrc-resources/best-practices>

- **Why disclose?**
- **What to disclose?**
- **To whom?**
- **By whom?**
- **How to disclose?**

ACTC: Training and Didactics



A comprehensive training program in clinical trials for Alzheimer’s disease and related dementias.

Applications open February 2024 for August 2025

Professionals Track (4 days) To further their knowledge and advance their careers in ADRD trials.

For study team members (e.g. clinicians, study coordinators, psychometricians, and other)

Fellowship Track (7 days)

Training for future PIs in ADRD trials

<https://impact-ad.org/>

ACTC Ethics Didactics

“Are we there yet” with PET as a suitable surrogate endpoint” Internal Ethics Committee holds debate to inform regulatory review of Alzheimer’s drugs

Dennis Selko and Christopher van Dyck

“Putting Research Participants First When Trials End Early” Emily Largent

Recordings at:

www.actcinfo.org/news



ACTC is seeking new Projects!



- Only brief synopsis required to apply
- Three review cycles each year (Aug 5, Dec 5, Mar 5)
- Looking for novel therapeutics, repurposed, nonpharmacological approaches, combination trials, platform trials
- Leverage ACTC infrastructure of expert sites, biorepository, coordinating center
- Collaborative Grant development after Steering Committee approval
- www.actcinfo.org/submit-a-proposal/

ACTC SESSION

2023 Hybrid Spring ADRC Meeting
Tuesday, May 2nd

9:30 - 9:50am ET

20min Presentation

Synergy Between ADRCs and
Alzheimer Clinical Trial Consortium (ACTC) Initiatives

Paul Aisen, MD
ACTC MPI

Reisa Sperling, MD
ACTC MPI; Massachusetts ADRC

Ron Petersen, PhD, MD
ACTC MPI; Mayo Clinic ADRC

Laurie Ryan, PhD
NIA



Example Spanish Language Materials from NIA & Other ADRCs



La Enfermedad de Alzheimer 101

UW Memory and Brain Wellness ...
245 subscribers

Subscribe

5

Share

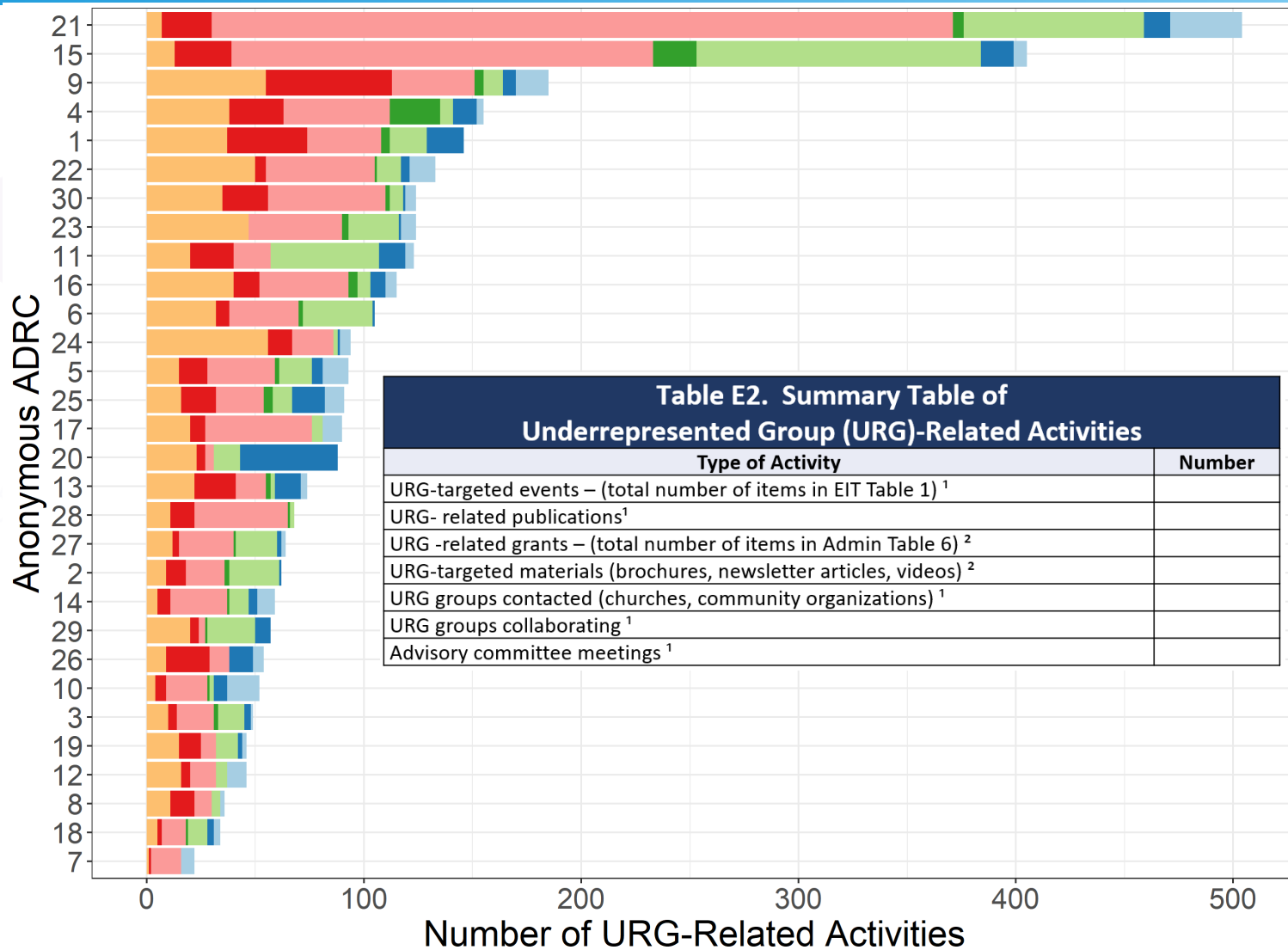
Download

...

<https://www.youtube.com/watch?v=VTngaJJHm9Y>

<https://www.nia.nih.gov/espanol/donacion-cerebro-regalo-generaciones-futuras>

DEI Follow Up: Summary of FY22 RPPR Table E2



URG-Related Activity

- Advisory committee meetings¹
- URG-related grants²
- URG-related materials²
- URG-related publications¹
- URG-targeted events¹
- URG groups collaborating¹
- URG groups contacted¹

¹ = current reporting period
² = cumulative

Represents data from 30/37 ADRCs

Congressional Inquiry Survey Results – Thank You!

Between January 2017 and December 2022:

Participant Engagement*



103, 828
participants
engaged*

*Average of 2,800
participants per ADRC*

Number of Clinical Trials



327 unique
clinical trials

*Average of 27 clinical trials
per ADRC*

ADRC Registries



485,152
participants
enrolled in
ADRC registries

*Clinical trial participant engagement defined as participants educated, screened, consented, referred, or enrolled into a clinical trial by an ADRC

In Memoriam



Guy McKhann



Murray Grossman

Thank you